Who am I?

Melissa Walter, MPH, RDN, LDN, is a dietitian employed by UNC's Department of Nutrition in the Gillings School of Global Public Health, and, as part of her role in the department, teaches oncology nutrition to residential and online Master of Public Health/Nutrition Students. Melissa also teaches in the community related to aging, brain health (Alzheimer's, Parkinson's, concussion, etc.), and oncology.

Melissa is passionate about how food grows, how it tastes, and how it nourishes us both physically and emotionally. She spends her spare time on local farms and in her garden, nourishes old friendships through intimate and sometimes emotional meals shared, and forges new friendships through nutritious and delicious food adventures. She supports her patients in finding healthy and delicious ways to enjoy their favorite foods and embrace their food traditions.

You can reach Melissa at melissawalter@unc.edu

1

Conflict of Interest

Melissa Walter, MPH, RDN, LDN, is the owner of (YUM) good living, which provides specialized nutrition consulting. This presentation contains no solicitation.

2

NUTRITION *and the aging brain* IN CANCER CARE

UNC
GILLINGS SCHOOL OF GLOBAL PUBLIC HEALTH
Nutrition

3

Objectives

Our brains change as we age. These alterations become more complicated and often accelerated when combined with cancer, radiation therapy, and/or chemotherapy. At the end of this lecture participants will be able to:

1. Describe brain and neurological changes that occur as a result of chemotherapy and radiation treatments in cancer care.
2. Identify critical elements of a diet that provides support for age-related changes in brain function and cognition.
3. Discuss ways to provide basic nutrition support and to make dietitian referrals to lessen cognitive and neurological impacts of chemotherapy and radiation.

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What is cognition?

Cognition is the mental process involved in knowing, learning, and understanding things; it is our ability to perceive, process, and assimilate information and convert it to knowledge. Cognition includes:

- Intellectual development
- Learning
- Attention
- Memory
- Language
- Reasoning
- Decision-making
- Evaluation
- Interpretation

https://www.collinsdictionary.com/us/dictionary/english/cognition; https://www.cognifit.com/cognition; Image by Gerd Altmann from Pixabay

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Risk factors *for* cognitive decline

CANCER	AGING/AGE RELATED DISEASE
Direct treatment toxicity	
Hormonal changes: estrogen and testosterone	Hormonal changes: estrogen and testosterone
Oxidative stress	Oxidative stress
Inflammation (and pro-inflammatory cytokines)	Inflammation (and pro-inflammatory cytokines)
Shortened telomeres	Shortened telomeres
Genes	Genes
- APOE4 alleles: ↓cognition	- APOE4 alleles: ↓cognition
- COMTVal158, BDNF	- COMTVal158, BDNF
- genes related to neuroplasticity, DNA damage/repair	- genes related to neuroplasticity, DNA damage/repair
Sleep disorders	Sleep disorders
Fatigue	Fatigue
Depression, anxiety, stress	Depression, anxiety, stress
Pain	Pain
Gut dysbiosis/altered gut integrity	Gut dysbiosis/altered gut integrity
Low cognitive reserve	Low cognitive reserve
NUTRITIONAL DEFICIENCIES	NUTRITIONAL DEFICIENCIES

Ahles 2012; Ahles 2018; Mandelblatt 2018.

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Brain reserve or cognitive reserve?

Brain reserve: a quantitative concept related to brain size and architecture: the amount of grey or white matter, the number of neurons and synapses, etc. (*passive reserve*)

Cognitive reserve: a qualitative concept related to the brain's pre-existing cognition (cognitive stores related to language, memory, processing, reasoning, experience, etc.) and ability to enlist compensatory approaches during times of cognitive challenge. (*active reserve*)

Cognitive reserve offers cognitive resilience in the face of decreased brain reserve. It is increased by:

- Life experiences
- Mentally enriching activities
- Level/amount of education
- Occupational attainment
- Socioeconomic status
- Physical exercise

Stern 2013. Image by Gerd Altmann from Pixabay

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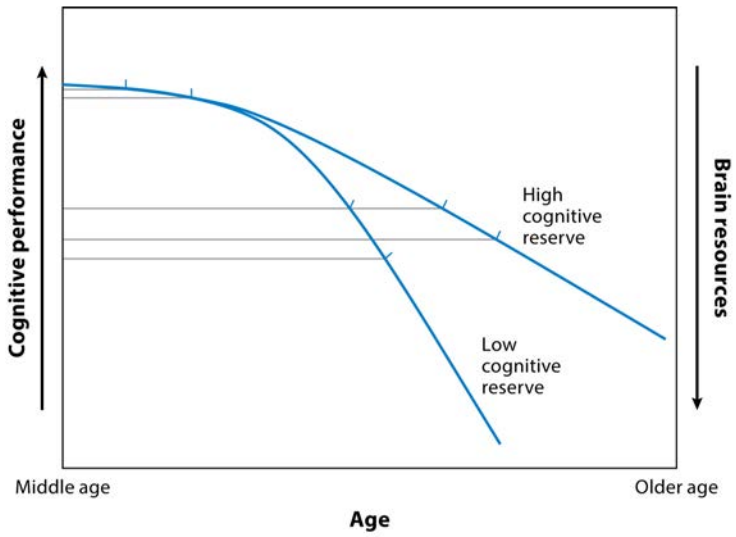
Cognitive reserve *and* cognitive decline



Ahles TA, Root JC. 2018. *Annu. Rev. Clin. Psychol.* 14:425–51

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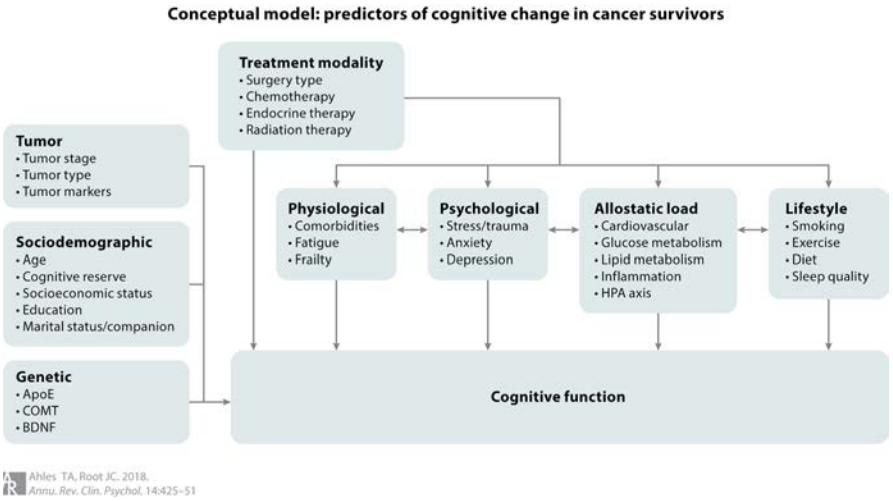
Predictors *of* cognitive decline *in* cancer survivors



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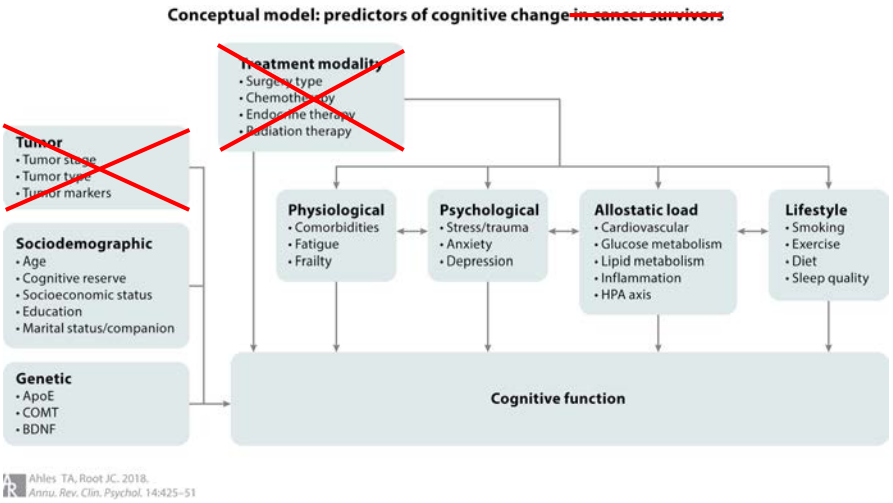
Predictors *of* cognitive decline



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Nutrition therapy *for* cognitive decline

CANCER	AGING/AGE RELATED DISEASE
NUTRITION to reduce oxidative stress	NUTRITION to reduce oxidative stress
NUTRITION to lessen inflammation	NUTRITION to lessen inflammation
NUTRITION to lengthen telomeres	NUTRITION to lengthen telomeres
NUTRITION to minimize epigenetic changes re:	NUTRITION to minimize epigenetic changes re:
- APOE4 alleles: ↓cognition	- APOE4 alleles: ↓cognition
- COMTVal158, BDNF	- COMTVal158, BDNF
- genes related to neuroplasticity, DNA damage/repair	- genes related to neuroplasticity, DNA damage/repair
NUTRITION and treatments to improve sleep length/quality	NUTRITION and treatments to improve sleep length/quality
NUTRITION and treatments to improve fatigue	NUTRITION and treatments to improve fatigue
NUTRITION and treatments to alleviate depression, anxiety, stress	NUTRITION and treatments to alleviate depression, anxiety, stress
NUTRITION for gut dysbiosis	NUTRITION for gut dysbiosis
IMPROVED NUTRITION	IMPROVED NUTRITION

Ahles 2012; Ahles 2018; Mandelblatt 2018. Image by Ulrike Leone from Pixabay.

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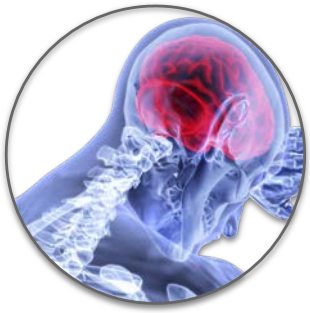
Nutrition *and* oxidative stress



Oxidative stress:

can activate transcription factors and result in the expression of over 500 different genes, including those for growth factors, inflammatory cytokines, chemokines, cell cycle regulatory molecules, etc.
activates inflammatory pathways leading to transformation of a normal cell to tumor cell, tumor cell survival, proliferation, chemoresistance, radioresistance, invasion, angiogenesis and stem cell survival
implicated in many diseases of aging, including dementias

Antioxidant diets include:

diets high in fruits and vegetables
- vitamins C and E, selenium, carotenoids (beta-carotene, lycopene, lutein, and zeaxanthin), etc.

While there is some debate about the use of antioxidant foods or supplements counteracting cancer treatments that work by creating ROS, a 2007 literature review indicates that these foods/supplements enhance the effectiveness of treatments, decrease their side effects, protect normal tissue, and may increase survival.

Reuter 2010; Simone 2007; NIH Antioxidants, Image by VSRao from Pixabay.

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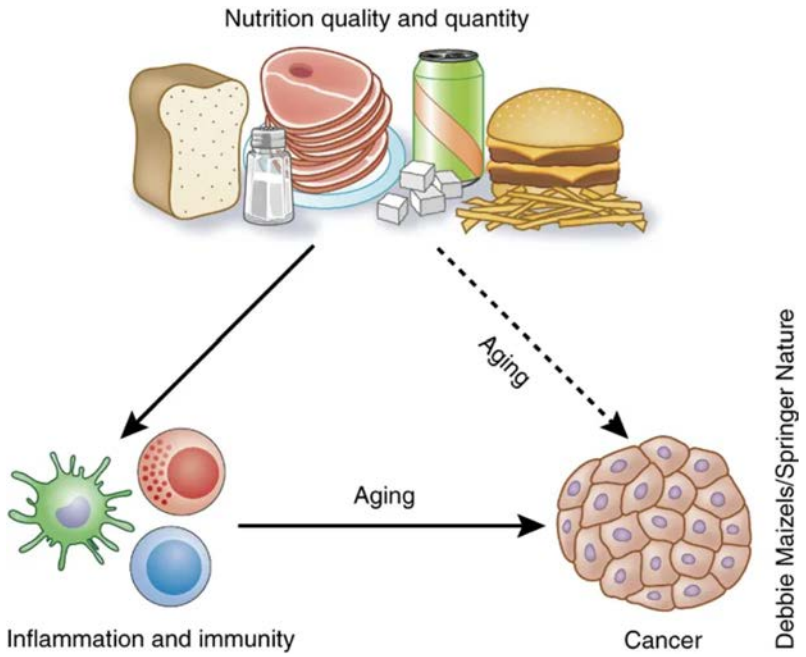
Nutrition, inflammation, aging, *and* cancer



Zitvogel et al. 2017

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Nutrition *and* inflammation

Inflammation: part of the immune system's response to defend body against infection—but affects the brain and cognition, too.

Nutrition can have a direct impact upon inflammatory processes in both aging and cancer.

Anti-inflammatory diets include:

- 4-5 daily servings fruits & vegetables for vitamins, minerals, fiber, polyphenols, other antioxidants → lower levels of inflammatory markers
- Whole grain foods → lower levels of inflammatory markers
- Decreased caloric intake (independent of weight loss) → lower levels of inflammatory markers
- Weight loss → lower levels of inflammatory markers

Franz 2014; Warnberg 2009; Zitvogel 2017

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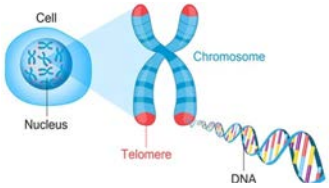
Nutrition *and* telomere length

Telomere: protective cap on the end of chromosomes; protects the end of the chromosome from deteriorating or fusing with other chromosomes.

Telomere length:

Decreased in aging
Decreased with cancer and treatment
Increased with dietary changes:

- Mediterranean Diet
- DASH Diet
- USDA Healthy Eating Index
- USDA Alternate Healthy Eating Index



Crous-Bou 2014; Leung 2018. Image Fancy Capis/Shutterstock.

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Nutrition, nutrigenomics, aging *and* cancer

Nutrigenomics: the role of nutrients and bioactive food compounds in gene expression (epigenetics and nutrition!)

Major plant constituents with evidence of epigenetic modifications

Major plant	Bioactive component
Tomatoes	Lycopene
Turmeric	Curcumin
Cinnamon	Coumaric acid
Cashew nuts	Anacardic acid
Apples	Phloretin
Soybean	Genistein
Tea	Epigallocatechin gallate (EGCG)
Grapes	Resveratrol
Citrus	Hesperidin
Coffee	Caffeic acid
Broccoli	Isothiocyanates
Garlic	Allyl mercaptan

Fenech 2011; Nicastro 2012.

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Nutrition *and* sleep

Glymphatic system: removal of "wastes" from the brain; named for glial cells in the brain that control this system in way similar to the lymphatic system

- "Cleans" the brain each night
- If impaired (age, brain injury, etc.) may allow amyloid-beta and tau proteins to accumulate (hallmark of Alzheimer's disease and others)

Sleep disorders are tied to age, Alzheimer's and other neurodegenerative diseases, brain injuries, and psychiatric disorders: which comes first?!

How can nutrition help?

- Lose weight if needed. Overweight—even 5-10 lbs—can lead to sleep apnea by compromising respiratory function. Apnea and fatigue can lower motivation to eat right and exercise—and can decrease cognition!
- Avoid spicy foods, chocolate, fatty foods, etc. at dinner (or later) if you have reflux/heartburn.
- Eat larger meals earlier in the day and lighter meals for dinner; avoid evening snacks.
- Avoid low fiber and high fat/high sugar diets; these are associated with lighter, less restorative sleep with more arousals.

Xie 2013. Image Eiko Ojala in NY Times 2014.

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Nutrition *and* mental health

Numerous studies have found correlations between nutrient-deficient diets and poor mental health...

- Low-carb diets can increase depression

...and have found correlations between improved diet and improved mental health:

- Link between high fish consumption and low incidence of mental illness
- Supplements and foods containing amino acids (used to make neurotransmitters) reduce symptoms; amino acids found in protein-rich foods
- Folate, B12, iron, iodine, chromium, lithium, selenium, zinc (many antioxidants and micronutrients found in fruits and vegetables) can also reduce symptoms

Sathyanarayana Rao 2008. Image from Pixabay.

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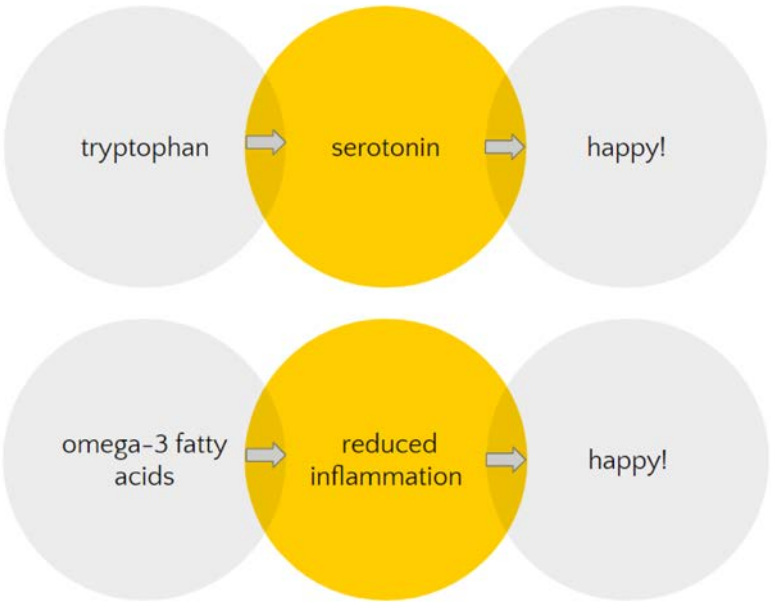
Nutrition *and* mental health



Katz 2015.

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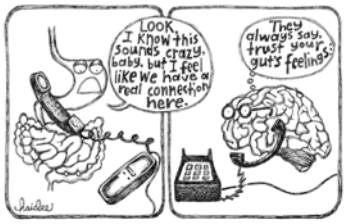
Nutrition *and* gut health



Both aging and chemotherapy alter and often destroy the microbiota (bacteria) in our guts. What do we really lose?

Nutrient extraction (from food) and conversion to useful forms
- Digestion of insoluble fiber → SCFA → energy
- Butyrate (a SCFA) decreases depression, anxiety; activates vagus nerve

Vitamin production (K, B12)

Regulation of inflammation

Drug detoxification (including chemotherapy detoxification!)

70% of our immunity
- Defense against infections

Regulation of angiogenesis (blood vessel formation)

Behavioral support/NT support
- Neurotransmitters secreted by gut (like brain!) decrease symptoms of depression, anxiety, even autism. They don't cross the blood brain barrier, though…they send signals via the vagus nerve.

Hsaio 2013; Loman 2019.

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Nutrition *and* gut health

"The Hadza people of Tanzania have a gut microbiome diversity that is one of the richest on the planet and about 40% higher than the average American and about 30% higher than the average Brit. The average Hadza person eats around 600 species of plants and animals in a year and has huge seasonal variation. They have virtually none of the common Western diseases such as obesity, allergies, heart disease and cancer. In contrast, most Westerners have fewer than 50 species in their diet and are facing an epidemic of illness and obesity."

How do we feed and support our bacteria?

- Eat more plants/fiber
- Eat pre- and probiotics (possibly consider supplementing)
  - Pre: non-digestible plants - fibrous veggies, garlic, onions, oats, beans
  - Pro: fermented foods - sauerkraut, kimchi, kombucha, pickled veggies, yogurt, kefir
- Avoid antibiotics and NSAIDs when possible
- Avoid artificial sweeteners
- Limit use of hand sanitizers and antimicrobial soaps
- Get more fresh air
- Get a dog!
- Get dirty!

Spector 2019.

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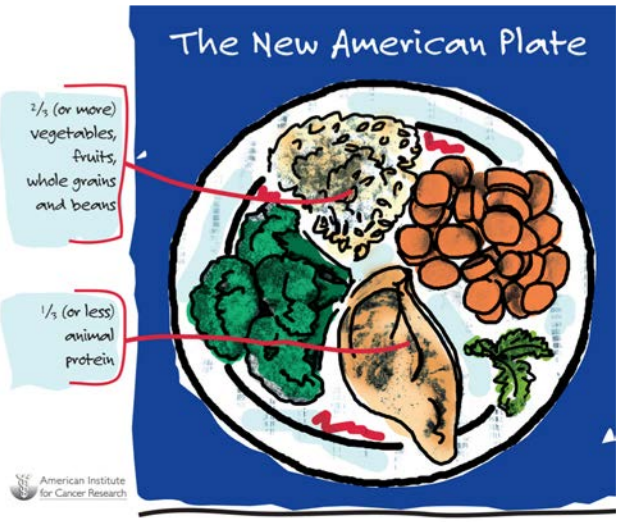
Nutrition *for* cancer prevention

The best diet is high in fiber and rich in a variety of vegetables, fruits, whole grains, and legumes (beans)

- provides vitamins, minerals, and protective and naturally-occurring plant substances known as phytochemicals (phyto = plant) and can help to defend the body against cancer and other diseases.

There are no real "super-foods!"

- We need a combination of MANY fruits, vegetables, whole grains to provide necessary nutrients for antioxidant and nutrigenetic support
- Greater effectiveness from foods than supplements
- Supplementation of some compounds appear to be cancer causing (e.g. folic acid) while food sources are cancer fighting (folate)



aicr.org.

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The MIND Diet

MIND Diet: *Mediterranean-DASH Intervention for Neurodegenerative Delay*

- Anti-inflammatory diet
- Flexible diet - no calorie limits, no elimination of food groups
- Combines plant fibers and antioxidants, omega-3s, lean protein
- Includes all important macro- and micronutrients
- Reduces added sugars, saturated and trans fats
- Shown to reduce Alzheimer's risk by 35-53% with MODERATE adherence

The MIND Diet: what to do? *(yep, eat more plants!)*

- Daily: 3 servings whole grains, 1 serving leafy greens plus at least one more vegetable, glass of wine (any kind!), cook with olive oil
- Most days: snack on nuts
- Every other day: ½ cup beans
- AT LEAST twice/week: poultry, ½ cup berries
- AT LEAST once/week: fish (cold water/omega 3)
- Exercise

LIMIT red meat (< 4 servings per week), butter/margarine (< 1 tablespoon per day), cheese (< 1 serving per week), sweets (<5 servings per week), fried and fast foods (< 1 serving per week)

Morris 2015.

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The MIND Diet:

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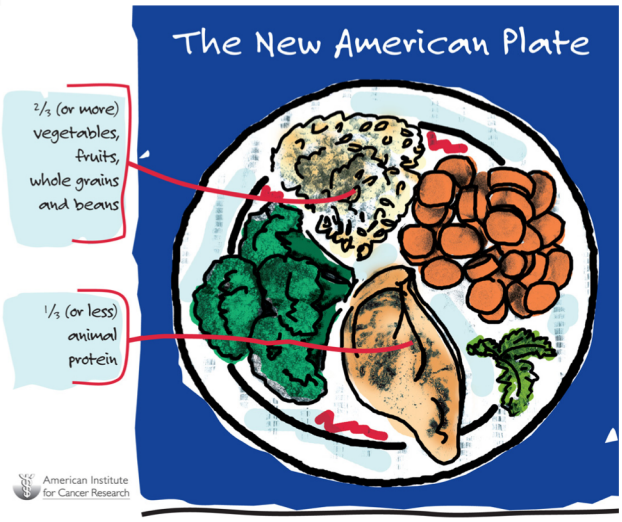
Morris 2015.



aicr.org.

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NUTRITION RISKS WITH CANCER TREATMENT

Psychological distress
Pain
Fatigue
Anorexia
Alimentary tract disturbances: changes in taste and smell (dysgeusia), dry mouth (xerostomia), thick saliva, swallowing challenges (dysphagia), stomatitis/mucositis, reflux, indigestion, flatulence/bloating, N&V, diarrhea, constipation, lactose intolerance
Malnutrition
- Dehydration
- Protein deficiencies
- Vitamin and mineral deficiencies

Weight loss OR weight gain
Sarcopenia
Cachexia

Weight loss → greater tx side effects → missed treatments → poorer response and prognosis

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Is it aging?

Is it cancer *and* treatment?

Visual changes
Fewer taste buds
Fewer olfactory buds
Less saliva production
Tooth decay
Decreased tactile sense (self-feeding)
Decline in muscle/motor function to chew
Weakness
Lesser appetite (less active, medication side effect, etc.)
Altered absorption and metabolism of food
Depression, loneliness, irritability, loss of memory, confusion, brain fog

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...or
is it
malnutrition?

Malnutrition:

Insufficient calories = depression, irritability, apathy, aggression, nervousness, restlessness, hypochondriasis, hysteria

Dehydration = poor memory, confusion, fatigue, low or high blood pressure, joint pain

↓ Carbohydrate = headache, confusion, brain fog, irritability

↓ Protein = confusion, moodiness, sleep disturbances, poor wound healing, muscle loss

↓ Fat = depression, brain fog, irritability, overwhelm, vitamin deficiencies

↓ Vit A = night blindness, decreased sense of taste, impaired wound healing, dry eyes/skin

↓ Vit B1 = loss of motor coordination, pain, headaches, weakness, loss of appetite

↓ Vit B2 = visual changes, burning eyes, peripheral nerve damage, weakness, skin cracking

↓ Vit B3 = disorientation, confusion, apathy, depression, memory deficit, paranoia

↓ Vit B6 = depression, confusion, mania, mood changes, fatigue, weakened immunity

↓ Vit B9 = peripheral nerve problems, memory disorder, weakness, palpitations, SOB

↓ Vit B12 = depression, confusion, poor concentration, severe dementia, weakness, white matter (brain) degeneration, GI issues, neuropathy, vision loss

↓ Vit C = joint pain and swelling, impaired wound healing, easy bruising, dry/rough skin

↓ Vit D = depression, fatigue, bone pain/loss, muscle pain, hair loss, frequent infection

↓ Vit E = disorientation, vision problems, muscle weakness, walking and balance problems

↓ Zinc = taste/smell loss, loss of appetite, apathy, depression, hair loss, weakened immunity

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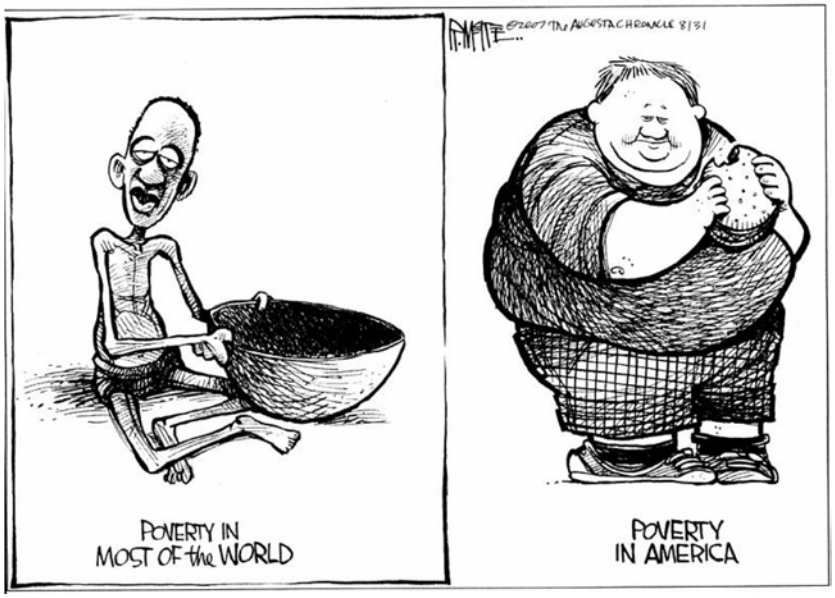
Malnutrition
and obesity?

Absolutely.



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Common nutrient deficiencies *in* aging

https://ods.od.nih.gov/factsheets/list-all/

Nutrient	Foods
Protein	Lean (low-fat) proteins include poultry (white meat), fish, eggs, beans, nuts, oats, quinoa, cottage cheese, greek yogurt. Some in broccoli, Brussels sprouts.
Omega-3 FA	Fish, nuts and seeds, plant oils, fortified foods
Fiber	Fruits, vegetables, beans, whole grains. *Not a nutrient, but important for reduction of multiple health risks; also important to "feed" beneficial bacteria.*
Calcium	Dark, leafy greens (collards/spinach/kale); dairy; sardines; canned salmon; white beans; almonds; poppy/sesame/chia seeds. *Evidence does not support supplementation; may increase risk of kidney and cardiovascular disease, colon polyps, aggressive prostate cancer.*
Vitamin D	Fatty fish (tuna, salmon, mackerel); cheese; egg yolk; Vit D fortified foods: OJ, milk. *A few minutes of sunlight each day can aid in Vit D production in the body; harder for those with darker skin.*
Magnesium	Dark, leafy greens; broccoli; nuts and seeds; beans; whole grains; low-fat dairy; avocado, dk chocolate
Vitamin C	Brightly colored F&V: citrus fruits, strawberries, cantaloupe, sweet potatoes, tomatoes, bell peppers, etc.; broccoli, cauliflower, kale
Vitamin E	Trout, shrimp, broccoli, spinach, squash, kiwifruit, nuts and seeds; vegetable oils. *Supplementation is NOT recommended.*
Vitamin B6	Poultry, pork, fish, eggs, organ meats, starchy vegetables, spinach
Vitamin B12	Clams, beef liver, all meat, trout, tuna, salmon, fortified foods: whole grains, nutritional yeast, etc.
Selenium	Brazil nuts (1 per day for men to reduce prostate cancer risk!), tuna, oysters, pork, beef, chicken, tofu, whole wheat pasta, shrimp, mushrooms

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Hydration *and* cognition

Lose ability to sense thirst with age; often drink less with chemotherapy and side effects

Dehydration: leading cause for admission to ERs and hospitals for older adults

Less water → "shrinking" brain and cells

- **Reduces cognition: short-term memory, numerical ability, psychomotor function, sustained attention**
- **Increases confusion, disorientation, fatigue**
- **Impacts mood negatively**
- **Leads to headache**

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Collaboration *is* critical

Nutrition-related side effects of cancer and cancer treatment can be challenging to manage—as can nutrition-related "side effects" of aging! Nurses and physicians are nutrition's front line. Interprofessional collaboration is essential.

Early and regular nutrition assessment and intervention and a multidisciplinary approach to nutrition care result in improved treatment tolerance for patients.

During the acute phase of curative oncology treatment, adequate nutrition support has been shown to improve short-term outcomes by reducing the number of complications and thus shortening the recovery phase.

Maintaining appropriate supportive nutrition can reduce the risk for cognitive decline and can sometimes reverse decline—whether from cancer and treatment, from aging, or both.

Image by Canva Studio by Pexels.

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When to refer *to a* dietitian

Registered Dietitians can help patients and practitioners manage nutrition-related side effects of treatments, including cognitive changes:

- Make recommendations on foods and eating strategies to complement medication management of side effects
- Offer strategies for preparing healthy foods in palatable ways to accommodate nutrition symptoms
- Aid in management of multiple, chronic side effects that affect eating and digestion
- Provide support—psychological and nutritional!—when oral intake is poor or anticipated to be poor (with or without weight loss)
- Monitor significant weight and/or muscle loss
- Aid in prevention, identification, and treatment of malnutrition
- Manage tube feedings and formulas
- Provide weight management and dietary guidance in survivorship
- Answer in-depth nutrition questions of patients and caregivers

To talk with an oncology dietitian at UNC, visit https://unclineberger.org/nutrition/

Image by Dreamstime.

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