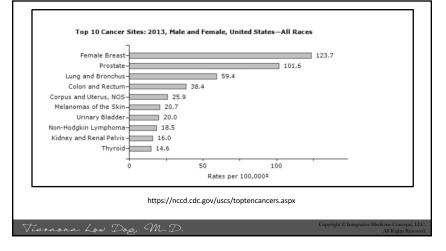




#### Statistics

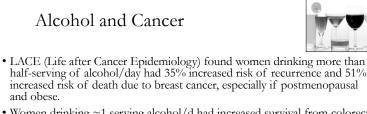
- In 2010, 1.6 million people were diagnosed with cancer.
- In 2030, estimated to increase to 2.3 million.
- Cancer rates are increasing globally, people being diagnosed at younger and younger ages.
- In US, one in four people will die from cancer.
- But many people survive the disease.
- >12 million people have survived cancer treatment and are looking to prevent cancer recurrence.



#### Recommendations for Cancer Prevention WCRF/AICR

- Do not smoke or use tobacco products.
- Body Fatness be as lean as possible within normal range of body wt.
- Physical Activity be physically active as part of everyday life
- Foods and Drinks that Promote Weight Gain limit consumption of energydense foods. Avoid sugary drinks
- Plant Foods eat mostly foods of plant origin
- · Animal Foods limit intake of red meat, avoid processed meat
- Alcoholic Drinks limit 2 serving/d men, 1 serving/d women
- · Preservation, Processing, Preparation limit consumption of salt
- Breastfeeding mothers to breastfeed, children to be breastfed
   Cancer Survivors follow recommendations above

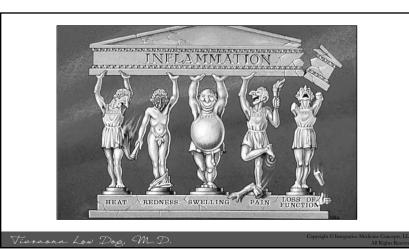
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- Women drinking ~1 serving alcohol/d had increased survival from colorectal cancer compared to non-drinkers.
- Mixed picture. Clear evidence moderate wine consumption has beneficial effects on CVD, longevity.

Kwan ML, et al. J Clin Oncol 2010; 28(29):4410-6. Fung TT, et al. PLoS One 2014; Dec 15;9(12):e115377 Artero A, et al. Maturitas 2015; Jan;80(1):3-13

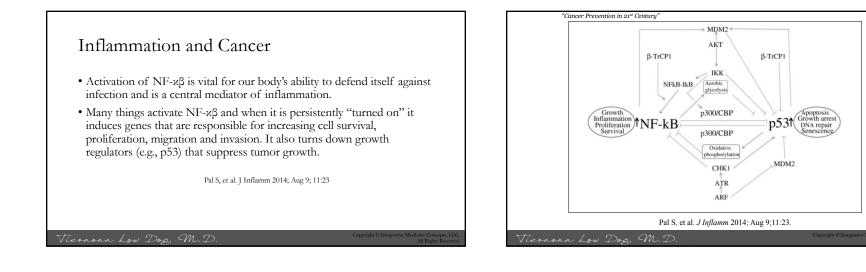
Ecraona Low Dog, M.D.



#### Diabetes, Inflammation, Cancer

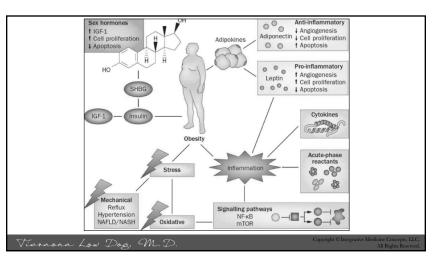
- Poorly regulated blood sugar in diabetic patients is often accompanied by increased levels of chronic inflammatory markers, e.g., interleukin (IL)-1β, IL-6, and TNF-α; emerging evidence has highlighted activation of the immune response in the progression and development of cancer cells.
- Uncontrolled pro-inflammatory responses create a chronic inflammatory state, promoting a tumor-favorable microenvironment and potentially triggering immune over-activation and cancer growth.

Chang SC, Yang WV. Crit Rev Oncol Hematol 2016; 108:146-153

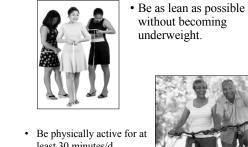


### Factors That Drive Inflammation and Insulin Resistance

- Sedentary lifestyle, lack of exercise
- Pattern of central obesity
- Western-dietary pattern, high fructose
- Prolonged psychosocial stress
- Environmental exposures (smoke, toxins, chemicals)
- Alterations in oral and gut flora and intestinal permeability



#### WCRF/AICR Recommendations to Reduce Cancer Risk



least 30 minutes/d.

#### Obesity and Cancer: What is The Connection? • Fat cells, particularly those in the belly, produce and react to hormones and proteins that drive inflammation and insulin resistance, which promote cell growth. The more often cells divide, the more opportunity there is for cancer to develop.

- · Waist measurements indicating increased risk:
  - 31.5 inches or more for women
  - 37 inches or more for men
- High risk
  - 35 inches or more for women
  - 40 inches or more for men





#### Obesity and Insulin Growth Factors

- Obesity is associated with multiple factors that may cause an increased risk for cancer and cancer-related mortality including insulin resistance, high blood sugar and insulin-growth factors (IGF).
- Elevated insulin increases tumor growth and aggressiveness.
- IGF-1 and IGF-2 have been identified as tumor promoters in multiple studies.

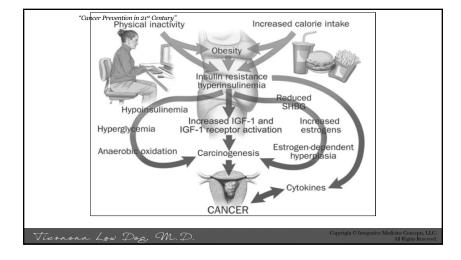
Belardi V, et al. J Mammary Gland Biol Neoplasia 2013; 18(3-4):277-89

#### "Cancer Prevention in 21st Century"

• According to AICR, estimated number of US cancers that are currently linked to excess body fat include:

#### Estimated Cancers

Percentage	Cancer Site	Cases Per Year
49	Endometrial cancers	21,300
35	Esophageal cancers	5,824
28	Pancreatic cancers	12,079
24	Kidney cancers	13,978
21	Gallbladder cancers	2,050
17	Breast cancers	35,540
9	Colorectal cancers	12,831
	TOTAL	103,602



#### Tumor Type

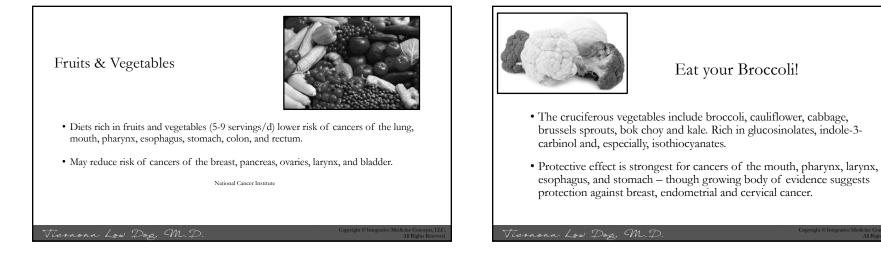
- The Women's Healthy Eating and Living (WHEL) trial found carbohydrate restriction associated with a striking five-fold reduction in breast cancer recurrence in 50% of subjects, specifically those whose tumors expressed the IGF-1 receptor.
- Unfortunately, IGF-1 testing of tumors is not yet a routine clinical practice.

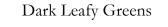
Edmond JA, et al. Cancer Epidemiol, Biomarkers Prev 2014; DOI: 10.1158/1055-9965

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 Diet and Cancer
 Study > 2000 women confirmed "Western" diet increased breast cancer risk, while Med Diet rich in fruits, vegetables, legumes, oily fish and vegetable oils lowered risk of all breast cancer subtypes, particularly triple-negative tumors.
 Another review found strong evidence of a beneficial role of the Mediterranean diet on oral and pharyngeal cancer.
 High adherence to MD associated with a significant reduction in the risk of overall cancer mortality (10%), colorectal cancer (14%), prostate cancer (4%) and aerodigestive cancer (56%)
 Castello A, et al. Br J Cancer 2014; 111(7):1454-62 Filomeno M, et al. Br J Cancer 2014; 111(5):81-65. Schwingsheck I, et al. Int J Cancer 2014; 111(5):81-65.
 Schwingsheck I, et al. Int J Cancer 2014; 113(5):1884-97.







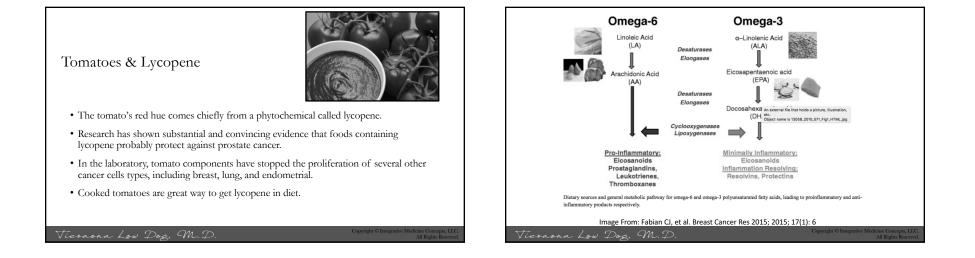
- Spinach, kale, romaine lettuce, leaf lettuce, mustard greens, collard greens, chicory and Swiss chard are excellent sources of **fiber**, **folate** and a wide range of **carotenoids** such as lutein and zeaxanthin, along with saponins and flavonoids.
- Research has found that the carotenoids in dark green leafy vegetables can inhibit the growth of certain types of breast cancer cells, skin cancer cells, lung cancer and stomach cancer.

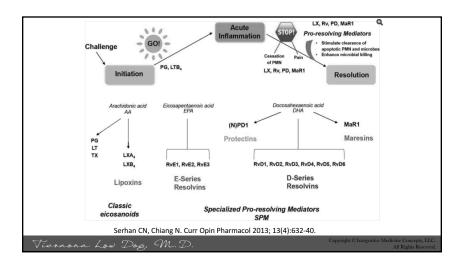
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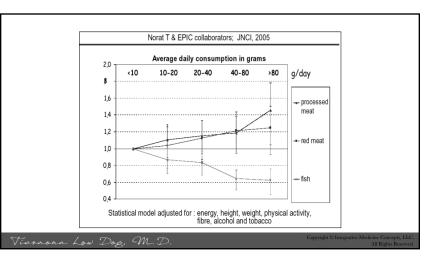


The Allium Vegetables

- Garlic belongs to the *Allium* family, which also includes onions, scallions, leeks and chives.
- In an impressive number of published studies, the consumption of onions and garlic has demonstrated protective effects against stomach, prostate and esophageal cancer.
- For cancer protection, AICR experts suggest including garlic as part of a well-balanced diet.







#### Canadians and Omega 3

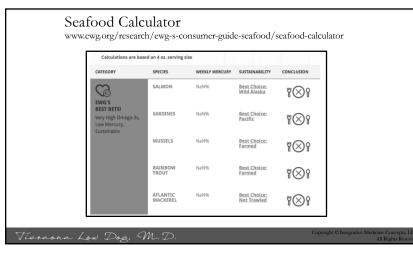
- The Omega-3 Index indicates the percentage of EPA+DHA in red blood cell fatty acids.
- Canadian government found that the mean Omega-3 Index level of Canadians aged 20-79 was 4.5%.
  - Levels higher for women, older adults, Asians and other non-white Canadians, omega-3 supplement users, and fish consumers; levels lower for smokers and people who were obese.
- Fewer than 3% of adults had levels associated with low CHD risk; 43% had levels associated with high risk.

Langlois K, et al. Health Rep 2015; Nov 18;26(11):3-11

Vieraona Low Dog, M.I

# Omega 3 and Prostate Cancer? SELECT trial raised concerns about potential link between omega 3s and increased prostate cancer/aggressive cancer. European Food Safety (EFSA) concluded, "there is no evidence for a role of EPA and/or DHA intake in the development of prostate cancer." Also, "supplemental intake of EPA and DHA combined at doses up to 5 g/d does not give rise to safety concerns for adults." EFSA Journal 10(7): doi:10.2903/j.efsa.2012.2815

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# Dietary Fat and Cancer: Systematic Review No associations were found for prostate, esophageal, gastric, renal cell, bladder, lung, skin, or postmenopausal breast cancer by the total intake or types of dietary fat. There *may* be an association between total dietary fat and premenopausal breast cancer. Ovarian cancer there was limited-suggestive evidence for a positive association with intake of saturated fats.

#### "Cancer Prevention in 21st Century"

#### WCRF/AICR Recommendations to Reduce Cancer Risk

• Limit consumption of red meats (beef, pork, lamb) and avoid processed meats. Aim for no more than 18 ounces per week (10 ounces higher risk)



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#### "Cancer Prevention in 21st Century"

- **Red meat** refers to <u>beef</u>, <u>pork</u> and <u>lamb</u> *foods like hamburgers, steak, pork chops and roast lamb.* 
  - Studies show we can eat up to 18 ounces a week of red meat without raising cancer risk.
- **Processed meat** is red meat that is <u>preserved by smoking, curing,</u> <u>salting or adding other chemical preservatives</u>. *Sausage, bacon, ham and lunch meats (such as bologna, salami and corned beef) are processed meats.* 
  - Evidence is convincing that processed meats raise risk of colorectal cancer. For every ounce and half of processed meat eaten per day, <u>risk rises by 21%</u>.

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- Traditional Mediterranean diet low in processed foods and fructose.
- High fructose consumption associated with increased intestinal permeability, elevated toll-like receptor 4, endotoxemia and development of non-alcoholic fatty liver disease.

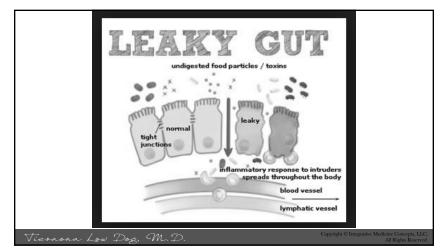
Jin R, et al. Nutrients 2014; 6:3187-3201

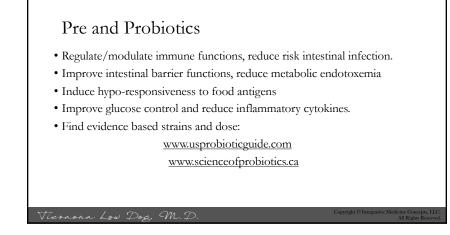
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#### Intestinal Permeability and Systemic Inflammation

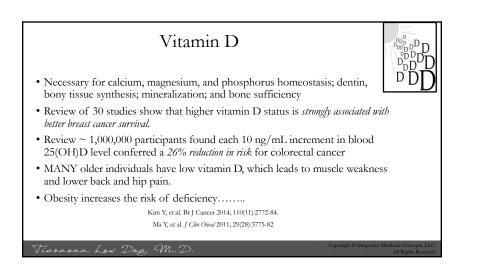
- When lipopolysaccharide (LPS), endotoxin from membrane of gram negative bacteria in intestinal lumen, enters bloodstream it binds Toll-like receptor 4, inflammation is activated, changing insulin signaling and triggering inflammatory mediators
- Chronic exposure to LPS may contribute to weight gain and type 2 DM. Obese people and diabetics have increased plasma LPS.

Boroni Moreira AP, et al. Nutr Hosp 2012; 27(2):382-90









#### Endocrine Society Guidelines

"For clinical care, it appears that all current (testing) methodologies are adequate if one targets a 25(OH)D value higher than current cut points; for example, a value of 40 ng/ml (100 nmol/L) is without toxicity and virtually ensures that the individuals 'true' value is greater than 30 ng/ml (75 nmol/L)."

Holick MF, et al. J Clin Endocrinol Metab 2011; 96(7):1911-30

Vieraona Low Doc. M.I

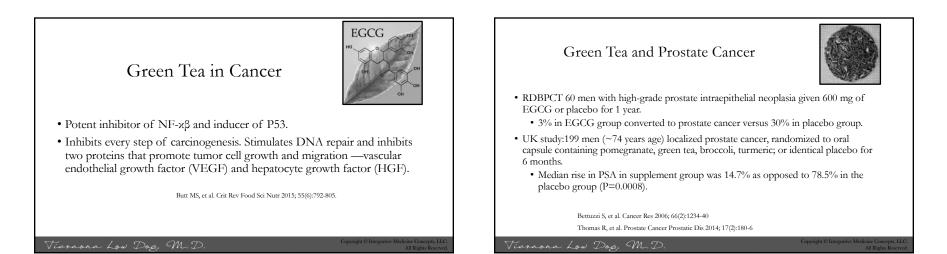
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#### Green Tea (*Camellia sinensis*)

- White, green, oolong and black teas contain polyphenols and flavonoids, particularly catechins.
- Dominant catechin in green tea is epigallocatechin gallate (EGCG), which exerts potent anti-inflammatory and antioxidant activity.

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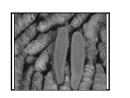
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## Turmeric (*Curcuma longa and others*)

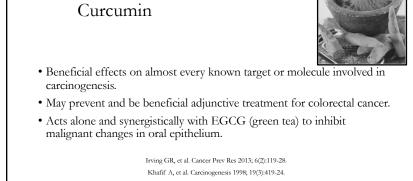
- Rhizomes provide bright yellow-orange culinary spice and dye.
- Yellow pigments = curcuminoids, one example is curcumin.
- Long history of medicinal use for respiratory, skin, digestive and inflammatory conditions in India.
- More than 65 clinical trials have shed light on its *potential* role in CVD, diabetes, cancer, fatty liver, arthritis, neuro/psych disorders.

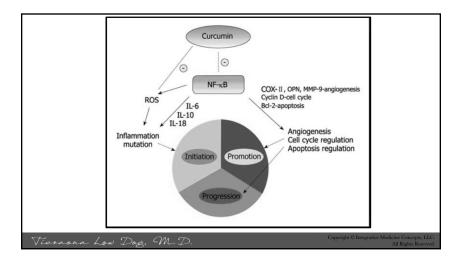
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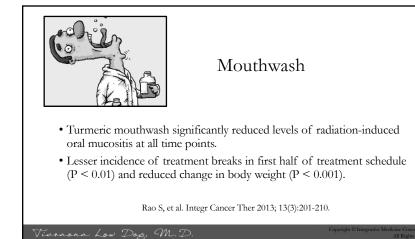


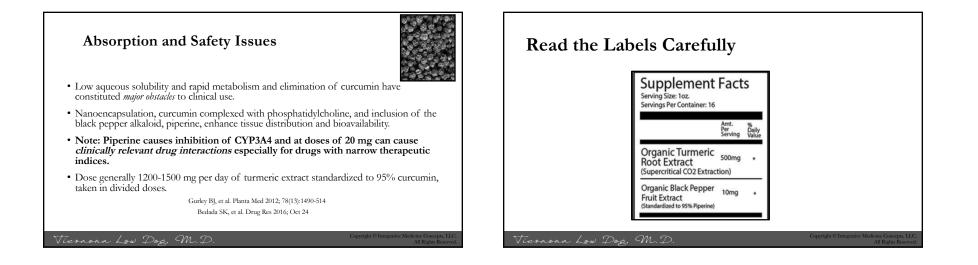
Kunnumakkara AB, et al. Br J Pharmacol 2016; Sep 17. doi: 10.1111/bph.13621.

Prasad S, et al. Biotechnol Adv 2014; 32(6):1053-1064

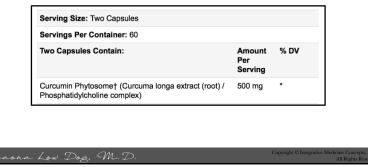


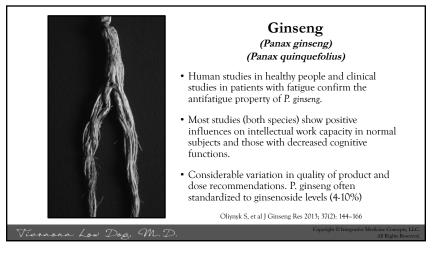






## Curcumin Bound to Phytosome: Safer If Taking Medications





#### **Cancer Related Fatigue**

- *P. quinquefolius* may reduce the risk of moderatesevere respiratory infections in patients with CLL
- Four RCT show that both species improve cancer related fatigue. Largest study 364 participants from 40 institutions.
- Randomized to receive placebo or 2000 mg/d of American ginseng for 8 weeks to determine effect on fatigue.
- Ginseng reduced fatigue by *almost double* that of placebo in those undergoing active cancer treatment. No discernible toxicities.
- Some experts recommend taking breaks every 12 weeks. Unclear if any clinical benefit or enhanced safety.

Vieraona Low Doc. M.D.



High KP, et al. J Support Oncol 2012; 10(5):195-201. Barton DL, et al. J Natl Cancer Inst 2013; 105(16): 1230–1238

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#### Herb-Drug Interactions

- No clinically significant drug interactions observed using approved CYP probe drugs and P-gp probe substrates when *P. ginseng* administered for 2 weeks in healthy volunteers.
- *P. quinquefolius* did not interact with indinavir (CYP3A4) in human volunteers.
- *P. ginseng* 1 gram/d for 6 weeks, no significant change in INR in patients on warfarin.

ieraona Low Dog, M.D.



Kim DS, et al. J Ginseng Res 2016; 40(4):375-81 Andrade AS, et al. BMC Complement Altern Med 2008; 8:50 Lee YH, et al. Int J Cardiol 2010; 145(2):275-6.

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Supplement Serving Size: 2 capsules Servings Per Container: 25	Fact
Amount Per Serving American Ginseng root (Panax quinquefolius)	1000 mg*
*Daily Value not established	

#### BENEFITS OF PHYSICAL ACTIVITY

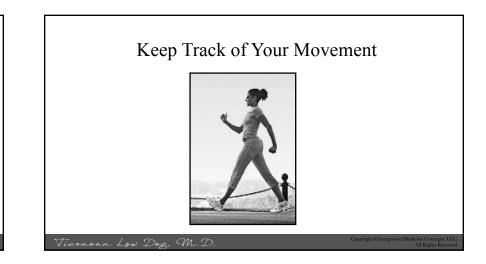
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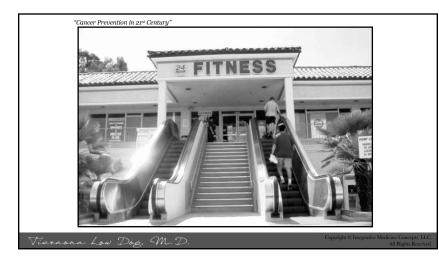


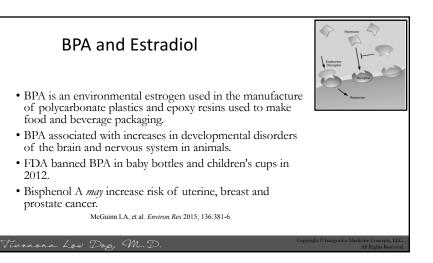
- Maintain healthy body weight and muscle tone.
- Reduces risk of heart disease and depression.
- Lowers risk of diabetes by enhancing skeletal uptake of blood sugar.
- American Cancer Society, exercise may reduce risk of cancer by reducing insulin and insulinlike growth factors levels, associated with increased cell/tumor growth.
- Review of 73 studies found 25% average risk reduction for breast cancer amongst physically active women.

Lynch, et al. Recent Results Cancer Res 2011; 186:13-42

Activity	In 1 hour	In 30 minutes		
Running (1 mile in 12 minutes or 5 miles/hour)	590	295		
Swimming (slow freestyle laps)	510	255		
Walking (1 mile in 13 minutes)	460	230		
Playing basketball	440	220		
Weight lifting (vigorous effort)	440	220		
Heavy yard work (chopping wood or clearing brush)	440	220		
Golfing (walking and carrying clubs)	330	165		
Dancing	330	165		
Light gardening/yard work	330	165		
Bicycling (more than 10 miles an hour)	290	145		
Walking (1 mile in 17 minutes)	280	140		
Weight lifting (general light workout)	220	110		
Source: USDA, www.mypyramid.gov				
w Dog, M.D.		Copy		







#### Canned Goods



- Canned goods are significant source of BPA.
- Researchers at the Harvard School of Public Health found that volunteers consuming one serving of canned soup each day for five days had a more than *1,000% increase* in urinary BPA concentrations compared with when the same individuals consumed fresh soup daily for five days.
- When possible, choose fresh, frozen or in glass.

Carwile JL, et al. JAMA 2011; 306(20):2218-20.

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#### Insecticides and Cancer

- Meta-analysis of 16 studies found childhood exposure to indoor residential insecticides associated with a significant increased risk of childhood leukemia and lymphomas.
- Positive but not statistically significant association also found for childhood brain tumors.
- Use integrated pest management.

Chen M, et al. Pediatrics 2015; 136(4):719-29.

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#### Hormone Therapy for Women

- Benefits likely outweigh risks for symptomatic women before the age of 60 years or within 10 years after menopause.
- Symptom control is used to determine the minimum required dose for each woman (not hormone testing!)
- When balancing benefits and risks dose, type and route of administration need to be considered.

deVilliers TJ, et al. Maturitas 2013; 391-2

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#### Route and Type

- **Transdermal estradiol** has least effect on lipids and renin as it avoids first pass effect on the liver, permitting lower doses to be used.
- Unopposed estrogen does not significantly increase risk of breast CA.
- **Progesterone** or dydrogesterone is associated with **lower risk of breast cancer** and venous thrombosis compared to synthetic progestogens.
- If symptoms primarily urogenital, vaginal estrogen can be used with minimal systemic absorption.

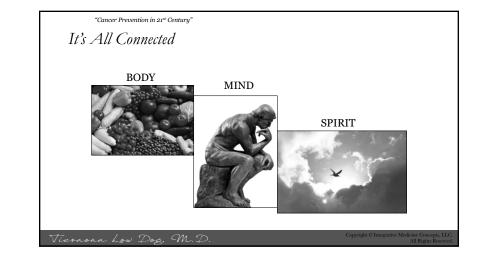
Bhupathiraju SN, et al. Endocr Prac 2014; 20:1201-13 L-Hermite M. *Climacteric*. 2013 Aug;16 Suppl 1:44-53. Hale GE, et al. Trends Cardiovasc Med 2015; 25(6):540-9

# HPV Vaccine An estimated 24,600 newly diagnosed cancers are attributable to the two high-risk HPV types targeted by all currently licensed HPV vaccines Routine HPV vaccination at age 11 or 12 years; and vaccination for females through age 26 years and males through age 21 who were not adequately vaccinated previously. 2 doses if before 15<sup>th</sup> birthday, 3 doses if after. CDC, from June 2006-March 2014, ~67 million doses of HPV vaccines distributed and ~ 25,000 adverse events were reported; 92% were classified as non-serious.

• After careful review, *none of these adverse events* were any more common after HPV vaccination than among comparison groups.

www.cdc.gov/vaccinesafety/vaccines/HPV/index.html https://www.cdc.gov/mmwr/volumes/65/wr/mm6549a5.htm

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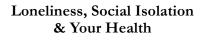


#### Stress and Cancer

- While stress *does not cause* cancer, there is growing evidence that chronic stress can promote the growth of tumors that are already present.
- Studies clearly demonstrate that social isolation and depression promote tumor growth.
- Excess sympathetic tone caused by emotional stress, can decrease cancer survival.

DeCouck M, et al. Oncol Rep. 2013; 30(5): 2435-2441.

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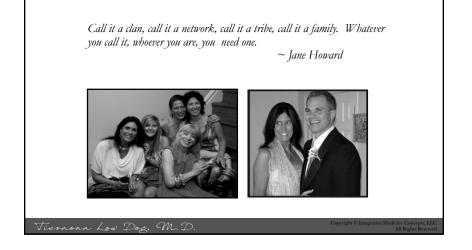


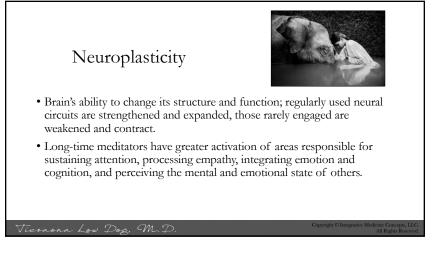


• 148 studies on the effects of social isolation on health found it is:

- As bad as smoking 15 cigarettes a day.
- As dangerous as being an alcoholic.
- As harmful as never exercising.
- Twice as dangerous as obesity.

Cacioppo JT, et al. Ann N Y Acad Sci 2011; 1231:17-22 Holt-Lunstad J, et al. PLoS Med 2010; 7:e1000316



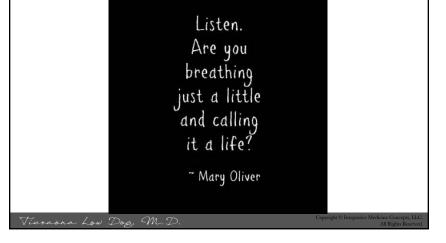


#### Mindfulness Meditation Systematic Review

- A review of 47 clinical trials (n=3515) found that mindfulness meditation improved:
  - Anxiety
  - Depression
  - Pain

Goyal M, et al. JAMA Intern Med 2014; 174(3):357-68





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