Complementary and Integrative Pharmacotherapy for Survivors of Cancer

Identifying the role of supplements, vitamins, and herbal products

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Nebraska Medicine

Disclosure

I have no financial relationship with any pharmaceutical companies, biomedical device manufacturers or distributors, or others whose products or services may be considered related to the content of my presentation.

Non-FDA-approved supplements and vitamins will be reviewed and discussed in this presentation.

Objectives

- Discuss the role of dietary supplements and complementary medicine practices in survivors of cancer.

- Identify available resources to augment the safe use(s) of supplements and complementary medicine, including how the team plays a role in articulating information for post cancer treatment and care to improve patient outcomes.

Definitions

Alternative

- In place of standard medical treatment

Complementary

- Alongside standard medical treatment

Integrative

- Combining standard medical treatments with complementary/alternative interventions
- Address mental, physical, and/or spiritual aspects of healthcare

Types of Complementary Medicine

Manipulative and body-based practices

Biologically based practices

Whole medical systems

Energy healing

Mind-body therapies

cancer.gov.

Biologically Based Practices

- Dietary supplements
  - Vitamins, minerals, and herbs, *alone or in combination*, to supplement the diet
- Vitamins
  - Nutrients needed for normal bodily function(s)
- Botanicals (*herbs*)
- Special diets

cancer.gov.

Benefits & Risks of Supplements & Complementary Medicine

Proposed Benefits

- Improve quality of life & health
- Prevent cancer recurrence
- Fill in dietary “gaps”
- Replace deficiencies

Proposed Health Benefits from Supplements, Vitamins, & Herbs

Intervention	Proposed Health Benefits
Vitamin B12	Nerve and blood cell health
Vitamin C	Antioxidant; immune support
Vitamin E	Antioxidant
Biotin	Hair, skin, & nail health
Echinacea	Immune support
Glucosamine	Joint health
Melatonin	Sleep regulation
St. John’s wort	Mood regulation
Turmeric	Anti-inflammatory; antioxidant

NIH Office of Dietary Supplements – ods.od.nih.gov.
National Center for Complementary and Integrative Health – nccih.nih.gov.

Proposed Benefits

- Improve quality of life & health
- Prevent cancer recurrence
- Fill in dietary “gaps”
- **Replace deficiencies**

Potential Risks

Financial toxicity	• Potential for high costs • Marketing & targeted audience
Lack of regulation	• Not approved by the FDA • No guarantee of safety or efficacy
Unknown composition	• Contaminated products • Is the dose on the label what is actually in the product?
Effect on other medications	• Drug interactions • May change the way the body responds to other therapies

NIH Office of Dietary Supplements – ods.od.nih.gov.
cancer.gov.

Financial Toxicity

- Supplements and complementary medicine typically not covered by insurance
- **~$30 billion** annual out-of-pocket expenses on complementary & alternative therapies

Product	Cost
Superfood powders	$100 (1-month supply)
Patches	$160 (1-month supply)
IV vitamin treatment	$200 (per treatment)
“Natural origin” supplements	$1200 (1-month supply)

J Clin Oncol 2013;31:3749-57. // Natl Health Stat Report 2016;22:1-11.
Google “Shopping”.

How Are Supplements Regulated?

Dietary Supplement Health and Education Act (DSHEA) of 1994

- Defined “dietary supplement”

> “a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients – 1) vitamin, 2) mineral, 3) herb or other botanical, 4) an amino acid, 5) a dietary substance for use by man to supplement the diet by increasing the total dietary intake, or 6) a concentrate, metabolite, constituent, extract, or combination of any [previously mentioned] ingredient”

- Required following of good manufacturing practices (GMP)

> “minimum … practices necessary for activities related to manufacturing, packaging, labeling, or holding dietary supplements to ensure the quality of the dietary supplement”

- Outlined labeling requirements

> Several requirements, include use of the words “dietary supplement, product serving size, listing of ingredients, disclaimer statement

NIH Office of Dietary Supplements – DSHEA.
FDA – Current Good Manufacturing Practices of Dietary Supplements.

How Are Supplements Regulated?

Role of the FDA

- Limited to banning a supplement if product is found to be dangerous
- Does not evaluate for safety or efficacy
  - Labeling requires "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease."

Just because the label says "safe" or "effective for…" doesn't guarantee the product is

NIH Office of Dietary Supplements – DSHEA.

“Natural Does Not Always Mean Safe”

Tainted supplements

- Analysis of the FDA’s “Tainted Dietary Supplement Database” revealed over 1000 adulterated dietary supplements
- Can contain other prescription drugs, medications that have previously been removed from the market
- Also risk for contamination by bacteria, heavy metals

Risk for overdose

- Products can contain more than the maximum recommended daily dose of a specific nutrient
- Labels may not list all ingredients or exact ingredient amounts
- No standardization

J Clin Pharmacol 2022 – doi/10.1002/jcph.2046. // Annals Pharmacother 2020;54:815-9.
NIH Office of Dietary Supplements – ods.od.nih.gov.

Effects on the Body & on Other Medications

Adverse Effects

- Impact quality of life
- Increase toxicity of other medications

Drug Interactions

- Absorption
- Distribution
- Metabolism
- Excretion

cancer.gov.
Br J Clin Pharmacol 2018;84:679-93.

Choosing Dietary Supplements, Vitamins, & Herbs

- Talk to your healthcare team
- Read the labels
- Look for seals of quality assurance
  - Organizations conducting quality tests
  - Specific standards met during manufacturing
  - Ingredients are accurate & lack contaminants

cancer.org.
qualitymatters.usp.org. // nsf.org.

Guideline Recommendations

American Institute for Cancer Research (AICR)
Children's Oncology Group (COG)
American Society for Transplantation and Cellular Therapy (ASTCT)
National Comprehensive Cancer Network (NCCN)

AICR
Cancer Prevention Recommendations

"Although supplements are popular for cancer prevention, we recommend you meet your nutritional needs through diet alone."

COG
Long-Term Follow-Up Guidelines

"Vitamin supplements are not a replacement for good eating habits … Healthy eating and taking supplements when medically needed helps ensure children and adolescents have a wide range of the nutrients and vitamins needed to remain healthy and function properly."

ASTCT

"Supplement guidance needs to be individualized, particularly in the setting of deficiency treatment & should come from a credible source."

"It is important for healthcare providers to take the initiative to ask their patients about CAM use in such a way that patients do not feel uncomfortable disclosing the information."

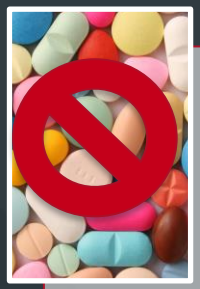
"Despite the well-known importance of nutrition in stem cell transplant survivors, there are sparse data regarding about the effect and the use of CAM in this population."

"No robust study results have been published so far to suggest that nutritional supplementation improves survival after a cancer diagnosis."

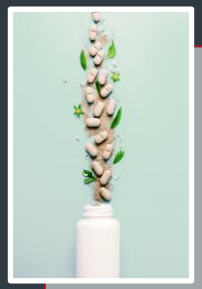
CAM = complementary and alternative medicine

Transplantation and Cellular Therapy 2021;27:467-73.

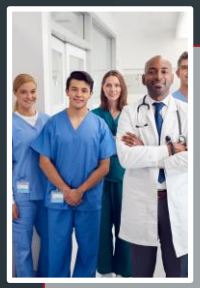
NCCN
Survivorship Guidelines



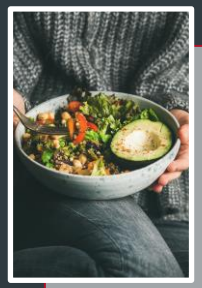
Supplement use is **not recommended for most survivors**, except in instances of documented deficiencies, inadequate diet, or comorbid indications.



Little data exist to support the use of vitamins or other dietary supplements for the purposes of cancer control, recurrence, or prevention.



Providers should assess supplement use at regular intervals. Ask about reasons for supplement use and supplement ingredients.



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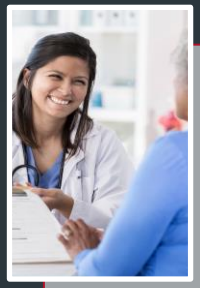
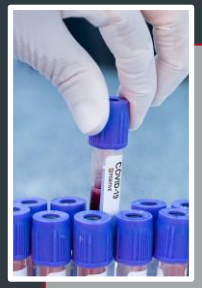
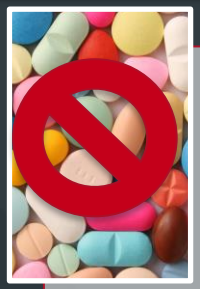


Refer survivors using multiple and/or unfamiliar supplements to a **registered nutritionist/dietitian.**



Survivors of certain cancers are at risk for vitamin deficiencies based on their cancer treatment. **Deficiencies should be assessed and repleted as needed.**

NCCN
Survivorship Guidelines



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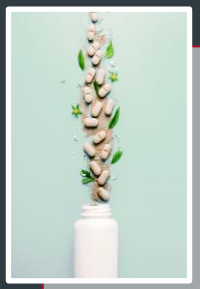

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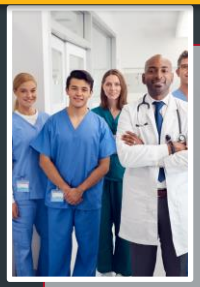

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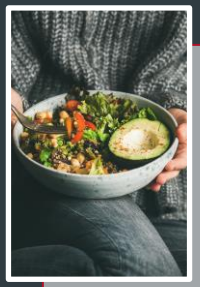

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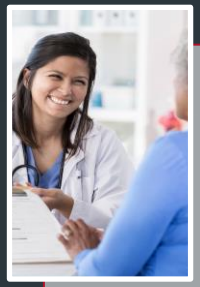

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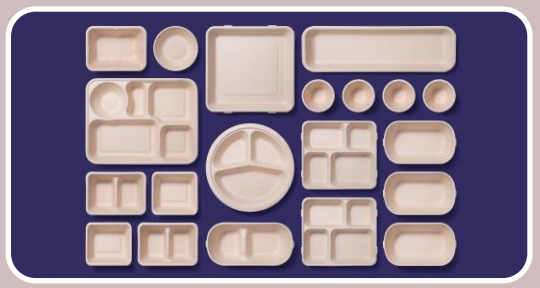
Who Might Need Supplementation?

Documented deficiencies of vitamins & minerals

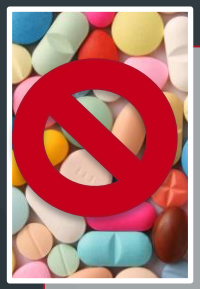


Inadequate dietary intake

Comorbidities

- Osteoporosis
- Macular degeneration
- Crohn's disease
- Pregnancy

NCCN
Survivorship Guidelines



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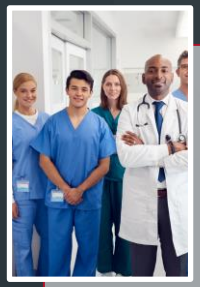

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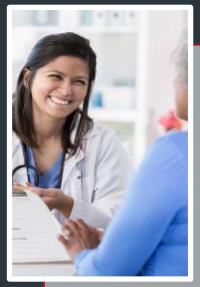

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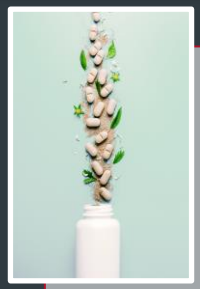

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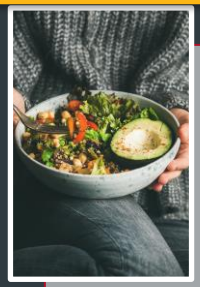

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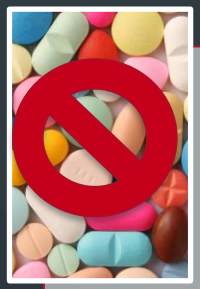
Do Supplements Prevent the Recurrence of Cancer or Help with Disease Control?

- At this time, no definitive evidence to support this question

Supplement	Disease State	Outcome(s)	Reference
Vitamin D3	• All cancer types • Breast	No reduction in cancer incidence	• NEJM 2019;380:33-44 • Front Nutr 2021;8:655727
Selenium	All cancer types	Conflicting results, but no clear prevention	Cochrane Review 2014
Antioxidants	Gastrointestinal cancers	No benefit in cancer prevention	Cochrane Review 2008
Vitamins (*variety*)	Skin cancers	No benefit in cancer prevention	Dermatology 2011;223:36-44

NCCN
Survivorship Guidelines



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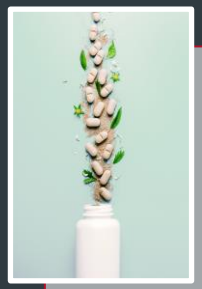

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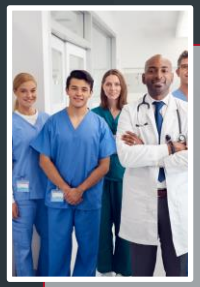

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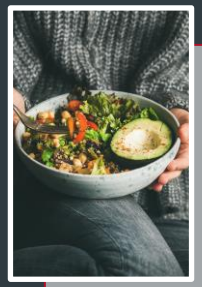

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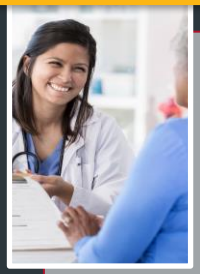

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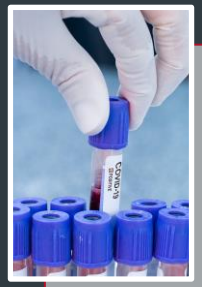

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"Prevalence and Nondisclosure of Complementary and Alternative Medicine Use in Patients With Cancer and Cancer Survivors in the US"

Survey of over 3000 survivors of cancer

Assessing CAM usage in the past 12 months

Over 1000 survey responders reported using CAM therapies

herbal supplements, chiropractic or osteopathic manipulation, massage, yoga/tai chi, spiritual meditation, special diets, acupuncture, others

Over 1/3 of users of CAM did not report usage to their healthcare teams

CAM = complementary and alternative medicine

JAMA Oncol 2019;5:735-7.

“Prevalence and Nondisclosure of Complementary and Alternative Medicine Use in Patients With Cancer and Cancer Survivors in the US”

What were the patients’ reasons for not sharing CAM usage?

Physician / Healthcare team

- Did not ask
- Had discouraged CAM use in the past

Patients

- Did not think that the healthcare team needed to know
- Did not feel like the physician would know much about the CAM therapy
- Worried about a negative reaction from the team
- Worried about being told “no”

CAM = complementary and alternative medicine

JAMA Oncol 2019;5:735-7.

Assessing for Dietary Supplement, Vitamin, & Herb Usage

- Important for the healthcare team to ask and patients to disclose
- Inquire/Share at every visit
  - What is being used
  - What is specifically in the product(s)
  - Why is it being used

NCCN Guidelines – Survivorship.
ASHP.org – Medication Reconciliation Guidance Document for Pharmacists.

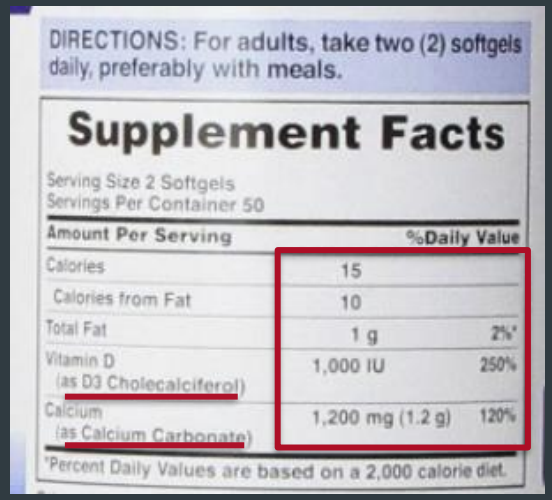
Examples of Product Variability

DIRECTIONS: For adults, take one (1) tablet daily, preferably with a meal.

Supplement Facts

Serving Size 1 Tablet

Amount Per Serving		%Daily Value
Magnesium (as Magnesium Oxide)	500 mg	119%



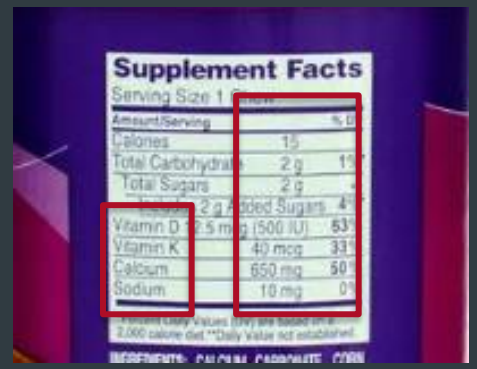
DIRECTIONS: For adults, take two (2) softgels daily, preferably with meals.

Supplement Facts

Serving Size 2 Softgels
Servings Per Container 50

Amount Per Serving		%Daily Value
Calories	15	
Calories from Fat	10	
Total Fat	1 g	2%*
Vitamin D (as D3 Cholecalciferol)	1,000 IU	250%
Calcium (as Calcium Carbonate)	1,200 mg (1.2 g)	120%

*Percent Daily Values are based on a 2,000 calorie diet.



Supplement Facts

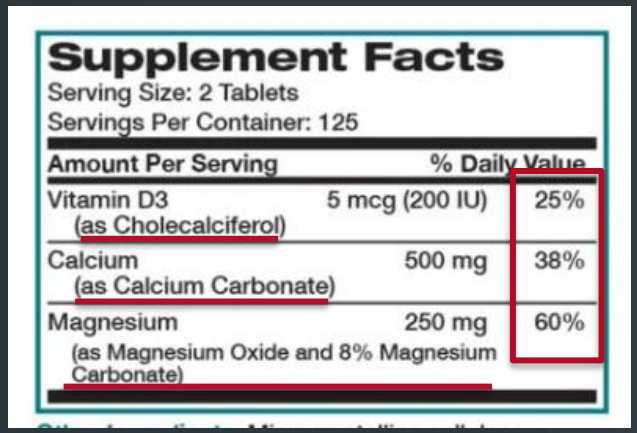
Serving Size 1

Amount/Serving		% D
Calories	15	
Total Carbohydrate	2 g	1%
Total Sugars	2 g	
Vitamin D	12.5 mcg (500 IU)	63%
Vitamin K	40 mcg	33%
Calcium	650 mg	50%
Sodium	10 mg	0%

Supplement Facts

Serving Size 1 tablet

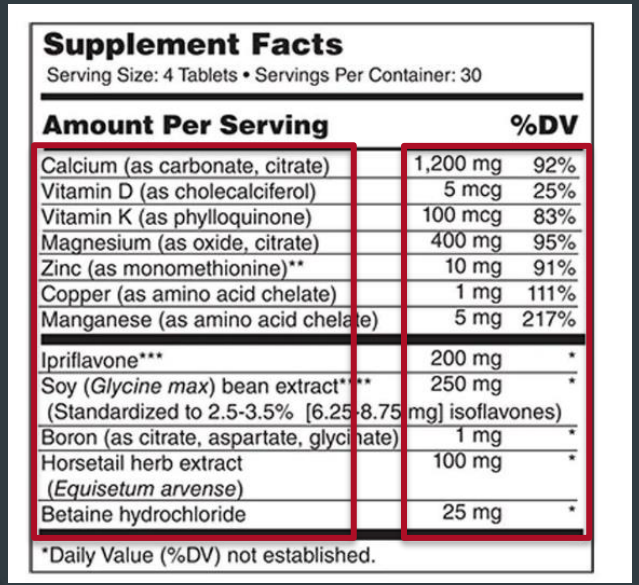
Amount Per Tablet		% Daily Value
Vitamin D_3 (as Cholecalciferol)	400 IU (10 mcg)	100%
Calcium (as Calcium Carbonate)	500 mg	50%



Supplement Facts

Serving Size: 2 Tablets
Servings Per Container: 125

Amount Per Serving		% Daily Value
Vitamin D3 (as Cholecalciferol)	5 mcg (200 IU)	25%
Calcium (as Calcium Carbonate)	500 mg	38%
Magnesium (as Magnesium Oxide and 8% Magnesium Carbonate)	250 mg	60%

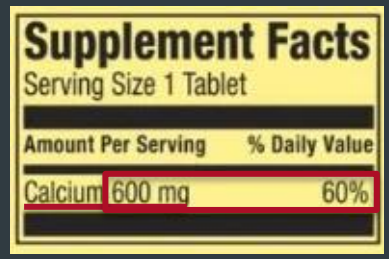


Supplement Facts

Serving Size: 4 Tablets • Servings Per Container: 30

Amount Per Serving		%DV
Calcium (as carbonate, citrate)	1,200 mg	92%
Vitamin D (as cholecalciferol)	5 mcg	25%
Vitamin K (as phylloquinone)	100 mcg	83%
Magnesium (as oxide, citrate)	400 mg	95%
Zinc (as monomethionine)**	10 mg	91%
Copper (as amino acid chelate)	1 mg	111%
Manganese (as amino acid chelate)	5 mg	217%
Ipriflavone***	200 mg	*
Soy (*Glycine max*) bean extract*** (Standardized to 2.5-3.5% [6.25-8.75 mg] isoflavones)	250 mg	*
Boron (as citrate, aspartate, glycinate)	1 mg	*
Horsetail herb extract (*Equisetum arvense*)	100 mg	*
Betaine hydrochloride	25 mg	*

*Daily Value (%DV) not established.



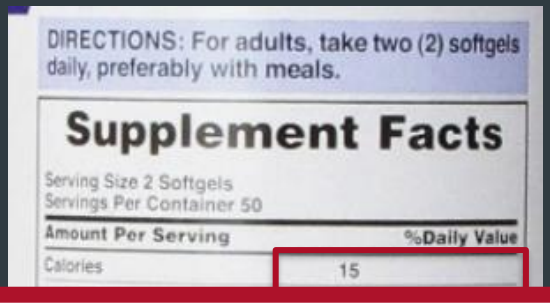
Supplement Facts

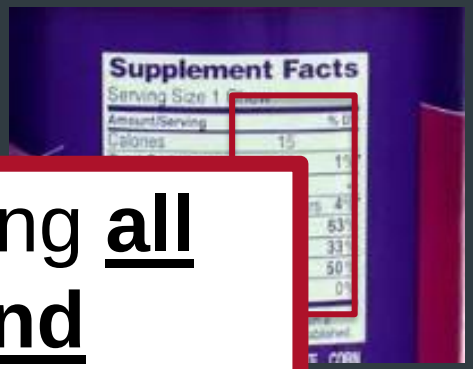
Serving Size 1 Tablet

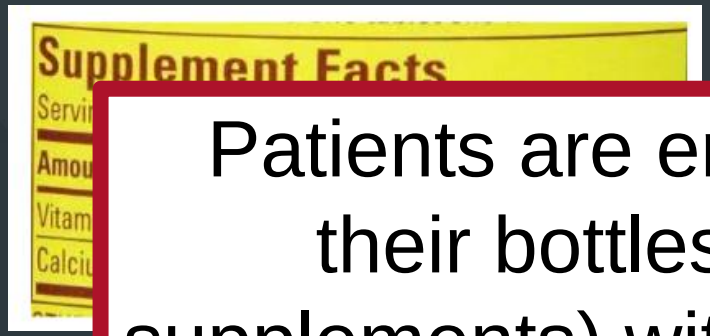
Amount Per Serving	% Daily Value
Calcium 600 mg	60%

Google “Shopping”.

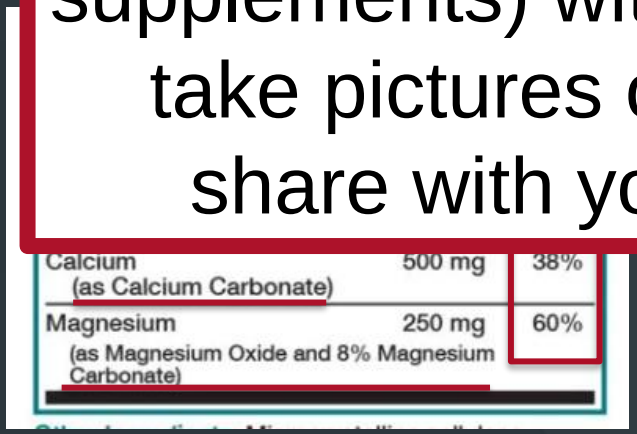
Examples of Product Variability

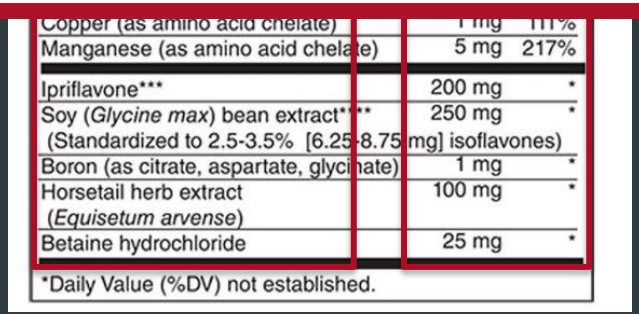


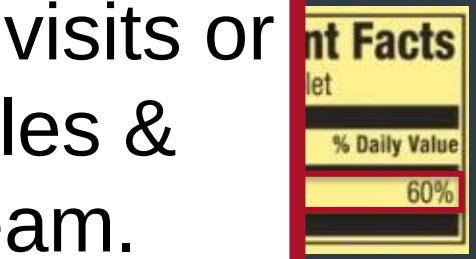




Patients are encouraged to bring **all** their bottles (medications **and** supplements) with them to office visits or take pictures of the labels/bottles & share with your healthcare team.

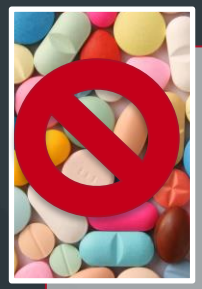






Google “Shopping”.

NCCN
Survivorship Guidelines



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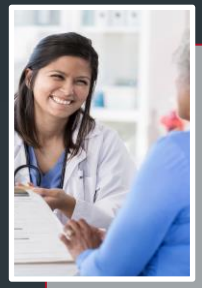
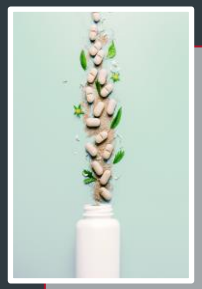
Providers should assess supplement use at regular intervals. Ask about reasons for supplement use and supplement ingredients.



Refer survivors using multiple and/or unfamiliar supplements to a **registered nutritionist/dietitian.**



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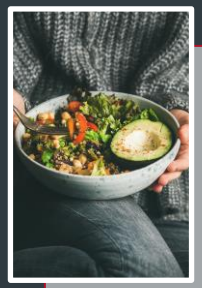

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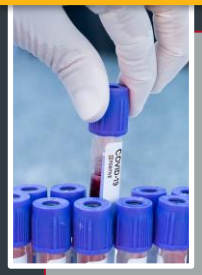


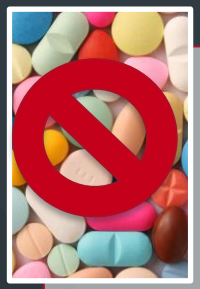
Survivors of certain cancers are at risk for vitamin deficiencies based on their cancer treatment. **Deficiencies should be assessed and repleted as needed.**

Dietary Sources

- Obtain nutrients from foods rather than supplements
- Supplement use should not replace healthy eating habits
- Follow USDA dietary guidelines as able

USDA = US Department of Agriculture
NCCN Guidelines – Survivorship. // MyPlate.gov.

NCCN
Survivorship Guidelines



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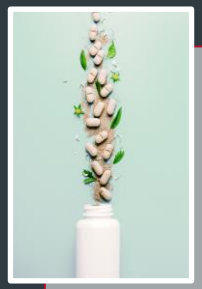

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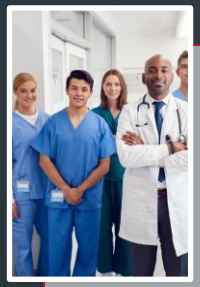

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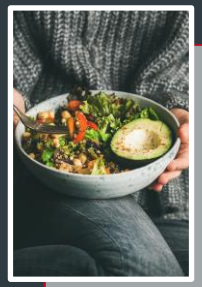

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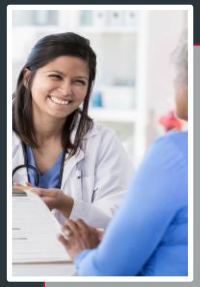

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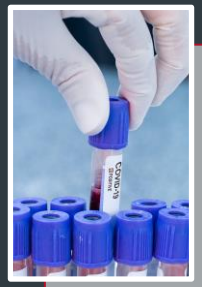
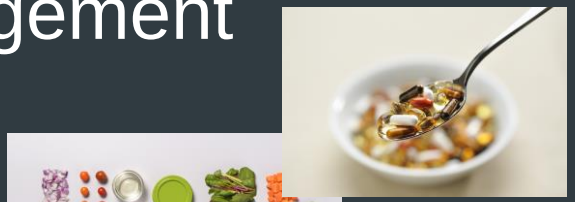


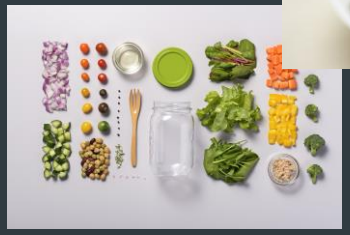
Survivors of certain cancers are at risk for vitamin deficiencies based on their cancer treatment. **Deficiencies should be assessed and repleted as needed.**

Registered Dietitians

- Important member of the healthcare team

- Can be especially useful in complicated cases related to
  - Malnutrition & weight management
  - Vitamin deficiencies
  - Supplement usage





NCCN Guidelines – Survivorship.
cancer.gov.

NCCN
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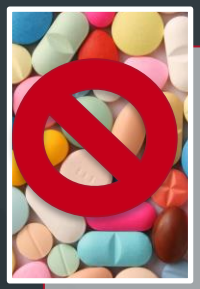

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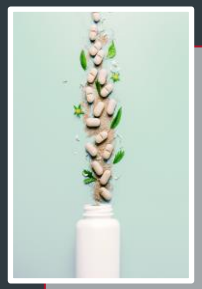

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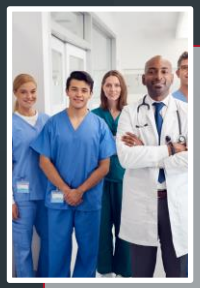

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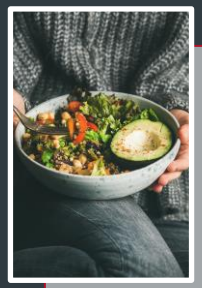

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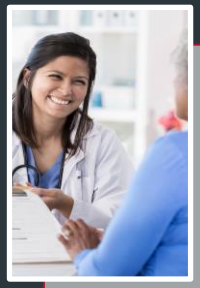

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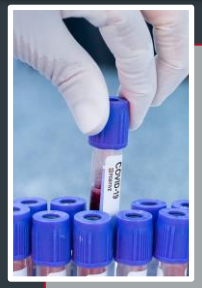

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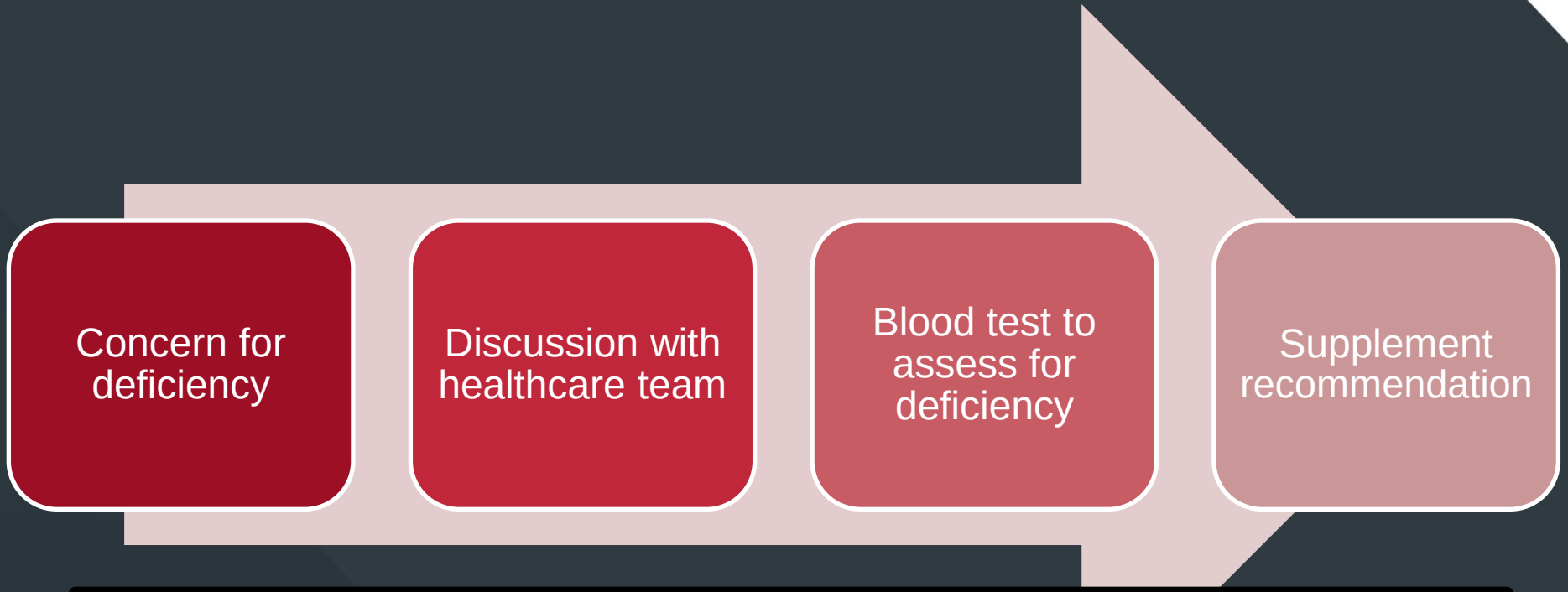
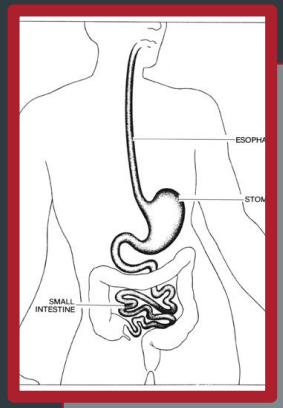
Monitoring for Deficiencies



Supplement should be taken at an **appropriate dose** for the **shortest time needed** to resolve the deficiency

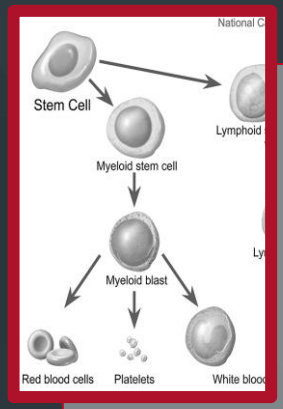
NCCN Guidelines – Survivorship.
cancer.org.

Potential Deficiencies Encountered During Survivorship Care



Gastric

- Vitamin B12
- Iron



After stem cell transplant

- Calcium
- Vitamin D
- Magnesium

NCCN Guidelines – Gastric Cancer.
Transplantation and Cellular Therapy 2021;27:467-73.
cancer.gov.

The Team Supporting the Survivor

How Pharmacists Can Help

- Assess for drug interactions, therapeutic effectiveness, safety concerns
- Ensure accuracy of medication lists
- Educate patients about supplements & CAM
- Help identify patients who might be at risk for deficiencies
- Assist in product selection

Pharmacy 2020;8:170.

Other Resources

National Institute of Health

- Office of Dietary Supplements: ods.od.nih.gov
- National Center for Complementary and Integrative Health: nccih.nih.gov

NCCN Guidelines – Survivorship Care for Healthy Living

- Website: nccn.org/patients

Memorial Sloan Kettering Cancer Center (MSKCC) Integrative Medicine services

- Website: mskcc.org (search “integrative medicine”)
- Smartphone app: “About Herbs”

Natural Medicines

- Website: naturalmedicines.therapeuticresearch.com
- Available by subscription only

Summary & Recommendations

Supplement use is **not recommended for most survivors**, except in instances of documented deficiencies, inadequate diet, or comorbid indications.

Supplement use should not replace healthy eating habits. **Obtain nutrients from one's diet if possible.**

If supplement use is being considered, **risk/benefit assessment & interaction analysis** should be conducted.

Patients are encouraged to talk to their healthcare team before taking any supplements.

Complementary and Integrative Pharmacotherapy for Survivors of Cancer

Identifying the role of supplements, vitamins, and herbal products

Emily Kathol, PharmD, BCOP

Clinical Pharmacist Practitioner – Ambulatory Oncology Clinics

Nebraska Medicine