Calorie Restriction & Cancer: Could Less be More?

with Greta Macaire, MA, RD, CSO
Overview

• Background
• Types of Calorie Restricting Diets
• Research findings on Calorie Restriction for Longevity, Health and Cancer
• Caveats and Concerns with Calorie Restriction
• Healthy Eating Suggestions
30-35% of cancers in the U.S. are related to obesity, poor diet and inadequate physical activity.
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**HOW COULD OBESITY LEAD TO CANCER?**

Research has identified three main ways:

1. **Oestrogen**
   - After the menopause, oestrogen made by fat cells can make cells multiply faster in the breasts and womb, increasing the risk of cancer.

2. **Insulin and Growth Factors**
   - Excess fat can cause levels of insulin and other growth factors to rise, which can also tell cells to divide more rapidly.

3. **Inflammation**
   - Cells in fat called macrophages release chemicals called cytokines, encouraging cells to divide (including cancer cells).

There are other theories too, but these are the main ideas being studied. More research is needed to understand this in more detail.
Food, nutrition, obesity, physical activity, and cellular processes linked to cancer

- DNA repair
- Proliferation
- Hormonal regulation
- Differentiation
- Inflammation and immunity
- Apoptosis
- Cell cycle
- Carcinogen metabolism

Food, nutrition, obesity, and physical activity
AICR Guidelines for Cancer Prevention

Choose mostly plant foods, limit red meat and avoid processed meat

Be physically active every day in any way for 30 minutes or more

Aim to be a healthy weight throughout life

And always remember - do not smoke or chew tobacco
AICR’s Guidelines for Cancer Survivors

1. Be as lean as possible without becoming underweight.
2. Be physically active for at least 30 minutes every day.
3. Avoid sugary drinks, and limit consumption of energy-dense foods (particularly processed foods high in added sugar, low in fiber or high in fat).
4. Eat more of a variety of vegetables, fruits, whole grains and legumes such as beans.
5. Limit consumption of red meats (such as beef, pork and lamb) and avoid processed meats.
6. If consumed at all, limit alcoholic drinks to two for men and one for women a day.
7. Limit consumption of salty foods and foods processed with salt (sodium).
8. Do not rely on supplements to protect against cancer.
Background on Fasting/Calorie Restriction

• Fasting is one of the oldest therapies in medicine.

• The Greek physician Hippocrates, known as the father of medicine, believed that fasting enabled the body to heal itself.

• Fasting, in various forms, is a part of most spiritual traditions in the world.

"I fast for greater physical and mental efficiency."

-Plato
• World War I - Denmark (1917)
  – Danish government enforced a 2 year food restriction on men and women. The diet was well planned and nutrient dense and was linked to a 34% lower death rates.

• World War II – Oslo, Norway (1941-1945)
  – A forced 20% calorie restriction for 4 years without significant changes in diet quality occurred. Mortality rates dropped by 30% compared to pre-war levels. The women experienced reduced breast cancer risk later in life.

*Ageing Res Rev. 2016 Aug 17*
Blue Zones – Longevity Hotspots

Genetics = ~20%
The Centenarians of Okinawa

Okinawa, one of the longest-lived and healthiest populations in the world, practice a principle they call hara hachi bu: Eat until you are 80 percent full.

— Michael Pollan —
The Traditional Okinawan Diet

- Plant based, ~17% fewer calories than adults on Japanese mainland and 40% less than adults in the U.S.

Ageing Res Rev. 2016 Aug 17
Calorie Restriction Society - CRONies

- Group that voluntarily restricts calorie intake by ~30% for an average of 15 years with the overall goal of prolonging their lifespan.

- Practice “Calorie Restriction with Optimal Nutrition” (CRON) → Diet meets all recommendations for essential nutrient requirements, is high in vegetable fiber and phytonutrients and has a low glycemic load.

- CRONies have lower metabolic and hormonal risk factors linked to the development of type 2 diabetes, heart disease, stroke, cancer and dementia.

Calorie Restriction
Improves Health Span in Lab Animals

Clive McKay, 1935

http://lpi.oregonstate.edu/sites/lpi.oregonstate.edu/files/images/doh2015.ppsx
Calorie Restriction Improves Health Span in Lab Animals

- Increases:
  - Memory/learning
  - Muscle mass
  - Mitochondrial function
  - Insulin sensitivity

- Decreases:
  - Cancer
  - Renal Disease
  - Autoimmune Disease
  - Alzheimer’s Disease
  - Atherosclerosis
  - Sarcopenia

http://lpi.oregonstate.edu/sites/lpi.oregonstate.edu/files/images/doh2015.ppsx
Calorie Restriction Lowers Cancer Risk

<table>
<thead>
<tr>
<th>Types of Fasting/Calorie Restricting Regimens</th>
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<tbody>
<tr>
<td><strong>Calorie Restriction</strong></td>
</tr>
<tr>
<td>20-40% reduction in calorie intake over a long period of time.</td>
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<tr>
<td><strong>Complete Alternate Day Fasting</strong></td>
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<tr>
<td>Alternating fasting days (no calories consumed) with eating days (calories consumed freely).</td>
</tr>
<tr>
<td><strong>Modified Fasting Regimens</strong></td>
</tr>
<tr>
<td>20-25% of calorie needs consumed on scheduled days and calories consumed freely on other days. Basis for the popular 5:2 Diet and the Periodic Fasting Mimicking Diet.</td>
</tr>
<tr>
<td><strong>Time-Restricted Feeding</strong></td>
</tr>
<tr>
<td>Consume calories freely within a defined window of time in the day with fasting the other 12 – 21 hours per day.</td>
</tr>
<tr>
<td><strong>Religious Fasting</strong></td>
</tr>
<tr>
<td>A wide variety of fasting regimens are undertaken for religious or spiritual purposes.</td>
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</tbody>
</table>
CALERIE Study: (Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy)

• 2 year study including 220 healthy, non-obese adults.

• Goal was 25% calorie restriction vs usual intake:
  – Average 12% calorie restriction was achieved.
  – Calorie restriction = ~10% weight loss and improvements in biomarkers linked with cardio metabolic disease.
  – Caloric restriction slowed biological aging independent of the effects of weight loss.

Calorie Restriction and Change in Biological Age

Randomized to
Ad Libitum
Caloric Restriction

Change in Biological Age (years)

Baseline  12-months  24-months
CALERIE Assessment

Calorie Restriction is Difficult!

Good
- Less Disease Risk
- Possible Longer life

Bad
- Spartan Lifestyle
- Social/Behavioral Modification
- Less Ability to Fight Infection

Are there ways to keep the “Good” & limit the “Bad” aspects of caloric restriction?

http://lpi.oregonstate.edu/sites/lpi.oregonstate.edu/files/images/doh2015.ppsx
Modified Fasting Regimens - 5:2 Diet

Day 1: Normal TDEE
Day 2: Normal TDEE
Day 3: Fasting
   - 500 (female)
   - 600 (male)
Day 4: Normal TDEE
Day 5: Fasting
   - 500 (female)
   - 600 (male)
Day 6: Normal TDEE
Day 7: Normal TDEE

Calories (per day)
TDEE = total daily energy expenditure

Source: Br J Diabetes Vasc Dis (c) 2013 Sage Publications, Inc.
Modified Fasting Regimens - 5:2 Diet
What does a 500 calorie day look like?

- **Breakfast:**
  - 1 egg + 2 cups raw spinach = 94 kcals

- **Lunch:**
  - 1 ½ cup vegetable bean soup = 190 kcals

- **Snack:**
  - ½ cup blueberries + 5 almonds = 77 kcals

- **Dinner:**
  - 1 cup cauliflower rice with herbs, 3 oz baked salmon with lemon = 150 kcals

- **Fluids:**
  - Water, black coffee/tea, herbal tea
Modified Fasting Regimens - Periodic Fasting Mimicking Diet

Valter Longo Ph.D.
USC Longevity Institute
Periodic Fasting Mimicking Diet

• Diet formulated to mimic effects of periods of fasting – tested in 100 healthy adults.

• 750-1090 calories per day for 5 days (34-54% of normal intake). After 5 days, subjects ate their normal diet for 25 days. Eating cycle was repeated 3 times.

• Diet is plant based, 9-10% protein; 34-47% carbohydrates; 44-56% fat, supplemented with vitamins/minerals/omega-3 fatty acids

Time Restricted Feeding & Cancer
Prolonged Nightly Fasting & Breast Cancer

• In women with early stage breast cancer, fasting for ≥13 hours at night, i.e. 5:00 pm – 7:30 am, was associated with a 36% lower risk of breast cancer recurrence, longer sleep duration and healthier blood sugar levels.

  *JAMA Oncol.* 2016; 2 (8): 1049 - 1055

• Habitually eating after 10 pm was associated with a 50% higher risk of breast cancer among Chinese women in Hong Kong.

Calorie Restriction during Cancer Treatment
Cell/mice studies

- Reduced normal cell toxicity
- Reduced side effects
  - Akt/mTOR, RAS/MAPK
  - Autophagy
  - Growth
  - Senescence

CR/Fasting/FMD

- Increased sensitivity to anti-mitotic agents

- Reduced substrate availability
- Reduced growth factors
- Reduced Inflammation
  - Leptin, Adiponectin
  - VEGF, PAI-1
  - IL-6, TNFα, MCP1
  - Insulin
  - Glucose
  - Ketones
  - IGF-1

Circulation

- Tumor Microenvironment
  - Desmoplasia
  - Inflammation
  - Tregs
  - Cytotoxic T cells

Increased drug delivery
Enhanced tumor clearance

BMC Medicine. 2017; 15:106
Average self-reported severity of symptoms in patients that have received chemotherapy with or without fasting.

10 patients, range of cancers and treatment regimens, 48-140 hour pre-chemo and 5-56 hour post-chemo water only fasting regimens.

Cell Cycle. 2010 Nov 15; 9(22): 4474–4476
Calorie Restriction during Cancer Treatment – Human Studies

- Based on positive results from cell/mice studies, several human studies are underway:
  - [www.clinicaltrials.gov](http://www.clinicaltrials.gov)
  - Different regimens in combination with chemotherapy or radiotherapy are being tested.
  - Calorie restriction mimicking drugs and diets are also being studied.

- At this time, evidence to recommend any type of fasting regimen during cancer treatment in humans is lacking. Until we know more about the safety and effects in humans, fasting while on treatment is not recommended.
Caveats & Concerns

• Unintended weight loss during cancer treatment is linked with poorer outcomes.
  – Fasting accelerates loss of muscle and cancer related wasting, especially in older adults.
  – 30-40% of people with cancer are already malnourished at diagnosis.

• Chronic calorie restriction decreases immune function and impairs wound healing.

• It is difficult to meet vitamin and mineral requirements on a calorie restricted diet.

• Fasting for people with diabetes or on certain medications may be contraindicated.
# General Guide for Calorie Needs

<table>
<thead>
<tr>
<th>Condition</th>
<th>Energy Needs per Pound</th>
<th>Example: 150 lb.</th>
<th>Example Energy Needs per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactive</td>
<td>12 calories</td>
<td>X 150 lbs.</td>
<td>1800 calories per day</td>
</tr>
<tr>
<td>Moderately active</td>
<td>15 calories</td>
<td>X 150 lbs.</td>
<td>2250 calories per day</td>
</tr>
<tr>
<td>Physical stress (surgery or chemoradiation treatment)</td>
<td>16 calories</td>
<td>X 150 lbs.</td>
<td>2400 calories per day</td>
</tr>
</tbody>
</table>

1 lb = 3500 calories, add/subtract 500 calories per day to gain/lose 1 lb. per week
<table>
<thead>
<tr>
<th>Condition</th>
<th>Protein Needs per Pound</th>
<th>Example: 150 lb.</th>
<th>Example Protein Needs per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal maintenance</td>
<td>0.4-0.5 gm</td>
<td>X 150 lbs.</td>
<td>60-75 gm per day</td>
</tr>
<tr>
<td>During cancer treatment – chemoradiation/surgery</td>
<td>0.6-0.7 gm*</td>
<td>X 150 lbs.</td>
<td>90-105 gm per day</td>
</tr>
<tr>
<td>Individual needs vary and may be lower with certain medical conditions such as kidney or liver disease.</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Dietary protein is best used by the body when spread between meals instead of eaten mostly at one meal.
NOT ALL CALORIES ARE CREATED EQUAL
Choose Mostly Plant Foods

Higher amounts of vitamins, minerals, fiber, prebiotics, and phytonutrients.

Less calories, animal fats and protein, processed foods, and added sugars.
The New American Plate

- \( \frac{2}{3} \) or more vegetables, fruits, whole grains and beans
- \( \frac{1}{3} \) or less animal protein

www.aicr.org
Replace Energy Dense with Nutrient Dense Foods

350 kcal/100gm  0% vitamin A

OR

76 kcal/100gm  284% vitamin A

250 kcal/100gm  2% vitamin C

OR

26 kcal/100gm  98% vitamin C
200 kcal/1 cup
0% vitamin C

25 kcal/1 cup
70% vitamin C

0 gm fiber  OR  8 gm fiber
**LEGUMES**

- 1/2 cup split peas: 8.1g
- 1/2 cup lentils: 7.8g
- 1/2 cup black beans: 7.7g
- 1/2 cup chickpeas: 6.2g

**VEGETABLES**

- 1 cup sweet potatoes: 6.6g
- 1 cup broccoli: 5.1g
- 1 cup carrots: 4.7g
- 1 cup Brussels sprouts: 4.1g

**FRUIT**

- 1 cup raspberries: 8 g
- 1 cup blackberries: 7.6 g
- 1 medium pear: 5.5 g
- 1 medium apple: 4.4 g

**WHOLE GRAINS**

- 1 cup whole-wheat spaghetti: 6.3 g
- 1 cup pearled barley: 6 g
- 1 cup quinoa: 5.2 g
- 1 cup steel cut oatmeal: 5 g

Limit Added Sugars/Refined Grains

• Diets high in added sugars and refined grains

  =

• High glycemic load
• Low nutrient value
• Negative effects on the immune system
• Blood sugar fluctuations → swings in mood, energy and thinking ability
• Weight/fat gain
Tips for Eating a Low Glycemic Load Diet

- **Eat real, whole foods!**

- Avoid eating “naked” carbs; combine carbs with protein/healthy fats (ex: piece of fruit with nuts or whole grain bread with nut butter).

- Eat foods in their natural packages → Vegetables, fruits, nuts/seeds, beans, etc....

- Minimize processed foods → Refined grains, added sugars, desserts, fried, fast foods

- Limit/avoid sugary beverages → Fruit juices, juice drinks, sweetened tea/coffee, sodas
# Serving Size Counts

<table>
<thead>
<tr>
<th>1 serving of whole grain =</th>
</tr>
</thead>
<tbody>
<tr>
<td>foto</td>
</tr>
<tr>
<td>½ cup cooked</td>
</tr>
</tbody>
</table>

- 4 servings
- 4 servings
Sugar

Current US daily intake:

22 tsp Sugar Daily → 355 calories daily

Recommended Guidelines:
(added in processing, cooking or table)
≤100 calories daily – females
≤150 calories daily – males

How many teaspoons is that? Daily:
5 tsp for females/ 9 tsp for males

Source: American Heart Association 2009; USDA
# Where’s the Added Sugar?

<table>
<thead>
<tr>
<th>Meal</th>
<th>Added Sugar per serving</th>
<th>Daily Total: 53 grams (212 calories)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast: Sweetened yogurt</td>
<td>10 grams</td>
<td></td>
</tr>
<tr>
<td>Lunch: Salad with bottled dressing</td>
<td>8 grams</td>
<td></td>
</tr>
<tr>
<td>Snack: Energy Bar</td>
<td>21 grams</td>
<td></td>
</tr>
<tr>
<td>Dinner: Chicken with teriyaki sauce</td>
<td>14 grams</td>
<td></td>
</tr>
</tbody>
</table>

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*Daily Total: 53 grams (212 calories)*
Meal Makeovers

Breakfast: Plain yogurt + blueberries + walnuts + cinnamon

Lunch: Mixed salad with 2 T olive oil, herbs and lemon juice dressing

Snack: ¼ cup almonds + small apple + 1 oz dark chocolate (>72% cocoa)

Dinner: Chicken baked with herbs and spices, brown rice and broccoli

Daily Total: 10 grams (40 calories)

Added Sugar

0 grams

0 grams

10 grams

0 grams
Spa Water

- Orange Lemon Lime
- Blueberry Orange Lemon
- Mint Cucumber Lime
- Strawberry Lemon
Healthy Fats

Omega-3 (EFA-PUFA) rich foods:
- Cold water fatty fish: salmon, sardines, black cod, trout, herring – Include 2 x week
- Ground flax seeds, walnuts, pumpkin seeds, chia seeds

Omega-9 (MUFA) rich foods:
- Olive oil, olives, almonds, avocado, canola oil, macadamia nut oil
Balance Your Essential Fatty Acids (EFAs)

Omega-6 fatty acids
Decrease Sources:
Meats (especially grain-fed), dairy fat, egg yolks, sunflower oil, safflower oil, cottonseed oil, corn oil, & processed foods made with these oils.

Omega-3 fatty acids
Increase Sources:
Cold-water fish (wild salmon, trout, sardines, herring, black cod), flaxseeds, chia seeds, walnuts, pumpkin seeds, & purslane.

Pro-Inflammatory Compounds:
- Promote inflammation,
- tumor growth, progression & angiogenesis
- Suppress immune function

Anti-Inflammatory Compounds:
- Inhibit tumor growth & angiogenesis
- Immune enhancing

Standard American Diet (SAD) contains far more omega-6 than omega-3 fats. Imbalance can have negative affects on various aspects of health.

Eicosanoid Production
Additional Tips

• Before reducing calories, make sure that the foods in your diet provide the best nutrition!
  – Calorie intake will decrease naturally.

• Don’t try to wing it!
  – Look at the week ahead to balance out heavier eating days with lighter eating days.
  – If dinner has to be late – eat light & skip the after dinner snacks.

• Plan in some form of physical activity daily.
Stock your Refrigerator
Organize your Pantry
Life Hack: Batch Cooking
Resources

**Cookbooks**


**Websites**

- **Cronometer – Calorie & Nutrient Tracker:** [https://cronometer.com](https://cronometer.com)
- **American Institute for Cancer Research:** [http://www.aicr.org](http://www.aicr.org)
- **UCSF Cancer Resource Center:** [http://cc.ucsf.edu/crc](http://cc.ucsf.edu/crc)
Practice Precaution

• Always discuss changes in diet & supplement use with your health care practitioner(s).
Words of Wisdom

• “Let food be your medicine & medicine be your food.”
  » Hippocrates