

# Integrative Cancer Care

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# Donald Abrams Disclosures

- Scientific Advisor
  - AXIM
  - Insys Therapeutics
  - Intec Pharma
  - VIVO Cannabis
  - Maui Wellness
  - Scriptyx
  - Tikun Olam
- I did go to college in the '60's
- And I will be discussing off-label use
  - Of an illegal substance

# Integrative Cancer Care

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

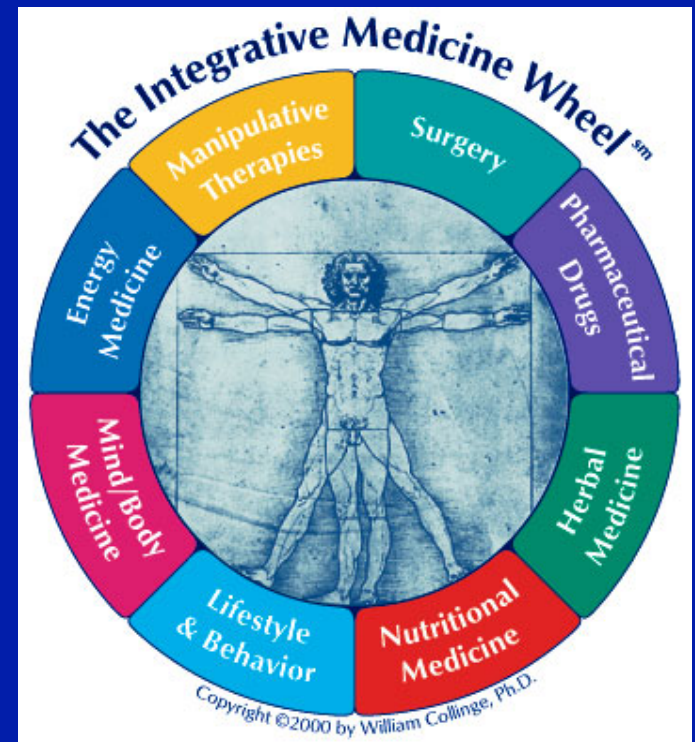
Moses Maimonides and

Sir William Osler



# 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

- Research suggests that our presence as medical or mental health clinicians, the way we bring ourselves fully into connection with those for whom we care, is one of the most crucial factors supporting how people heal- how they respond to our therapeutic efforts.

» Daniel Siegel **The Mindful Therapist** 2010

# 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 prevention & maintenance of health
- Maintains that healing is always possible even when curing is not

# Oncologists and CAM

- Most oncologists admit to (very) limited knowledge about CAM
- In direct observations of oncology visits MD/Pt communication re: CAM is suboptimal
- CAM/cancer patients identified 3 barriers
  - Physician's indifference or opposition
  - Physician's emphasis on scientific evidence
  - Patients' anticipation of a negative response from their physician
- Just asking a directed question about CAM during history-taking increased disclosure from 7 to 43%

# Men's Choices of CAM in Prostate CA

- Survey of 34 men using CAM in the UK
- Choice of particular therapies was based on forms of “evidence” that were personally meaningful
  1. Personal stories of people helped by CAM
  2. Long history and enduring popularity of the Rx
  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 CAM therapies

Evans et al 2007

# 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 any possible salvage therapy
- Seeking integrative end-of-life care
- Seeking optimal survivorship 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

# Three Closing Questions

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

Let your food be your medicine  
And your medicine be your food

Hippocrates

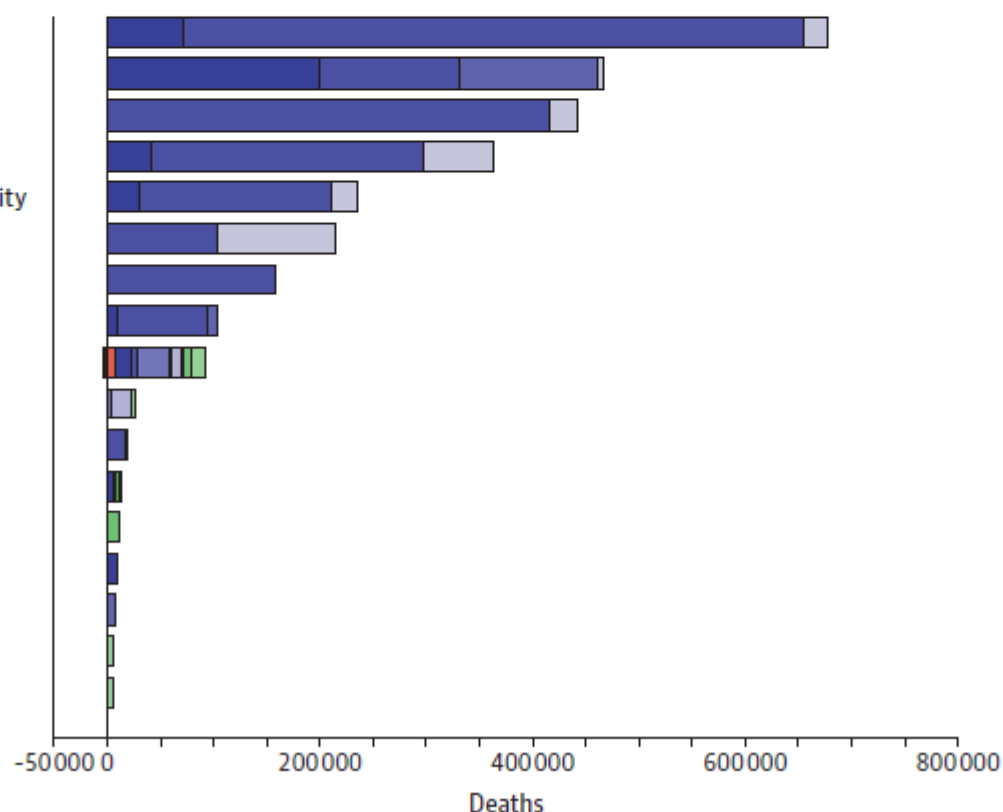


**Figure 3. Number of Deaths and Percentage of Disability-Adjusted Life-Years Related to the 17 Leading Risk Factors in the United States in 2010 for Both Sexes Combined**

**A** Risk factors and related deaths

**Risk Factors**

Dietary risks  
Tobacco smoking  
High blood pressure  
High body mass index  
Physical inactivity and low physical activity  
High fasting plasma glucose  
High total cholesterol  
Ambient particulate matter pollution  
Alcohol use  
Drug use  
Lead exposure  
Occupational risks  
Low bone mineral density  
Residential radon  
Ambient ozone pollution  
Intimate partner violence  
Childhood sexual abuse



**Diseases and injuries**

- Intentional injuries
- Unintentional injuries
- Transport injuries
- Other noncommunicable
- Musculoskeletal disorders
- Diabetes/urogenital/blood/endocrine
- Mental and behavioral disorders
- Neurological disorders
- Digestive diseases
- Cirrhosis
- Chronic respiratory diseases
- Cardiovascular and circulatory diseases
- Cancer
- Other communicable
- Nutritional deficiencies
- Neonatal disorders
- Maternal disorders
- Neglected tropical diseases and malaria

# 14 Components of Dietary Risk

- **Diets low in:**

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

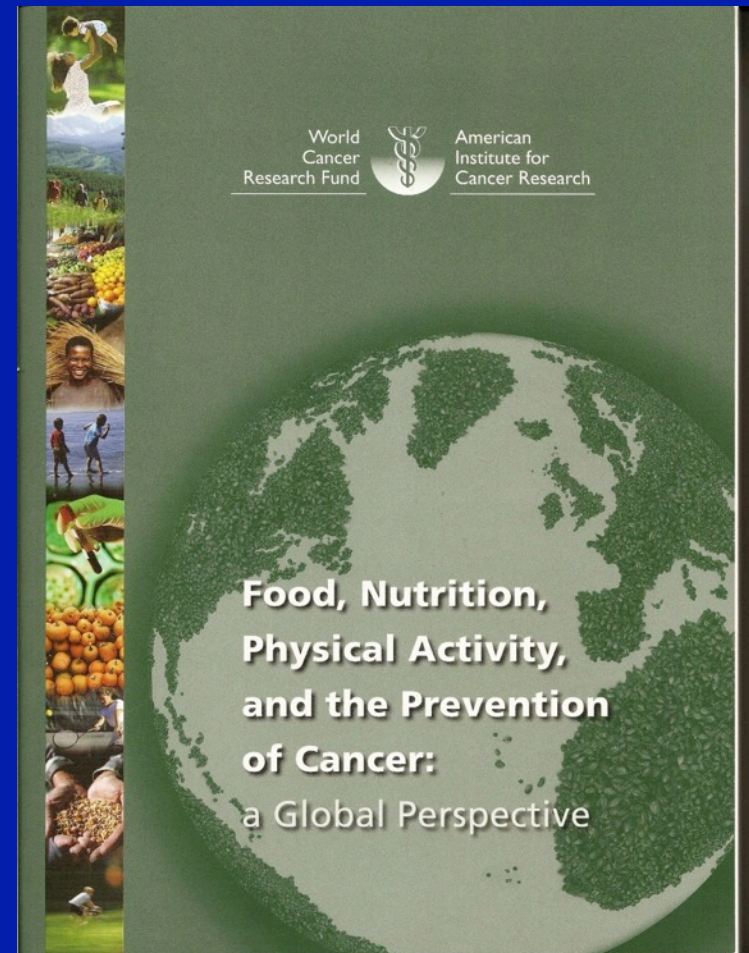
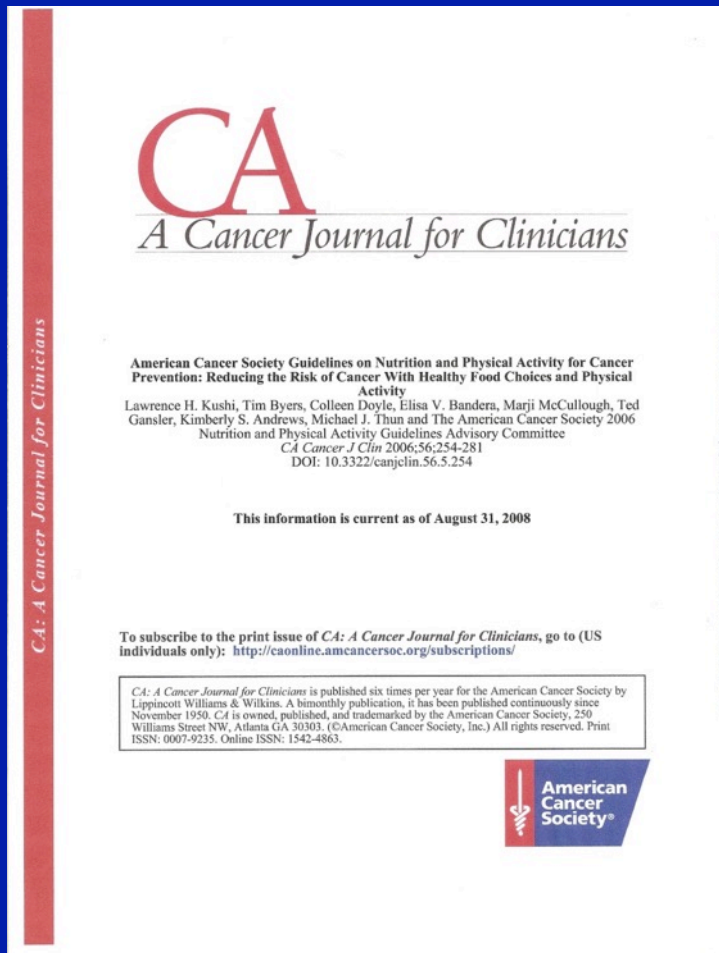
- **Diets high in:**

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

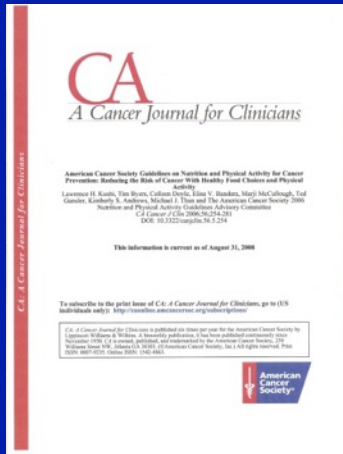
# Diet and Cancer

- Probably involved in 30-35% of all cancers
- Certainty about diet less firm than tobacco
  - Contradictory study results i.e. fiber
  - Hard to define what the diet actually is
    - Diets are very complex
    - Diets vary over time
- Is it what we ate in the past? Or perhaps what our mothers ate? Or theirs?

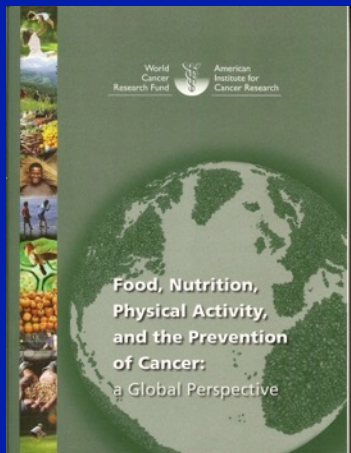
# ACS and WCRF/AICR Guidelines



# WEIGHT GUIDELINES



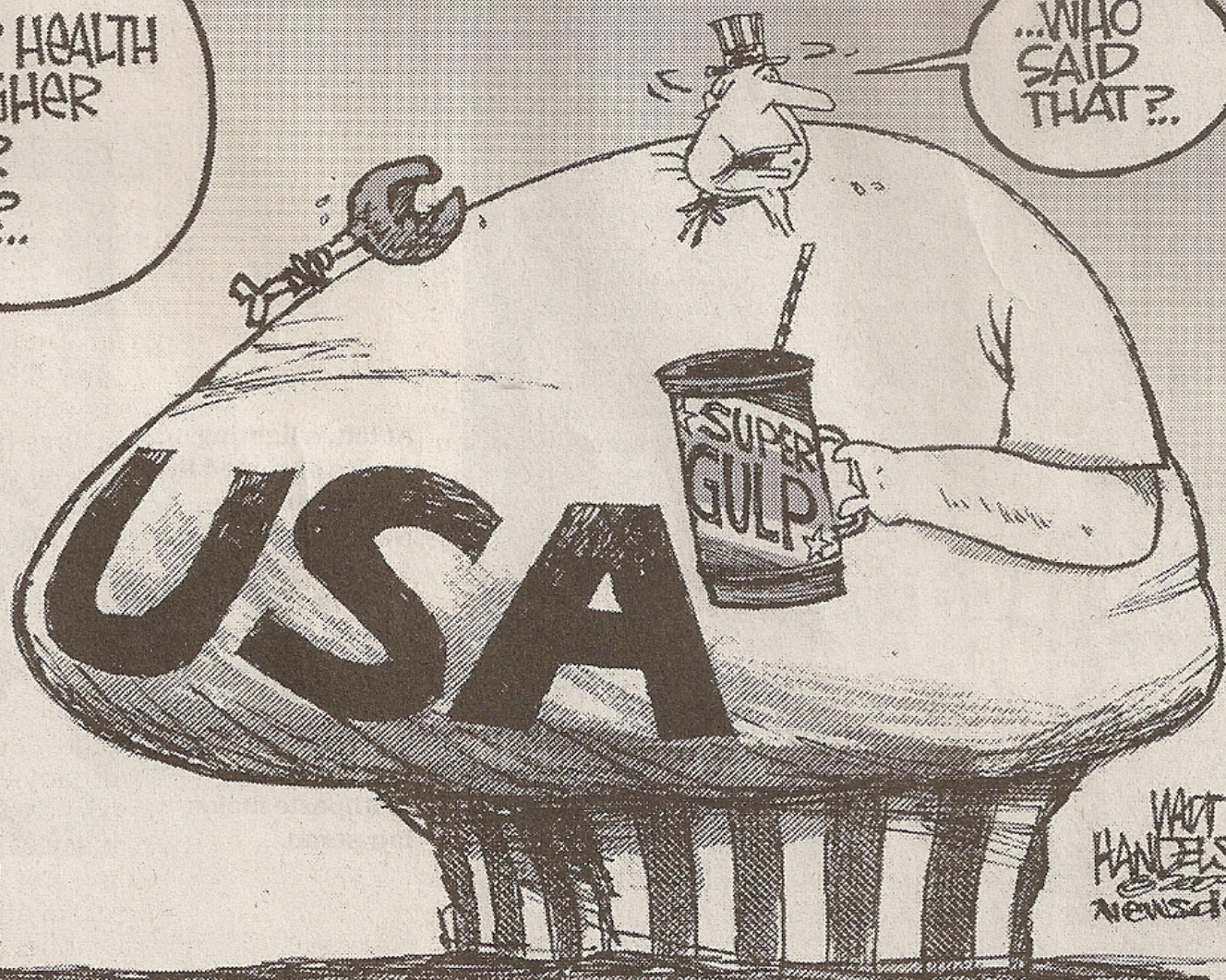
- Maintain a healthy weight throughout life
  - Balance caloric intake with physical activity
  - Avoid excessive weight gain throughout the life cycle
  - Achieve & maintain a healthy weight if currently overweight or obese



Be as lean as possible  
without becoming underweight

BUT WHY ARE OUR HEALTH  
CARE COSTS HIGHER  
THAN OTHER  
COUNTRIES?...

...WHO  
SAID  
THAT?...



VALT  
HANDELMAN  
newsday

# 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 approx 115,000 preventable deaths a year in the US

# 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

# WCRF/AICR Recommendations to Reduce Cancer Risk 2007

1. Be as lean as possible without becoming underweight
2. Be physically active for at least 30 minutes every day

# Exercise in Cancer Survivors

- 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

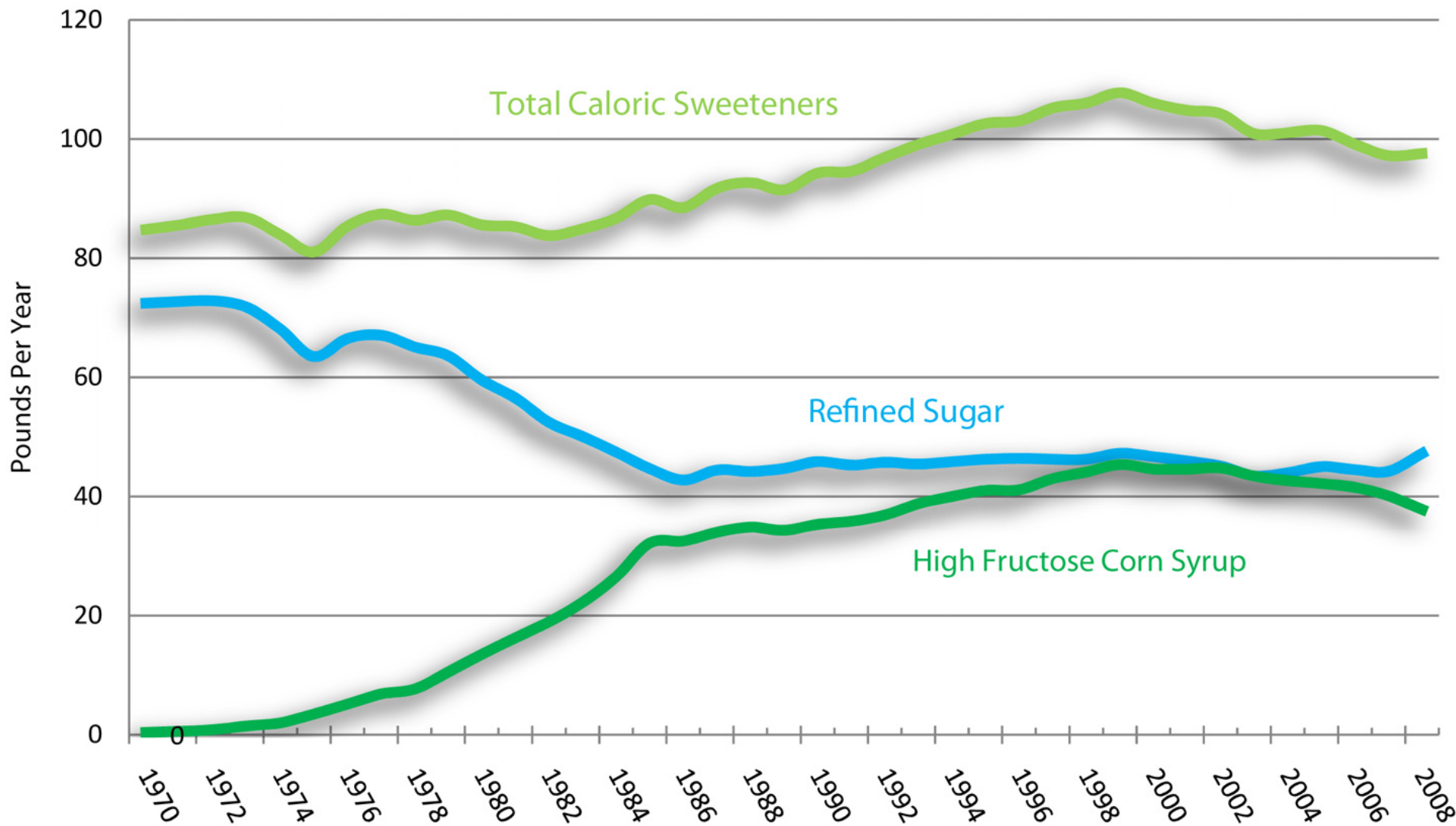
# WCRF/AICR Recommendations to Reduce Cancer Risk 2007

1. Be as lean as possible without becoming underweight
2. Be physically active for at least 30 minutes every day
3. **Avoid sugary drinks**

Limit consumption of energy dense foods

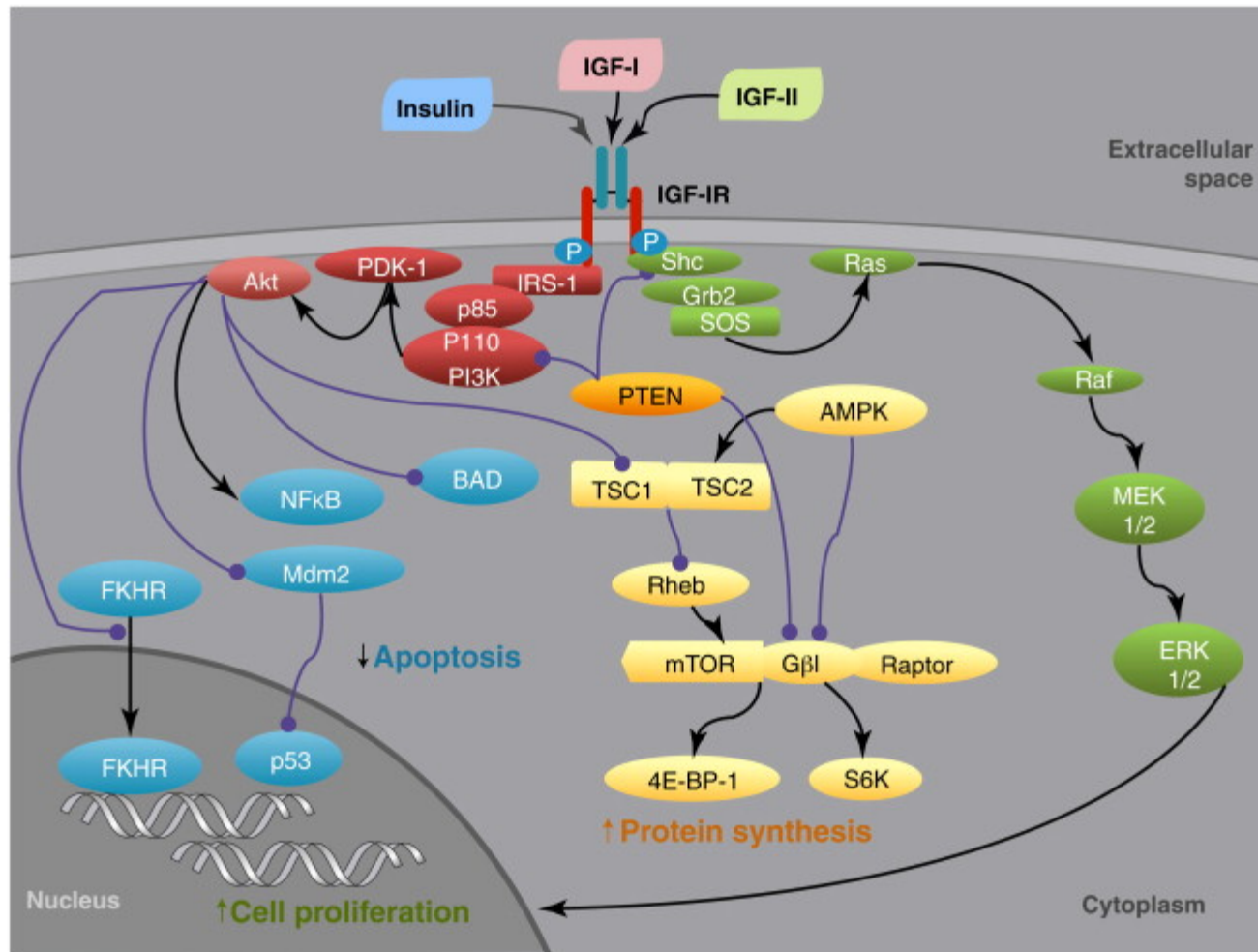
Particularly processed foods high in added sugar, low in fiber or high in fat

# Per Capita Consumption of Caloric Sweeteners 1970 - 2008



Source: US Department of Agriculture

# Insulin and IGF-1 and Cancer



TRENDS in Endocrinology & Metabolism

NONI



Out of Stock at the company



\$19.18 Now Acai Concentrate 16oz (454g)  
\$34.39 Nature's Way Organic Acai Berry Juice 32 fl. oz. (946 mL)  
\$19.18 Now Acai Juice Superfruit Tomato Juice 32 fl. oz. (946 mL)  
\$26.38 Nature's Way Alive! Organic Goji Berry Juice 16 fl. oz. (473 mL)  
\$16.96 Pure Fruit Goji-zen 1 Liter (33.8 fl. oz.)  
\$24.99 Pure Planet Tart Cherry Conc 16 fl. oz. (473 mL)



Out of Stock at the company



\$16.96 Pure Fruit Mangoni 16 fl. oz. (473 mL)  
\$28.78 Nature's Way Superfruit 16 fl. oz. (473 mL)  
\$16.96 Pure Fruit Ultra Mangosteen 16 fl. oz. (473 mL)  
\$10.99 Pure Fruit Ultra Mangosteen 8 fl. oz. (236 mL)

# But What About Metformin?

- Relative of isoamylene guanidine, active ingredient in French lilac (*Galega officinalis*) used for polyuria in diabetics
- Epidemiologic studies show decreased cancer risk in patients on metformin
- Exerts *in vitro* inhibition of prostate, ovarian and breast CA cells
- Selectively kills cancer stem cells
- Currently in 199 cancer clinical trials

# WCRF/AICR Recommendations to Reduce Cancer Risk 2007

## 4. 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

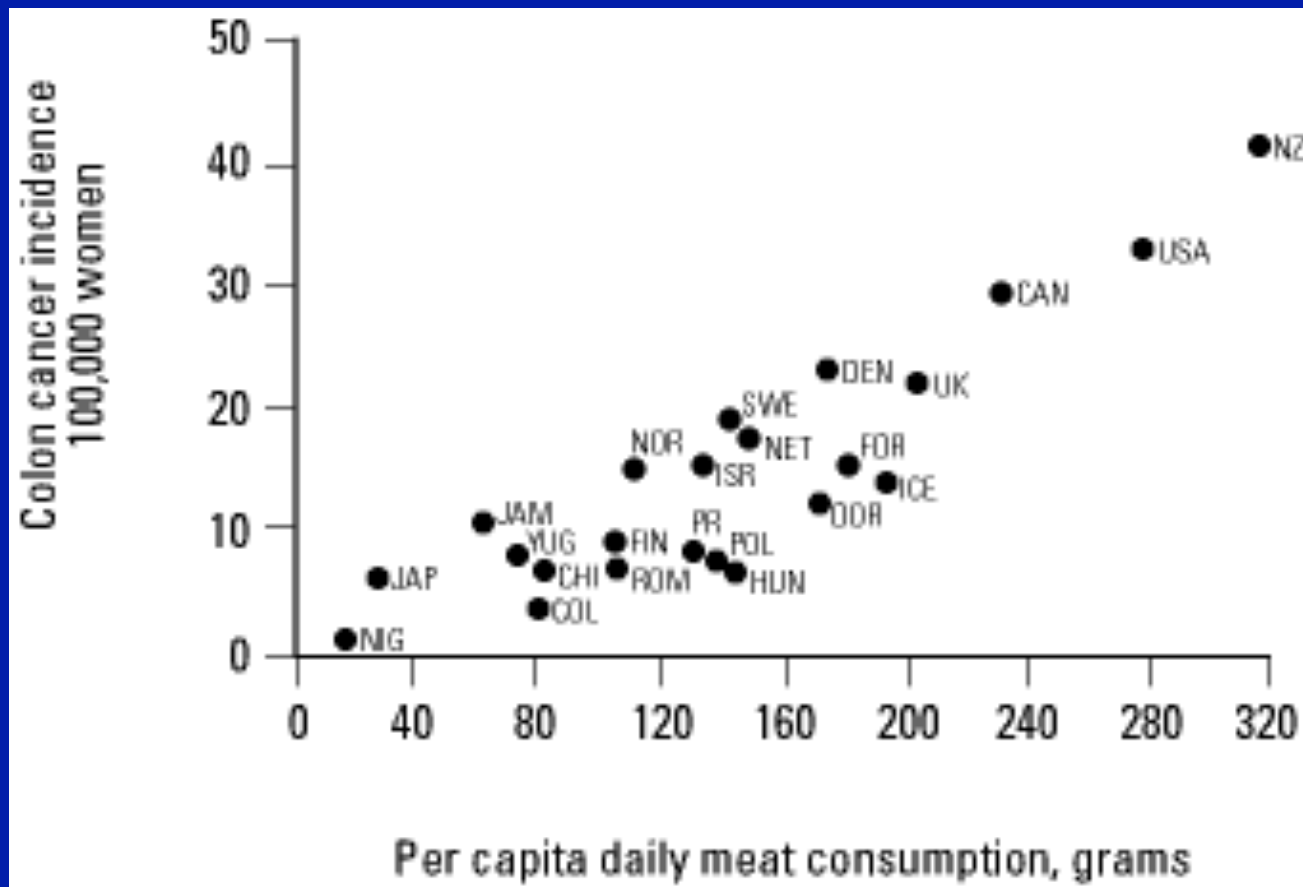


# LACE Study of Soy in Breast CA

- Life After Cancer Epidemiology Study followed 1954 breast CA survivors dx 97-00 for 6.3 yrs
  - 282 breast CA recurrences ascertained
  - Isoflavone intake assessed
- Soy intake at levels comparable to those consumed in Asian population
  - May reduce the risk of recurrence in women who have been treated with tamoxifen
    - In postmenopausal women (HR 0.48, 0.21-0.79,  $p=0.008$ )
  - Does not appear to negate the effects of tamoxifen
- Shanghai Breast Cancer Survival Study confirmed 30% ↓ in recurrence and mortality; WHEL analysis also confirmed benefit of soy

# WCRF/AICR Dietary Recommendations to Reduce Cancer Risk 2007

5. Limit consumption of red meats (beef, pork and lamb) and avoid processed meats

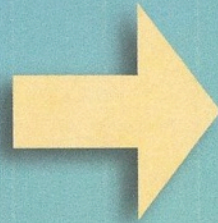


# Dietary Fats & Inflammation

## 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

# Fats, Fatty Acids and Prostate CA

- Preclinical studies had suggested that ↓ dietary fat and ↓ n-6:n-3 lowers risk and slows progression of prostate cancer
- 48 men undergoing radical prostatectomy
- Randomized to low fat (15%) diet and 5 gm fish oil (n-6:n3 2:1) or control Western diet (40% fat, n6:n3 15:1) for 4-6 wks pre-op
- Food prepared by UCLA chefs
- Serum IGF-1 levels selected as primary endpoint

Aronson et al, 2011

# Fats, Fatty Acids and Prostate CA

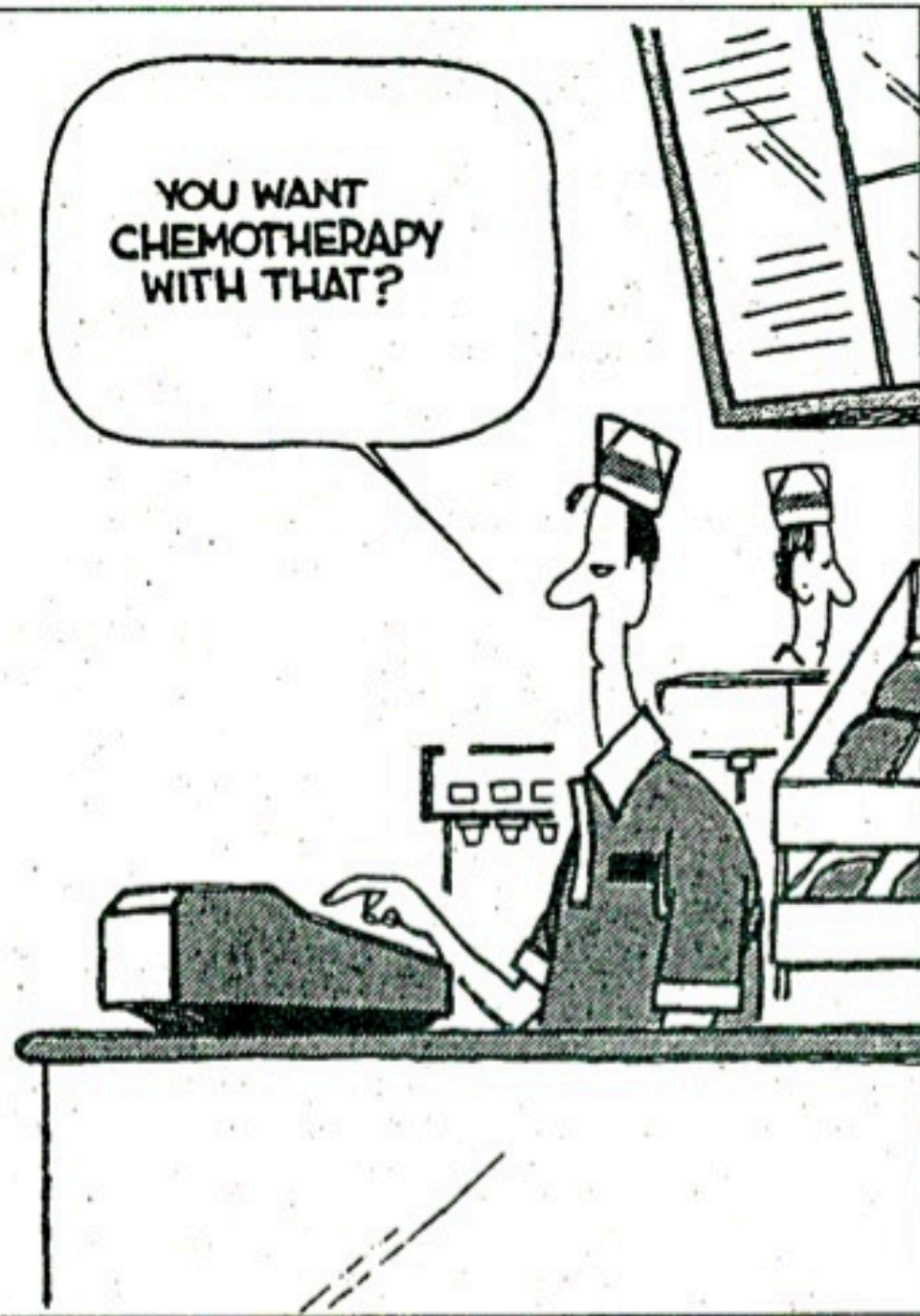
- No effect on serum IGF-1 levels
- Low fat, high n-3 group had:
  - Lower omega-6:omega-3 ratios in blood and prostate
  - Less prostate tissue (benign and malignant)
  - Reduced cancer cell proliferation (Ki-67 index)
  - Reduced prostate cancer cell proliferation in vitro with their blood added c/w controls

# 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

I'LL HAVE THE  
HALF-POUND  
DOUBLE-DELUXE  
BACON STEERBURGER,  
PLEASE...

YOU WANT  
CHEMOTHERAPY  
WITH THAT?



Does It Really Matter  
After A Cancer  
Diagnosis?

## Nutrition

6. Please describe your typical diet:

Breakfast Buttered, toasted bagel; orange juice; coffee  
Lunch Rarely  
Dinner Restaurants / burgers + fries / frozen dinners  
Snacks Occasional ice cream

7. Do you change your eating habits when you are upset, worried, or sad? ☐ Yes ☒ No

8. Do you eat when you are rushed? ☒ Yes ☐ No

9. Do you skip meals? ☒ Yes ☐ No

☐ Breakfast

☒ Lunch

☐ Dinner

10. How many glasses of fluids (water, juice) do you drink a day? five to eight

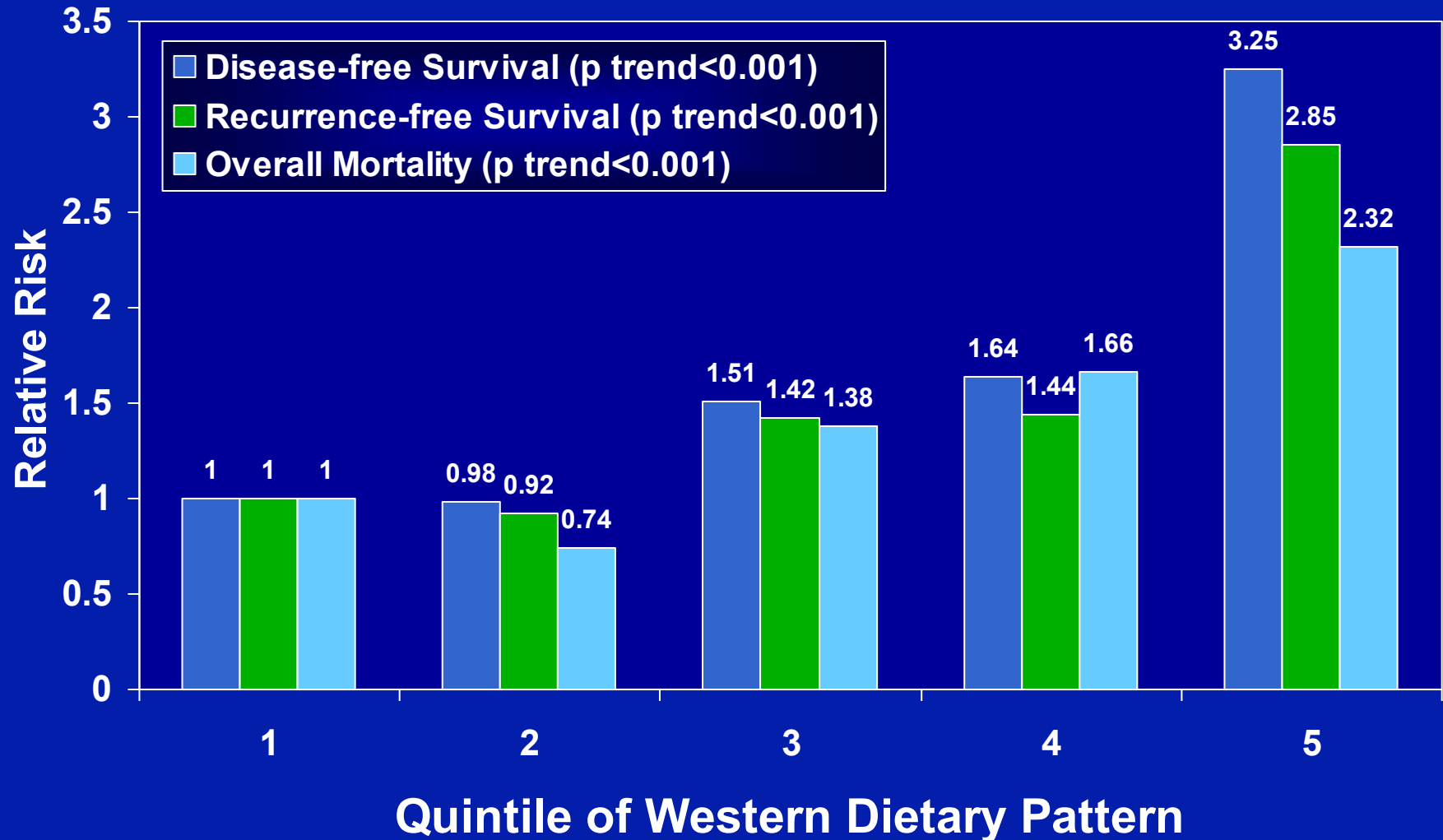
11. How many cups/cans of caffeinated drinks (coffee, tea, soda) do you drink/day? six to eight

# Dietary Patterns in Colon CA

- Prospective observational study of 1009 pts with Stage III colon cancer enrolled in CALGB 89803 between 4/99-5/01
  - Pts reported on dietary intake using a ffq during and 6 months after the trial
  - Two major dietary patterns recognized
- Two major dietary patterns identified
  - **Western pattern** characterized by high intakes of meat, fat, refined grains, and dessert
  - **Prudent pattern** characterized by high intakes of fruits and vegetables, poultry and fish
  - Every patient scored along the spectrum of both
- Patients were followed up for cancer recurrence or death

# 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



# Dietary Patterns in Colon CA

- Highest quintile in Western diet had daily median
  - 1 serving of red meat
  - 5 servings of refined grains
  - 2 sugar desserts
- Lowest quintile in Western diet had daily median
  - 0.3 serving red meat (2 per week)
  - 2 servings refined grain
  - 0.5 sugar desserts (3 per week)
- “So the recommendation is more of an avoidance than an increase in diet components”

# Doc, Can I Take This?



Photo by Lawenda

# Herb-Drug Interactions: CYP3A4

## Anticancer Agents

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

## Herbal Products

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

# 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

# Antioxidants and Chemo: Teams

## 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
- C0-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

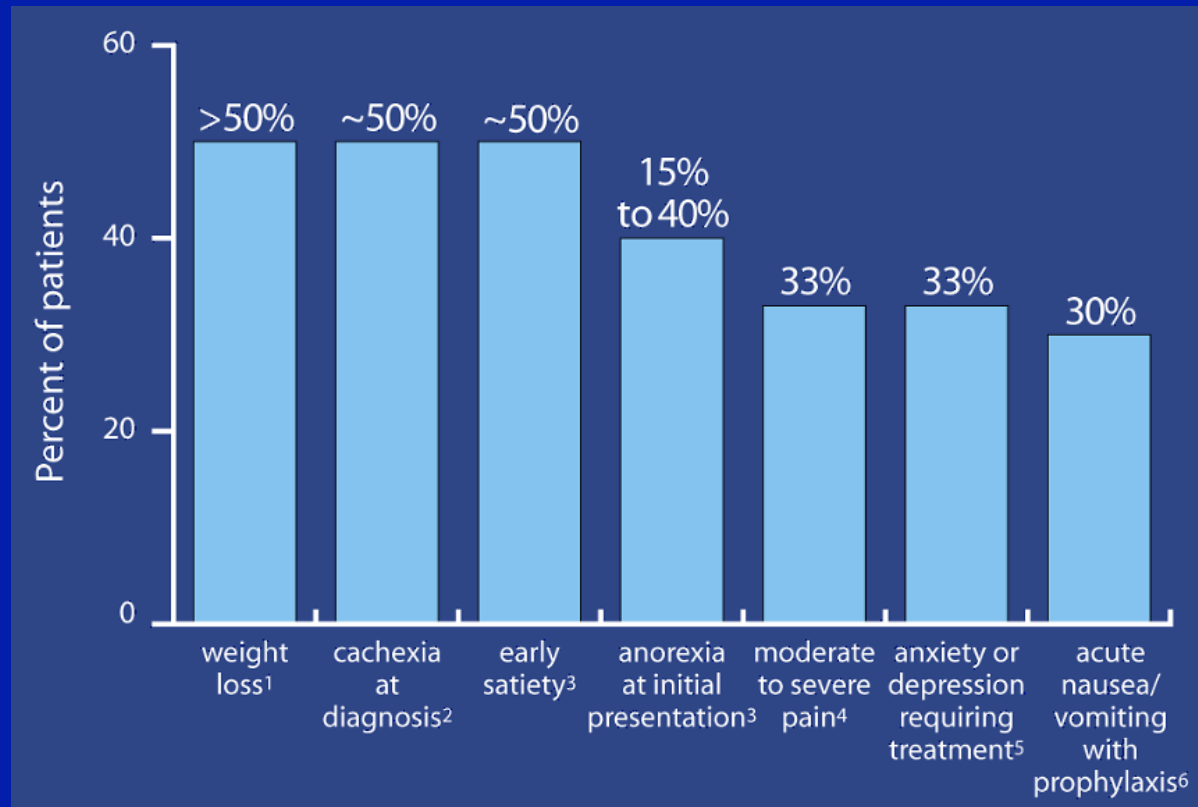
- Vitamin D3 (depending on 25OHD level)
- Calcium/Magnesium
- Omega 3's
- Medicinal Mushrooms
- Turmeric
- Probiotic

# Recommended Supplements

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



# Symptom Management Challenges Associated with Cancer and Its Treatments



1. Arnold SM, et al. In: DeVita VT, et al, eds. *Cancer: Principles & Practice of Oncology*. 2001.

2. Damsky D. *Clin J Onc Nursing*. 2002;6(4):235-238.

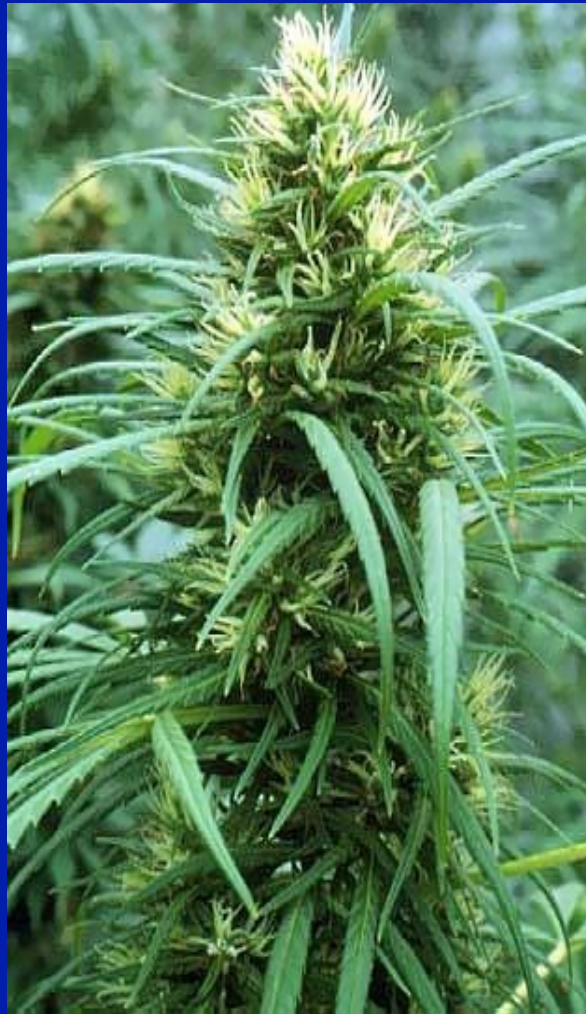
3. Body JJ. *Curr Opin Oncol*. 1999;11:255-260.

4. Foley KM. In: DeVita VT, et al, eds. *Cancer: Principles & Practice of Oncology*. 2001.

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6. Carlson RH. *Oncology Times*. 2001;23(3):19-23.

# *Cannabis sativa*



# Cannabis as Medicine

- Contains over 400 chemical compounds
- Highest concentration of bioactive compounds in resin exuded from flowers of female plants
- Main psychoactive component believed to be delta-9-THC
- At least 100 other cannabinoids identified in pyrolysis products
- delta-8-THC similar in potency but only in small concentration
- Cannabidiol (CBD) is non-psychoactive but analgesic, anti-inflammatory and anticonvulsant

# 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.

# Oral Delta-9 THC: An Approved Drug

**INTRODUCING**  **(dronabinol)** Warning: May be habit forming  
capsules 2.5 mg



**FOR THE TREATMENT OF ANOREXIA ASSOCIATED WITH WEIGHT LOSS IN PATIENTS WITH AIDS**

A significant appetite improvement was achieved at week 4 of a 6-week study.<sup>1</sup> Trends toward improved body weight and mood, and decreases in nausea were also seen during the same 6-week study, but these results were not statistically significant.<sup>1</sup>

MARINOL was well tolerated. Side effects were generally mild and reversed by dosage reduction. The most frequent adverse reactions included: euphoria (13%), dizziness (7%), thinking abnormal (7%), sinusitis (6%), somnolence (6%).<sup>1</sup> Although no drug/drug interactions were discovered during clinical trials of MARINOL, cannabinoids

may interact with other drugs, including amphetamines, atropine, and amitriptyline.

MARINOL has the potential for abuse. The same care in prescribing and accounting for MARINOL should be used as for other Schedule II drugs. Prescriptions should be limited to the amount necessary for the period between visits.

A Patient Assistance Program is available. For information call: 1-800-274-8651.

<sup>1</sup>The USAN name for delta-9-tetrahydrocannabinol (THC). Please see Brief Summary of Full Prescribing Information on adjacent page.

**APPETITE CHANGE FROM BASELINE**



Time Point	MARINOL 2.5 mg (n=112)	Placebo (n=112)
Week 2 (P<0.05)	~10	~5
Week 4 (P<0.001)	~15	~5
Week 6 (P<0.001)	~18	~5

Results of a 6-week, multicenter, double-blind, placebo-controlled study of 139 AIDS patients with anorexia and weight loss of at least 5 pounds. Data shown are based on all patients treated (112 who stayed in the study for at least 4 weeks). Data indicate mean change from baseline values on a 100 mm visual analog scale in which 0 mm represented "not hungry" and 100 mm represented "extremely hungry." Appetite was rated on a 100 mm visual analog scale 3 times during baseline and 3 days/week thereafter. Patients recorded their hunger by marking the scale 3 times during baseline and 3 days/week thereafter.

Approved in 1986 for N&V from chemoRx; AIDS anorexia in 1992

# Cannabis as an Anti-Cancer Agent

- In 1975 NIH investigators reported that delta-9-THC, delta-8-THC and CBD inhibited Lewis lung adenocarcinoma cell growth in vitro and in mice
- 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

# Cannabinoids and Cancer

- Cannabinoids induce apoptosis in mouse gliomas
- Cannabinoids administration in mouse models differentiates tumor vascular hyperplasia
  - Associated with reduced expression of VEGF and VEGF receptors (inhibition of tumor angiogenesis)
- Cannabinoids decrease the activity of matrix metalloproteinase-2; hence may also modify glioma invasiveness (inhibition of metastasis)
- Despite above, normal glial cells unaffected

# Cannabinoids and Cancer

- 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
  - Thyroid epithelioma
  - Lymphoma
  - Glioma



# CURE YOUR OWN CANCER

Empty Pill Capsules & Oral Syringes for

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## PLUS +CBDoil

100% Legal Industrial Hemp  
Ships To All 50 States

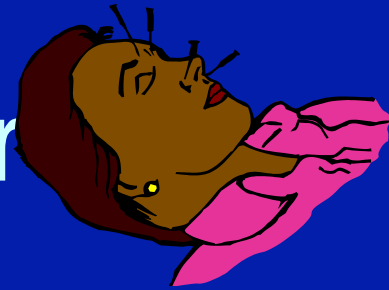
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CER

# 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

# Acupuncture for AI Arthralgias

- Aromatase inhibitor induced arthralgias and muscle stiffness in 5-50% pts
- 51 participants randomized to true or sham AP (sham= superficial needle insertion at locations not recognized as true acupoints)
- 38 pts evaluable (58 yrs, 55% Hispanic, 70% anastrozole)
- At 6 wks, pain reduced 50% in TA from baseline with no change in SA group

# 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

# Bridging the Gap



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

*Ambroise Pare*

