Practical Practice Tips for Widely-Used Dietary Supplements

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Speakers

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About CRN

CRN is a trade association of dietary supplement, functional food and nutritional ingredient manufacturers and marketers, who join together to sustain and enhance a climate for our member companies to responsibly develop, manufacture and market dietary supplements, functional foods and their nutritional ingredients.

About CRN

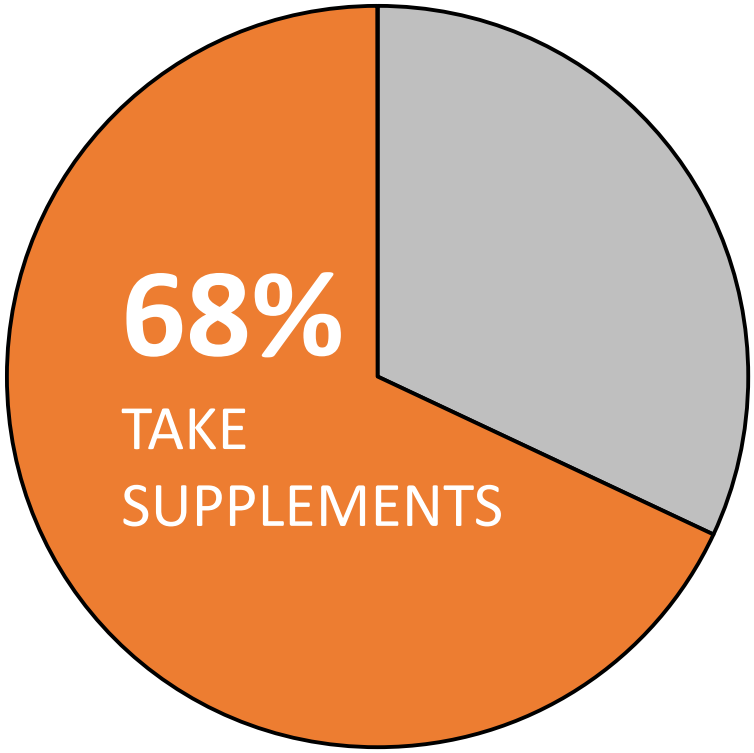
Association	Amount with CRN
Staff	16
Voting Members	105
Manufacturers	54
Suppliers	51
Associate members	49
Annual budget	$5.2 million
Years in existence	41

Also contains: scientific, regulatory, international, media relations and government relations expertise not found anywhere else.

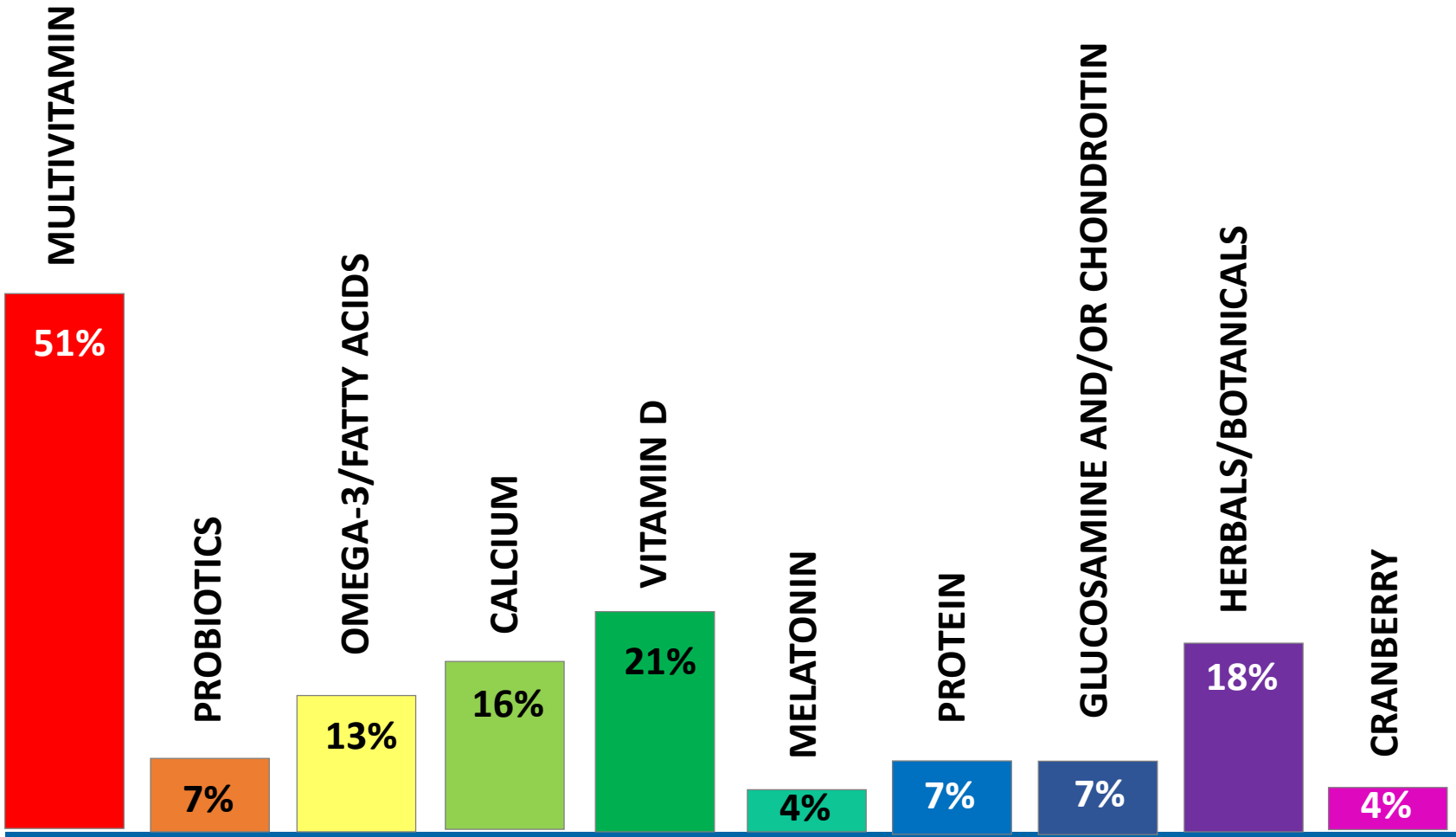
Some of CRN's Members

Who takes dietary supplements?

According to the 2014 CRN Consumer Survey on Dietary Supplements, 68% of all U.S. adults take dietary supplements.

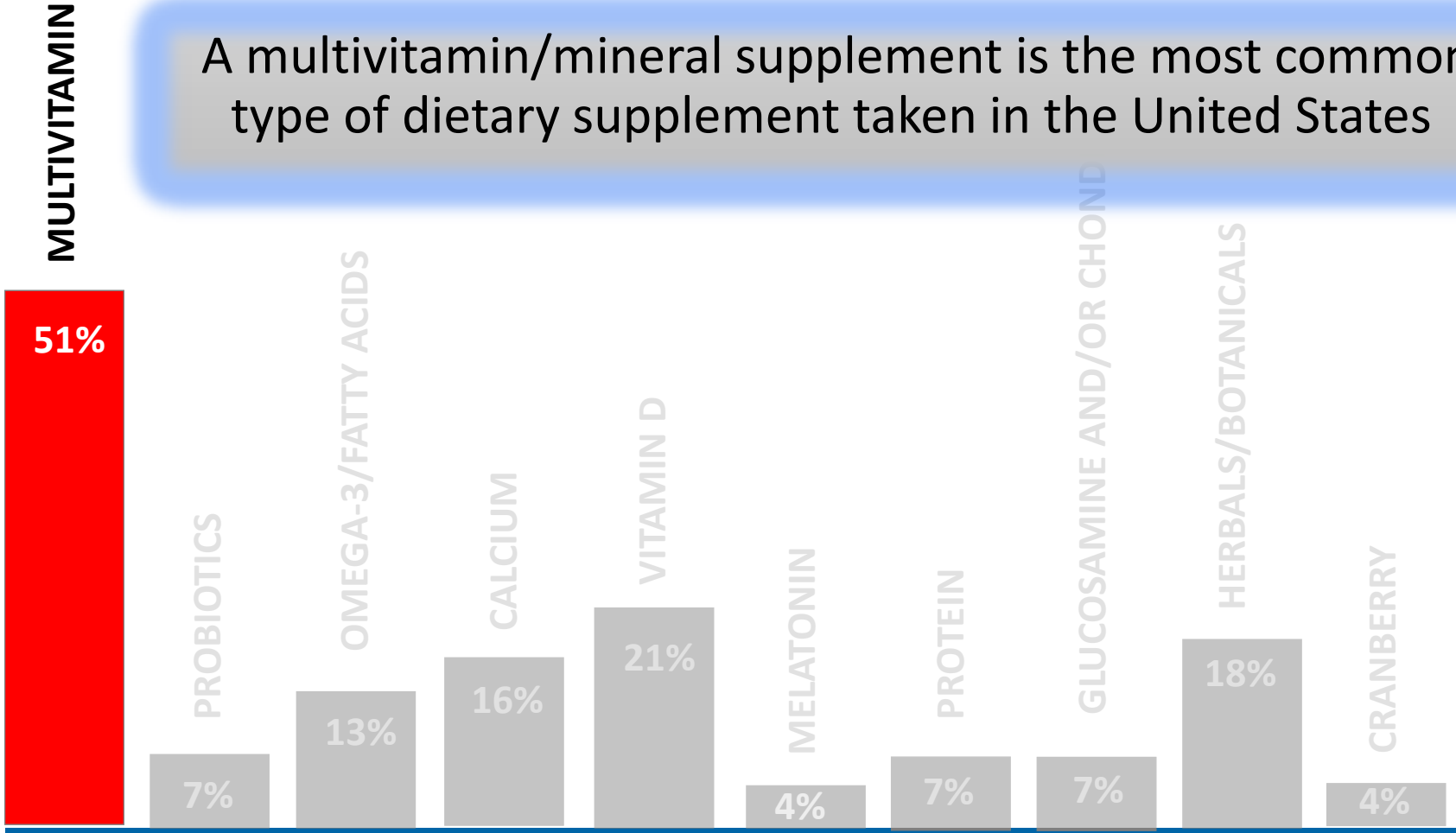


What do they take?



Multivitamin – Who?

A multivitamin/mineral supplement is the most common type of dietary supplement taken in the United States



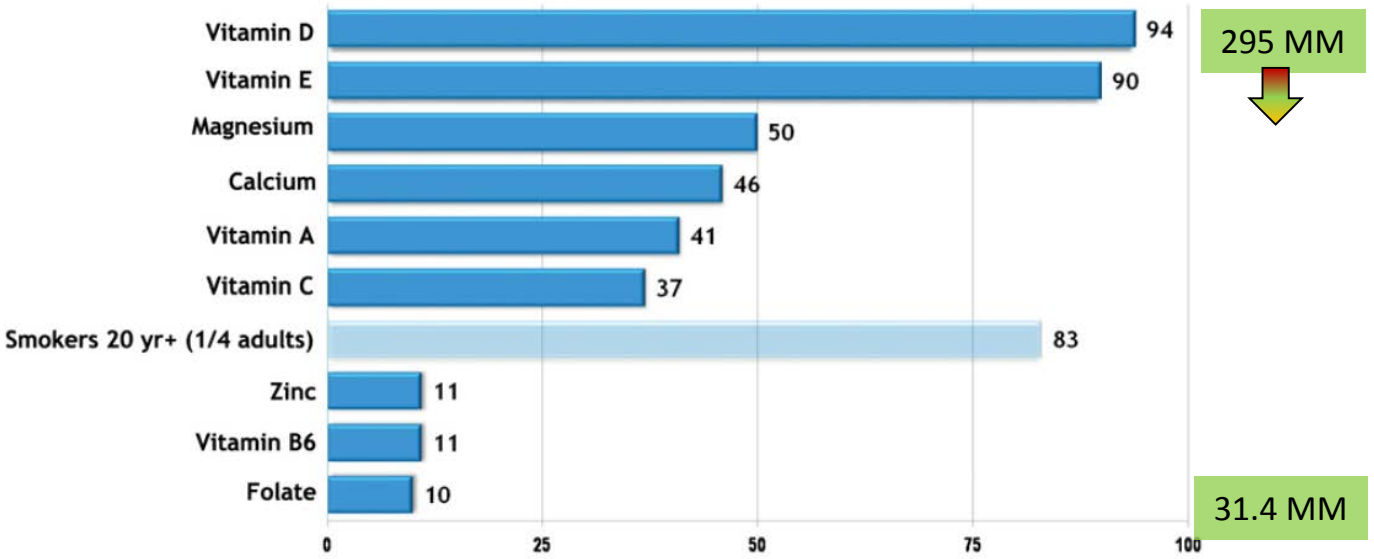
Why take a multivitamin/mineral?

Multivitamin/mineral supplementation helps individuals achieve targeted nutrient intakes

Are there nutrient gaps to fill?

% Americans with Usual Intakes <EAR

NHANES 2005–2008

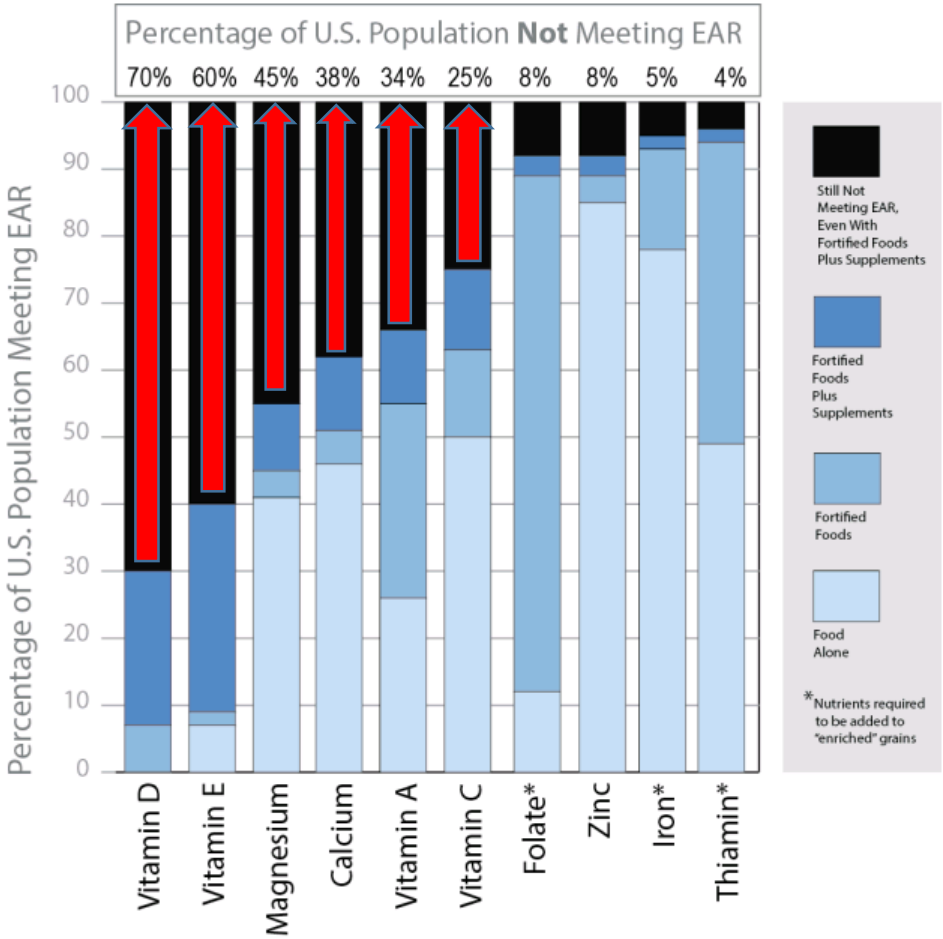


Source: Dwyer TD, et al., *Nutr Rev* 2014. Vol. 72:127–141.

*Data are from What We Eat in America, NHANES 2005–2008
Includes individuals aged ≥1 year, excluding breastfed children and pregnant or lactating females.

Significant portions of the U.S. population do not meet the EAR for key nutrients even when the contribution of fortification and supplementation are considered

EAR estimated to meet the need of 50% of the population



Derived from: Fulgoni, et al. *J Nutr 2011;*141:1847. NHANES: 2003 - 2006

Multivitamin/Mineral for Disease Risk Reduction

Dietary Supplements, including the MVM are not intended treat disease	• However, when a study fails to show that a MVM is the magic bullet for chronic disease, some are ready to throw their vitamins away
Randomized Clinical Trials (RCTs) are considered the gold standard for showing effects of MVM on disease risk reduction	• RCTs have significant limitations when trying to measure the effects of nutrient interventions on chronic disease risk reduction

Limits of RCTs for Nutrition Research

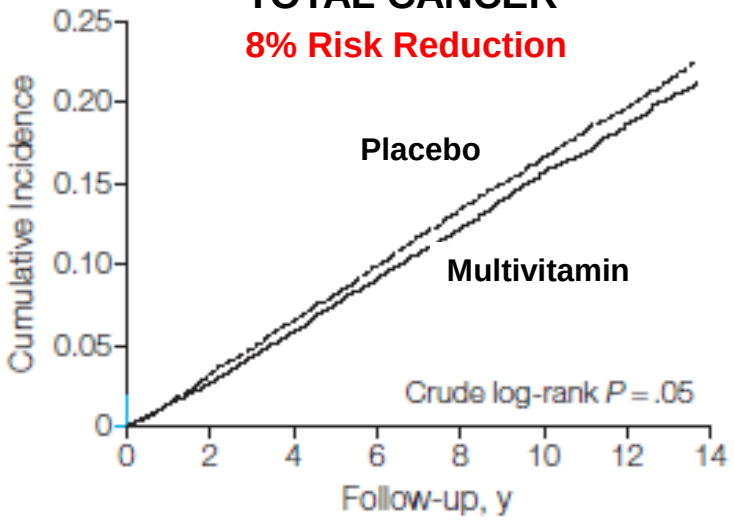
	Drugs	Nutrients
Control Group	Drug-free state	Nutrient free state unethical or impossible
Baseline Drug/Nutrient Status	No baseline status	Nutrient sufficiency at baseline may mask effect
Effect Size	Large (if no effect in 6 - 12 months, no continued funding for drug-approval process)	Modest Aggregate over time Combined with current standard of care, including Rx drugs
Scope of Effect	Single Target	Nutrients impact all tissues and organs

Multivitamins Reduce the Risk of Total Cancer

RCT, n=14,641 men, ≥50 y, 10.7-13.3 y duration

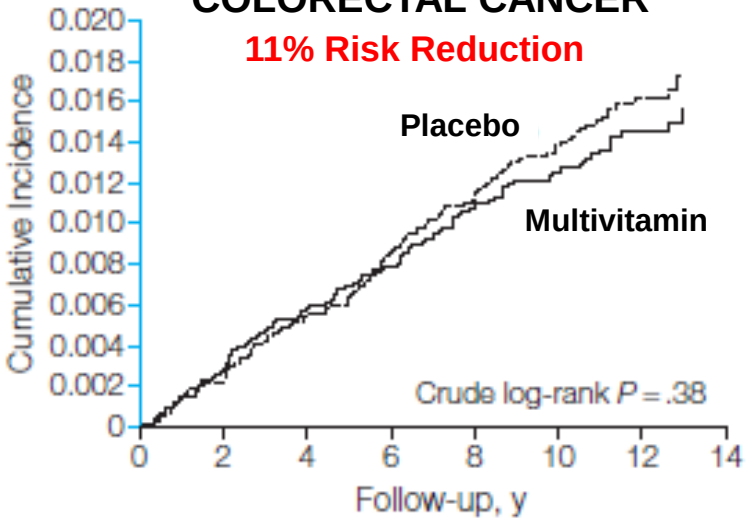
TOTAL CANCER

8% Risk Reduction



COLORECTAL CANCER

11% Risk Reduction

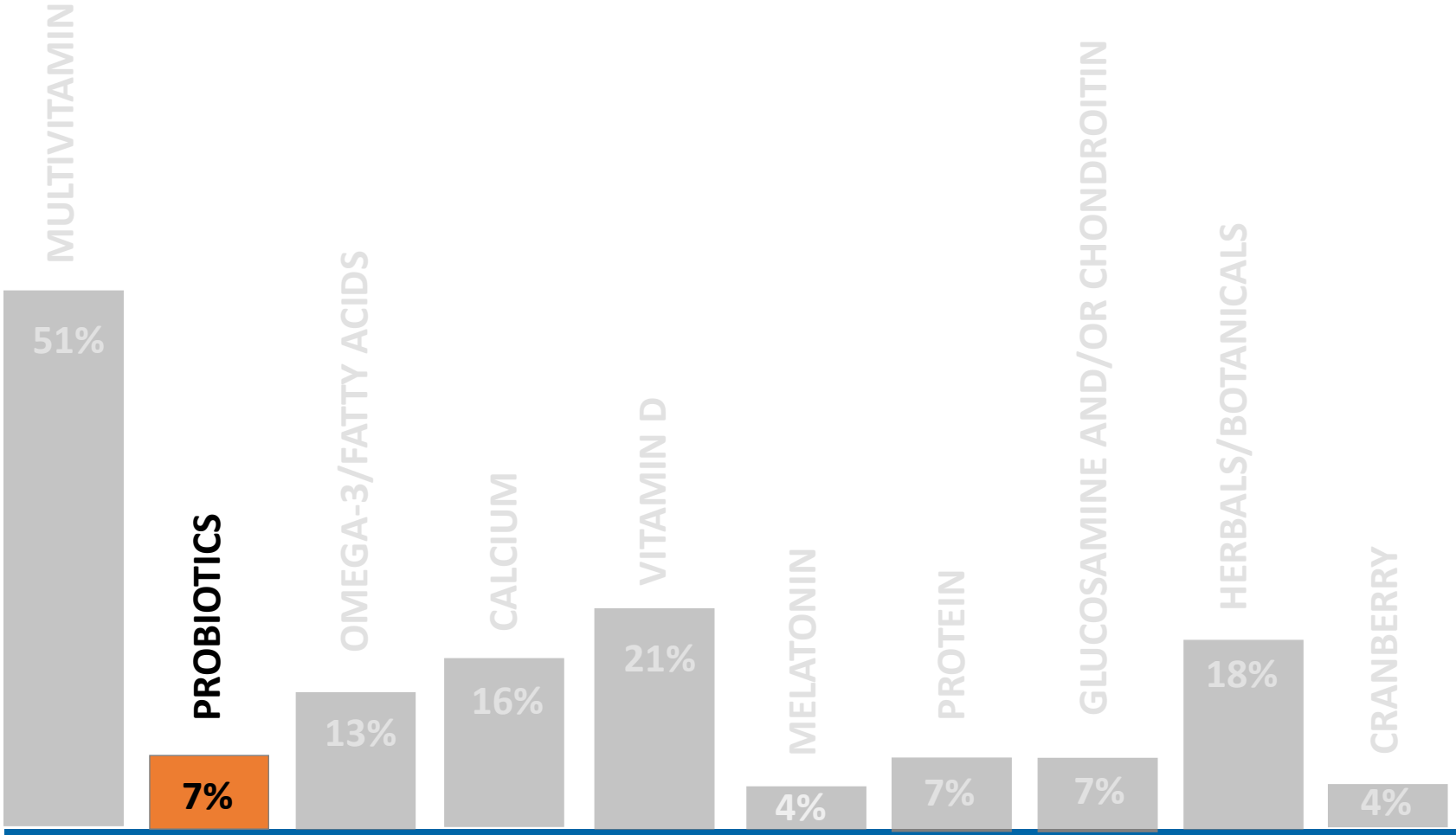


Gaziano et al. *JAMA* 2012

Hundreds of MVMs to choose from

Age/Gender	• Iron – men vs. women • Ca+/Mg+ • Fe+, folic acid, iodine – pregnancy • Adolescents • B12 – elderly
Delivery form	• tablet/capsule • liquid • gummy • powder • compliance
Levels/forms of nutrients	• RDA or less; higher levels • Taking other products - Ca+/Mg+; vitamin D. • Nutrient forms • Other ingredients – herbs, bioactives (Co Q10, lycopene, etc.)

Probiotics – Who?



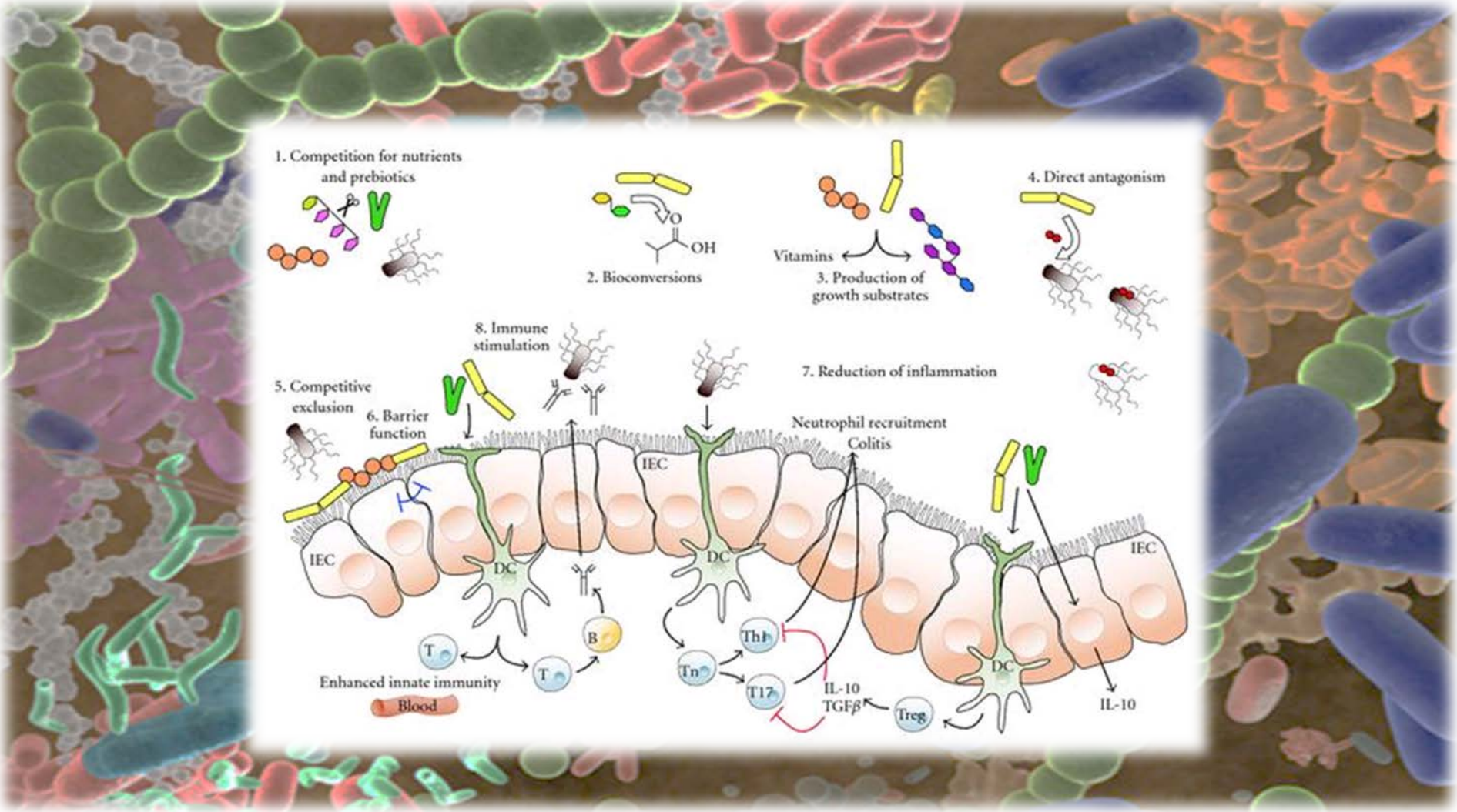
What are probiotics?

"Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host."

FAO/WHO Definition

(ISAPP consensus Oct. 13, 2013)

How do probiotics work?



Why take a probiotic?

- Gastrointestinal
  - Childhood diarrhea/acute
  - Antibiotic-associated/infectious diarrhea
    - Avoid side effects of *H. Pylori* tx
  - Necrotizing enterocolitis
    - Infection and inflammation of the intestines mostly seen in infants
  - *C. difficile* infection
  - Inflammatory Bowel Dz.
    - Ulcerative colitis/Crohn's
  - Preventing pouchitis
    - Inflammation of the intestines that can follow intestinal surgery
- Immune Health
  - Atopic eczema
  - Childhood respiratory illness
    - Some evidence for other infections such as ear infections, strep throat, and colds
  - Vaginitis
- Emerging Science
  - Cognitive
  - Cardiovascular
  - Irritable Bowel Syndrome
  - Weight Management

Choosing a probiotic

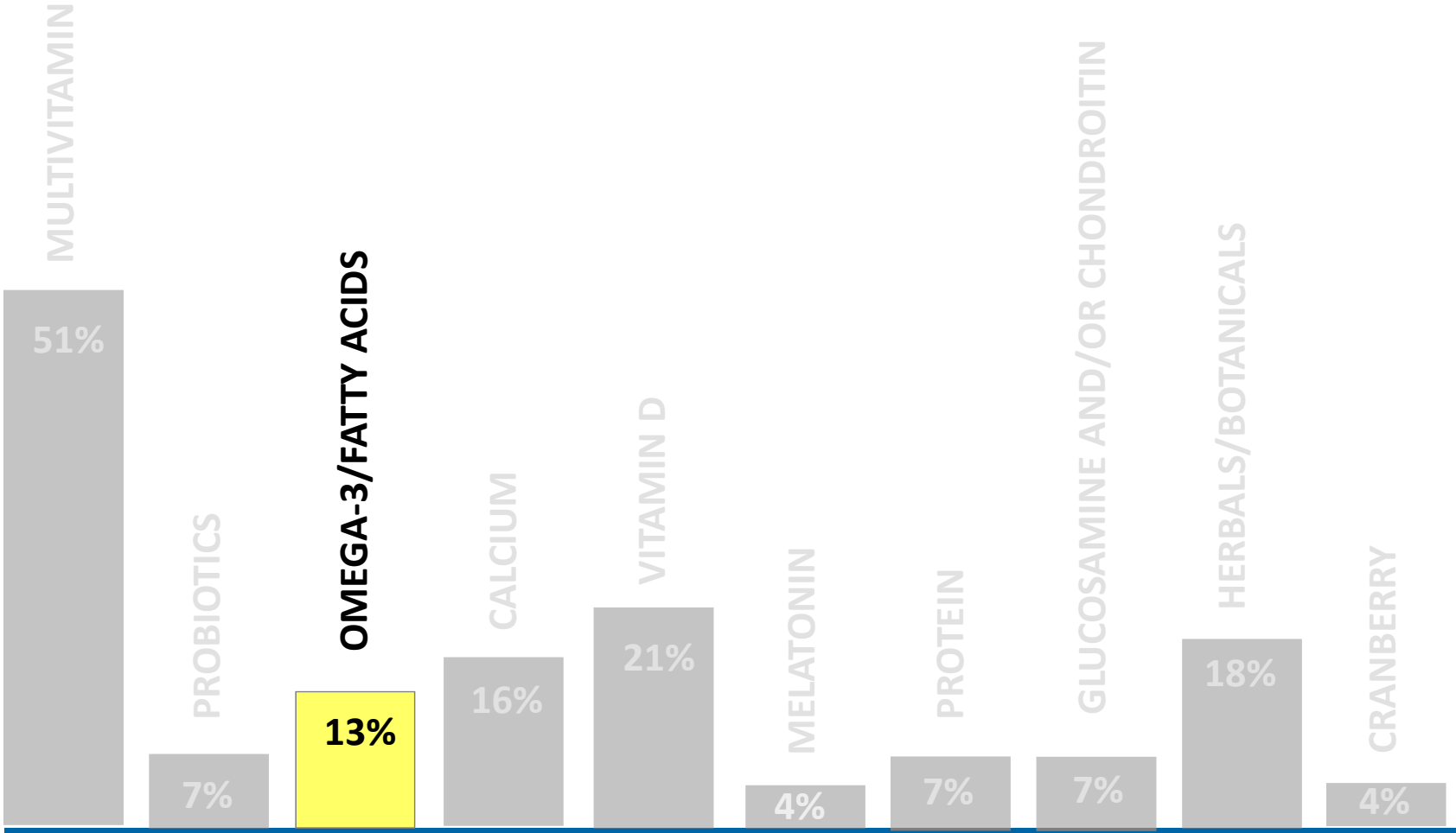
- It cannot be assumed that research published on one strain of probiotic applies to another strain, even of the same species.
  - However, strain attributes do overlap
- For general digestive health
  - Lactic acid producers
    - Lactobacillus acidophilus
    - Bifidobacterium lactis
- Probiotics have a strong safety profile
  - Infrequent mild GI side effects, gas
  - Risk of serious adverse effect higher in immune compromised or critically ill individuals

Meet the Bacteria

These microorganisms have been shown to boost health in scientific studies:

Strain	Benefits	Products
Bifidobacterium animalis DN-173 010 (marketing name: Bifidis Regularis)	Gut health and faster digestion	Dannon Activia yogurt
Bifidobacterium infantis 35624	Alleviates symptoms of irritable bowel syndrome	Procter & Gamble's Align supplement
Bifidobacterium lactis Bb-12	Helps immune system and digestive health	Yo-Plus yogurt, Nestle Good Start infant formula
Lactobacillus casei Shirota	Helps immune system and digestive health	Yakult fermented dairy drink
Lactobacillus casei DN-114 001 (marketing name: L. casei Immunitas)	Helps immune system; lessens duration of colds and flus in older people	Dannon's DanActive dairy drink
Lactobacillus rhamnosus GR-1 in combination with **Lactobacillus reuteri**	Improved vaginal health; helps eradicate vaginal infections	RepHresh Pro-B and Fem-Dophilus dietary supplements
Lactobacillus reuteri 55730	Helps treat colic,gingivitis, antibiotic-associated diarrhea	BioGaia tablets, drops and lozenges
Saccharomyces boulardii yeast	Helps prevent and treat antibiotic-associated diarrhea	Florastor dietary supplement

Omega-3/Fatty Acids – Who?

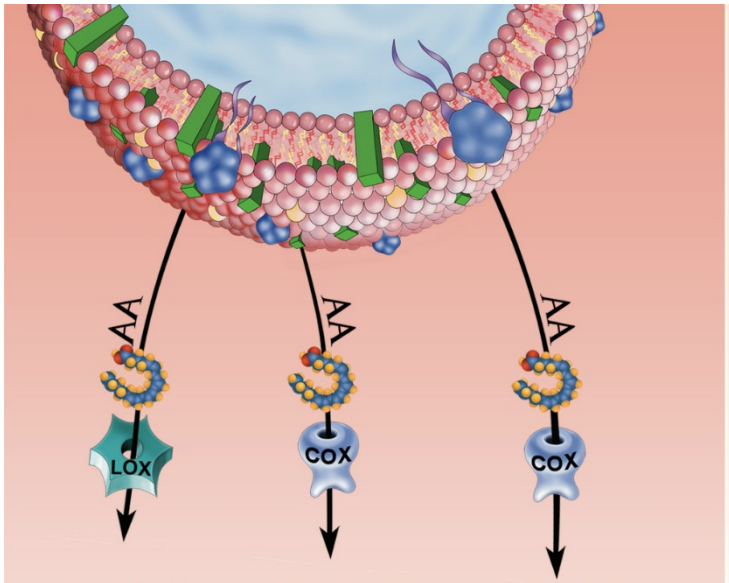


Dietary fatty acids

- **Omega-3s** (essential fat)
  - Essential for human development
  - Must be consumed through diet
  - Component of cell membranes
  - Fish-source proven most bioavailable
- **Omega-6s** (essential fat)
  - Good in moderation only
  - Excess increases inflammation
  - Mostly from processed vegetable oils
  - GLA is the beneficial Omega-6
- **Omega-9**
  - Important, not an essential fat
  - Olive oil is a good source

- **Saturated Fat** (non-essential)
  - Animal fat, solid at room temp
  - Increases disease risk
- ***Trans* fats** (non-essential)
  - "partially hydrogenated"
  - New to nature
  - Associated with disease risk

Omega-6



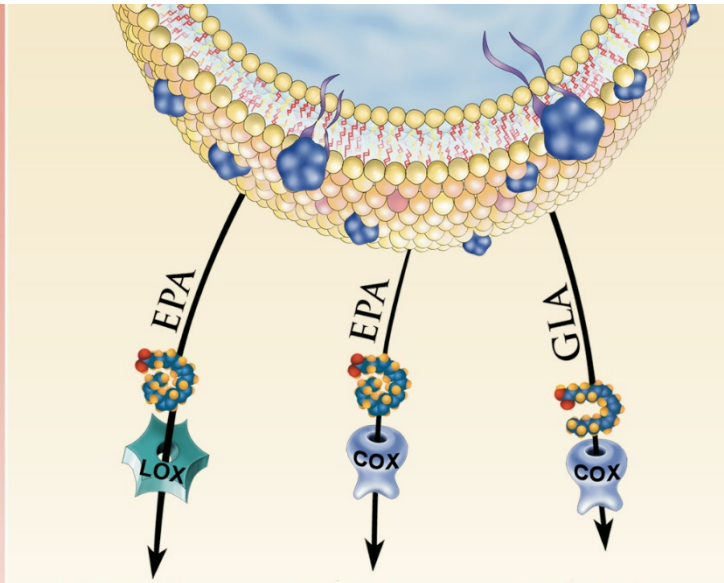
Leukotrienes-4 series
- Promotes inflammation
- Constricts airways
- Prolongs duration of inflammation

Thromboxane-A2
- Constricts blood vessels
- Constricts airways
- Increases blood clotting
- Reduces circulation

Prostaglandin-E2
- Increases sensitivity to pain
- Increases swelling
- Induces fever
- Constricts blood vessels

PRO-INFLAMMATORY

Omega-3



Leukotriene-5 series
- Relaxes blood vessels
- Increases circulation
- Relaxes airways
- Promotes anti-inflammatory response

Prostaglandin-E3
- Improves circulation
- Decreases sensitivity to pain
- Relaxes blood vessels
- Promotes anti-inflammatory response

Prostaglandin-E1
- Relaxes muscles spasms
- Reduces blood clotting
- Increases protective stomach secretions
- Improves circulation

ANTI-INFLAMMATORY

Omega-3 supplements

Fish Oil
- Fish Body Oil – 18% EPA: 12% DHA
- Concentrated Fish Body Oil – Variable concentrations and ratios EPA:DHA
- Fish Liver Oil – contains other fat soluble vitamins A & D

Krill Oil
- Phospholipid structure
- Emerging science

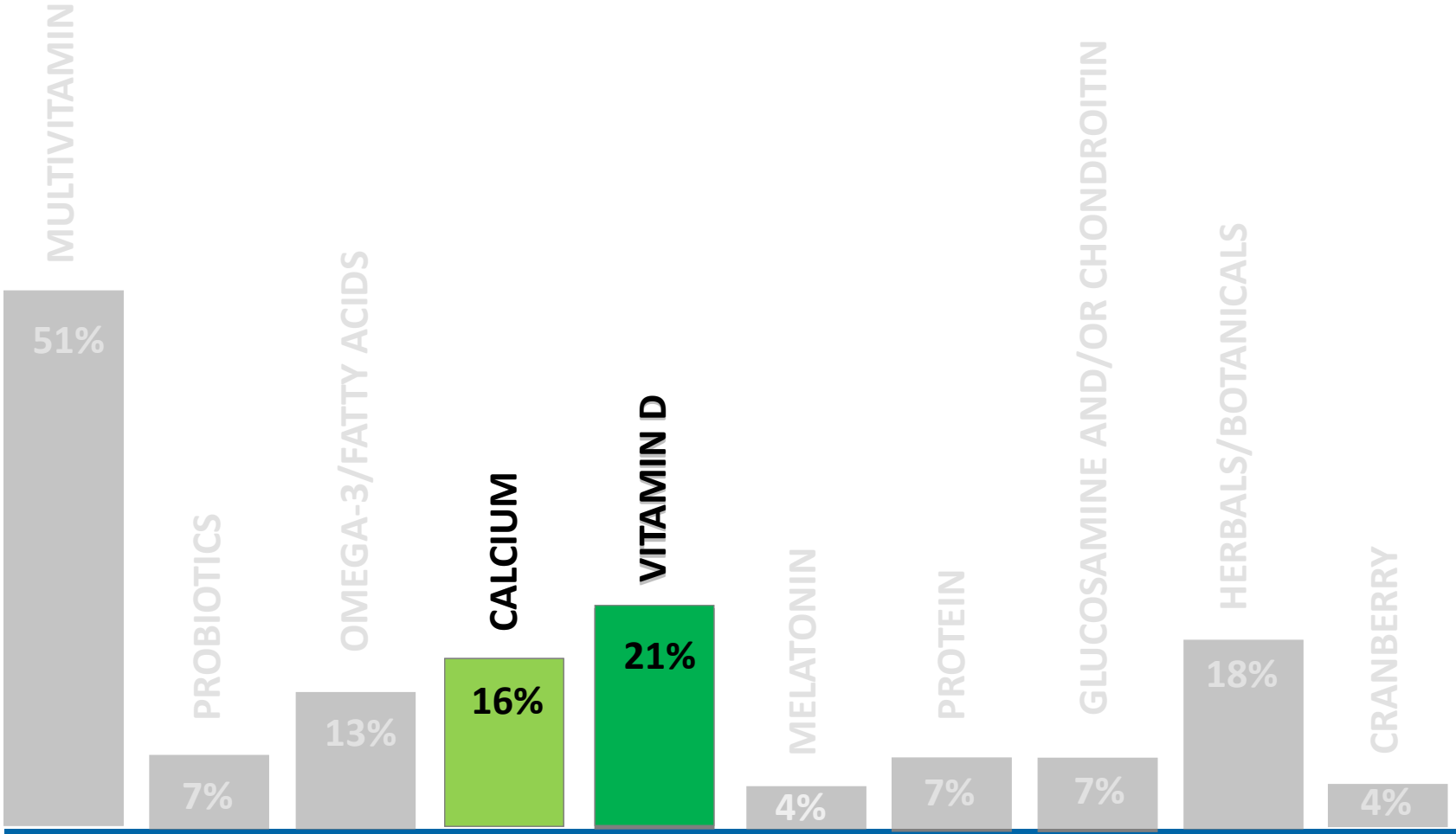
Vegetarian EPA/DHA
- Algae-based
- No fishy taste
- Vegetarian

Vegetarian omega-3
- 18 carbon Alpha-linolenic Acid (ALA)
- Needs to be converted to EPA:DHA

Omega-3 Recommended Intake

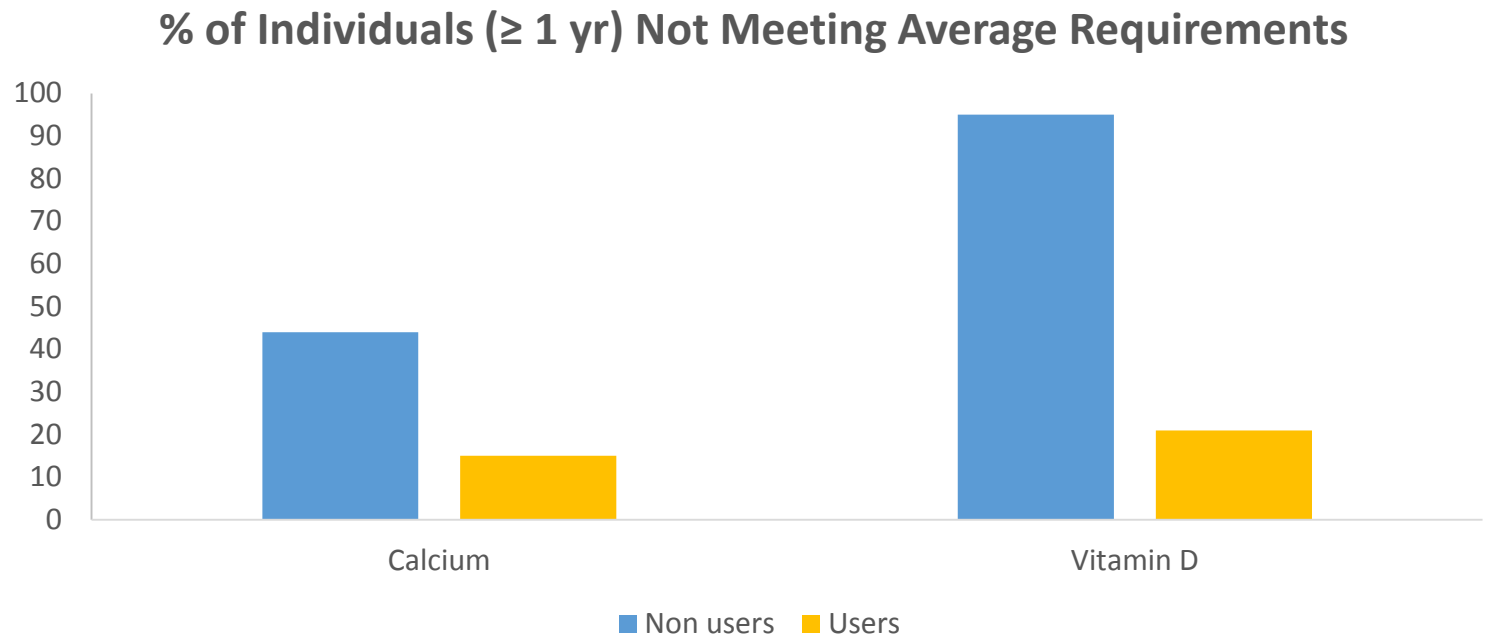
REFERENCE	DAILY DOSAGE of EPA & DHA
The ADA and Dieticians of Canada	500 mg/day EPA + DHA 2 servings of fatty fish/week (1/4 can of sardines/week)
ISSFAL	500 mg/day EPA + DHA
UK's Scientific Advisory Committee on Nutrition	450 mg/day EPA + DHA
Australia and New Zealand National Health and Medical Research Council	610 mg/day EPA + DHA 430 mg/day DPA
World Health Organization	200 - 700 mg/day EPA + DHA 1-2 servings of fish per week (1/4 can of sardines/week)
American Heart Association	500 - 1000 mg/day
British Nutrition Foundation Task Force	1000 - 1500 mg/day
UK Department of Health	200 mg/day
Institutes of Medicine Dietary Reference Intakes	110 - 160 mg/day (based on 10% of AI for ALA in 2002)
STUDIES	
1. Brownawell AM, Harris WS, Hibbelin JR	500 mg/d of EPA + DHA
2. Gebauer, Pstoa, Harris, Kris-Etherton	500 mg/d of EPA + DHA
3. Harris WS, Kris-Etherton PM	400 - 500 mg/d of EPA + DHA
4. Pepping. Am J Health-System Pharmacy	2 - 4g fish oil caps/day
5. Simopoulous AP, Leaf A, Salem N Jr	Minimum of 500mg of EPA + DHA/day
6. Kris-Etherton PM, Grieger JA, Etherton TD	Highly recommend establishing EPA + DHA DRI's above present 100mg

Calcium & Vitamin D – Who?



Calcium & Vitamin D – Why?

- Americans are falling short of these nutrients
- Supplements help to fill the gaps



Calcium & Vitamin D – Why?

- Calcium is important for strong bones and may reduce the risk of osteoporosis
- Vitamin D helps the body absorb calcium
- Vitamin D has other roles in the body, including:
  - Cell growth modulation
  - Neuromuscular function
  - Immune function
  - Anti-inflammation

Calcium – How Much & When?

- Amount depends on age, gender and dietary intake
- Absorption is best when consuming ≤500 mg at one time

IOM Recommended Dietary Allowances (mg)		
Age	Males	Females
19-30 yr	1,000	1,000
31-50 yr	1,000	1,000
51-70 yr	1,000	1,200
>70 yr	1,200	1,200

Vitamin D – How Much & When?

- Amount depends on age, sun exposure, and dietary intake

IOM Recommended Dietary Allowances (mcg) [IU]		
Age	Males	Females
19-70 yr	15 [600]	15 [600]
>70 yr	20 [800]	20 [800]

- National Osteoporosis Foundation:
  - 400-800 IU (<50 yr); 800-1000 IU (older adults)
- North American Menopause Society: 700-800 IU in women at risk for deficiency due to low sun

Vitamin D – How Much & When?

Sun exposure

- Vitamin D synthesis can be affected by season, time of day, length of day, cloud cover, smog, skin melanin content, and sunscreen

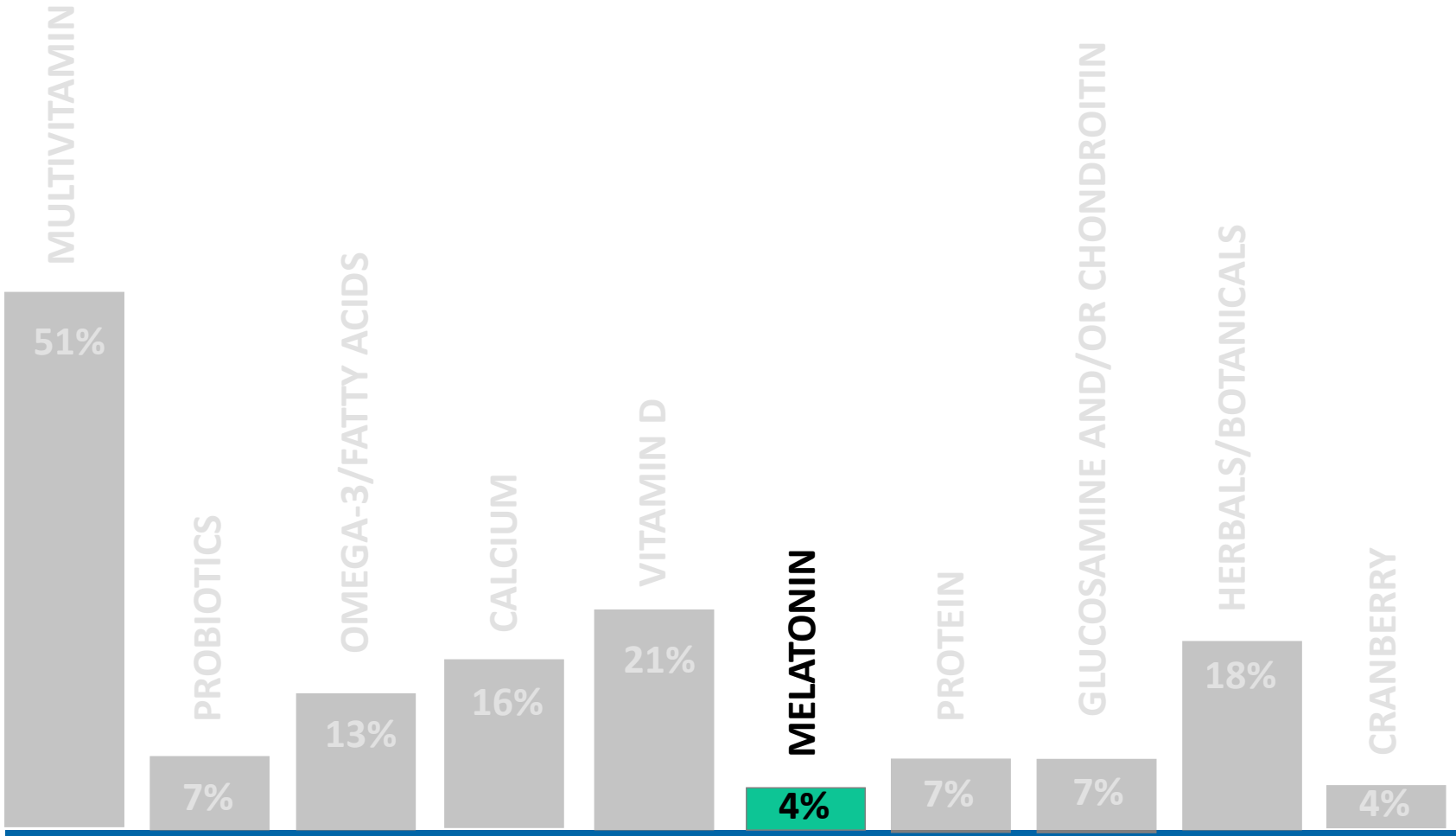
Food sources

- Few foods naturally contain vitamin D
- Some foods are fortified with vitamin D (e.g., milk)

Dietary supplements

- Vitamin D_2 (ergocalciferol) and D_3 (cholecalciferol) are available

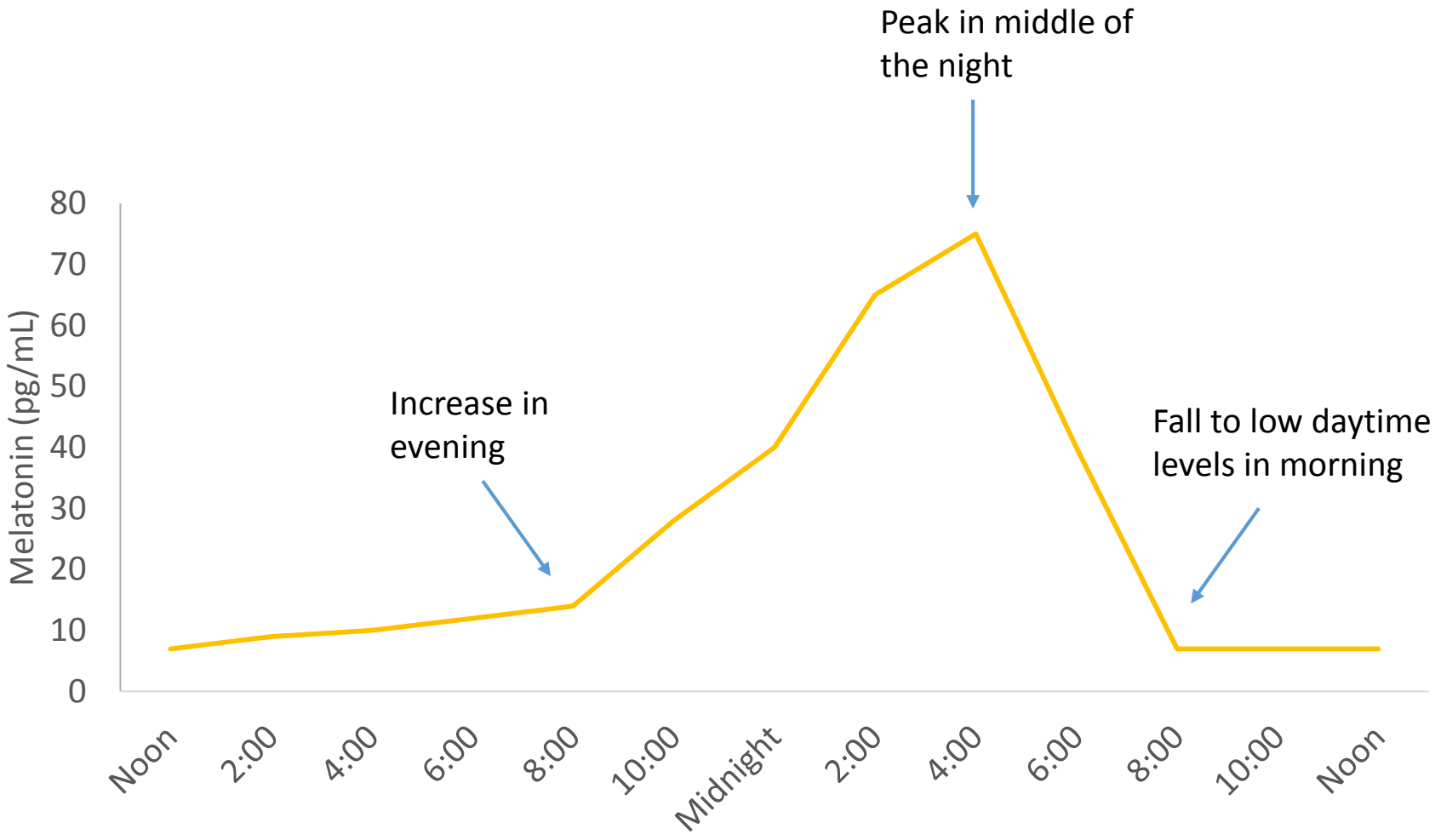
Melatonin – Who?



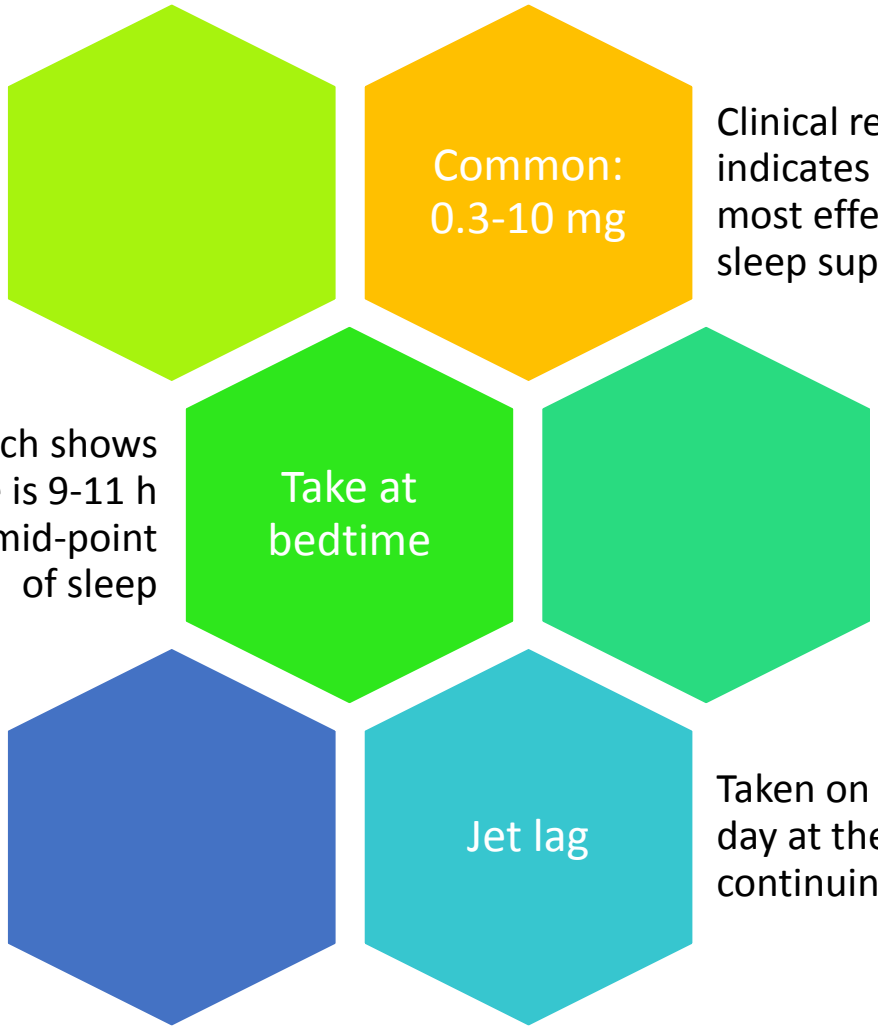
Melatonin – Why?

- Hormone produced by the pineal gland
- Involved in circadian rhythm
  - Production suppressed by bright light and increased in darkness
- Levels decline with age
- Used for sleep support and jet lag
- Other therapeutic uses

Endogenous Melatonin Levels



Melatonin – How Much & When?

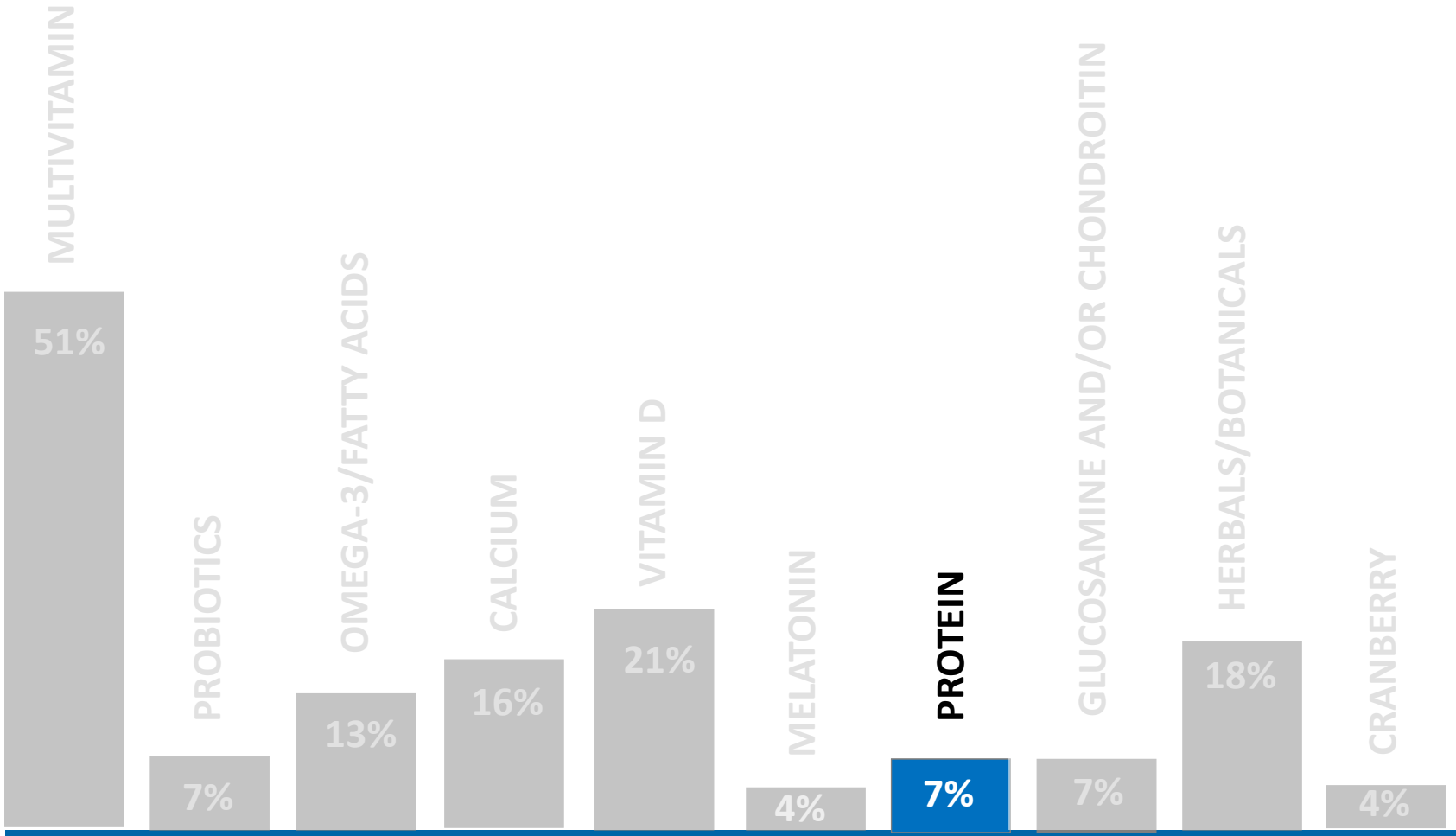


Clinical research indicates 0.3-3 mg most effective for sleep support

Some research shows optimal time is 9-11 h before the mid-point of sleep

Taken on the arrival day at the destination, continuing for 2-5 days

Protein – Who?


MULTIVITAMIN
51%
PROBIOTICS
7%
OMEGA-3/FATTY ACIDS
13%
CALCIUM
16%
VITAMIN D
21%
MELATONIN
4%
PROTEIN
7%
GLUCOSAMINE AND/OR CHONDROITIN
7%
HERBALS/BOTANICALS
18%
CRANBERRY
4%

Protein – Why?

Sports Nutrition

Weight Management

Healthy Aging

Protein for Healthy Aging

- Protein supplements can help preserve skeletal muscle mass in the elderly
- Research suggests that equally distributing protein intake at each meal maximally stimulates muscle synthesis
- Supplemental leucine may also increase muscle protein synthesis

Protein – Common Forms

Whey

- Concentrate
- Isolate
- Hydrolysate

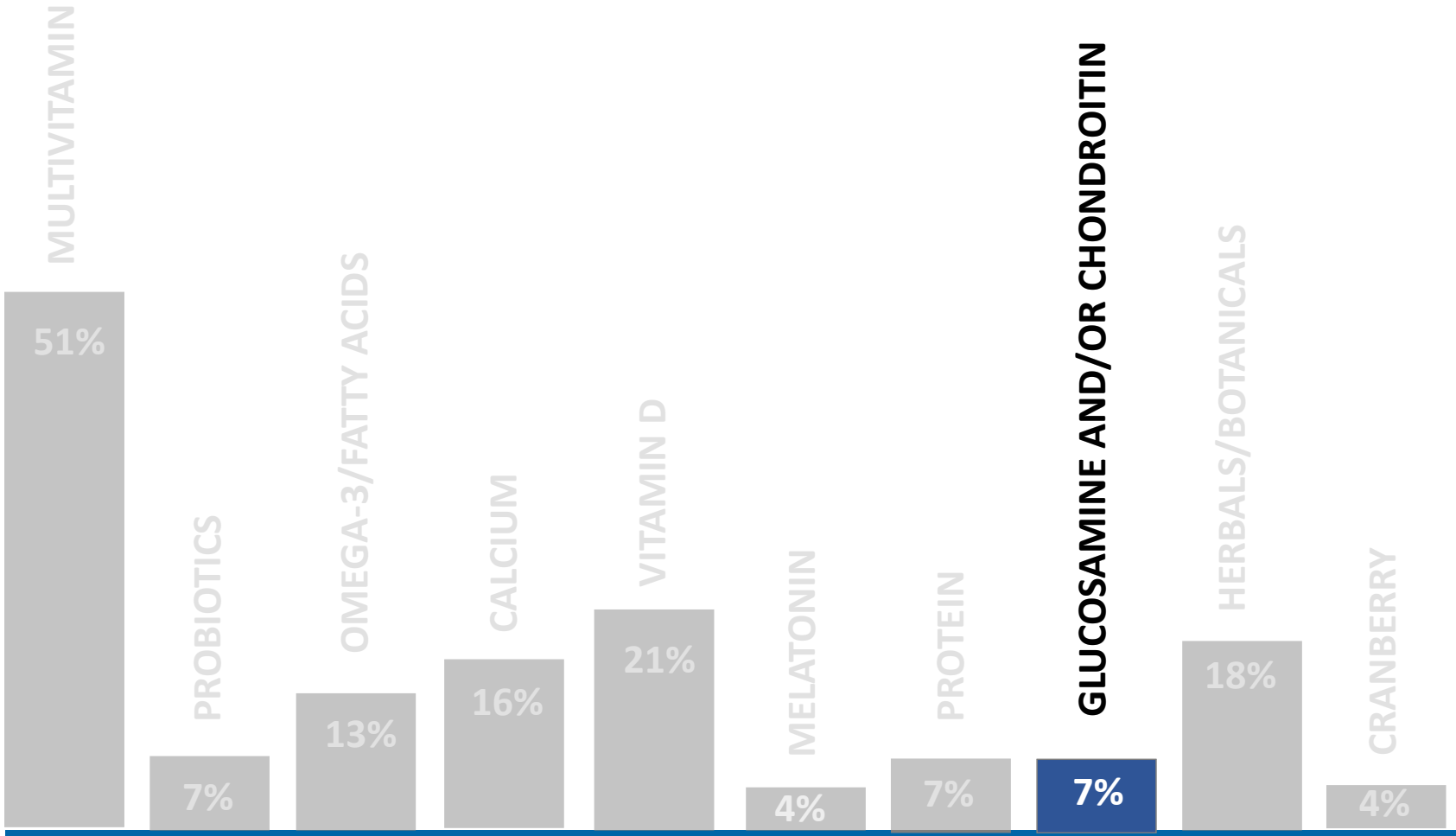
Casein

- Also from dairy

Vegan

- Soy
- Rice
- Pea

Glucosamine and/or Chondroitin – Who?



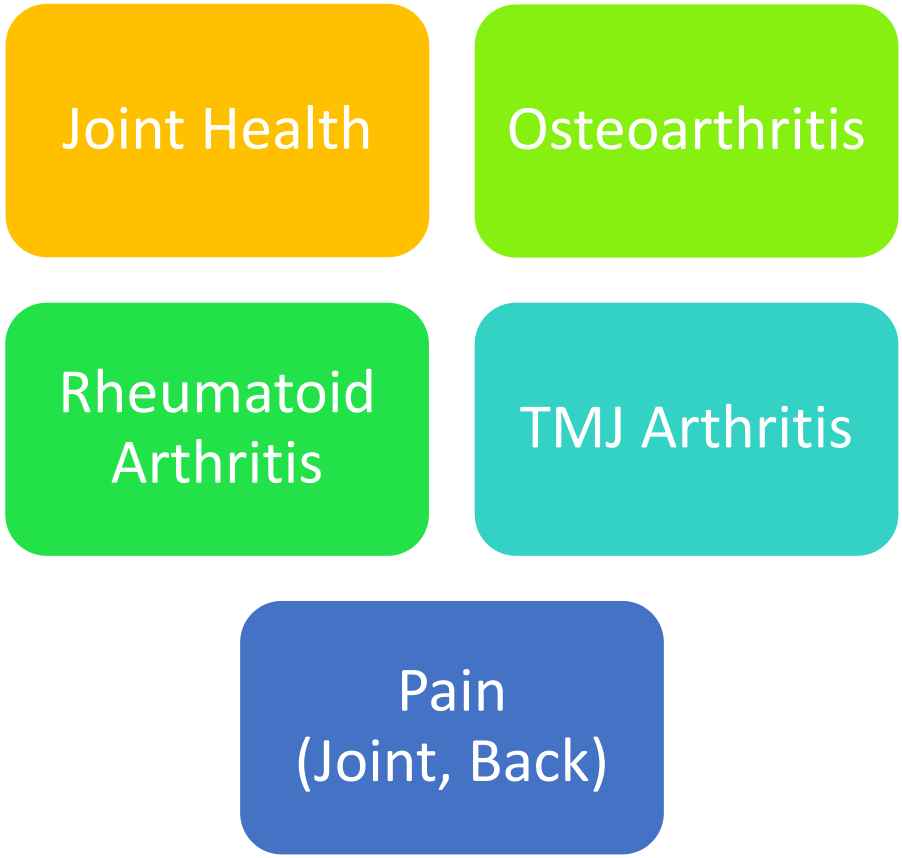
Glucosamine

- Aka chitosamine
- Amino sugar (2-amino-2-deoxyglucose…)
- Natural source – shellfish, “vegetarian”
- Synthetic
- Available forms
  - Glucosamine hydrochloride (G HCl)
  - N-acetyl-glucosamine (NAG)
  - Glucosamine sulfate (G SO_4)

Chondroitin

- Complex carbohydrate (chondroitin-4-…)
- Natural source – cartilage (shark/bovine)
- Synthetic
- Available forms
  - Chondroitin sulfate (Ch SO_4)

Glucosamine & Chondroitin – Why?



Glucosamine & Chondroitin – Things to Consider

- Side effects – mild GI – G & C
- Allergy - pre-existing “shellfish” allergy – G
- BSE – C
- Drug interactions
  - Warfarin/Coumadin/Blood thinners - G & C
  - Antimitotic chemotherapy agents - G

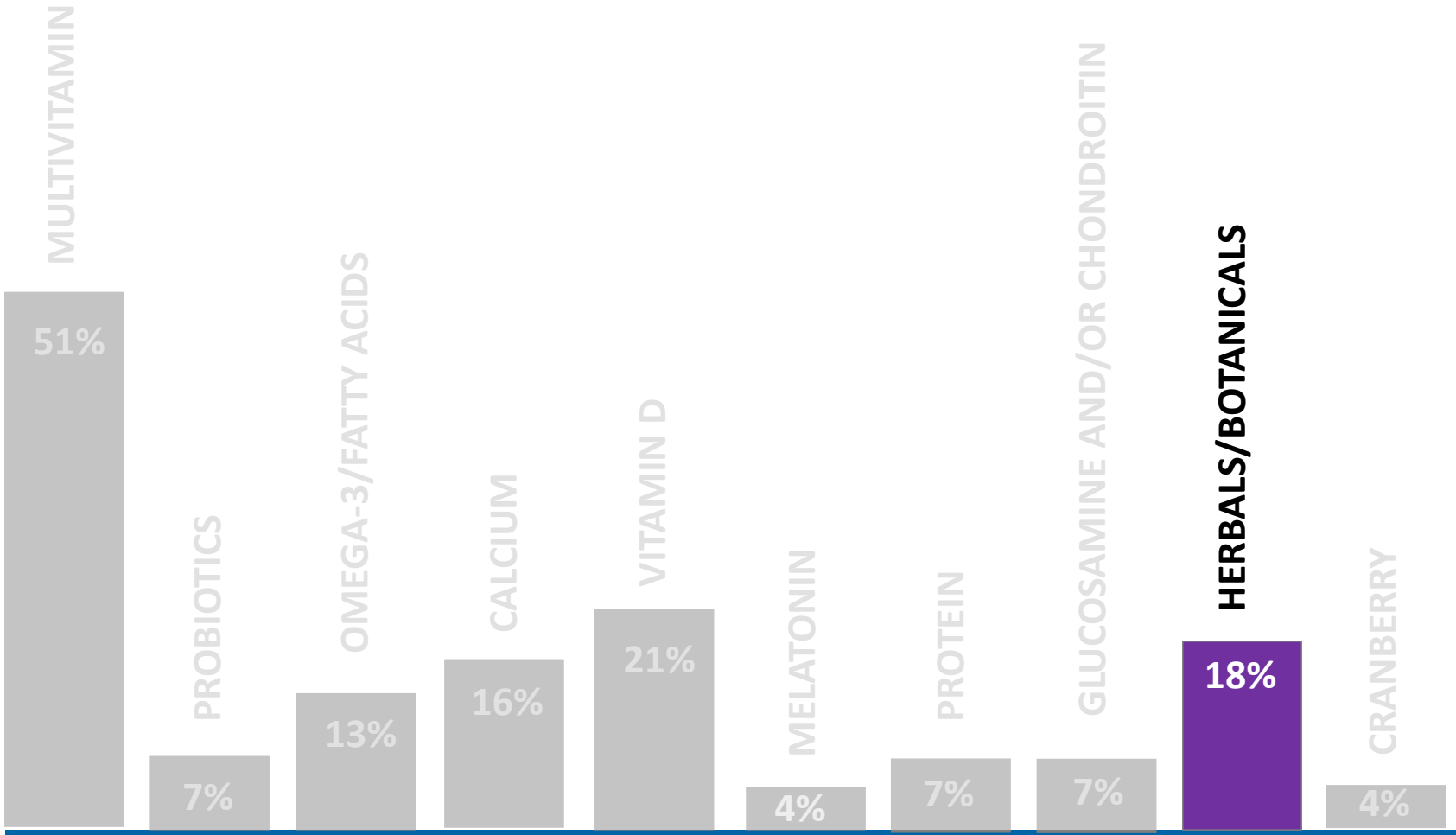
Glucosamine & Chondroitin – Evidence

- Evidence supports the role of glucosamine and chondroitin for:
  - Knee function/pain (G, G+C)
  - TMJ function/pain (G)
  - Hand osteoarthritis function/pain (C)
- Less evidence available for rheumatoid arthritis pain
- Inconsistencies in evidence
  - Study design; G HCl vs G SO_4; dose and dosing

Glucosamine & Chondroitin – How Much?

- Glucosamine Hydrochloride: 1500 mg (bolus or split t.i.d.)
- Glucosamine Sulfate: 1500 mg (bolus or split t.i.d.)
- Chondroitin Sulfate: Range of 200-400 mg b.i.d or t.i.d. (total: 400-1200 mg/day).
  - RCTs use 1200 mg (bolus or split t.i.d.)

Herbals/Botanicals – Who?



Botanicals / Herbals

Top 10 in Mainstream & Natural Channels (2013)

1. Horehound	1. Turmeric
2. Yohimbe	2. Grass (Wheat/Barley)
3. Cranberry	3. Flax Seed/Oil
4. Black Cohosh	4. Aloe
5. Senna	5. Spirulina
6. Cinnamon	6. Milk Thistle
7. Flax Seed/Oil	7. Elderberry
8. Echinacea	8. Echinacea
9. Valerian	9. Maca
10. Saw Palmetto	10. Saw Palmetto

Botanicals / Herbals

Others in Mainstream & Natural Channels (2013)

Ashwagandah
Bromelain
Cat's Claw
Chamomile
Chia
Evening Primrose
Garlic
Ginger
Ginkgo
Goldenseal
Green Coffee
Green Tea
Horny Goat Weed
Horsetail
Kava kava
Peppermint
Red Clover
Red Yeast Rice
St. John's Wort
Stevia

Botanicals / Herbals

- Botanical - having to do with plants / plant parts.
- Herb – plant used in cooking, tea and medicinal purposes.
- Herbal - having to do with medicinal/edible plants.
- Referred by Latin binomial, i.e., *Genus species*
  - Black Cohosh = *Actaea racemosa*
  - Ginger = *Zingiber officianale*
  - Kava kava = *Piper methysticum*

Botanicals / Herbals – Which Parts?

- Whole plant
- Fruit/Berries
- Flowers
- Bark
- Leaves
- Stems/Twigs
- Roots/Rhizomes/Tubers

Botanicals / Herbals – Dosage Forms

- Fresh
- Dried
- Extract (Specific solvent to remove targeted constituent)
  - Liquid or dried (evaporated liquid)
- Tincture (Alcohol/water solvent)
- Decoction (Boiled & simmered for specified time in water)
- Tea (Infusion steeped with addition of boiling water)
- Powders, Capsules, Tablets

Botanicals / Herbals - Quality

- Standardization
  - Identify / Quantify
  - Plant part / Labeling
- Batch-to-batch consistency; QC - Quality
  - Marker Compound(s)
- Batch-to-batch consistency; QC – Biological activity
  - Biomarker Compound(s)
- Quality
  - Brand recognition
  - Brand longevity
  - Third party certification/verification

Botanicals / Herbals - Quality

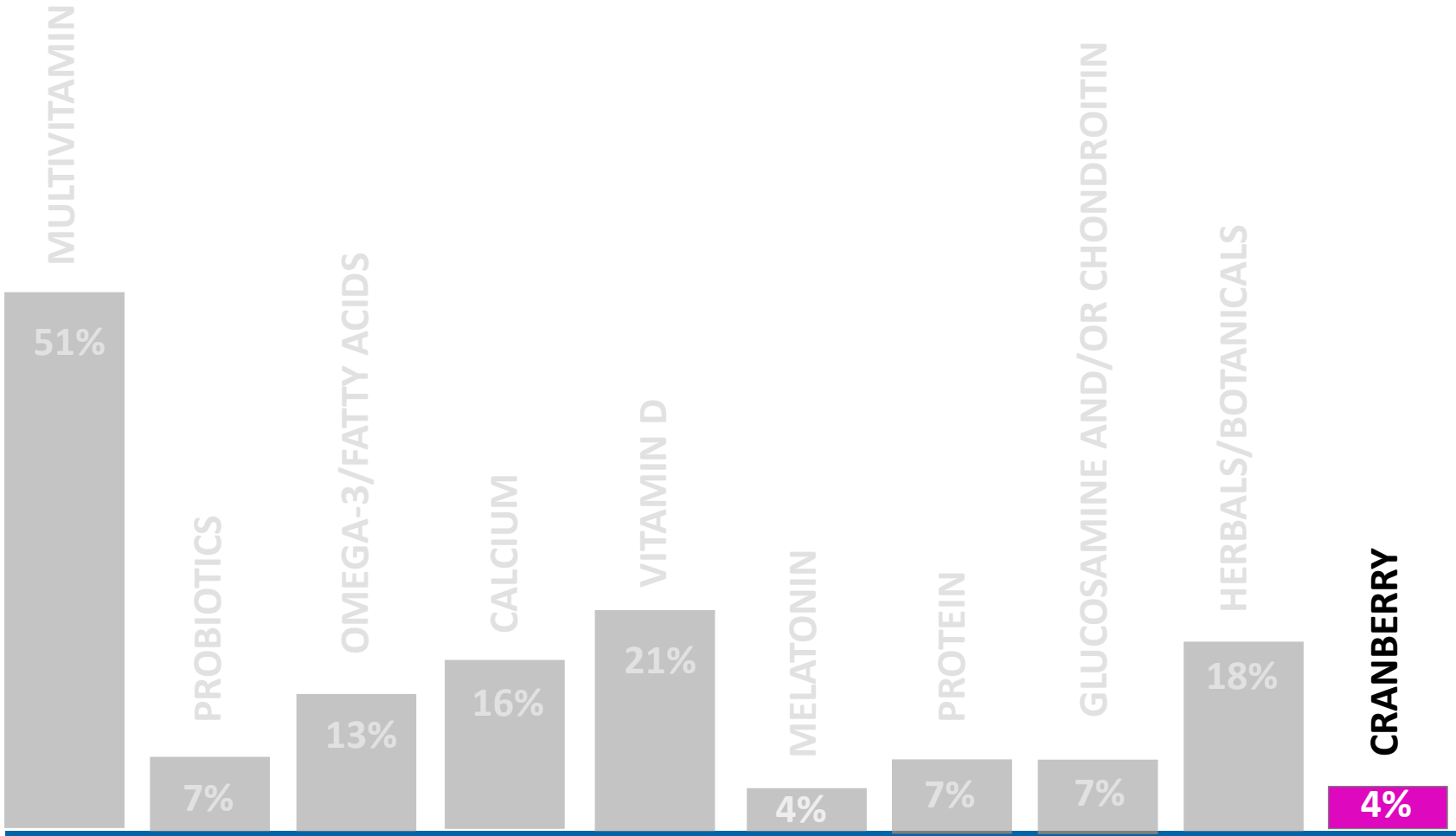
Good Manufacturing Practices (GMPs)

- Control for Quality
  - Processes
  - Personnel
  - Product
  - Documentation
- Aspects
  - Identification
  - Consistency
  - Solvent(s)
  - Contaminant(s); Heavy metals (inorganic); Pesticides; etc.
  - Adulterant(s)

Botanicals / Herbals – Things to Consider

- Diverse; Physiological action from mild to potent
  - Subtle long-term (chronic)
  - Dramatic, immediate (acute)
- Dependent on
  - Physiological activity/action
  - Dose / Dosing regimen
  - Chemical constituent(s), Extract?, Plant part(s)?, Geography?
  - Solvent(s)
  - Contaminant(s)
  - Adulterant(s)

Cranberry – Who?



Cranberry

Overview

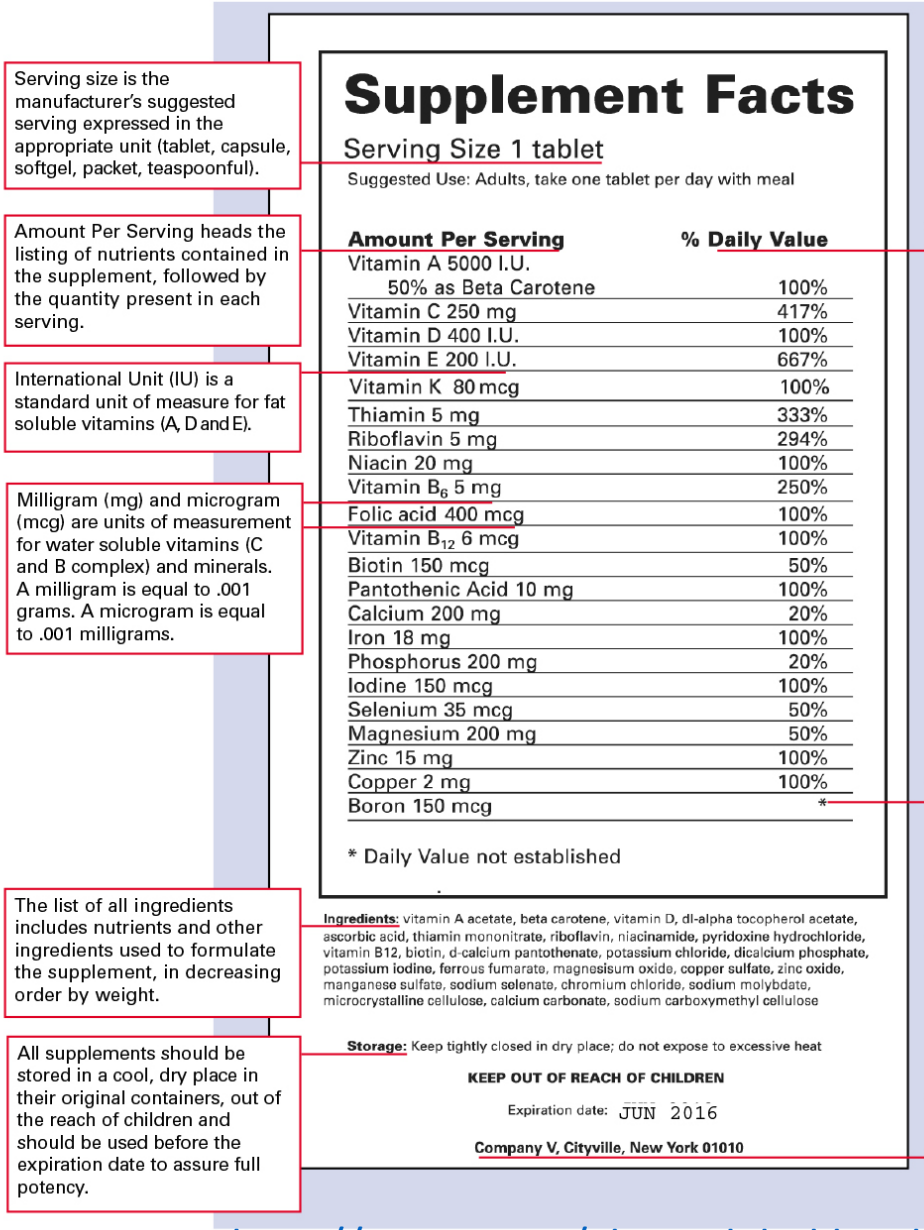
- *Vaccinium macrocarpos*; Family: Ericaceae
- Cranberry Juice; Cranberry Juice Extract
- Plant part: Berries
- Uses:
  - Urinary Tract Infection (UTI)
  - Neurogenic bladder
  - Urinary deodeorizer with incontinence
  - Benign Prostatic Hyperplasia (BPH)

Cranberry – Things to Consider

- Doesn't work for everyone…data on women with high risk for recurring UTI.
- Doesn't acidify urine or diminish bacteria.
- Acidity of Juice - increases GI problems
- Acidity of Juice – organoleptic problems
- Oxalates in Juice - can lead to stones.
- Drug interactions
  - Warfarin/Coumadin/Blood thinners

Practical Extras

How to Read a Supplement Label



http://crnusa.org/about_label.html

Proposed Labeling Changes

- FDA issued a proposed rule on changes to nutrition and supplement facts labeling
- Recommended daily intakes (RDIs) for many nutrients will change
- Units of measure will change (e.g., from IU to mg)

Nutrient	Current RDI	Proposed RDI
Calcium	1000 mg	1300 mg
Chloride	3400 mg	2300 mg
Vitamin E	30 IU	15 mg

Tainted Products Marketed as Supplements

- May contain the active ingredients in FDA-approved drugs or their analogs, or other compounds, such as novel synthetic steroids.
- Labeled as “alternative to [drug]” or “alternative to [anabolic steroid]”
- Common categories:
  - Body Building
  - Sexual Enhancement
  - Weight Loss
- Tools: FDA RSS feed and e-mail alerts

Helpful Resources

Natural Standard
The Authority on Integrative Medicine

https://naturalmedicines.therapeuticresearch.com/

NATURAL MEDICINES
COMPREHENSIVE DATABASE

http://naturaldatabase.therapeuticresearch.com/

NIH National Institutes of Health
Office of Dietary Supplements

http://ods.od.nih.gov/

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Thank you!

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