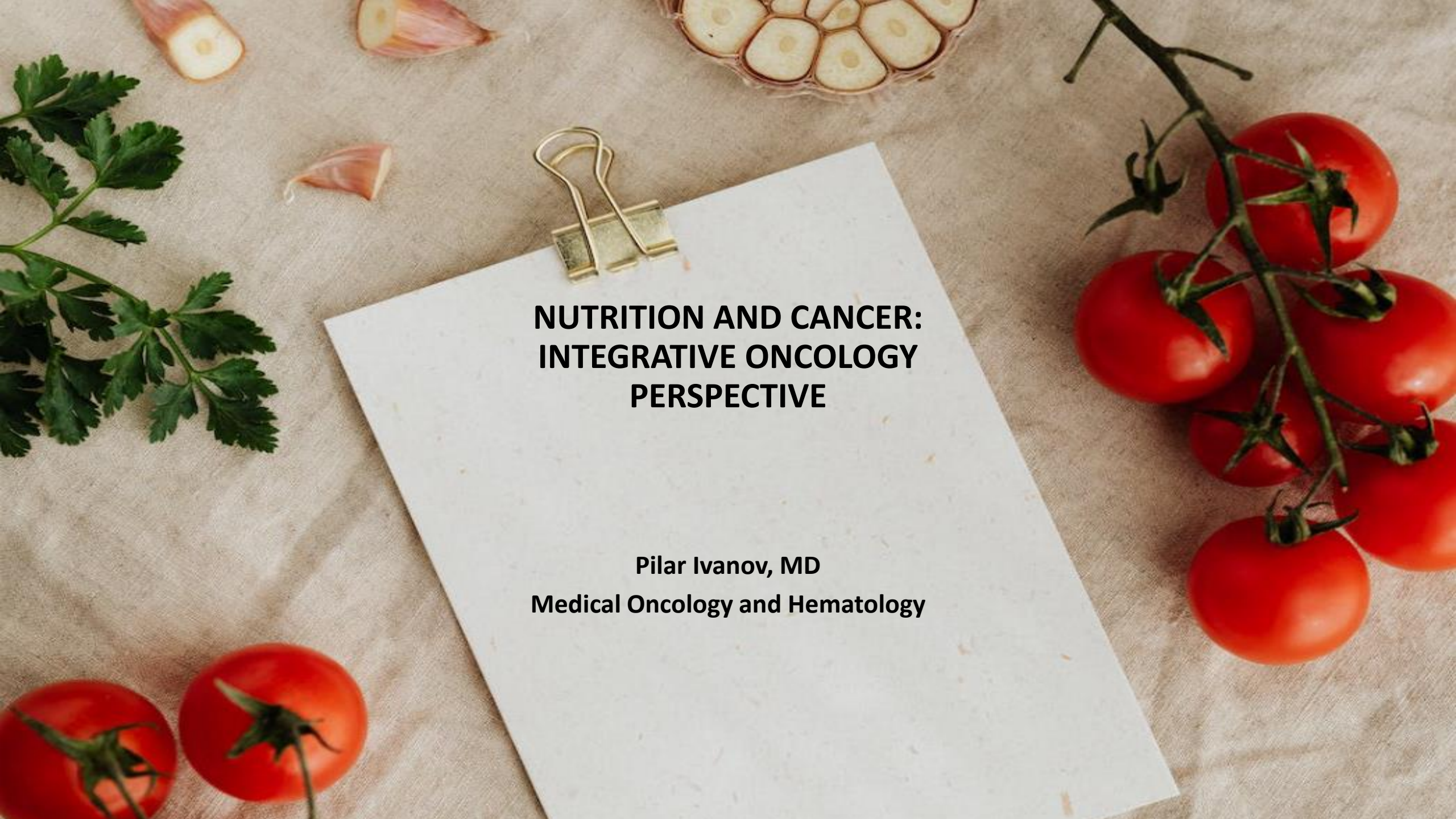


NUTRITION AND CANCER: INTEGRATIVE ONCOLOGY PERSPECTIVE

Pilar Ivanov, MD

Medical Oncology and Hematology

No Disclosures

Objectives

- Understand Integrative Oncology Concept and how it relates to nutrition
- Know the AICR and ACS guidelines for cancer prevention
- Recognize the link between diet and cancer risk
- Understand some popular diets and their concordance to AICR/ACS recommendations
- Obtain tips on how to guide patients regarding their chosen diet

Integrative Oncology

Definition

Integrative oncology is a patient-centered, **evidence-informed field of cancer care** that utilizes mind and body practices, natural products, and/or lifestyle modifications from different traditions **alongside conventional cancer treatments**. Integrative oncology aims to **optimize health**, quality of life, **and clinical outcomes** across the cancer care continuum and to **empower people** to prevent cancer and become active participants before, during, and beyond cancer treatment."

JNCI Monographs, Volume 2017, Issue 52, November 2017

Philosophy

- Patient centered—focus care on whole person. Acknowledge them as multidimensional
- Promote innate ability of each person to heal-individualized
- Compassionate
- More than just integrating lifestyle medicine to conventional care-but a philosophy of care
- Use Foundation of Wellness (Diet, Physical Activity, Sleep, Social Support/Community, Stress)
- Being proactive rather than reactive to their needs

Components of Integrative Oncology Consultation (2)

Lifestyle Management

- Nutrition and Diet
- Physical Activity and Exercise
- Sleep
- Stress management

Herb and Supplement Guidance

- Safety and potential herb-drug interaction
- Review Evidence and advice on appropriate herb or supplement use in cancer setting

Symptom Control

- Nausea, Vomiting
- Pain
- Fatigue
- Anxiety

The New York Times

Is ...

Celery Juice, Kombucha,
Activated Charcoal, CBD,
Turmeric, Fish Oil, Chlorophyll,
Intermittent Fasting,
The Keto Diet, Probiotics,
Collagen, Coffee, Zinc, B.M.I.,
Plant Milk, Natural Deodorant,
Lettuce Water, Aloe,
An At-Home Face-Lift,
Hydration,
A Stress-Relieving Drink,
Nasal Rinsing,
Cold Water Plunging

A Scam?

**Facts about wellness.
Will these trends change your life — or
take your money?**

Dietary Guidelines

Prevalence of Diet use

3% to 48% of cancer patients pursue “special diets” during their cancer experience (3,4)

Most common complementary approach patients ask about during treatment

During survivorship, most commonly asked resource or referral

Many studies are done on breast cancer patients

Female access this complementary approach more often than men

Why Diet

- Motivations to choose a diet are driven by (3,4,5,6):
  - The desire to mitigate symptoms and side effects of cancer and treatment
  - The desire to have some control over their life
  - To improve overall health
  - Popular perspective as presented by the media
  - Health care setting promoting a specific dietary/lifestyle recommendation
  - Philosophical, cultural, or ethical underpinnings

Dietary Guidelines During Cancer Treatment

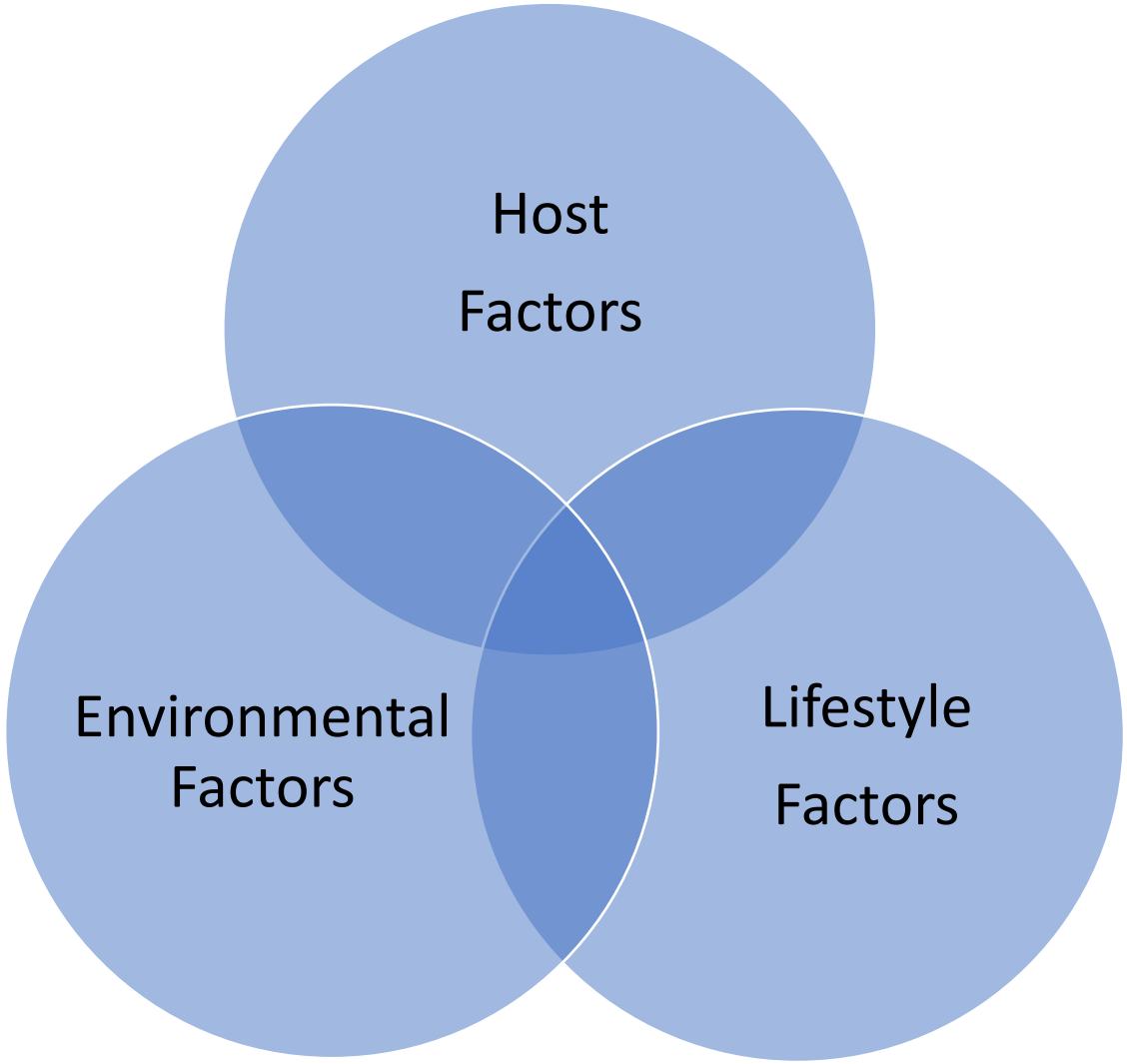
ASCO® AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Cancer.Net®
ASCO | KNOWLEDGE CONQUERS CANCER

NCCN GUIDELINES FOR PATIENTS®

NIH NATIONAL CANCER INSTITUTE

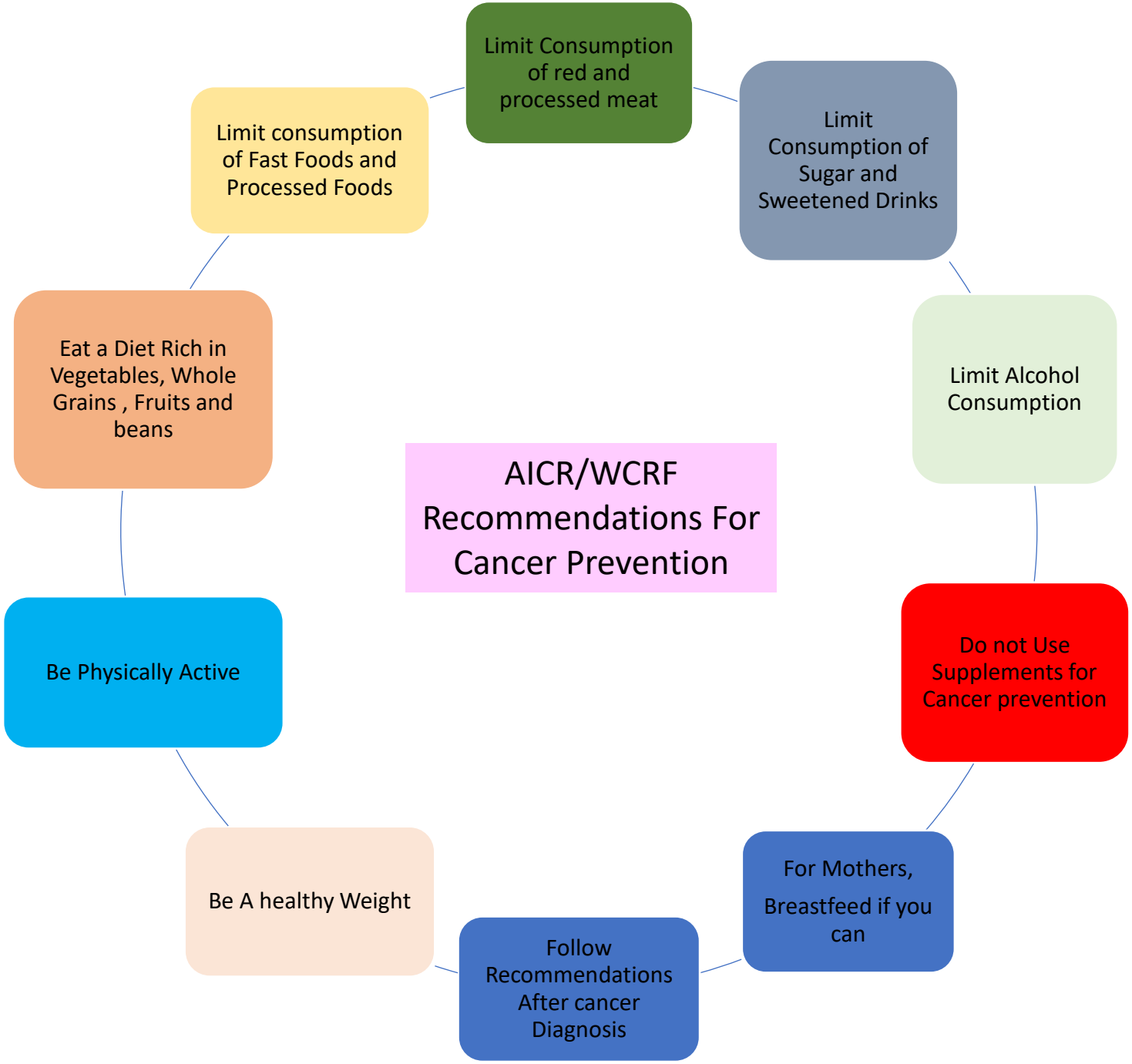
Dietary Guidelines For Cancer Prevention



Lifestyle, Environmental and Host factors interact to affect the cancer process

While following each individual recommendation offer cancer protection benefits, you gain the most by treating all recommendations as an integral package or way of life

- Not Smoking
- Avoid Excess Sun



World Cancer Research Fund | American Institute for Cancer Research

2020 American Cancer Society Guideline on Diet and Physical Activity for Cancer Prevention

1. Achieve and maintain a healthy body weight throughout life
2. Be physically active
3. Follow a healthy eating pattern at all ages
4. It is best not to drink alcohol

World Cancer Research Fund

American Institute for Cancer Research

CUP Continuous Update Project

Analysing research on cancer prevention and survival

Diet, Nutrition, Physical Activity and Cancer: a Global Perspective

A summary of the Third Expert Report

World Cancer Research Fund International

World Cancer Research Fund UK

Wereld Kanker Onderzoek Fonds

World Cancer Research Fund
世界癌症研究基金會

BE A HEALTHY WEIGHT

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

- Ensure that body weight during childhood and adolescence projects towards the lower end of the healthy adult BMI range
- Keep your weight as low as you can within the healthy range throughout life
- Avoid weight gain (measured as body weight or waist circumference) throughout adulthood

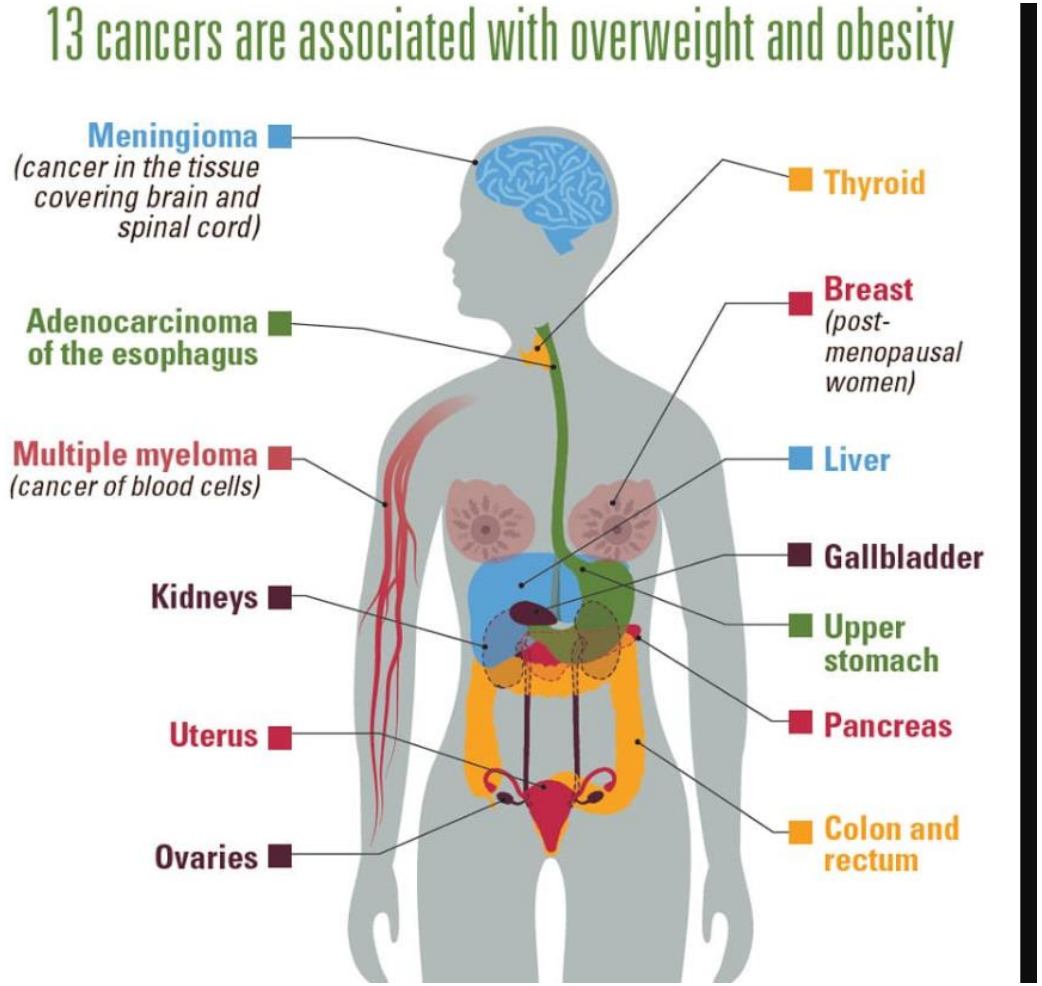
World Cancer Research Fund | American Institute for Cancer Research

BE A HEALTHY WEIGHT

•More than 684,000 obesity-associated cancers occur in the United States each year, including more than 210,000 among men and 470,000 among women.

•Breast cancer after menopause is the most common obesity-associated cancer among women. Colorectal cancer is the most common obesity-associated cancer among men.

•More than 90% of new obesity-related cancers occur in men and women who are 50 years old or older.



CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

EAT A DIET RICH IN WHOLE GRAINS , VEGETABLES, FRUIT AND BEANS

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

- consume a diet that provides at least 30 grams per day of fiber from food sources
- include in most meals foods containing whole grains, non starchy vegetables, fruit and pulses such as beans and lentils
- eat a diet high in all types of plant foods including at least five portions or servings of a variety of non starchy vegetables and fruit every day
- if you eat starchy roots and tubers as staple foods eat non starchy vegetables fruit and pulses regularly too if possible

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

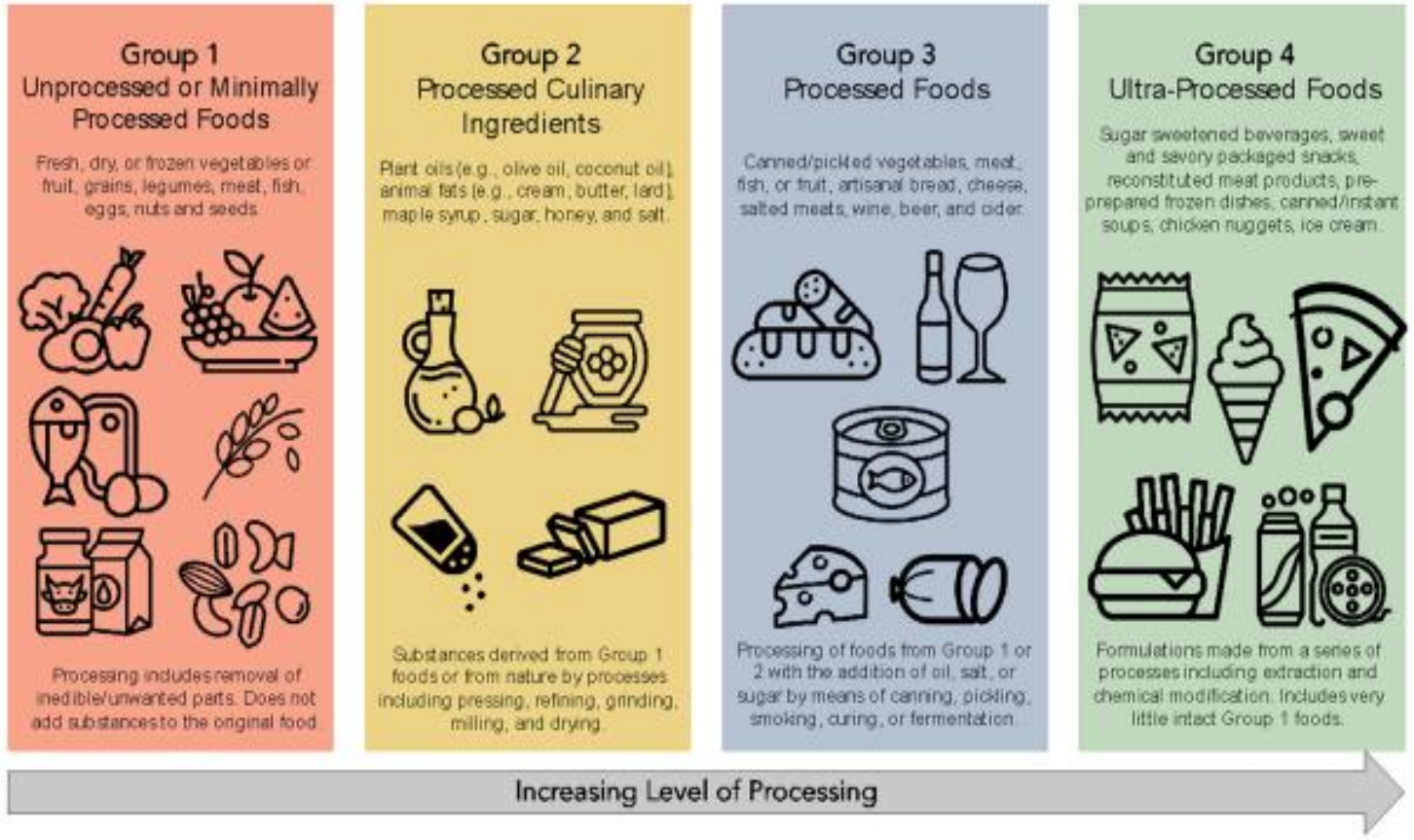
Limiting these foods help control calorie intake and maintain a healthy weight

- limit consumption of processed foods high in fat, starches or sugars –including fast foods , many pre-prepare dishes, snacks, bakery foods and desserts and confectionery.

World Cancer Research Fund | American Institute for Cancer Research

Spectrum of processing of foods based on the NOVA classification

- **Group 1** - Unprocessed or minimally processed foods
- **Group 2** - Processed culinary ingredients
- **Group 3** - Processed foods
- **Group 4** - Ultra-processed food and drink products



Current Obesity Reports (2022) 11:80–92

World Cancer Research Fund | American Institute for Cancer Research

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

- If you eat red meat, limit consumption to no more than about three portions per week. 3 portions is equivalent to about 350 to 500 grams (about 12 to 18 ounces) cooked weight of red meat.
- Poultry and fish are valuable substitutes for red meat. Eggs and dairy are also valuable sources of protein and micronutrients for people who do not eat other foods of animal origin

LIMIT CONSUMPTION OF SUGAR SWEETENED DRINKS

- drink mostly water and unsweetened drinks

LIMIT ALCOHOL CONSUMPTION

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

- Consuming alcoholic drinks is a cause of many cancers. There is no threshold for the level of consumption below which there is no increase in the risk of at least some cancers.

DO NOT USE SUPPLEMENTS FOR CANCER PREVENTION

Aim to meet nutritional needs through diet alone

- high dose dietary supplements are not recommended for cancer prevention.

AICR/WCRF Guidelines

World Cancer Research Fund | American Institute for Cancer Research

Emphasize

- Vegetables
- More than 15oz (5 serv.) per day

Fruits

- More than 15oz (5 serv.) per day

Whole grains
Beans

Use diverse foods to help prevent cancer, not dietary supplements

After a cancer dx, adhere to these recommendations

Limit or None

- Alcohol
- Sugar-sweetened drinks
- Fast food & processed food
- As little as possible
- Red meat
- < 12-18 oz (3 serv.) per week
- Processed meat

American Cancer Society Guidelines

Emphasize

Plant-based foods
2.5-3 cups of vegetables and 1.5-2 cups of fruit per day

Whole grains

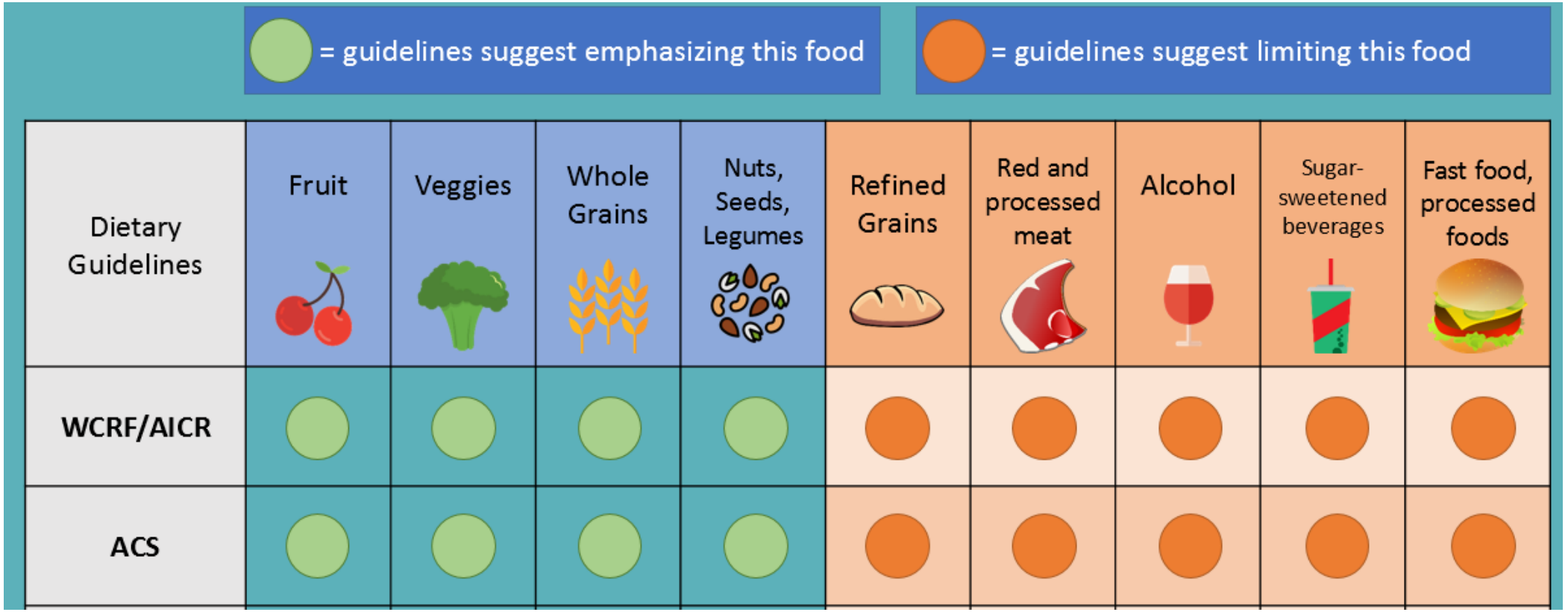
- Read food labels when possible
- Choose portion sizes that support a healthy weight
- “Low-fat” doesn’t mean “low-calorie”
- Cook meat with low-heat, low-fat cooking methods

Limit

Red and processed meats
Highly processed foods
Refined grain products
Sugar-sweetened beverages
Alcohol

- Choose smaller portion sizes when eating high-calorie foods
- Be careful to make healthy choices when eating away from home

Guidelines Similarities



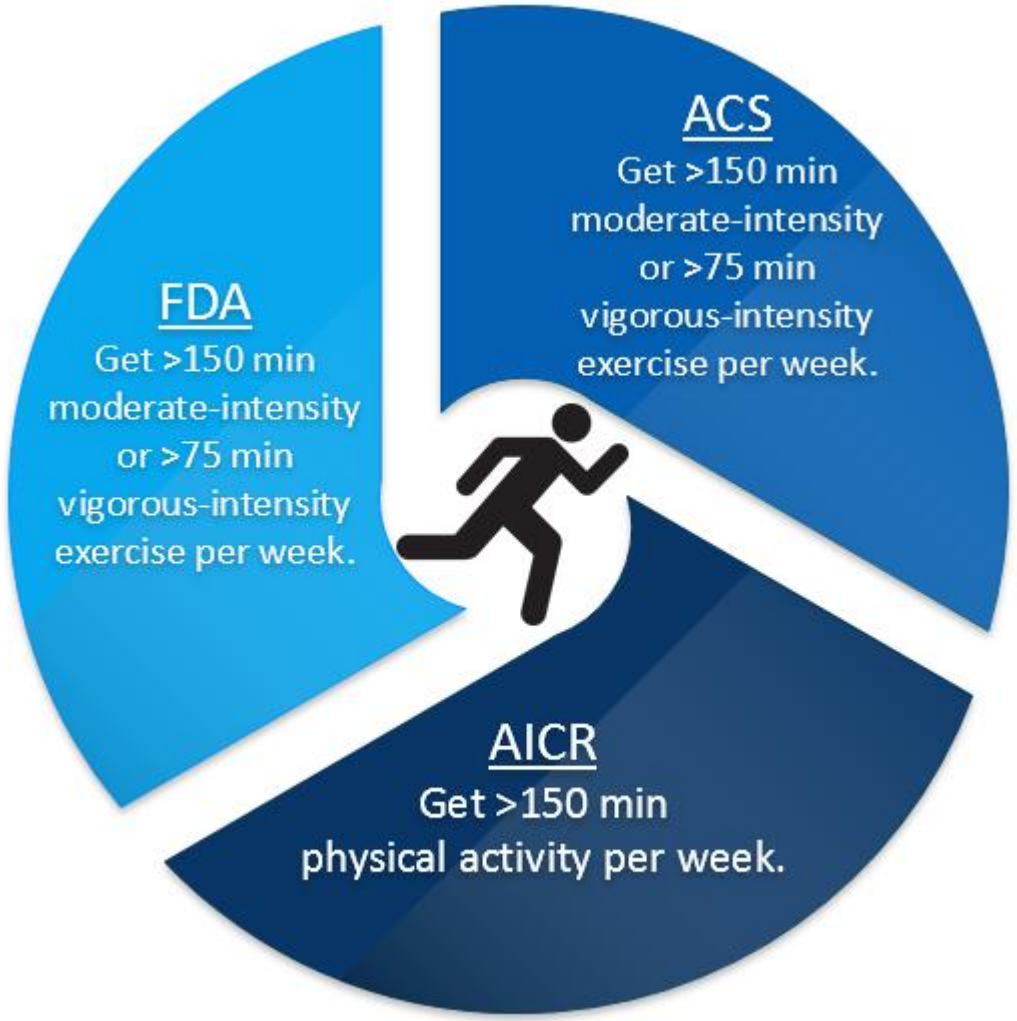
Dietary Guidelines	Fruit	Veggies	Whole Grains	Nuts, Seeds, Legumes	Refined Grains	Red and processed meat	Alcohol	Sugar-sweetened beverages	Fast food, processed foods
WCRF/AICR	●	●	●	●	●	●	●	●	●
ACS	●	●	●	●	●	●	●	●	●

BE PHYSICALLY ACTIVE

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

- Be at least moderately physically active, and follow or exceed national guidelines
- limit sedentary habits

- Spread physical activity throughout the day and the week



World Cancer Research Fund
American Institute for Cancer Research

Other Lifestyle Recommendations

- Avoid **smoking**
- Limit excessive sun exposure
- Participate in appropriate screenings
- Immunization for cancer prevention
- For mothers breastfeed your baby if possible

Impact on Cancer Incidence

Meta-Analysis of ACS & AICR/WCRF Diet and Physical Activity Guideline Studies

N = 12 studies (1,687,408 participants),

Type: Prospective Cohort Studies

Who: Americans, Europeans, Canadians

Dose: Adherence to ACS & AICR/WCRF recommendations calculated as points (0-8 or 0-11), higher more adherent to guidelines

Outcomes: Cancer incidence and site specific-cancer incidence

Association of specific-cancer incidence with highest vs. lowest adherence to AICR/WCRF & ACS guidelines

- **Incidence:**
- Colorectal: **35 - 52%** decrease
- Breast: **19 - 60%** decrease
- Endometrial: **23 - 60%** decrease
- Lung, ovarian, prostate: Non-significant decreases

- **For each additional point of adherence to guidelines= Delays the onset of cancer by 1.1 to 1.6 years**

- **All cancer**: **Average = 17% (range of 4 to 45%)** decrease

Impact on Mortality

Meta-Analysis of ACS & AICR/WCRF Diet and Physical Activity Guideline Studies[12]

N = 5 of the 12 studies (1,090,905 participants)

- Who: Americans, Europeans, Canadians

Type: Prospective Cohort Studies

Dose: Adherence to ACS & AICR/WCRF recommendations calculated as points (0-8 or 0-11), higher more adherent to guidelines

Outcomes: Cancer Specific Mortality

Association of cancer mortality with highest vs. lowest adherence to both AICR/WCRF & ACS guidelines

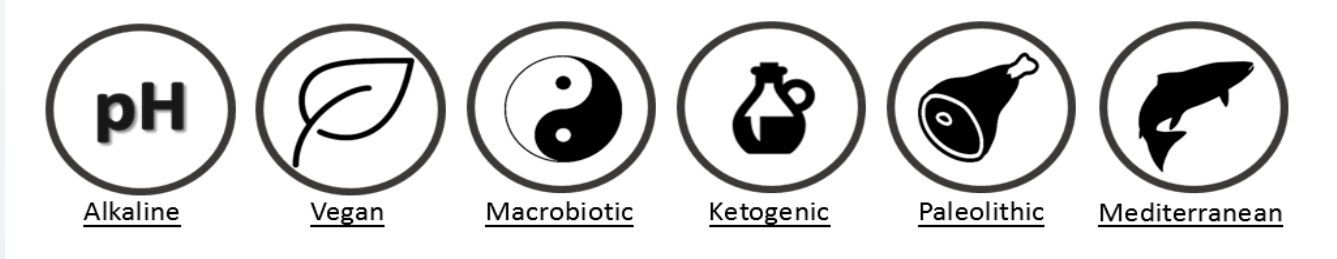
•Cancer Mortality:

• **All Cancers:**	**20 - 30 %** decrease
• Women:	**20 - 24%** decrease
• Men:	**20 - 30 %** decrease

For each additional point of adherence to guidelines
9 - 10% decrease

Overall cancer	**Range of 10 - 30%** decrease

POPULAR CANCER DIETS



Alkaline Diet Definition

Definition

- 80% of diet should be “alkaline” foods, 20% can be from “acidic” foods

Beliefs

- Foods range from “acid-forming” to “alkaline-forming”
- The “Western diet” - rich in meat, sugar, and processed foods - is considered highly acid-forming
- “Acidic” foods lead to inflammation of acid detoxification systems and then to cancer

Rationale

- Systemic pH is modifiable with diet
- Blood pH (and the pH of other systems) is associated with urine pH
- Extent of systemic pH change is great enough to dysregulate natural physiology
- Inflammation of acid-base balance systems leads to cancer
- All “alkalizing” foods are good; any “acid-forming” food is bad

Alkaline Diet

Alkaline (Ph scale 7-14) 80% of diet

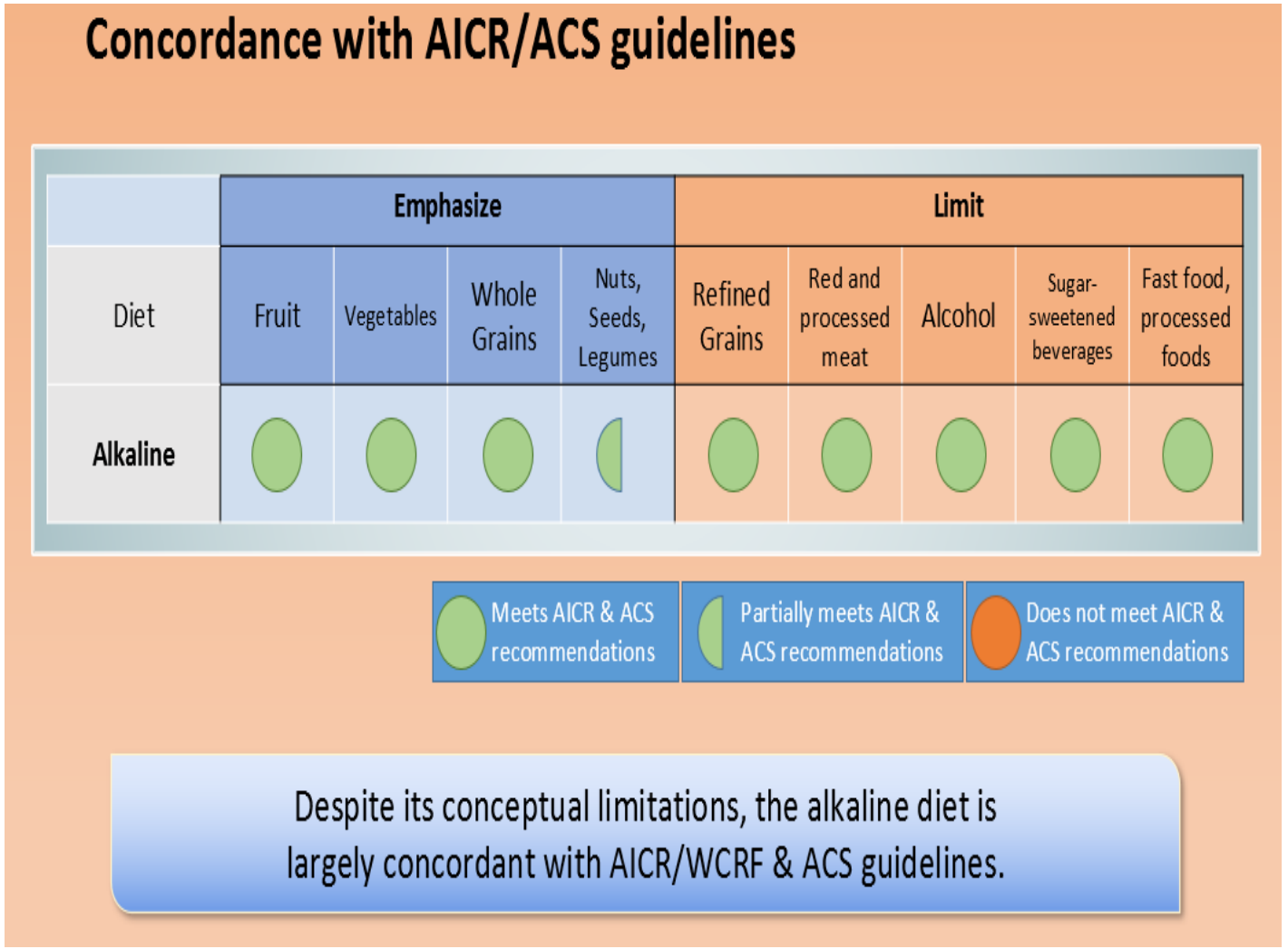
- Vegetables
- beets, broccoli, cauliflower, celery, cucumber, kale, lettuce, onions, peas, pepper, spinach; preferably raw
- Low sugar fruits
- apples, bananas, berries, grapes, lemons, oranges, melons, peach, pear
- Some legumes
- Alkaline ionized water

Acidic 20% of diet

- Red meat, pork, poultry, fish, eggs
- Dairy products
- Corn & wheat
- Coffee
- Sugar
- Alcohol

Alkaline Diet

- The logic behind the alkaline diet is faulty, and robust scientific evidence is lacking.
- The alkaline diet is highly congruent with dietary recommendations for cancer patients and survivors
- It may be an appropriate diet for cancer patients, but for different reasons than given by its proponents



Vegetarian/Vegan Diet

✓All plant-based foods:

✓Vegetables

✓Alternative milk products

✓Soy products

No animal products:

- Meat
- Dairy*
- Eggs*
- Honey*

*Permitted in some vegetarian diets

*Ovo-lacto **vegetarians** eat eggs and dairy products

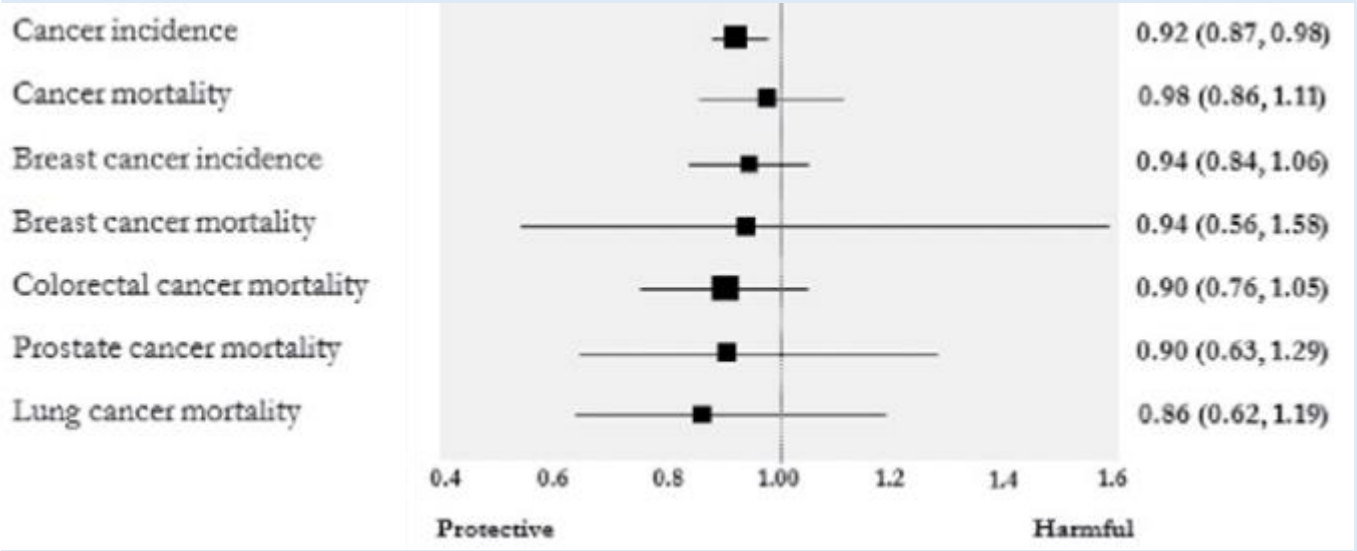
Evidence related to cancer: Vegetarian Diet[20]

Meta-analysis of studies among vegetarians

N = 7168 vegans

Type: 86 cross-sectional and 10 prospective cohort studies

Outcome: Cancer incidence, cancer mortality, etc.



Association of vegetarian diet compared to omnivorous diet:

Cancer Incidence RR = 0.92
(95% CI: 0.87 - 0.98)

Cancer Mortality RR = 0.98
(95% CI: 0.86 - 1.11)

Vegetarian diets are associated with a **8% reduced risk** for developing cancer, but not with all-cause mortality.

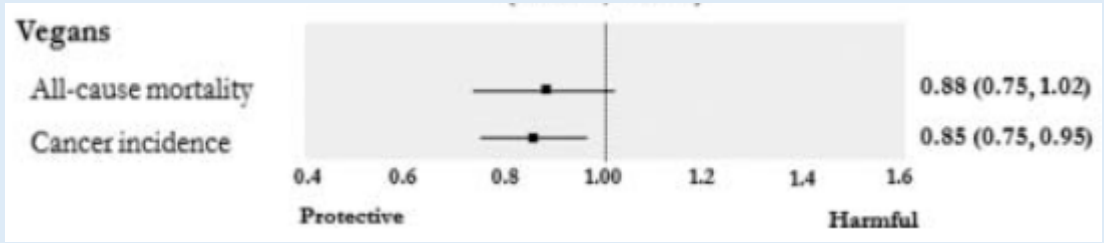
Evidence related to cancer: Vegan Diet[20]

Meta-analysis of studies among vegans

N = 7168 vegans

Type: 24 cross-sectional and 4 prospective cohort studies

Outcome: Cancer incidence, all-cause mortality



Association of vegan diet compared to omnivorous diet:

Cancer Incidence RR = 0.85
(95% CI: 0.75 - 0.95)

All-Cause Mortality RR = 1.72
(95% CI: 0.88 – 1.02)

Vegan diets are associated with a **15% reduced risk** for developing cancer, but they are not significantly associated with a change in all-cause mortality.

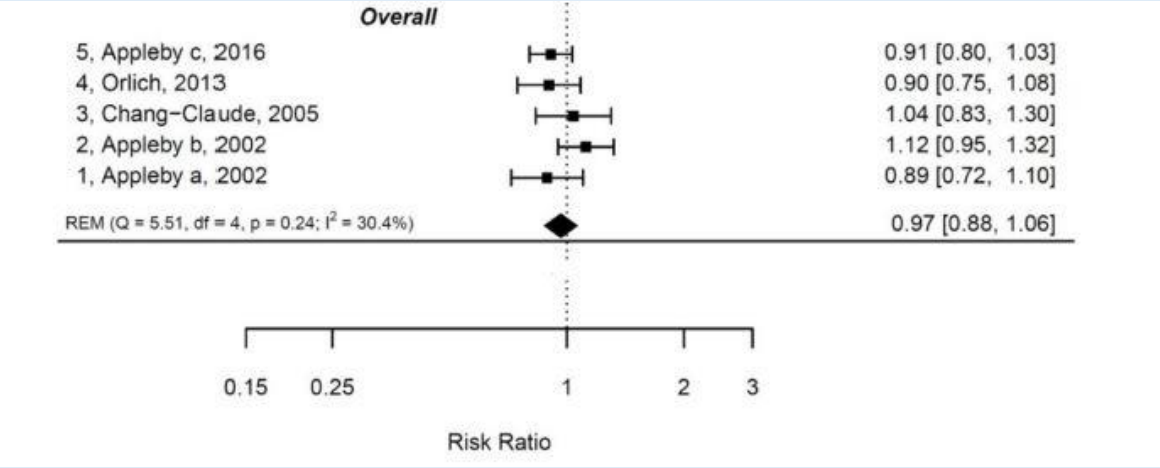
Evidence related to cancer: Vegan & Vegetarian Diet[49]

Rapid Review & meta-analysis of studies among vegans and vegetarians

N = 139,174 participants

Type: 5 cohort studies

Outcome: overall cancer mortality



Vegetarian diet compared to omnivorous diet:

Overall Cancer Mortality RR = 0.97
(95% CI: 0.88 - 1.06)

Vegetarian diets are non-significantly associated with a **3% reduced risk** of overall cancer mortality.

Clinical considerations: Vegan & Vegetarian Diet[21]

With an **unbalanced** diet, possible insufficiencies include:

- Calcium
- Zinc
- Iron
- Iodine

Contrary to popular belief, it is very rare for a vegan diet to cause protein insufficiency.

Recommendations

- A **varied diet** will mitigate most nutritional insufficiencies

- Advise on vegan sources of:
- **Calcium**:
  - leafy greens, nuts, seeds, sea vegetables, fortified nut milks
- **Zinc**:
  - Legumes, whole grains, nuts and seeds
- **Iron**:
  - leafy green, nuts, seeds, and whole grains
- **Iodine**:
  - Sea vegetables, iodized salt

Clinical considerations: Vegan & Vegetarian Diet[17,18,23]

Even with an balanced diet, some insufficiencies are still possible:

- Vitamin D
- Vitamin B12
- Essential fatty acids

Fun Fact

The type of vitamin B12 found in seaweed, nutritional yeast, and most other vegetable-sources is not bioavailable.

Recommendations

- Advise on vegan sources of:
- **Vitamin D**:
  - Fortified foods (orange juice, nut milks, cereals)
  - Supplements (synthetic or vegan preparations)
  - Adequate sun exposure (see module on vitamin D)
- **Vitamin B12**:
  - Fortified foods (cereals, nut milks)
  - Supplements (synthetic or made from specific algae)
- Omega-3 fatty acids, particularly eicosapentaenoic acid (**EPA**) from supplements

Bottom line

- Vegan/vegetarian diets may be beneficial for cancer prevention
- Advantages outside of impact on cancer risk include favorably affecting cardiovascular health and weight management
- People considering a vegan diet for cancer prevention should:
  - Choose whole-food options
  - Consider supplementing with vitamins D & B12, and EPA
- And should limit:
  - Refined grains
  - Alcohol
  - Processed foods and fast food
  - Energy-dense foods
  - Sugary beverages

Vegetarian/Vegan Diet

Concordance with AICR/ACS guidelines

	Emphasize				Limit				
Diet	Fruit	Vegetables	Whole Grains	Nuts, Seeds, Legumes	Refined Grains	Red and processed meat	Alcohol	Sugar-sweetened beverages	Fast food, processed foods
Vegan/ Vegetarian	●	●	●	●	●	●	●	●	●

● Meets AICR & ACS recommendations

◐ Partially meets AICR & ACS recommendations

● Does not meet AICR & ACS recommendations

Vegetarian & vegan diets should be followed alongside other dietary guidelines to ensure concordance with AICR/WCRF & ACS guidelines.

Macrobiotic Diet

- The macrobiotic diet is part of a lifestyle centered around balance
- Foods range in their “yin” and “yang” qualities
- The Western diet is imbalanced by being high in “yang” foods like meat and refined fats
- Imbalance leads to disease states

Macrobiotic diets are thought to affect cancer by:

- Increasing:
  - Nutrient-dense vegetables and fruit
  - Fiber-rich whole grains
- Limiting:
  - Portion sizes
  - Saturated fats
- Eliminating:
  - Red and processed meat
  - Dairy products

Macrobiotic Diet

Emphasis on	Limit
Whole grains (50-60%)	Almost all meat except some fish
Nuts, seeds, and legumes	Animal fats
Vegetables (25-30%)	Eggs
Beans and sea vegetables (5-10%)	Dairy products
White-meat fish	Refined sugars
Soy products	Processed foods
Green tea	Alcohol
	Nightshades

- Eat local & in season
- Moderate portion sizes
- Choose whole foods

Macrobiotic Diet

Concordance with AICR/ACS guidelines

	Emphasize				Limit				
	Fruit 	Veggies 	Whole Grains 	Nuts, Seeds, Legumes 	Refined Grains 	Red and processed meat 	Alcohol 	Sugary Drinks 	Fast food, processed foods 
Macrobiotic									

The macrobiotic diet is largely concordant with AICR/WCRF & ACS guidelines.

Clinical considerations: Macrobiotic Diet[28]

Possible insufficiencies include:

- Vitamin C
- Vitamin D
- Vitamin B12
- Calcium

Not so Fun Fact
Children following macrobiotic diets are at risk for clinical deficiency of these micronutrients.

Recommendations

- A **varied diet** will mitigate most nutritional insufficiencies
- Advise on macrobiotic-friendly sources of:
- **Vitamin C:**
  - Tree fruits and berries
- **Vitamin D**:
  - Fortified foods (orange juice, nut milks, cereals)
  - Supplements (synthetic or vegan preparations)
  - Fatty fish (mackerel and salmon, as well as tuna and sardines
  - Adequate sun exposure (see module on vitamin D)
- **Vitamin B12**:
  - Fortified foods (cereals, nut milks)
  - Supplements (synthetic or made from specific algae)
- **Calcium**:
  - leafy greens, nuts, seeds, sea vegetables, canned fish

Bottom line: Macrobiotic Diet[29]

- The macrobiotic diet is almost completely congruent with AICR/WCRF & ACS guidelines
- Additional benefits may include positive changes in self-efficacy, physical activity, weight, stress, and chronic disease burden.

Evidence related to cancer

No studies to date, one under way:

Diet and Androgens 5 Study (DIANA-5)[31]

N = 1208 women

Type: Randomized control trial

Intervention: Mediterranean-macrobiotic diet, nutrition education, physical activity

Outcome: Breast cancer recurrence

Paleolithic Diet

Assumptions

- Ancestral hunter gatherer- "Stone age diet" nutritionally superior to modern-day diets
- Human genes have not changed significantly since the Paleolithic period
- Archaeologists know what prehistoric diets looked like
- Modern "paleo-friendly" foods are equivalent to historical foods
- Late-occurring chronic diseases affect the natural selection and evolution of humans

- Industrial food and processed food resulted in genetic adaptation
- Human agricultural practices have substantially altered the genetics and nutritional quality of plants meant for consumption
- Modern Paleo Diet (Eaton and Konner)

Paleo Diet

Emphasis on

- Animal products (except dairy)
- Fish
- Eggs
- Vegetables
- Fruit

  - Choose grass-fed or wild-caught meats
  - Choose organic, whole fruit and veggies

Limit

- Processed foods
- Grains
- Some seeds
- Refined oils high in Omega-6s
- Dairy products*
- Nightshades*
- Starchy vegetables*
- Legumes*

Paleo Diet

- “Paleo” diets share characteristics with other healthy diets (emphasis on vegetables, fruit, nuts, and abstinence from sugar and processed foods)
- An improperly implemented “paleo” diet can lead to imbalanced food choices (i.e. excessive meat consumption)
- Strict adherence may eliminate food groups (whole grains, beans, etc.) proven beneficial for cancer prevention and general health.

Possible deficiencies

- **Vitamin D**:
  - Fortified foods (nut milks)
  - Supplements (synthetic or vegan preparations)
  - Fatty fish (mackerel and salmon, as well as tuna and sardines
  - Adequate sun exposure (see module on vitamin D)
- **Calcium**:
  - Leafy greens, nuts, seeds, sea vegetables, canned fish
- **Iodine**:
  - Sea vegetables, iodized salt

Concordance with AICR/ACS Guidelines Partial

	Emphasize				Limit				
	Fruit	Veggies	Whole Grains	Nuts, Seeds, Legumes	Refined Grains	Red and processed meat	Alcohol	Sugary Drinks	Fast food, processed foods*
Paleolithic	●	●	●	◗	●	●	●	●	◗

*Minimally processed meats such as hamburger are not considered "processed foods", however smoked, salted, and cured meats are.

● Meets AICR & ACS recommendations

◗ Partially meets AICR & ACS recommendations

● Does not meet AICR & ACS recommendations

Evidence related to cancer : Paleo Diet

Paleolithic Diet Pattern Score and Risk of Incident, Sporadic Colorectal Adenomas[36]

N = 564 cases, 1202 controls

Type: Case-control study

Comparison: Highest adherence vs. lowest adherence to a Paleolithic-style diet

Outcome: Incidence of Colorectal Adenomas

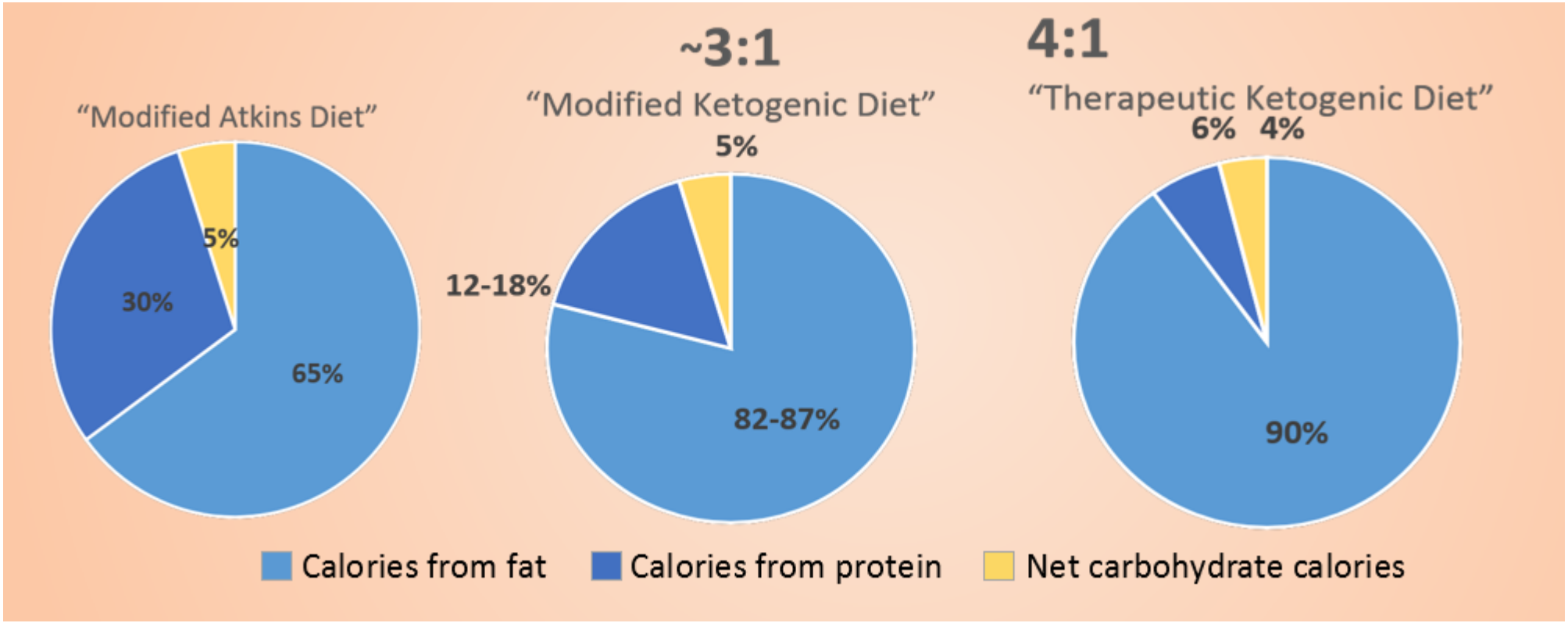
Association of CRC adenoma incidence with highest adherence vs. lowest adherence to a "paleo" dietary pattern

CRC adenoma incidence OR = 0.71
(95% CI: 0.50 - 1.02; $p_{trend} = 0.02$)

Compared to low adherence to a Paleolithic-style dietary pattern, high adherence is non-significantly associated with a **29% decrease** in risk for colorectal cancer adenoma.

Ketogenic Diet

Ketogenic diets are high fat, low protein, very-low carbohydrate diets that force the body to utilize fat (ketones) instead of carbohydrates (glucose) for fuel.



Net Carbohydrates limited to 20-60 gms a day

Ketogenic Diet Rationale for Cancer

Ketogenic diets are thought to fight cancer by:

- Lowering blood glucose, IGF-1, & insulin and raising ketone bodies deprives cancer cells of preferred growth substrates

→

- Ketogenic diets do not lower blood glucose consistently, but do lower insulin and IGF-1
- Some cancer cells are able to metabolize ketones

- Inducing cancer cell-specific oxidative stress which potentiates cancer cells to therapy

→ Conclusions from human and animal studies are inconclusive

- Protein-sparing effect preserves lean body mass in the setting of cancer cachexia or weight loss

→ The conclusions from few animal studies are promising, but eating enough calories on a keto diet may prove problematic

Ketogenic Diet

Emphasize	Limit
Most sources of fat	Most carbohydrate sources
Oils & fats	Grains
Meat from all sources	Sugar
Eggs	Legumes
Low net-carb vegetables (green vegetables, avocado)	Milk
High-fat dairy (cream, cheese)	Fruit
High fat nuts	Starchy vegetables
	High net-carb vegetables

Evidence related to cancer: Research Highlight

KetoLung & KetoPan Phase I Clinical Trials: The University of Iowa Experience

N = **9 Participants**

Participants: patients with locally advanced non-small cell lung cancer (NSCLC; 7 patients) or pancreatic cancer (2 patients) undergoing chemotherapy and radiation

Type: Open label clinical trial

Intervention: 4 to 5 weeks ketogenic diet provided by medical center

Outcome: Safety and tolerability of diet

Measurement of safety, adherence, and oxidative damage in patients with cancer receiving radiation therapy.

No significant conclusions due to high dropout rate (1 pancreatic & 2 NSCLC patients completed study)

Limited results suggest combination of keto diet and radiation might increase oxidative damage in tumors

Non-compliance and **adverse events** may be expected when implementing a processed-foods ketogenic diet in patients with locally advanced cancer.

Systematic review of human and animal studies

Studies: 14 human case reports,
10 cohort studies (human),
27 RCTs (animal)

Outcome: pro- or anti- tumor effects

72% of animal studies suggest an anti-tumor effect

42% of human studies suggest an anti-tumor effect

27% of human studies are inconclusive

4% of human studies suggest a pro-tumor effect

50% of human studies suggest improved QOL

Available evidence is of **low quality** (no control) and likely suffers from **reporting bias**.

Adverse events are associated with extreme versions of the diet (≥90% of kcal from fat or highly processed).

Evidence suggests **possible benefit** and **improbable harm**, but definitive conclusions cannot be drawn.

Evidence related to cancer

Feasibility of a modified Adkins diet in glioma patients during radiation and its effects on radiation sensitization

N = 29 participants
Participants: Men and women diagnosed with grades II-IV astrocytoma
Type: Retrospective study
Intervention: The modified Atkins diet (MAD) (< 20 g carbs daily) with 6 weeks of radiation and temozolomide therapy
Outcome: Adverse events, serum beta-hydoxybutyrate (BHB), and rate of pseudoprogression (PSP) after treatment

Measurement of safety, feasibility, and effects on radiation sensitivity of MAD in adults undergoing treatment for glioma

Safety: No serious adverse events occurred

Feasibility: Ketosis was achieved in all 29 participants (100%) when defined as serum BHB level $\geq$ 0.5 mmol/L, and 23 participants (79%) when defined as serum BHB level $\geq$ 1 mmol/L

Radiation sensitivity: PSP occurred in 16 of 29 patients (55%)

A modified Atkins diet is safe, feasible, and may play a role as a radiation sensitizer in adults undergoing treatment for glioma

Concordance with AICR/ACS Guidelines

	Emphasize				Limit				
	Fruit	Veggies	Whole Grains	Nuts, Seeds, Legumes	Refined Grains	Red and processed meat	Alcohol	Sugary Drinks	Fast food, processed foods
Ketogenic	●	◗	●	●	○	●	●	○	●

○ Meets AICR & ACS recommendations

◗ Partially meets AICR & ACS recommendations

● Does not meet AICR & ACS recommendations

Advanced nutritional counseling is required to implement a prudent ketogenic diet.
Its severe restrictions preclude agreement with any dietary recommendations.

Ketogenic Diet

A ketogenic diet is not a classically “healthy” diet, particularly it is:

Low in fiber

High in saturated fats

- Incur risk for micronutrient deficiency when improperly implemented
- Are high in saturated fat, typically low in fiber, may include processed foods, and exclude entire food groups such as fruits, legumes, and many vegetables which have been shown to be beneficial for cancer prevention and mortality
- Research is not definitive enough to draw conclusions on their effect on cancer
- They are exceedingly difficult to implement without professional dietary counseling

Clinical Considerations

Possible <u>insufficiencies</u> include:

- Vitamin D
- Calcium
- Electrolytes (K, Na, Mg

Adverse Events

Ketosis increases water excretion, so it is important to drink more water to stay hydrated.

Research is mixed,but suggests that extended ketogenic regimens may increase risk for kidney stones.

<u>Recommendations</u>

- Consider a multivitamin with calcium and vitamin D
- Advise on “keto”-friendly sources of:
- **Vitamin D**:
  - Fortified foods (dairy products, nut milks) and supplements
  - Fatty fish (mackerel and salmon, as well as tuna and sardines)
  - Adequate sun exposure (see module on vitamin D)
- **Calcium**:
  - Leafy greens, nuts, seeds, sea vegetables, canned fish
- **Electrolytes**:
  - Leafy greens, salmon, mushrooms, nuts, avocado, pickled and fermented vegetables, sea salt, supplements

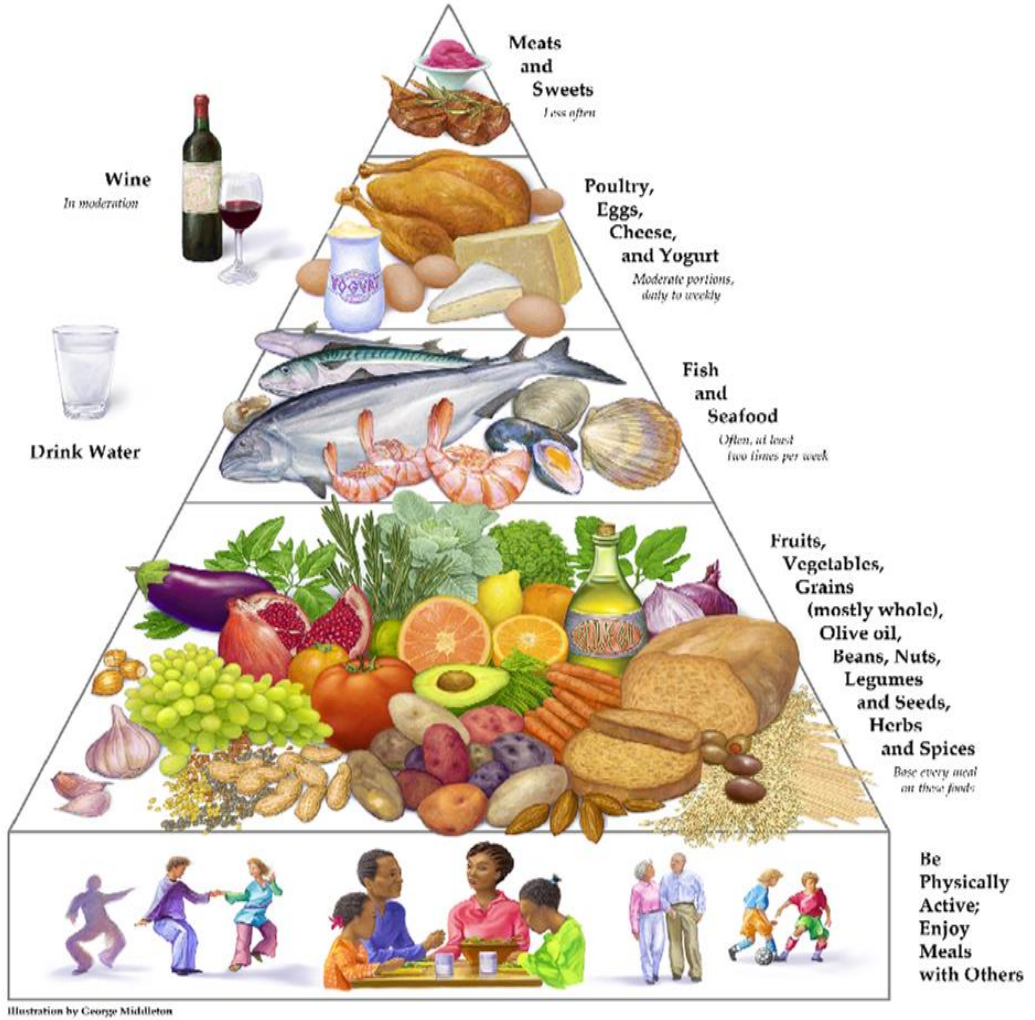
Mediterranean Diet

Based on the traditional diet and lifestyle of the Mediterranean region

Includes whole vegetables, fruit, and whole grain products at every meal

Noted for

- Liberal use of olive oil
- Regular and moderate consumption of red wine
- A physical activity and social component



Mediterranean Diet Food Pyramid. OldWayPT.org

Mediterranean Diet

Emphasize

Whole grains

Vegetables

Fruit

Extra virgin olive oil

Fish

Nuts, legumes, and seeds

- Choose diverse, colorful food options
- Eat with friends and family often

Limit

Refined grains

Added sugars

Processed foods

Moderate

Meat (except for fish)

Dairy products

Eggs

Concordance with AICR/ACS Guidelines

	Emphasize				Limit				
	Fruit	Veggies	Whole Grains	Nuts, Seeds, Legumes	Refined Grains	Red and processed meat	Alcohol	Sugary Drinks	Fast food, processed foods
Mediterranean	●	●	●	●	●	●	●	●	●

● Meets AICR & ACS recommendations

◐ Partially meets AICR & ACS recommendations

● Does not meet AICR & ACS recommendations

Evidence related to Mediterranean diet & cancer incidence

Meta-analysis[46]

N = 2,130,753 subjects

Type: 2 RCTs, 30 case-control studies, and 51 prospective cohort studies

Outcome: specific-cancer incidence

*Data is reported preferentially from multiple types of studies, then RCTs, then case-control studies, and lastly from cohort studies

Association of incidence with highest adherence vs. lowest adherence to a Mediterranean dietary pattern

	Incidence Hazard Ratio*:
Colorectal:	**0.82** (95% CI: 0.75 - 0.88)
Breast:	**0.92** (0.89 - 0.96)
Prostate:	**0.90** (0.64 - 1.26)
Gastric:	**0.65** (0.53 - 0.79)
Head & neck:	**0.46** (0.32 - 0.67)
Respiratory:	**0.71** (0.49 - 1.02)

People with the highest adherence to the Mediterranean diet may have a lower risk of cancer incidence.

Evidence related to Mediterranean diet & cancer mortality

Meta-analysis[46]

N = 2,130,753 subjects

Type: 2 RCTs, 30 case-control studies, and 51 prospective cohort studies

Outcome: Cancer mortality, specific-cancer mortality

Association of mortality with highest adherence vs. lowest adherence to a Mediterranean dietary pattern

Cancer Mortality RR = 0.86
(95% CI: 0.81 - 0.91)

Cancer Mortality for cancer survivors
RR = 0.95 (95% CI: 0.82 - 1.12)

People with the highest adherence to the Mediterranean diet may have a 14% lower risk of cancer mortality.

Clinical considerations[47]

The greatest risk with implementing the Mediterranean diet is the possibility for misinterpretation.

Common misconceptions:

- **It's a rigid diet plan**
- **It's a low-fat / high-fat diet**
- **It's vegetarian**
- **Pizza is ok!**
- **Drinking is ok!**

However, the "Med" diet is actually:

- An accommodating dietary pattern.
- Moderate in all macronutrients.
- Plant-based but still includes meat
- Limiting in junk food
- Moderate in polyphenol-rich alcohol, but if you don't drink you don't have to start now!

"Inspiring good health through good food traditions"

OLDWAYS

With the input of public health entities like the WHO and Harvard School of Public Health, OldWaysPT developed a food pyramid, diet plan, recipes, and other resources on the Mediterranean diet.

Bottom line

The Mediterranean diet is in complete harmony with AICR/WCRF & ACS guidelines

Significant decrease in incidence & mortality

Additional benefits may include positive changes in physical activity, weight management, stress management, and chronic disease burden.

Diets compared

Meets AICR & ACS recommendations | Partially meets AICR & ACS recommendations | Does not meet AICR & ACS recommendations

Top 3 Diets	Emphasize				Limit				
	Fruit	Veggies	Whole Grains	Nuts, Seeds, Legumes	Refined Grains	Red and processed meat	Alcohol	Sugary Drinks	Fast food, processed foods
Mediterranean	●	●	●	●	●	●	●	●	●
Macrobiotic	◐	●	●	●	●	●	●	●	●
Alkaline	●	●	●	◐	●	●	●	●	●

Diets compared

Meets AICR & ACS recommendations | Partially meets AICR & ACS recommendations | Does not meet AICR & ACS recommendations

Bottom 3 Diets	Emphasize				Limit				
	Fruit	Veggies	Whole Grains	Nuts, Seeds, Legumes	Refined Grains	Red and processed meat	Alcohol	Sugary Drinks	Fast food, processed foods
Ketogenic	◐	◐	●	◐	●	●	●	●	●
Paleolithic	●	●	●	◐	●	◐	●	●	●
Vegan	●	●	●	●	●	●	●	●	●

Dietary Fiber

The National Academy of Medicine defines fiber as: 1) dietary fibers (nondigestible carbohydrates and lignans) that occur naturally in plants, and 2) functional fibers that are extracted from plants or synthetically made and are nondigestible with a beneficial health effect in humans.

- Soluble
- Insoluble

- Fermentable
- Non fermentable

- Latest AICR report shows that each 10-grams increase in dietary fiber is linked with a 7 percent lower risk of colorectal cancer. May also lower breast cancer risk.
- May help lower cholesterol, manage blood sugar and contributes to satiety and therefore may help with weight loss
- Helps with constipation
- Studies shows improved response to Immunotherapy

Clinical considerations[48]

For the patient-provider relationship to thrive, consider that:

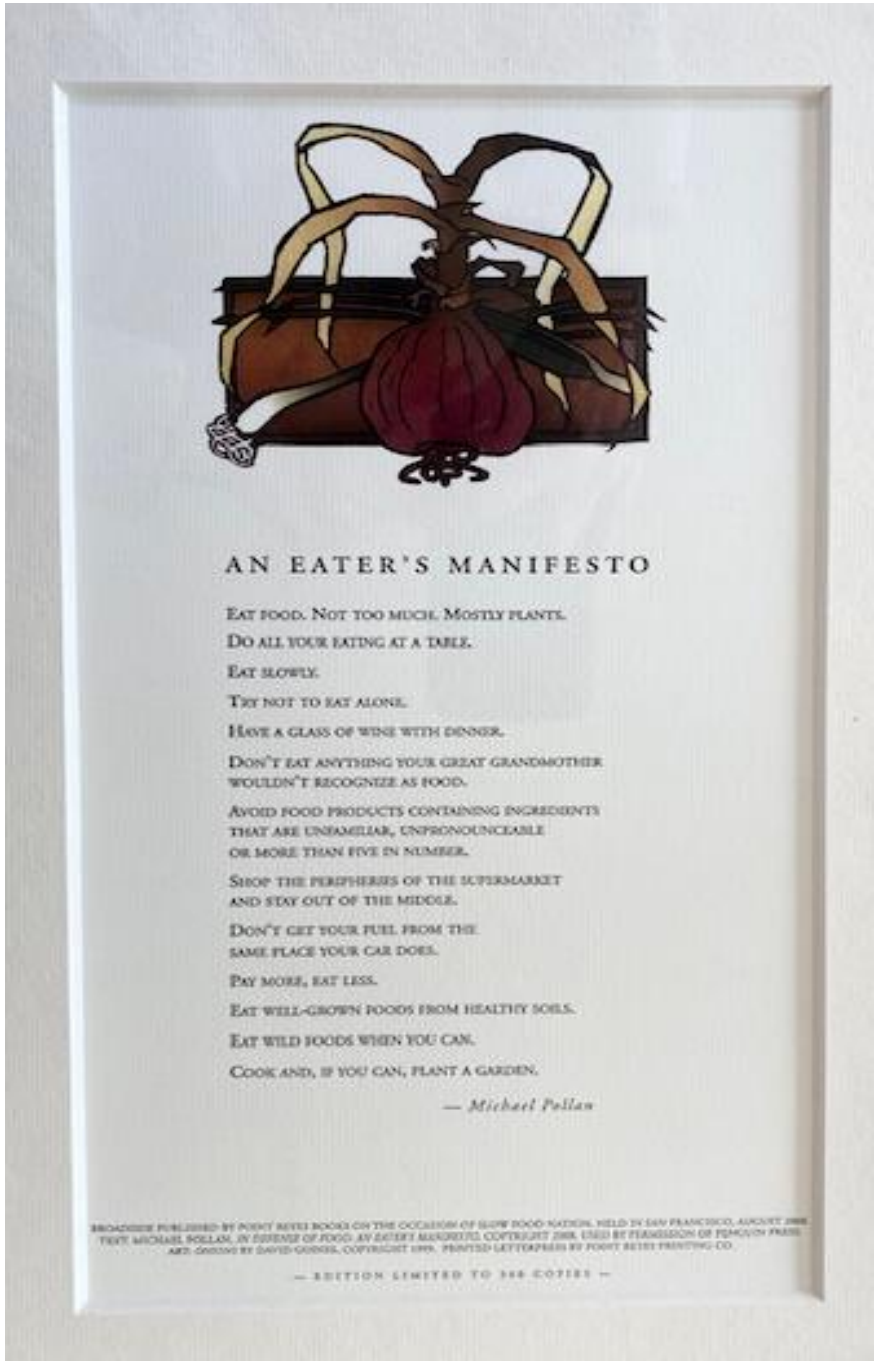
- Some diets (especially ketogenic, paleo, and alkaline), emphasize certain foods and limit others to a potentially unhealthy extent
- Many diets are chosen as much for their philosophical, cultural or ethical underpinnings as for any scientific evidence of benefit
- The choice of diet may not matter so much as the patient's desire for control and autonomy in their life
- Negative or contradictory statements about a patient's diet can lead to defensiveness and lack of trust

Clinical considerations[48]

In the face of a patient who wants to stick to their diet, consider these strategies to build trust and encourage evidence-based dietary change:

- Emphasize positive aspects and provide helpful resources of the diet that align with ACS and AICR/WCRF dietary guidelines
- Suggest foods that are congruent with patients' dietary strategies to address any nutrient concerns
- Remind patients that a strict diet may interfere with their quality of life and a more adaptable dietary pattern may yield similar long-term benefits.
- Refer patients to a registered dietitian as needed to help guide their choices.
- <u>The best diet is one that your patient can stick to!</u>

Eat Food
Not Too Much
Mostly Plants



AN EATER'S MANIFESTO

EAT FOOD. NOT TOO MUCH. MOSTLY PLANTS.

DO ALL YOUR EATING AT A TABLE.

EAT SLOWLY.

TRY NOT TO EAT ALONE.

HAVE A GLASS OF WINE WITH DINNER.

DON'T EAT ANYTHING YOUR GREAT GRANDMOTHER WOULDN'T RECOGNIZE AS FOOD.

AVOID FOOD PRODUCTS CONTAINING INGREDIENTS THAT ARE UNFAMILIAR, UNPRONOUNCEABLE OR MORE THAN FIVE IN NUMBER.

SHOP THE PERIPHERIES OF THE SUPERMARKET AND STAY OUT OF THE MIDDLE.

DON'T GET YOUR FUEL FROM THE SAME PLACE YOUR CAR DOES.

PAY MORE, EAT LESS.

EAT WELL-GROWN FOODS FROM HEALTHY SOILS.

EAT WILD FOODS WHEN YOU CAN.

COOK AND, IF YOU CAN, PLANT A GARDEN.

— *Michael Pollan*

BROADSIDE PUBLISHED BY POINT REYES BOOKS ON THE OCCASION OF SLOW FOOD NATION, HELD IN SAN FRANCISCO, AUGUST 2008.
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Key Resources

- AICR/WCRF dietary guidelines
- ACS dietary guidelines
- NCI Eating Hints
- NCCN guidelines for cancer treatment
- FDA Dietary Guidelines for Americans
- AHA recommendations for portion sizes
- Harvard School of Public Health's Healthy Eating Plate and Healthy Eating Pyramid
- Charlie Foundation – nonprofit focusing on providing ketogenic diet resources
- Old Ways – nonprofit dedicated to fostering health through traditional foodways, especially useful for Mediterranean diet resources
- Division of Cancer Prevention and Control, Centers for Disease Control and Prevention
- Cancer.net
- NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Survivorship

THANK YOU

Types of Edible Soy Products[3,4]

Soy Foods

Unfermented

-Soybean/Edamame

-Tofu

-Soy Milk

-Soy Flour

-Soy Oil

Fermented

-Miso

-Natto

-Tempeh

-Soy Sauce

Click Here!
Learn about kinds of fermented nd unfermented soy foods

Soy Supplements

-Soy protein isolate

-Soy isoflavone extracts with combined or individual isoflavones

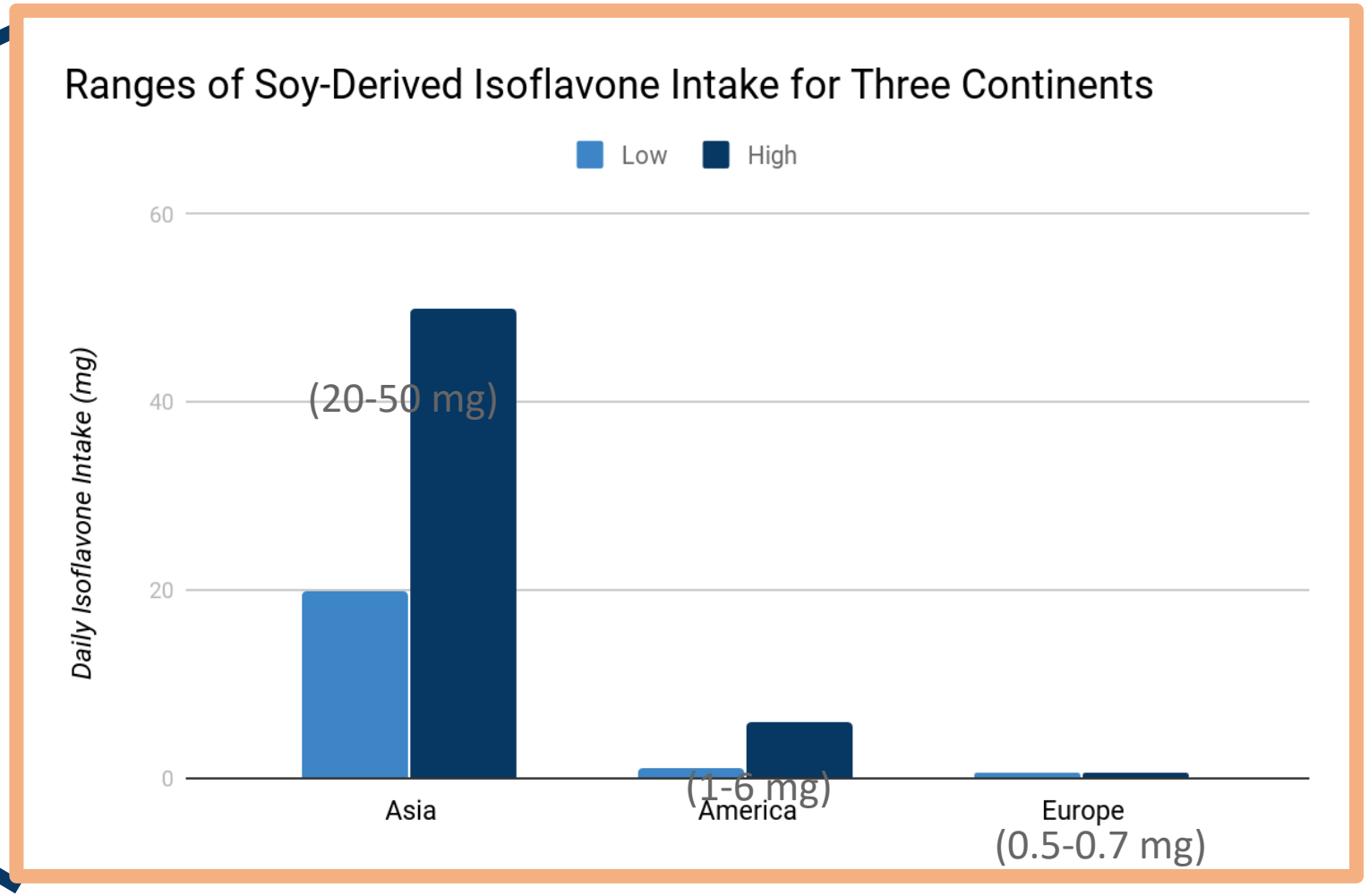
-Soy lecithin granules

-Soy-based infant formula

Purported Physiological Influences of Soy Intake[5,6]

- Carcinogenesis Prevention
- Heart Disease Prevention
- Cholesterol Reduction
- Menopause Treatment
- Bone Loss Prevention

Data indicate that soy-derived isoflavone consumption and overall soy product consumption is highest in asian countries[4]



Nutritional Composition of Soy[6,7]

Macronutrient Distribution		
CARBS	FAT	PROTEIN
~28%	~25%	~47%
Caloric Distribution		
~32%	~38%	~30%
%Daily Value		
~7%	~18%	~44%
-Low glycemic index -Good amount of soluble and insoluble fiber	-Primarily essential polyunsaturated and monounsaturated fatty acids. -Some plant-based saturated fatty acids.	-Contains all 9 essential amino acids, and, thus, is a **complete protein.**

Good Source of:		Also Contains:	
Micronutrient	% Daily Value	Micronutrient	%Daily Value
Vitamin C	51%	Riboflavin	16%
Folate	50%	Niacin	11%
Manganese	45%	Zinc	11%
Thiamin	31%	Copper	11%
Iron	35%	Vitamin A	6%
Potassium	28%	Vitamin B6	5%
Phosphorus	28%	Selenium	4%
Magnesium	27%	Vitamin B5	2%
Calcium	26%	Sodium	1%

Amino Acids in Soy[6,7]

Essential	Conditionally Essential	Nonessential
Histidine	Arginine	Alanine
Isoleucine	Cysteine	Aspartic Acid
Leucine	Glutamine*	Asparagine*
Lysine	Glycine	Glutamic Acid
Methionine	Proline	Serine
Phenylalanine	Tyrosine	
Threonine		
Tryptophan		
Valine		

⇒ Soy foods are excellent sources of plant-based protein for this reason, as well as a good source in many micronutrients. They, therefore, serve as an invaluable asset to one's diet.

Types of Bioactive Compounds in Soy[4,8,9]

- Isoflavones
- Phenolic Acids
- Tocopherols
- Amino Acids
- Peptides

Isoflavones are the most prominent type of bioactive compound in soy

Disease Prevention:

Protect DNA against oxidation

Deactivate carcinogens

Inhibit carcinogenic mutations and oncogene expression

Detoxify xenobiotics

Highly Antioxidative

Scavenge free radicals

Suppress lipid peroxidation

Prevent metal chelation and free radical formation

Phytoestrogens:

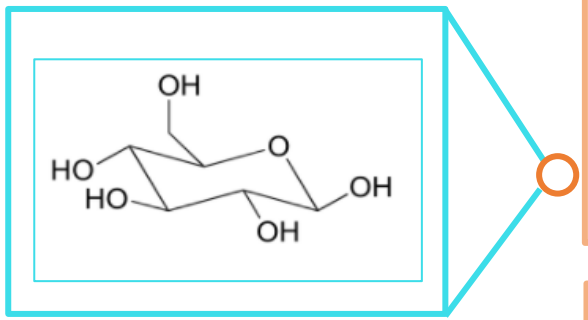
Estrogen-like structures

Hormonal influence misunderstood

Soy's Isoflavones are Phytoestrogens[10,11,12]

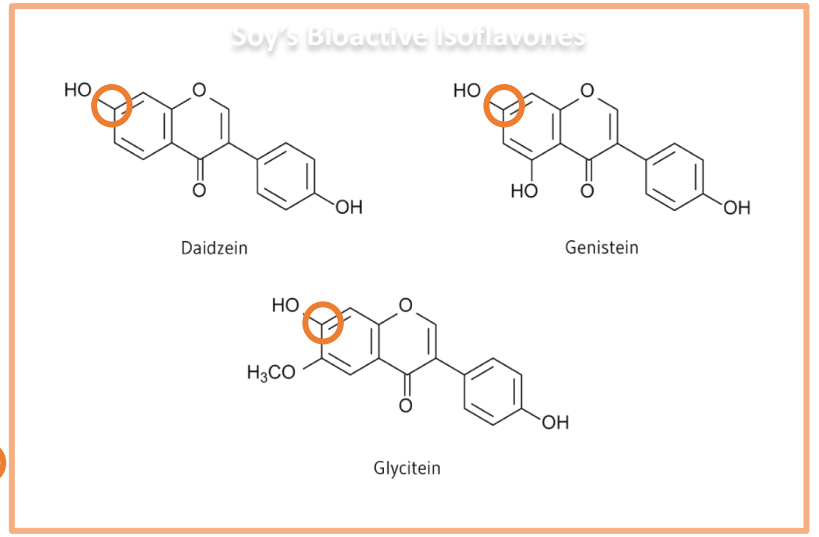
- **Biologically Inactive: β-glycosides**
  *Contain glucose on 7' carbon
  Derived from unfermented soy products
  (soybean/edamame, tofu, soy milk, soy flour soy oil)
  - Genistin
  - Daidzin
  - Glycitin

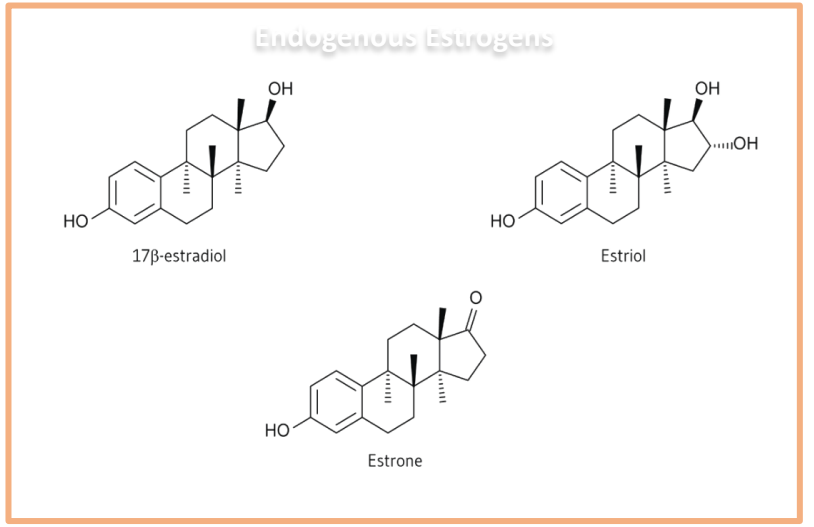
- **Biologically Active: aglycones**
  Derived from fermented soy products
  (miso, natto, tempeh, soy sauce)
  - Genistein (50%)
  - Daidzein (40%)
  - Glycitein (10%)



Most similar to hormone 17β-estradiol

Most prominent isoflavone in soy





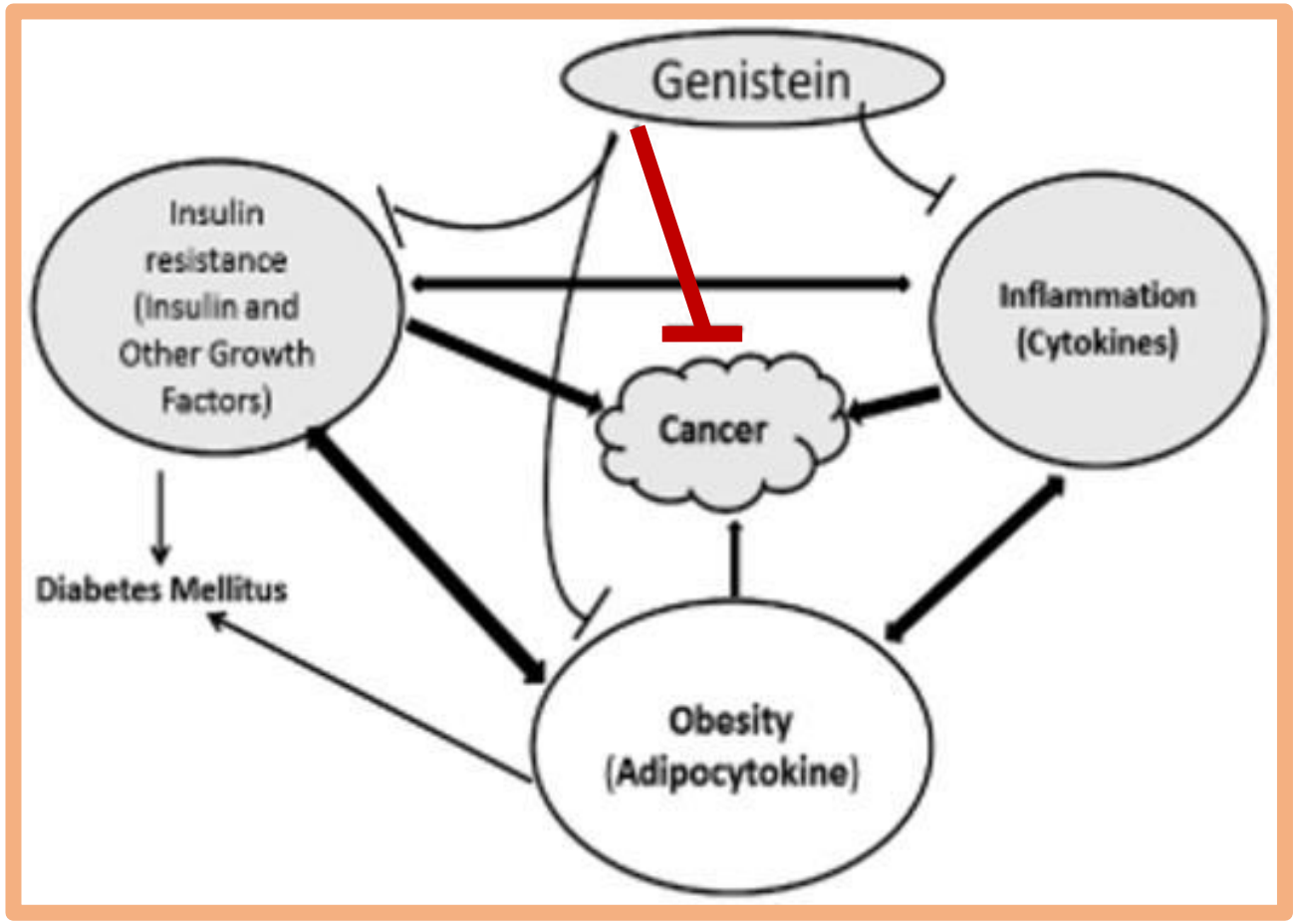
Soy Isoflavone Content in Common Soy Foods[13]

Food Product	Common Serving Size	Total Isoflavones (mg)	Genistein (mg)	Daidzein (mg)
Soy flour, full fat, roasted	1 cup (85 g)	140.28	72.35	76.04
Soy protein isolate	1 ounce (28 g)	25.50	16.04	8.63
Tempeh	3 ounces (84 g)	50.91	30.37	19.03
Miso paste	1 tablespoon (18 g)	7.46	4.18	2.96
Soybeans, raw sprouted	½ cup (35 g)	12.04	6.57	4.50
Soybeans, cooked	1 cup (94 g)	16.84	6.64	6.97
Soy yogurt	8 oz. container (224 g)	74.30	37.16	30.84
Tofu, soft, silken	1 slice (84 g)	24.56	17.35	7.22
Tofu, firm, cooked	1 slice (84 g)	18.52	9.10	8.62
Soy milk	1 cup (243 g)	26.07	14.75	11.76
Vegetarian burger	1 patty (64 g)	4.09	3.21	1.68
Soy cheese, cheddar	¼ cup (28 g)	1.92	0.59	0.51

*Values are expressed in mg per **common serving size** of fresh weight of edible portion of food

Genistein and Cancer[17]

Genistein is known to reduce risk of developing cancer, as well as other chronic diseases.



The Effects of Soy Intake on Cancer Takeaway

According to overall data from observational studies and randomized clinical controlled trials investigating the influence of soy intake with different types of cancers, frequent ***soy food*** *intake appears to provide protection against cancer and remediation of carcinogenesis. Whereas concentrated* ***soy supplement*** *intake may also provide protection and remediation of carcinogenesis, but may also induce proliferation of cancer cells under certain circumstances.* ***Research is less clear about the effects of soy supplement intake and carcinogenesis.***

Recommendations for Different Soy Products

SOY PRODUCTS		SUBTYPES	HEALTH EFFECTS	RECOMMENDATIONS	CONTRAINDICATIONS	ADVERSE EFFECTS
Food Advisable	**Unfermented**	**Soybean** **Tofu** **Soy Milk** **Soy Flour** **Soy Oil**	• Provides beneficial nutrients and helps a person fulfill nutrient adequacy. • Tends to protect against carcinogenesis, particularly when consumed throughout the lifespan.	• Consume regularly as a part of a diet that is also balanced with fruits, vegetables, whole grains, nuts, seeds, lean proteins, healthy fats, and few refined, processed foods. • Choose to consume more whole soy products instead of processed foods with soy ingredients in them. • Lifelong, regular soy food consumption is encouraged and may provide the strongest	• Allergy	• Soy foods contain anti-nutrients such as oxalates and phytates, which inhibit iron absorption. • Bloating
	Fermented	**Miso** **Natto** **Tempeh** **Soy Sauce**				
Supplement Not advisable		**Protein Powder** **Isoflavone Extract** **Soy Lecithin Granules**	• Research is unclear regarding the effects of soy isoflavone supplement intake and cancer. • May protect or possibly promote carcinogenesis.	• Denote that there are conflicting results regarding the effects of soy supplement intake on cancer prevention and increased cancer risk. • Use with caution: soy supplements are not regulated by the FDA.	• Allergy • Could contain contamination due to lack of FDA regulation	• Potential cell proliferation • Ingestion of potentially harmful contaminants

Most clinical research investigating the effects of soy and breast cancer has been conducted in ***pre-diagnostic populations****, and, thus, focus primarily on* ***prevention*** *rather than* ***remediation****.*

Breast Cancer: Observational Data

Pre-diagnosis: Childhood and Adolescence:

- Risk of cancer development appears to be significantly reduced if soy foods are consumed throughout the lifespan, particularly during early childhood and adolescence.

Pre-diagnosis: Pre and Postmenopausal

- The most recent meta-analysis suggests that **soy isoflavone consumption has a protective effect against breast cancer for both pre and postmenopausal asian women** and only marginal protection against breast cancer for pre and postmenopausal western women.

Post-diagnosis: Different Breast Cancer Types

- Soy intake appears to be associated with better survival in breast cancer patients.
- There were strong associations between soy food intake and reduced mortality in ER-positive, ER-negative, premenopausal, postmenopausal women with breast cancer.
- There were strong associations between soy food intake and reduced recurrence of cancer in ER-negative, ER-positive, PR-positive and postmenopausal, women with breast cancer

Soy and Breast Cancer: Bottom Line[31]

Observational Data: (Pre Diagnosis) Soy intake is inversely associated with the odds of getting breast cancer in pre and postmenopausal asian women, whereas the odds of getting breast cancer are only marginally reduced in western women.
(Postdiagnosis) Soy intake significantly reduces mortality risk in ER+ breast cancer women, ER- breast cancer, premenopausal and postmenopausal women with breast cancer.
Soy intake appears to significantly reduce breast cancer recurrence in women with ER- breast cancer, women with ER+/PR+ breast cancer, and postmenopausal women with breast cancer.

Clinical Data: Many clinical trials investigating the effects of soy supplement intake on breast cancer are very mixed, though studies soy food intake appears to reduce breast cancer risk.

Proposed Mechanism: Soy-derived isoflavones such as genistein appear to prevent breast cancer via a variety of pathways.

There is urgent need for larger randomized clinical trials with soy food intake to take place in order clearly depict the impact of soy food and soy supplement intake on breast cancer.

The Effects of Soy Intake on Cancer Takeaway

According to overall data from observational studies and randomized clinical controlled trials investigating the influence of soy intake with different types of cancers, frequent ***soy food*** *intake appears to provide protection against cancer and remediation of carcinogenesis. Whereas concentrated* ***soy supplement*** *intake may also provide protection and remediation of carcinogenesis, but may also induce proliferation of cancer cells under certain circumstances.* ***Research is less clear about the effects of soy supplement intake and carcinogenesis.***

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The Overall Influence of Soy on Cancer

PROTECTION: ✓ REMEDIATION: ✓ PROLIFERATION:?

Isoflavones may have different types of influences on cancer depending on how they are consumed

Soy Food: Isoflavone-containing soy foods appear to provide sufficient chemopreventive effects, particularly when consumed throughout the lifespan.

Soy Supplements: Concentrated soy isoflavone extract and protein have shown to be effective in vitro and animal models, but often fail to provide chemopreventive or therapeutic benefits when taken by the patients in clinical trials.