

Hairy Cell Leukemia:

Dietary Guidelines for Cancer Prevention, Therapy, and Survivorship

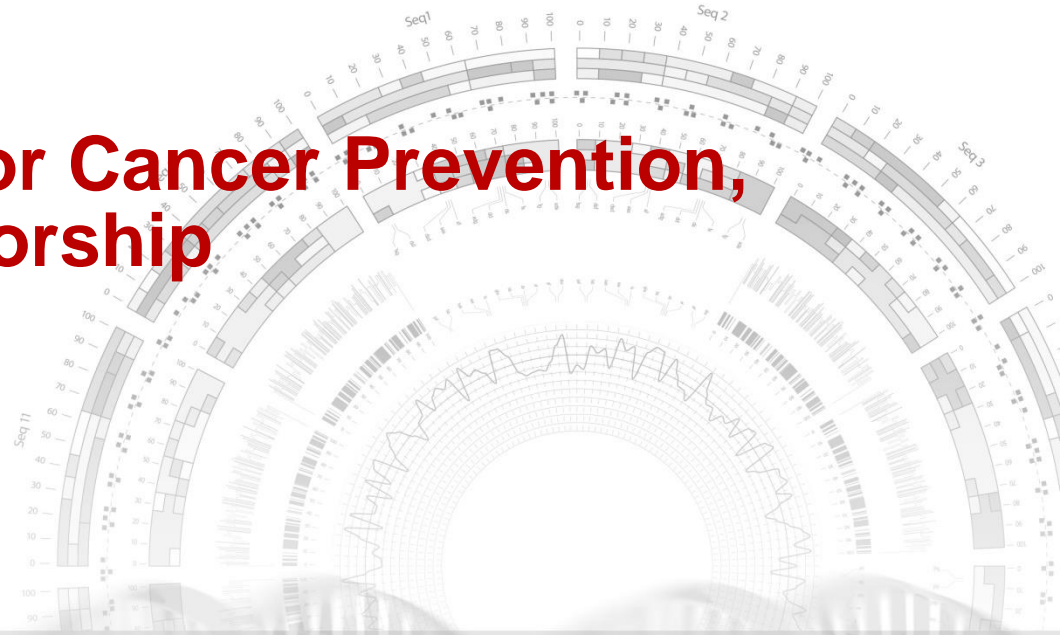
Steven K. Clinton, MD, Ph.D.



THE OHIO STATE UNIVERSITY




A Comprehensive Cancer Center Designated by the National Cancer Institute



Why me ?

- **Dietary Guidelines for America 2015-2020**
 - Congressionally mandated, 5 year intervals
 - Oversight by USDA and NIH
 - Impacts all food and nutrition policies of the US government
- **National Academy of Sciences – Institute of Medicine**
 - Dietary Reference Intakes for Nutrients
 - Vitamin D and Calcium
 - Access to Nutrition Care in Cancer Centers
 - Determinants of Nutritional Requirements of Humans
- **National Cancer Institute – National Institutes of Health**
 - Nutrition Access and Cancer Health Outcomes (NACHO) Committee
- **World Cancer Research Fund – World Health Organization**
 - Food, Nutrition, and Physical Activity for the Prevention of Cancer

Evidence-Based Standards of Care: Hairy Cell Leukemia



National
Comprehensive
Cancer
Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Hairy Cell Leukemia

Version 2.2018 — September 26, 2017

NCCN.org

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NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2018 Panel Members Hairy Cell Leukemia

[NCCN Guidelines Index](#)
[Table of Contents](#)
[Discussion](#)

| | | |
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‡ Hematology/Hematology oncology § Dermatology
§ Radiotherapy/Radiation oncology ¶ Patient advocacy
Bone marrow transplantation * Discussion Writing Committee
‡ Pathology Member

[NCCN Guidelines Panel Disclosures](#)

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NCCN Guidelines Version 2.2018 Hairy Cell Leukemia

INDICATION FOR TREATMENT⁹

- Evaluate for indications for treatment:
- Systemic symptoms
 - Splenic discomfort
 - Recurrent infection
 - Hemoglobin <11g/dL
 - Platelets <100,000/mcL
 - ANC <1000/mcL
 - Symptomatic organomegaly
 - Progressive lymphocytosis or lymphadenopathy
 - Unexplained weight loss (>10% within prior 6 months)
 - Excessive fatigue

No indication → Observe

Indication present →

INITIAL TREATMENT^j

- Purine analogs**
- Cladribine^h
 - Pentostatin^h

Complete responseⁱ → Observe until indication for treatment

< Complete responseⁱ →

See monoclonal antibody and viral reactivation ([HCL-C](#))

FOLLOW-UP

Relapse at ≥2 years^g →

Relapse at <2 years^g →

RELAPSED/ REFRACTORY THERAPY^j

- Retreat with initial purine analog ± rituximab
- Alternative purine analog ± rituximab
- Rituximab, if unable to receive purine analog

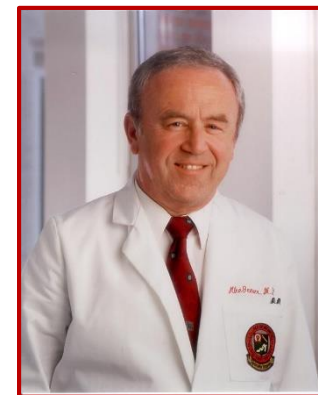
- Clinical trial
- Alternate purine analog ± rituximab
- Interferon alpha
- Rituximab, if unable to receive purine analog

Progression →

- Clinical trial
- or
- Vemurafenib^k ± rituximab
- or
- Ibrutinib^l

Evolution of Hairy Cell Leukemia Therapy: Translational Research

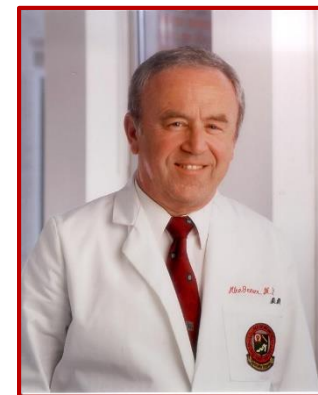
- 1950's
 - Discovery and characterization as Subtype of B-cell Leukemia
 - Splenectomy to correct “cytopenias”
- 1980's
 - Alpha-Interferon (80% response, 20% CR)
 - Pentostatin (75% CR, durable remissions)
- 1990's
 - Cladribine (90% CR, durable remissions)
 - Rituximab (anti-CD20)
- 2000's
 - Vemurafenib (BRAfV600E targeting)
 - Ibrutinib (targets BTK)



Evolution of Hairy Cell Leukemia Therapy: Translational Research

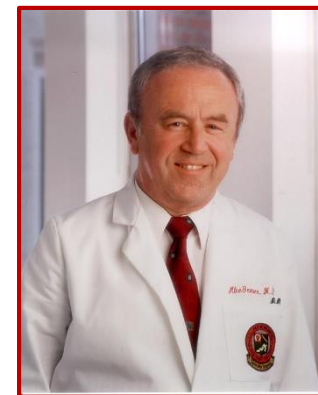
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IMPACT: HOW DOES THIS THIS HAPPEN ?



Evolution of Hairy Cell Leukemia Therapy: Translational Research

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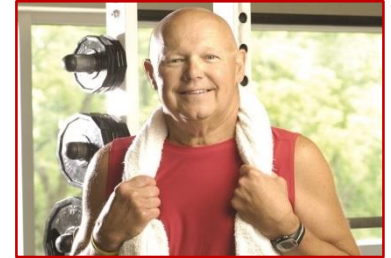
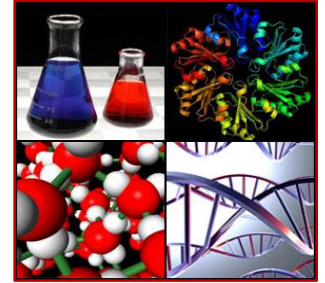


IMPACT: HOW DOES THIS THIS HAPPEN ?

RESEARCH

Diet and Nutrition - Health Outcomes: The “Scientific” Approach to Guidelines and Recommendations

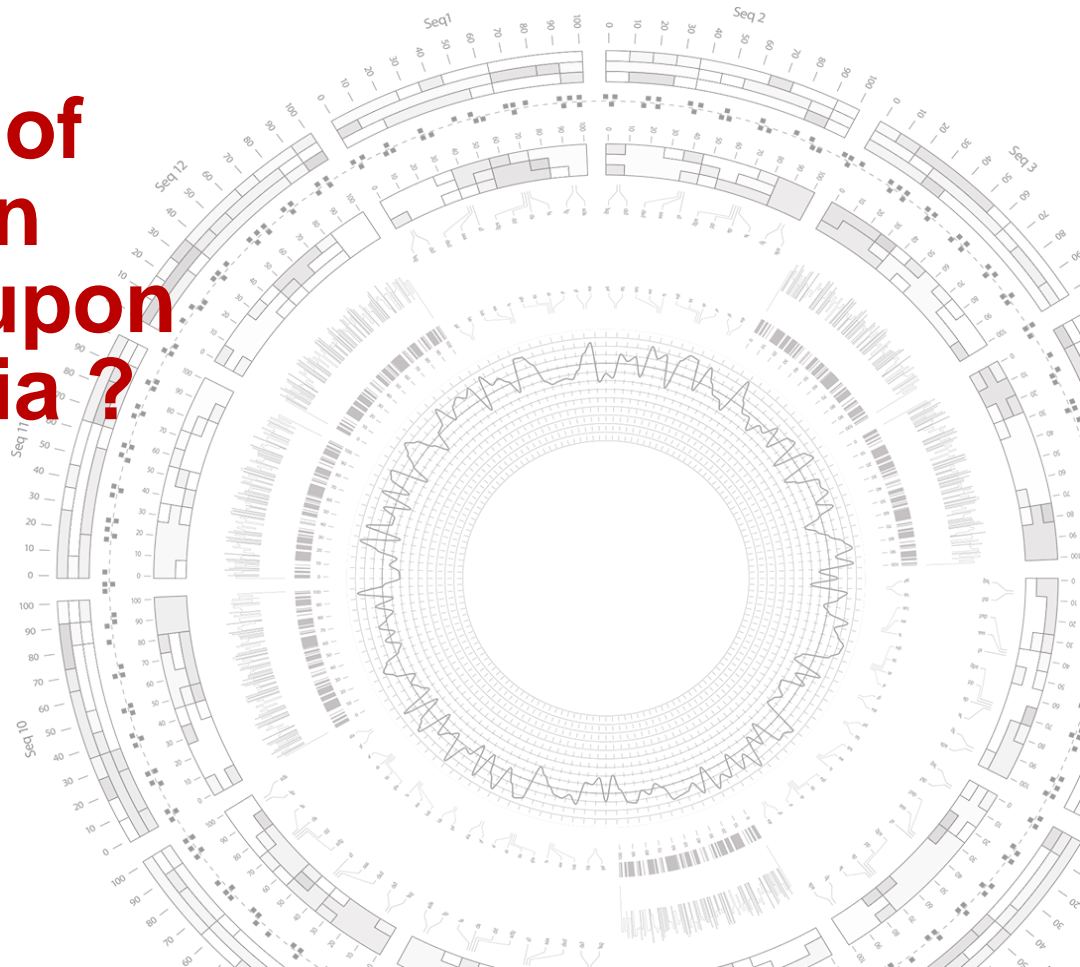
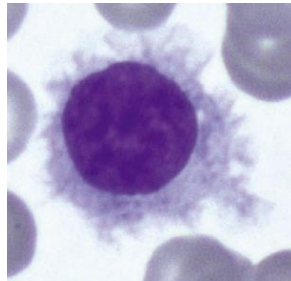
- Biochemistry / Molecular
- Cell biology
- Experimental Models
- Epidemiology
- Human studies
 - Clinical trials
 - Community / Populations
- Systematic reviews of data
- Standards of medical care
- Public Health / Policy / Regulation



} Committee



What is the state of diet and nutrition research focusing upon Hairy Cell Leukemia?



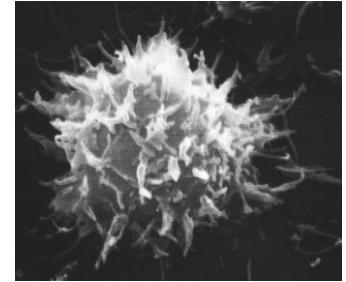
Why is the data so limited?

- Incidence (cases / million / year)
 - Hairy Cell Leukemia - 3
 - Colon/Rectal - 400
 - Breast - 1200
 - Prostate - 1198



What are some observations suggesting “hypotheses” regarding the origins of Hairy Cell Leukemia

- **Age:**
 - Rises up to 40-50 then plateaus
 - median age of 58 in men, 63 in women
- **Gender:** 4-times more common in males
- **Ethnicity:** More common in Whites vs Black/Asian
- **Exposures:**
 - Pesticides, herbicides
 - Petrochemicals, fuels
 - Duration of farming occupation
 - Early life infections
- **Genetics:**
 - Some familial clustering



Opportunities for Research: Diet, Nutrition, and Hairy Cell Leukemia

- Etiology and Prevention
- Initial Therapy
 - Enhancing efficacy :
 - Reducing toxicity:
 - Drug specific toxicity
 - Non-specific: fatigue, anorexia, endocrine, body composition changes
 - Optimizing immune function / risks of infection
- Early Post-Therapy
 - Maintaining durable complete remission
 - Recovery from toxicity
- Cancer Survivorship
 - Complications of therapy (endocrine, bone, cardiovascular, cognitive, etc.)
 - Second primary cancers

Hairy Cell Leukemia: Survivorship

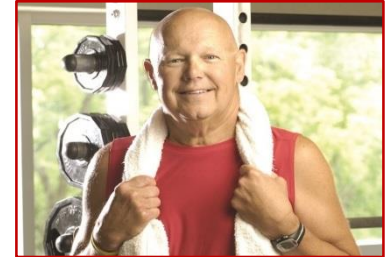
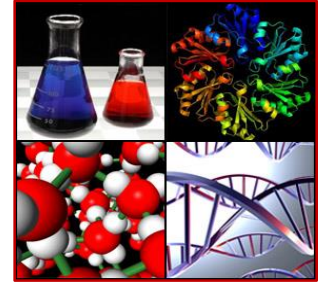
Risk of Second Malignancy

- Data
 - NCI SEER:
 - Approximately 20% increased risk
- Why?
 - Aging
 - Genetics / Family History
 - Field effect of cancer
 - Prior cancer therapy / immunosuppression
 - Diet and lifestyle



Diet and Nutrition - Health Outcomes: The “Scientific” Approach to Guidelines

- Biochemistry / Molecular
- Cell biology
- Experimental Models
- Epidemiology
- Human studies
 - Clinical trials
 - Community / Populations
- Systematic reviews of data
- Standards of medical care
- Public Health / Policy / Regulation



} Expert
Committees



Define ?

- **Nutrition**
- **Diet**

Nutrient = requires a deficiency syndrome

- **Water**
- **Energy (carbohydrates, lipids, protein, alcohol)**
- **Protein**
 - **Essential Amino Acids**
 - **Non-essential Amino Acids**
 - **Conditional Amino Acids**
- **Essential fatty acids**
 - **Alpha-linolenic acid (an omega-3), linoleic acid (an omega-6)**
 - **Conditional:**
 - **Docosahexanenoic acid (an omega-3) and gamma-linolenic acid (an omega-6)**
- **Minerals**
- **Vitamins**
 - **Fat soluble (A, D, E, K)**
 - **Water soluble (thiamine, riboflavin, niacin, panthothenic acid, pyridoxine, biotin, folate, C, cyanocobalamin)**

Minerals

| | | | | | | | | | | | | | | | | | | | |
|----|----|----|----|----|----|----|----|----|----|----|----|----|-----|----|-----|----|-----|-----|--|
| H | | | | | | | | | | | | | | | | | | He | |
| Li | Be | | | | | | | | | | | | B | C | N | O | F | Ne | |
| Na | Mg | | | | | | | | | | | | Al | Si | P | S | Cl | Ar | |
| K | Ca | | Sc | Ti | V | Cr | Mn | Fe | Co | Ni | Cu | Zn | Ga | Ge | As | Se | Br | Kr | |
| Rb | Sr | | Y | Zr | Nb | Mo | Tc | Ru | Rh | Pd | Ag | Cd | In | Sn | Sb | Te | I | Xe | |
| Cs | Ba | * | Lu | Hf | Ta | W | Re | Os | Ir | Pt | Au | Hg | Tl | Pb | Bi | Po | At | Rn | |
| Fr | Ra | ** | Lr | Rf | Db | Sg | Bh | Hs | Mt | Ds | Rg | Cn | Uut | Fl | Uup | Lv | Uus | Uuo | |
| | | | | | | | | | | | | | | | | | | | |
| | | * | La | Ce | Pr | Nd | Pm | Sm | Eu | Gd | Tb | Dy | Ho | Er | Tm | Yb | | | |
| | | ** | Ac | Th | Pa | U | Np | Pu | Am | Cm | Bk | Cf | Es | Fm | Md | No | | | |

The four organic basic elements

Quantity elements

Essential Trace Elements

Possible structural or functional role in mammals

The Science of Nutrition Informs Public Health Interventions



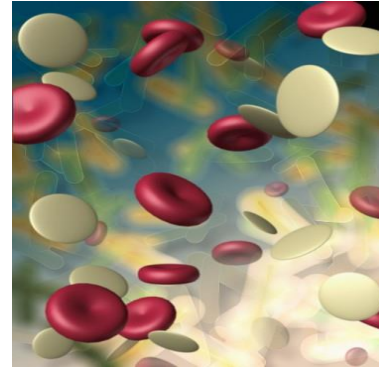
Rickets
Vit D



Pellagra
Niacin



Goiter
Iodine



Anemia
Iron

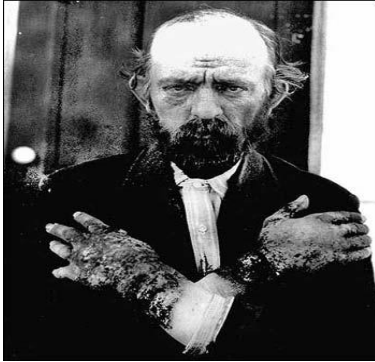


Neural tube
Defects
Folate

The Science of Nutrition Informs Public Health Interventions



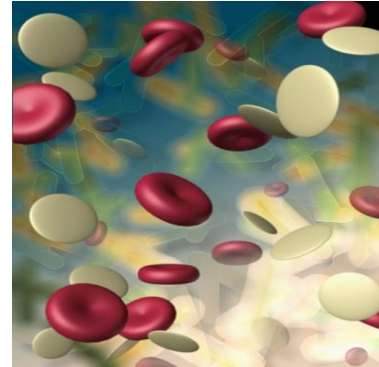
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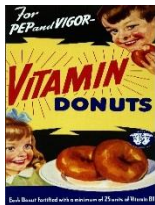
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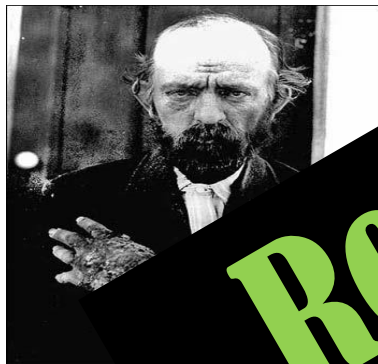
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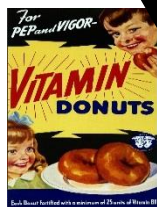
Science Informs Public Health Interventions by the Government



Rickets
Vit D



Pellagra
Niacin



Anemia
Iron



Neural tube
Defects
Folate



Research
IMPACT

Diet = everything consumed

- Vehicle for carcinogens / anti-carcinogens / toxins.
- Compounds produced during storage and processing.
- Compounds produced during cooking.
- Food additives.
- Phytochemicals.
 - Herbs, Spices
 - Fruits, Vegetables
 - Fungi
- Fiber.
 - Fermentable
 - Non fermentable
- Alcohol
- Infectious agents



What do you need to do?

- Obtain expert advice when undergoing therapy (RD or RDN)
- Meet the needs for essential nutrients
 - Healthy individuals do not need supplements if consuming a diet defined by Dietary Guidelines for Americans
 - Individuals with medical issues need personalized evaluation and therapy (RD RDN)
- Optimize dietary patterns
 - Dietary Guidelines for Americans
 - AICR-WCRF recommendations

World
Cancer
Research Fund



American
Institute for
Cancer Research

in partnership with



World Health
Organization

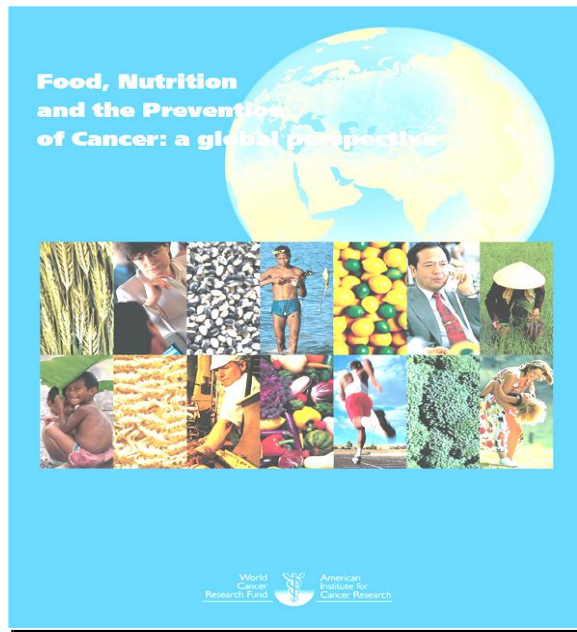
Systematic Reviews: Subcontract



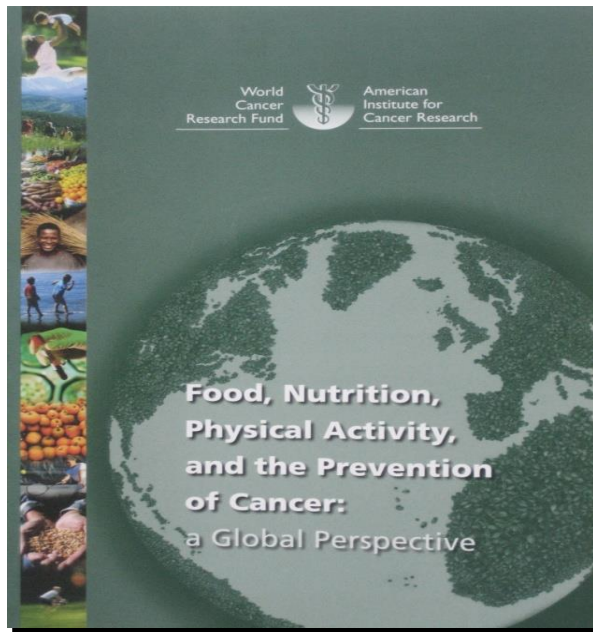
Imperial College
London

www.aicr.org

2007 World Cancer Research Fund American Institute for Cancer Research (WCRF / AICR) www.aicr.org



1997

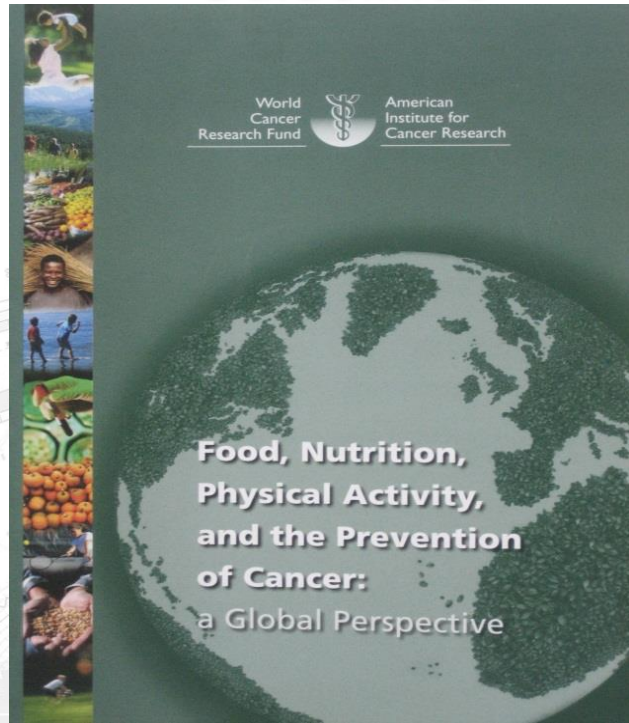


2007



2018

AICR / WCRF Global Public Health Guidelines



RECOMMENDATIONS

BODY FITNESS

Be as lean as possible within the normal range of body weight

PHYSICAL ACTIVITY

Be physically active as part of everyday life

FOODS AND DRINKS THAT PROMOTE WEIGHT GAIN

Limit consumption of energy-dense foods
Avoid sugary drinks

PLANT FOODS

Eat mostly foods of plant origin

ANIMAL FOODS

Limit intake of red meat and avoid processed meat

ALCOHOLIC DRINKS

Limit alcoholic drinks

PRESERVATION, PROCESSING, PREPARATION

Limit consumption of salt
Avoid mouldy cereals (grains) or pulses (legumes)

DIETARY SUPPLEMENTS

Aim to meet nutritional needs through diet alone

BREASTFEEDING

Mothers to breastfeed; children to be breastfed

CANCER SURVIVORS

Follow the recommendations for cancer prevention

The Continuous Update Program (CUP)

AICR/WCRF's CUP systematically collects the evidence and updates the research on an ongoing basis. The evidence is added to a central database, the world's largest resource of existing scientific literature on food, nutrition, physical activity and cancer.

Once the database is fully up-to-date for all cancer types, the AICR/WCRF CUP expert panel will evaluate whether any adjustments need to be made to AICR/WCRF's Recommendations for Cancer Prevention.

The process of updating the database on a rolling basis is underway, adding systematic literature reviews of new evidence, cancer site by cancer site



The Continuous Update Program (CUP)

2010: Breast Cancer

2011: Colorectal Cancer

2012: Pancreatic Cancer

2013: Endometrial Cancer

2014: Ovarian Cancer

2014: Prostate

2014: Breast Cancer Survivors

2015: Liver

2015: Gallbladder

2015: Kidney

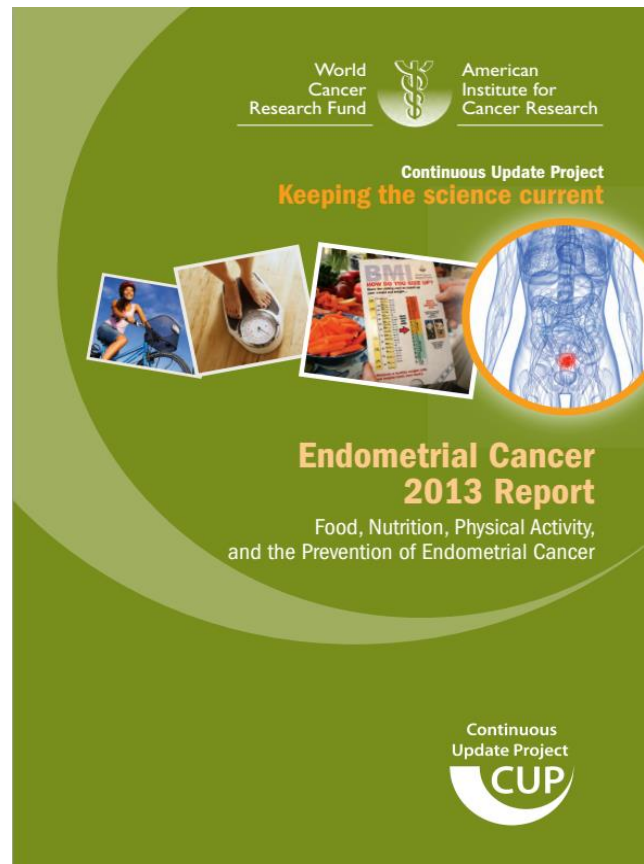
2015: Bladder

2016: Lung

2016: Esophagus

2016: Stomach

2017: Colorectal Cancer



Endometrial Cancer: AICR/WCRF CUP

Excess body fat is one of the strongest factors that increases risk for this cancer.

A high-glycemic-load diet (a diet high in sugary foods, sugary drinks and processed foods high in carbohydrates) increases risk.

Daily moderate physical activity reduces the risk.

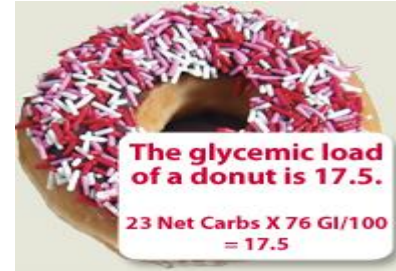


Figure 84 Nonlinear dose-response figure for BMI and endometrial cancer

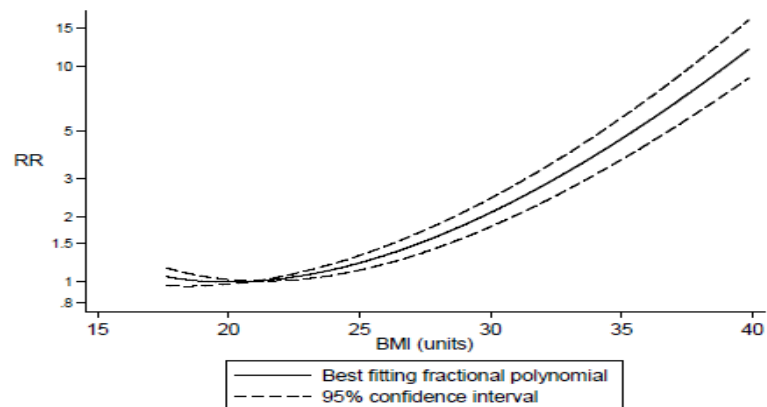


Figure 85 Scatter plot of risk estimates for BMI and endometrial cancer

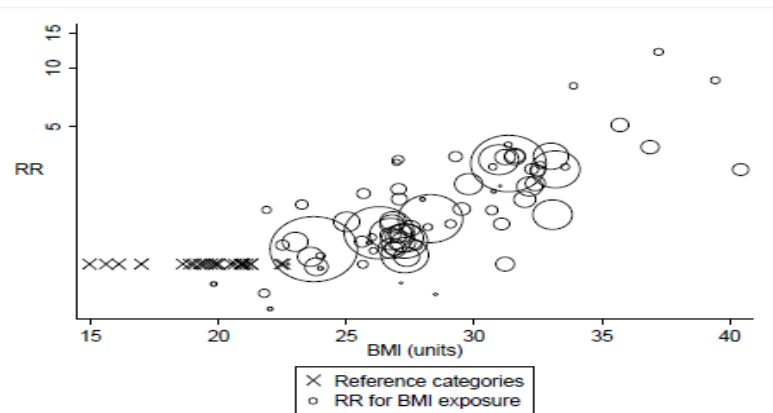


Figure 90 Nonlinear dose-response figure for BMI at age 18-25 and endometrial cancer

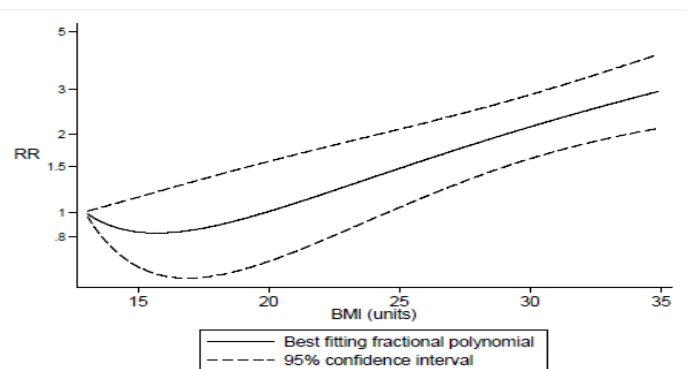
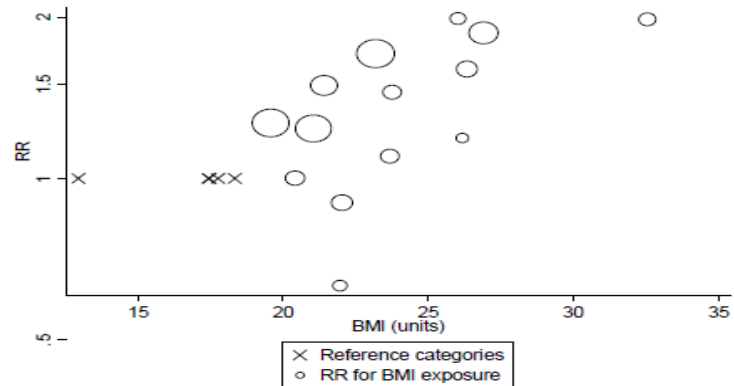


Figure 91 Scatter plot of risk estimates for BMI at age 18-25 and endometrial cancer



CUP : Endometrial Cancer

The American Institute for Cancer Research estimates that

59%

of U.S. endometrial cancer cases, or about

3 in 5



could be prevented by being at a healthy weight and being physically active.²

That's roughly **29,200** cases each year that never have to happen.

BODY FATNESS, AND THE RISK OF CANCER

In the judgement of the Panel, the factors listed below modify the risk of cancer. Judgements are graded according to the strength of the evidence.

2007
Report

| | | INCREASES RISK | |
|--|-----------------|-------------------|--|
| | | Exposure | Cancer site |
| Convincing | | Body fatness | Oesophagus ¹ Pancreas Colorectum Breast (postmenopause) Endometrium Kidney |
| | | Abdominal fatness | Colorectum |
| Probable | | Body fatness | Gallbladder ² |
| | | Abdominal fatness | Pancreas Breast (postmenopause) Endometrium |
| | | Adult weight gain | Breast (postmenopause) |
| Limited — suggestive | | Body fatness | Liver |
| | | Low body fatness | Lung |
| Substantial effect on risk unlikely | None identified | | |

DIETARY GUIDELINES FOR AMERICANS 2015-2020

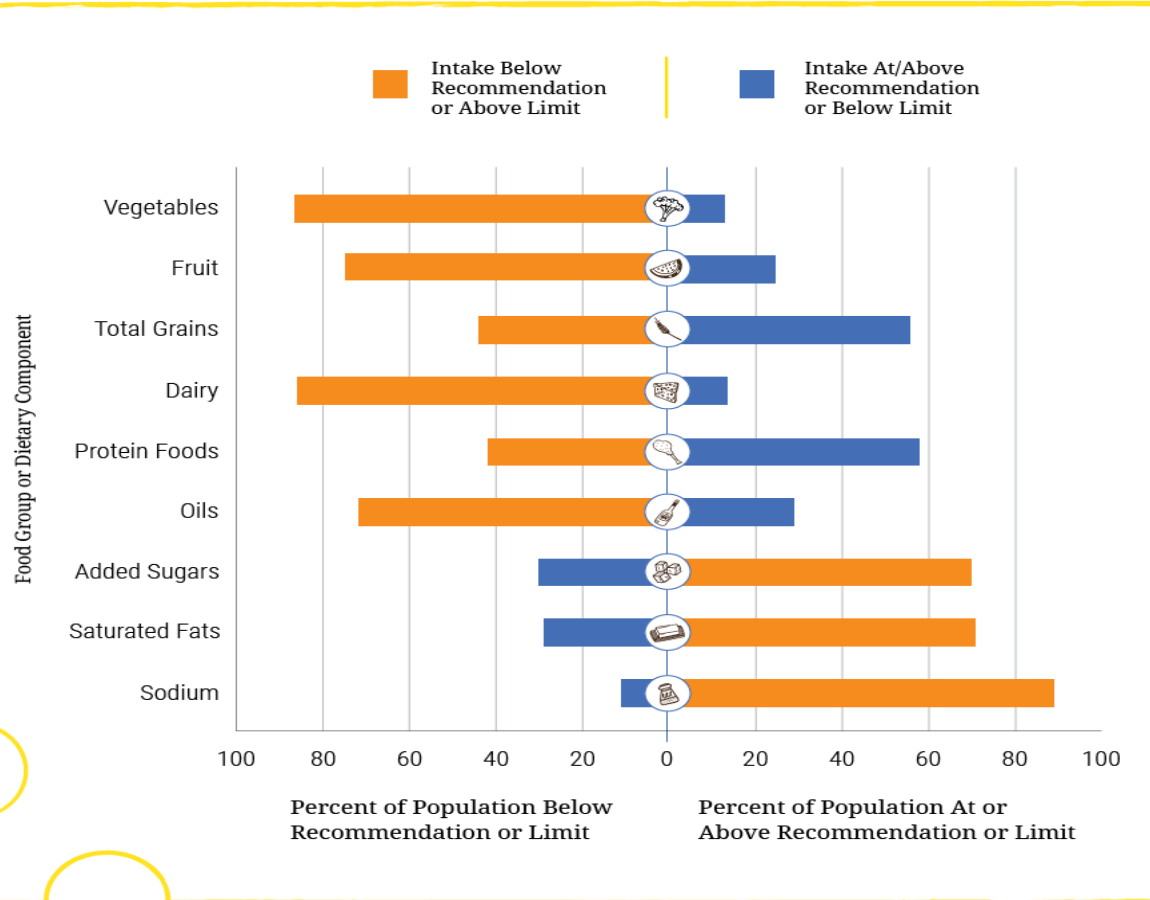


Available at: <http://health.gov/dietaryguidelines/2015/guidelines/>



Current Eating Patterns in the United States

% of the U.S. population ages 1 and older who are below, at, or above dietary goal or limit

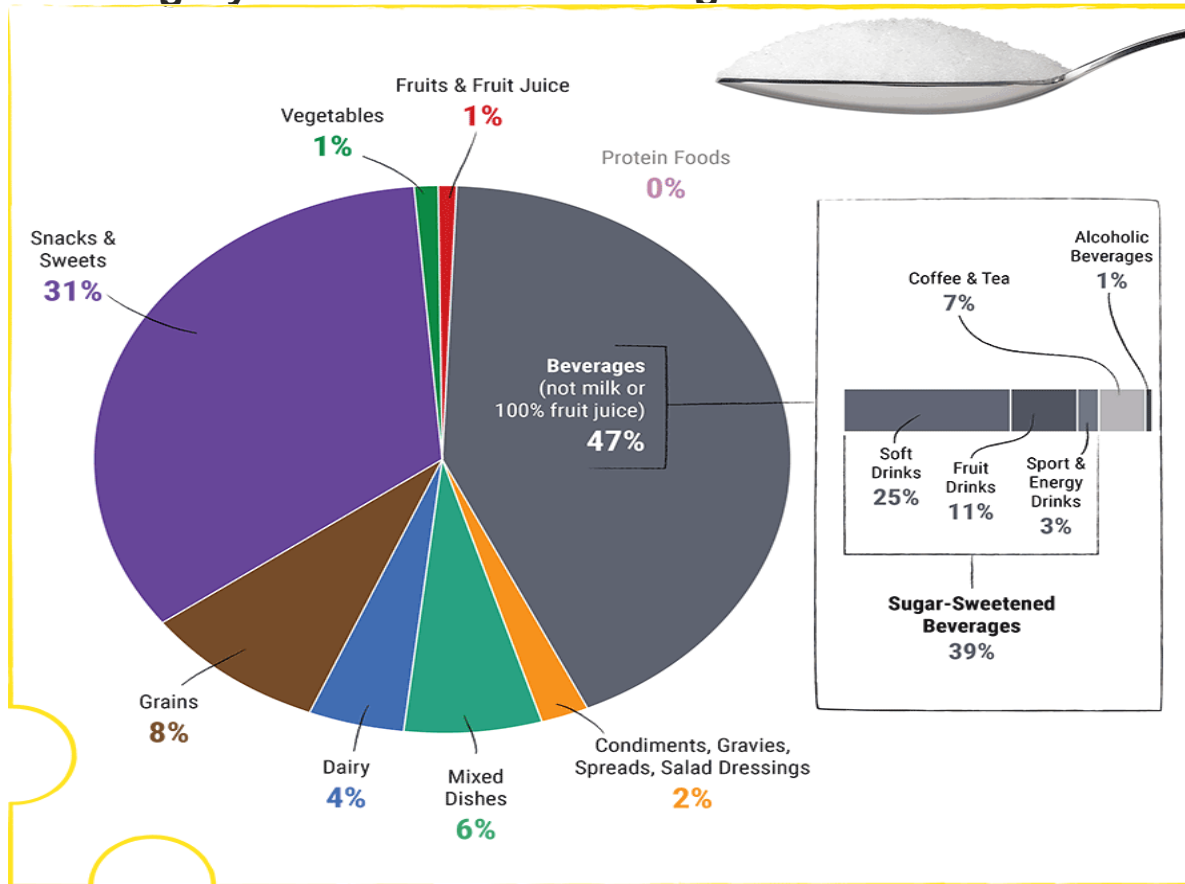


Note: The center (0) line is the goal or limit. For most, those represented by the orange sections of the bars, shifting toward the center line will improve their eating pattern.

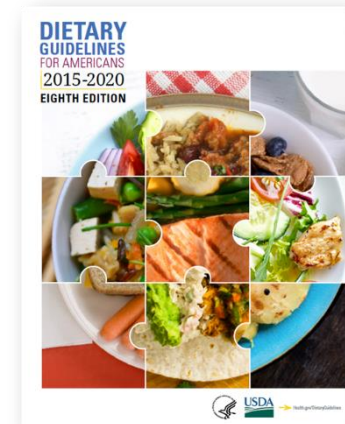
Data Source: What We Eat in America, NHANES 2007-2010 for average intakes by age-sex group. Healthy U.S.-Style Food Patterns, which vary based on age, sex, and activity level, for recommended intakes and limits.

Food Sources of Added Sugars

Food Category Sources of Added Sugars

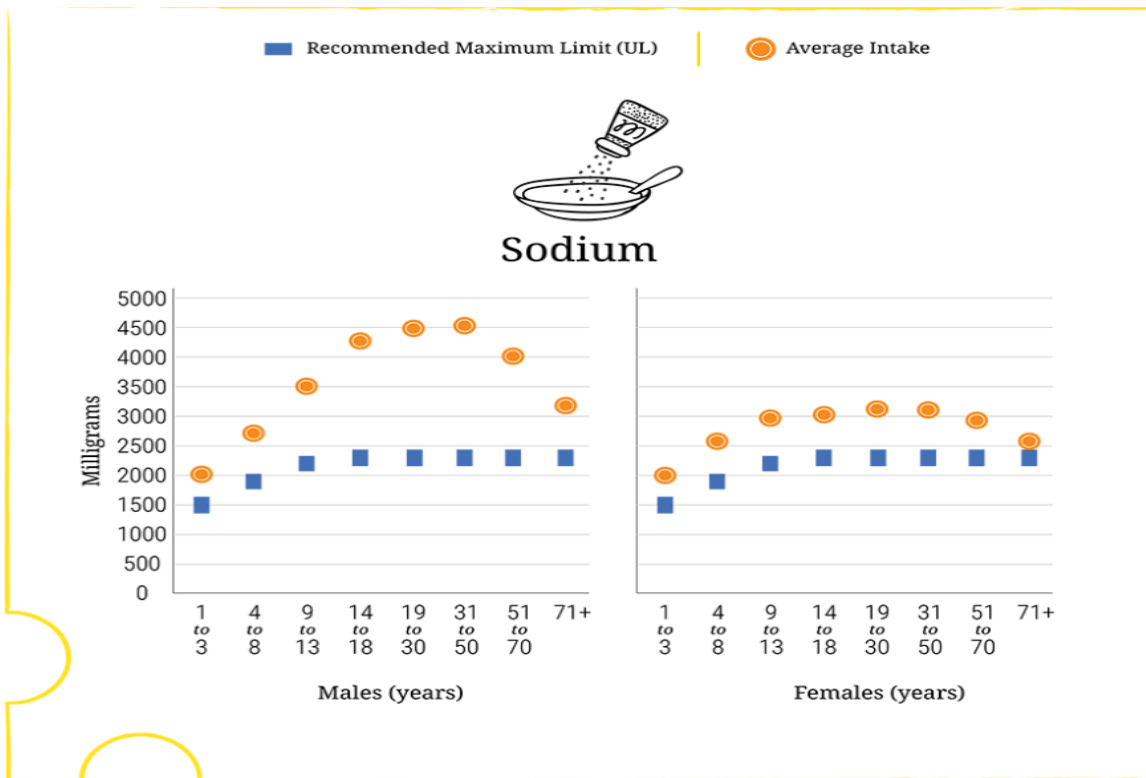


Data Source: What We Eat in America (WWEIA) Food Category analyses for the 2015 Dietary Guidelines Advisory Committee. Estimates based on day 1 dietary recalls from WWEIA, NHANES 2009-2010.

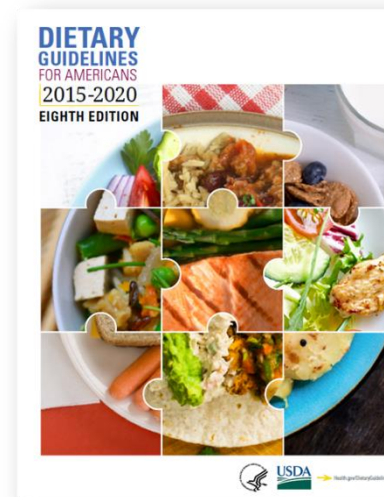


Sodium: Intakes and Limits

Average Intake of Sodium in Milligrams per Day by Age-Sex Groups, Compared to Tolerable Upper Intake Levels (UL)



Data Sources:
What We Eat in America, NHANES 2007-2010 for average intakes by age-sex group. Institute of Medicine Dietary Reference Intakes for Tolerable Upper Intake Levels (UL).



Politics and Regulatory Issues



SNAKE-OIL LINIMENT
RELIEVES INSTANTANEOUSLY
AND CURES HEADACHE, NEURALGIA, TOOTHACHE, EARACHE, BACKACHE, SWELLINGS, SPRAINS, SORE THROAT, SWELLING OF THE THROAT, CONTRACTED CORDS AND MUSCLES, STIFF JOINTS, WRINCENESS, DISLOCATIONS, CUTS AND BRUISES.

It Quickly takes out the Swellings and Inflammation from Corns, Bunions, Insect and Rupture Bites.

The best External Preparation for RYCHLISMS and ATLETISMS. It makes the Muscles supple and Relaxes the Cords. Loosens the Joints and gives a Feeling of Freshness and Vigor to the whole System.

SNAKE-OIL LINIMENT CURES ALL ACHES AND PAINS.

If you are suffering from Rheumatism, ALWAYS take LA-CAS-KA internally for the Blood and use SNAKE-OIL LINIMENT externally. When used together we GUARANTEE A CURE in every instance or MONEY REFUNDED.

If You Are Afflicted With DEAFNESS
Get Our Specially Prepared
PURE Rattlesnake Oil



Dietary Supplements



CANCER CAN BE CURED

I WANT TO SEND TO ALL SUFFERERS FROM CANCER. THESE TWO BIG BOOKS ABSOLUTELY FREE

and these statements prove it

Read the Proof!

TWO FREE BOOKS: CANCER AND ITS CURE TESTIMONIAL BOOK

DR. JOHNSON REMEDY CO. Kansas City, Mo.

Lessons from the Wizard of Oz



The great and powerful
Wizard of OZ



The Truth

Quackery, Deceit, Fraud.....

Dr. Oz: A Modern Day Purveyor of Wizardry.



<https://www.youtube.com/watch?v=WA0wKeokWUU>

Dr. Oz: A Modern Day Purveyor of Wizardry.



Dr Oz Best Weight Loss
Garcinia Cambogia



FRAUDULANT

“ Last Night Dr Oz Spoke About Green Coffee Beans & How They Can Help You Lose Weight “



Order Now



DR OZ
GARCINIA CAMBOGIA
for Quick Weight Loss

ORDER NOW & FREE BOTTLES
ON SELECT PACKAGES

Lose 3-5lbs a week



Raspberry Ketones as featured in Dr Oz Show



Supplement Industry / Food Labeling



Smart cookies? They're just white flour, sugar, and oil... plus a dose of whole grain, processed fiber, and added calcium.

Each cup has 60 mg of omega-3s. A 6 oz. serving of salmon has 800-3,000 mgs



- **Political**
 - **DSHEA, repeal / revise**
 - **Enhance FDA oversight and the Office of Dietary Supplements**
 - **Demand safety, quality control, and accurate labels**

Dietary Supplement Health and Education Act



DSHEA of 1994 Provisions

- Dietary supplements do not need approval from FDA before they are marketed
- Firms do not need to provide FDA with information regarding safety, efficacy
- Manufacturers do not need to register their products with FDA before producing, marketing them
- Currently, no regulatory standards exist to ensure quality, purity of dietary supplements
 - FDA proposes to develop regulatory standards in future
 - Currently, the manufacturer is responsible for this
 - Contrast with drugs (Good Manufacturing Practices, Good Laboratory Practices)

Recommendations are derived from studies such as those at The Ohio State University !



The Cancer Survivors Garden:

A Comprehensive Garden-Based Nutrition and Physical Activity Education Program for Cancer Survivors

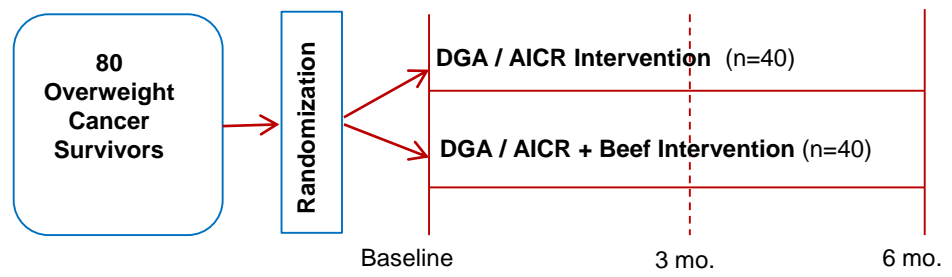
Success: 19% increase in “steps per day”, 12 lbs wt loss, 7% reduction in waist circumference, 10 point drop in resting BP, 8% drop in cholesterol, 25% increase in circulating carotenoids, improved healthy eating index, etc.



MICROBIOME



Fig 1. Growing Hope Study Design - 2017



Remember:

**Evidence –based
Recommendations!**

Thank You !



Questions

