Dietary Supplements & Cancer Survivors

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Optimizing Wellness
Cancer Survivorship

• More people diagnosed with cancer are surviving each year
• The overall 5-year survival rate for adults diagnosed with cancer in 1996–2003 is 65%†
• An estimated 11.1 million Americans are living with a previous diagnosis of cancer†

Dietary Supplement Utilization in Cancer Survivors

- Use is common, but studies are scarce
- Systematic review of 32 studies since 1999
- 64-81% all survivors use VM supplement
- 50% all US adults used DS
- 14-32% start use after diagnosis
- Breast cancer highest utilizers
- Prostate cancer lowest utilizers
- Most consistent predictors of use: female gender & higher education
- 68% MD unaware of use

DS Use in Cancer Survivors

• VITAL study (75,288 cohort)
• Cancer survivors (n=280)
  – 11 different cancers
  – Multiple DS queried
• Adjusted analyses for individual supplements & cancer types
  – Cranberry w/ bladder ca (OR 3.44)
  – Zinc w/ ovarian ca (2.19)
  – Soy w/ prostate ca (1.99)
  – Melatonin w/ cervical ca
  – VD w/ thyroid ca (1.66)

DS Use in High Risk Women

- 303 women underwent BRAC1/2 testing
- 51% used at least 1 DS
  - Ca++ (26%); MVI (17%); VD (14%); VE (12%) & VC (10%) most common
- Women > 50 more likely to use (p<0.0001)
- Inconclusive test assoc w/higher use (OR 2.6)
- Smoking inversely assoc w/ use (OR 0.3)

Elderly Survivors, Diet Adequacy & Supplements

- Long term survivors (>5 yrs) breast, prostate, colon ca > 65 y/o (n=753)
- 74% took supplements
  - MVI (60%); Ca++/VD (37%); AO (30%)
- Diet quality by Healthy Eating Index
  - Substantial portion below EAR
  - DS utilizers generally had better diet (p<0.01) over all & for 12 of 13 nutrients studied
  - Higher scores in Total Fruit, Whole Grain & Oil more likely to use DS

“Supplement use may reduce the prevalence of nutrient inadequacies in this population, though survivors who use supplements are the least likely to need them.”

ACS Cancer Risk Reduction Recommendations

- Maintain healthy weight
  - Balance caloric intake w/ physical activity
  - Avoid excessive wt. gain
  - Reduce weight if overweight
- Adopt physically active lifestyle
  - 30 min mod-vigorous physical activity 5d/wk (45-60 min preferred)
- Consume healthy plant based diet
  - Choose foods/beverages healthy weight
  - 5 or more servings variety Vegetables & Fruits/d
  - Whole grains > processed grains
  - Limit consumption processed and red meats
- Limit alcohol consumption
  - (1 drink women & 2 drinks men)

American Cancer Society, 2006.
Dietary Intake in Breast Cancer Survivors

3,084 women w/ early stage Br Ca
Higher F, V, Fiber
Lower intake high fat food
Older than 60 less likely to report any changes
Length of time from diagnosis more likely to make these choices


<table>
<thead>
<tr>
<th>Food</th>
<th>Percent who ate at 12 mo before diagnosis</th>
<th>How consumption changed since diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No change (%)</td>
<td>Decrease (%)</td>
</tr>
<tr>
<td>Vegetables</td>
<td>99.0</td>
<td>76.9</td>
</tr>
<tr>
<td>Fruits</td>
<td>97.7</td>
<td>86.8</td>
</tr>
<tr>
<td>Fatty</td>
<td>96.8</td>
<td>81.0</td>
</tr>
<tr>
<td>Vegetable oil</td>
<td>92.9</td>
<td>60.6</td>
</tr>
<tr>
<td>Grilled foods</td>
<td>61.1</td>
<td>66.0</td>
</tr>
<tr>
<td>Whole grains</td>
<td>90.5</td>
<td>57.3</td>
</tr>
<tr>
<td>Cheese</td>
<td>90.4</td>
<td>45.9</td>
</tr>
<tr>
<td>Pizza</td>
<td>90.3</td>
<td>30.6</td>
</tr>
<tr>
<td>Eggs</td>
<td>89.4</td>
<td>39.5</td>
</tr>
<tr>
<td>Fish</td>
<td>88.4</td>
<td>35.9</td>
</tr>
<tr>
<td>Nuts</td>
<td>87.4</td>
<td>29.5</td>
</tr>
<tr>
<td>Cakes/Sweets</td>
<td>86.9</td>
<td>44.0</td>
</tr>
<tr>
<td>Red Meat</td>
<td>86.5</td>
<td>36.7</td>
</tr>
<tr>
<td>Cofee</td>
<td>83.1</td>
<td>42.1</td>
</tr>
<tr>
<td>Reduced-fat</td>
<td>84.6</td>
<td>61.5</td>
</tr>
<tr>
<td>milk products</td>
<td>84.6</td>
<td>61.5</td>
</tr>
<tr>
<td>Sugar</td>
<td>81.4</td>
<td>61.6</td>
</tr>
<tr>
<td>Hamburger</td>
<td>79.4</td>
<td>46.0</td>
</tr>
<tr>
<td>Fốc</td>
<td>78.2</td>
<td>35.6</td>
</tr>
<tr>
<td>Margarine/shortening</td>
<td>74.4</td>
<td>39.9</td>
</tr>
<tr>
<td>Other fast</td>
<td>71.5</td>
<td>47.5</td>
</tr>
<tr>
<td>foods</td>
<td>71.5</td>
<td>49.2</td>
</tr>
<tr>
<td>Regular ice</td>
<td>69.6</td>
<td>55.6</td>
</tr>
<tr>
<td>Cream</td>
<td>66.4</td>
<td>62.8</td>
</tr>
<tr>
<td>Wine</td>
<td>64.5</td>
<td>61.3</td>
</tr>
<tr>
<td>Butter</td>
<td>64.5</td>
<td>30.7</td>
</tr>
<tr>
<td>Fisted foods</td>
<td>64.5</td>
<td>43.7</td>
</tr>
<tr>
<td>Reduced-fat</td>
<td>64.5</td>
<td>66.4</td>
</tr>
<tr>
<td>cheese</td>
<td>64.5</td>
<td>66.4</td>
</tr>
<tr>
<td>Spirits/hard</td>
<td>78.4</td>
<td>77.4</td>
</tr>
<tr>
<td>liquor</td>
<td>78.4</td>
<td>77.4</td>
</tr>
<tr>
<td>Beer</td>
<td>78.4</td>
<td>77.4</td>
</tr>
<tr>
<td>Whole milk</td>
<td>30.3</td>
<td>74.3</td>
</tr>
<tr>
<td>products</td>
<td>30.3</td>
<td>74.3</td>
</tr>
</tbody>
</table>
Controlled Trials Diet Breast Cancer Risk

• WHI
  – 48,835 post-menopausal women
  – Goal: Total fat 20% energy consumption; 5 serv F/V; 6 serv whole grain

• WINS
  – RMCT Early stage Br Ca survivors w/in 1st year (n=2437)
  – Goal: reduce fat intake to 20% daily calorie intake
  – No intent in weight reduction

• WHEL
  – 3088 Breast Can enrolled up to 4 years after dx
  – Goal: 5 V serv; 3 F serv; 16 oz Veg juice; 30 g Fiber; 15-20% intake fat
Fat reduced 57.3 g/d to 33.3 g/d in treatment group c/w 56.3 to 51.3 g/d in control; 6 weight difference ($p = .005$).

WHEL: Disease-Free Survival and All-Cause Mortality by Diet Group

Kaplan-Meier survival after Women's Healthy Eating and Living (WHEL) Study enrollment by four diet and physical activity categories
Mortality by diet and physical activity (PA) in Women’s Healthy Eating and Living Study comparison group: body mass index (BMI) categories
## Vitamin D Levels

<table>
<thead>
<tr>
<th></th>
<th>All (N = 80)</th>
<th>Sufficient (n = 15)</th>
<th>Insufficient (n = 59)</th>
<th>Deficient (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum 25(OH)D, ng/mL</td>
<td>24.1 (8.6)</td>
<td>36.6 (5.0)</td>
<td>22.5 (5.3)</td>
<td>9.0 (2.6)</td>
</tr>
<tr>
<td>Total vitamin D intake, IU/d</td>
<td>718 (37)</td>
<td>883 (300)*</td>
<td>721 (367)†</td>
<td>279 (238)</td>
</tr>
<tr>
<td>Dietary vitamin D intake, IU/d</td>
<td>271 (137)</td>
<td>259 (119)</td>
<td>280 (144)</td>
<td>213 (113)</td>
</tr>
<tr>
<td>Over-the-counter vitamin D intake, IU/d</td>
<td>447 (351)</td>
<td>623 (349)*</td>
<td>441 (337)†</td>
<td>67 (163)</td>
</tr>
<tr>
<td>Serum PTH, pg/mL</td>
<td>61.5 (36.3)</td>
<td>47.3 (26.5)</td>
<td>60.8 (31.7)</td>
<td>104 (66.3)</td>
</tr>
<tr>
<td>Calculated CrCl, mL/min</td>
<td>55.6 (18.3)</td>
<td>50.4 (16.8)</td>
<td>57.5 (19)</td>
<td>49.6 (13)</td>
</tr>
<tr>
<td>Adjusted serum calcium, mg/dL</td>
<td>9.6 (0.5)</td>
<td>9.6 (0.3)</td>
<td>9.6 (0.5)</td>
<td>9.5 (0.5)</td>
</tr>
<tr>
<td>Serum phosphorus, mg/dL</td>
<td>3.5 (0.6)</td>
<td>3.6 (0.6)</td>
<td>3.5 (0.6)</td>
<td>3.4 (0.3)</td>
</tr>
</tbody>
</table>

25(OH)D = 25-hydroxyvitamin D; PTH = parathyroid hormone; CrCl = creatinine clearance (calculated using the Cockcroft-Gault equation).  
*P < 0.01, compared with vitamin D-deficient patients using 1-way analysis of variance.  
†P < 0.05, compared with vitamin D-deficient patients using 1-way analysis of variance.
Incidence rates of prostate and breast cancers in different countries as functions of the mean latitude of the country

Moan J. et.al. PNAS 2008;105:668-673
FIGURE 1. Vitamin D [25(OH)D] sufficiency, insufficiency, and frank deficiency by race-ethnicity, geography, and season in a cohort of breast cancer survivors

VD & Cancer Risk

• Iowa Women’s Health Study Breast Cancer Risk*
  – 34,321 women followed 1986-2004
  – 800 IU vs 400 IU (0.89 (CI: 0.77-1.03) p=0.02
  – Association the strongest 1st 5 yrs.
  – Association stronger for ER - than ER + tumors

• Colon Cancer Risk**
  – Drawn from another trial
  – Median VD level 25.6 ng/ml (insufficient level)
  – Women more protected than men
  – VD > mean OR Women 0.59 (CI: 0.30,1.16); Men 0.95

Vitamin D & Cancer Risk

- 1180 healthy, post-menopausal women RDBPCT in 3 groups
  - Placebo both VD & Ca++
  - Ca++ only (Carb 1500 mg or Citrate 1400 mg)
  - Ca++ comb (as above) with 1000 IU VD
- 1024 (86.8%) completed 4 years
- Cancer incidence rate main secondary outcome
- Cases of Breast (19), Colon (3), Lung (7), Hem(10), Uterus (3) recorded
- RR for Ca-VD group (after 1st 12 mo) 0.232 (CI: 0.09, 0.60) p <0.005

FIGURE 2. Kaplan-Meier survival curves (i.e., free of cancer) for the 3 treatment groups randomly assigned in the cohort of women who were free of cancer at 1 y of intervention (n = 1085)

Kaplan-Meier Estimates of the Cumulative Hazard for Invasive Colorectal Cancer with Supplemental Calcium plus Vitamin D, as Compared with Placebo

36,282 post-menopausal women in WHI 1,000 mg Calcium carbonate + 400 IU Vitamin D for 7 years; Placebo group allowed to take calcium & vitamin D

Calcium & Colorectal Cancer Risk

• Systematic review by Cochrane Collaborative
• 2 randomized trials identified
• 1346 participants
• Outcome- development of adenomatous polyps
• Dosage:
  – Calcium 1200 mg/d X 4 yrs or 2000 mg/d X 3 yrs
• Reduction in polyp formation
  – OR 0.74 (CI 0.74-0.58)

Dose Response VD & Breast Ca Risk

**Determining Dosage VD**

- Goal attain a serum level of at least 55 ng/ml of 25(OH)D (range 55-90 ng/ml)
- Prevent 60,000 cases colorectal cancer and 85,000 cases breast cancer per year
- Worldwide 250,000 cases colon cancer & 350,000 breast cancer
- To reduce colon cancer risk by 50% estimated dose of 2000 IU would be required
- To reduce breast cancer risk by 50% estimated that a dose of 3500 IU would be required
- Routine minimal replacement of 1000IU recommended and 2000IU preferred in breast cancer patients
- Main toxicity hypercalcemia; Significant toxicity not demonstrated below 10,000 IU
- Mega doses at long intervals have also been assessed (50,000 & 100,000 IU)
- Sun exposure: 3-15 min/d within an hour of noon/ 40% of body/ No sunscreen
B Vitamins- Cancer Risk

• 848 incident breast cancer cases & Controls WHI*
  – Plasma concentrations of FA, B6, B12
  – No correlation w/ serum B vitamin level & Breast Cancer risk
  – No effect food vs supplement source
• Large cohort study B vitamins (thiamin, riboflavin, niacin, FA, methionine) + alcohol cancer risk Canadian women**
  – Breast (2491 cases); Endometrium (426); Ovary (264); Colorectal (617); Lung (358)
  – No significant associations of dietary or other intake w/cancer
• 869 prostate cancer cases & 1174 controls**
  – No sig assoc w/serum level FA or B12
  – Subgroup analysis: Advance stage- High B12 levels increased risk of increasing level

Table 4. Invasive Breast Cancer According to Treatment Assignment With Folic Acid, Vitamin B6, and Vitamin B12 vs Placebo by Tumor Characteristics at Diagnosis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Cases</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive breast cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment Group (n = 2721)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo Group (n = 2721)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hormone receptor status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ER+ /PR+</td>
<td>70</td>
<td>0.83 (0.60 to 1.14)</td>
<td>.24</td>
</tr>
<tr>
<td>ER+ /PR−</td>
<td>8</td>
<td>0.92 (0.92 to 1.36)</td>
<td>.66</td>
</tr>
<tr>
<td>ER− /PR+</td>
<td>15</td>
<td>0.90 (0.55 to 1.46)</td>
<td>.47</td>
</tr>
<tr>
<td>ER− /PR−</td>
<td>1</td>
<td>0.90 (0.34 to 2.44)</td>
<td>.95</td>
</tr>
<tr>
<td>Tumor size</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤2 cm</td>
<td>55</td>
<td>0.88 (0.61 to 1.27)</td>
<td>.49</td>
</tr>
<tr>
<td>&gt;2 cm</td>
<td>6</td>
<td>0.50 (0.21 to 1.06)</td>
<td>.11</td>
</tr>
<tr>
<td>Unknown</td>
<td>7</td>
<td>1.15 (0.59 to 2.33)</td>
<td>.90</td>
</tr>
<tr>
<td>Lymph nodes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No metastasis</td>
<td>46</td>
<td>0.86 (0.58 to 1.28)</td>
<td>.46</td>
</tr>
<tr>
<td>Metastasis to lymph nodes</td>
<td>14</td>
<td>0.82 (0.40 to 1.70)</td>
<td>.57</td>
</tr>
<tr>
<td>Unknown</td>
<td>10</td>
<td>0.70 (0.31 to 1.60)</td>
<td>.39</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ductal carcinoma</td>
<td>52</td>
<td>0.91 (0.62 to 1.32)</td>
<td>.60</td>
</tr>
<tr>
<td>Lobular carcinoma</td>
<td>6</td>
<td>0.60 (0.22 to 1.65)</td>
<td>.32</td>
</tr>
<tr>
<td>Duct and lobular carcinoma</td>
<td>3</td>
<td>0.38 (0.10 to 1.31)</td>
<td>.15</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>2</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Tubular adenocarcinoma</td>
<td>3</td>
<td>2.99 (0.31 to 2.73)</td>
<td>.34</td>
</tr>
<tr>
<td>Mucinous adenocarcinoma</td>
<td>2</td>
<td>0.66 (0.11 to 3.54)</td>
<td>.65</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>0.43 (0.08 to 2.04)</td>
<td>.22</td>
</tr>
<tr>
<td>Histologic grading and differentiation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well differentiated</td>
<td>19</td>
<td>0.82 (0.45 to 1.51)</td>
<td>.52</td>
</tr>
<tr>
<td>Moderately differentiated</td>
<td>26</td>
<td>0.76 (0.46 to 1.27)</td>
<td>.19</td>
</tr>
<tr>
<td>Poorly differentiated/anaplastic</td>
<td>15</td>
<td>1.06 (0.52 to 2.14)</td>
<td>.87</td>
</tr>
<tr>
<td>Unknown</td>
<td>9</td>
<td>0.74 (0.31 to 1.78)</td>
<td>.50</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; ER, estrogen receptor; NA, not applicable; PR, progesterone receptor.
Folic Acid & Colorectal Adenomas

- RDBPCT Phase III designed to test the efficacy & safety of 1 mg of FA to prevent colorectal adenomas in 1021 pts w/previous adenoma
- Pts were randomized separately to receive either FA/placebo OR ASA/placebo (2x2 factorial trial)
- First period of follow up: 3 yrs; second period: 3-5 years & adherence to study medication encouraged
- Outcomes
  - Primary: occurrence of adenoma
  - Secondary: Occurrence of advanced lesions (villous, dysplasia, > 1 cm, cancer, multiple adenoma)
- Fortification of food began during study—even the placebo group increased serum FA & decreased homocysteine; Second follow-up period was less standardized; FA results not reported separate from ASA results—tho no interaction suspected.

## Table 3. Risk of Adenoma After Randomization in the Intention-to-Treat Population

<table>
<thead>
<tr>
<th>End Point</th>
<th>First Follow-up Interval</th>
<th>Second Follow-up Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%) of Participants</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo (n = 486)</td>
<td>Folic Acid (n = 501)</td>
</tr>
<tr>
<td>Any adenoma</td>
<td>206 (42.4)</td>
<td>221 (44.1)</td>
</tr>
<tr>
<td>Advanced lesion</td>
<td>42 (8.6)</td>
<td>57 (11.4)</td>
</tr>
<tr>
<td>No. of adenomas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>168 (34.6)</td>
<td>174 (34.7)</td>
</tr>
<tr>
<td>≥3</td>
<td>38 (7.8)</td>
<td>47 (9.4)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; RR, risk ratio.

*The intention-to-treat population consisted of all randomized participants with a follow-up examination, including those participants who discontinued randomized supplementation. First follow-up interval included the initial 3-year protocol, and the second follow-up interval was 3 or 5 years later. P values are based on \( \chi^2 \) tests. For number of adenomas, \( P \) values are global for the 3 categories (0, 1-2, and ≥3 adenomas), and separate \( \chi^2 \)s are shown to summarize the effect of folic acid on each adenoma-multiplicity category.

## Table 4. Incidence of Serious Adverse Events After Randomization

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>No. (%) of Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (n = 505)</td>
</tr>
<tr>
<td>Death</td>
<td>19 (3.8)</td>
</tr>
<tr>
<td>Noncolorectal cancer</td>
<td>32 (6.3)</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>4 (0.8)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>8 (1.6)</td>
</tr>
<tr>
<td>Coronary revascularization</td>
<td>16 (3.2)</td>
</tr>
<tr>
<td>Stroke</td>
<td>5 (1.0)</td>
</tr>
</tbody>
</table>

# Adverse Events Known to Be Associated With the Study Supplements

**Table 5.** Adverse Events Known to Be Associated With the Study Supplements

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Placebo (n = 8696)</th>
<th>Vitamin E (n = 8737)</th>
<th>Selenium (n = 8752)</th>
<th>Selenium + Vitamin E (n = 8703)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Men</td>
<td>RR (99% CI)</td>
<td>No. of Men</td>
<td>RR (99% CI)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>206</td>
<td>1 [Reference]</td>
<td>220</td>
<td>1.06 (0.83-1.36)</td>
</tr>
<tr>
<td>Dermatitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grades 1-2</td>
<td>516</td>
<td>1 [Reference]</td>
<td>591</td>
<td>1.14 (0.98-1.32)</td>
</tr>
<tr>
<td>Grades 3-4</td>
<td>8</td>
<td>1 [Reference]</td>
<td>12</td>
<td>1.49 (0.46-4.83)</td>
</tr>
<tr>
<td>Halitosis</td>
<td>427</td>
<td>1 [Reference]</td>
<td>493</td>
<td>1.15 (0.97-1.36)</td>
</tr>
<tr>
<td>Nail changes</td>
<td>1035</td>
<td>1 [Reference]</td>
<td>1041</td>
<td>1.00 (0.90-1.11)</td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grades 1-2</td>
<td>566</td>
<td>1 [Reference]</td>
<td>604</td>
<td>1.03 (0.89-1.19)</td>
</tr>
<tr>
<td>Grades 3-4</td>
<td>24</td>
<td>1 [Reference]</td>
<td>29</td>
<td>1.20 (0.59-2.45)</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grades 1-2</td>
<td>203</td>
<td>1 [Reference]</td>
<td>191</td>
<td>0.94 (0.72-1.21)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>9</td>
<td>1 [Reference]</td>
<td>3</td>
<td>0.33 (0.06-1.85)</td>
</tr>
</tbody>
</table>

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**Abbreviations:** CI, confidence interval; RR, relative risk.

aThe RRs given for vitamin E, selenium, and selenium + vitamin E groups are compared with the placebo group. Maximum grade experienced by a participant are given. Alopecia, halitosis, and nail changes were only defined for grades 1 and 2. National Cancer Institute Common Toxicity Criteria were used for alopecia, nail changes, fatigue, and nausea. Halitosis and dermatitis were defined in the study protocol. Generally, grade 1 = mild, grade 2 = moderate, grade 3 = severe, and grade 4 = life-threatening.

b₂<.01.

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Characteristics of Chemopreventative Agent

- Able to be taken orally
- Adequate bioavailability
- Excellent safety margin over long period of use
- Effective at disrupting carcinogenesis at an early stage
Examples of Natural Chemopreventative Agents

Chemopreventive agents known to suppress tumorigenesis:

- Oleander (oleanderin)
- Tomato (lycopene)
- Garlic (diallyl sulfide, ajoene, S-ally cysteine, allicin)
- Carrots (β-carotenes)
- Artichoke (Silymarin)
- Red grapes, peanuts & berries (resveratrol)
- Red chilli (capsaicin)
- Turmeric (curcumin)
- Pomegranate (ellagic acid)
- Fennel, anise, corriander (anethol)
- Honey-bee propolis (caffeic acid, CAPE)
- Basil & rosemary (ursolic acid)
- Tea (catechins)
- Cloves (eugenol & isoeugenol)
- Ginger (zingiberol)
- Cruciferous vegetables (sulforaphane)
- Aloe (emodin)
- Soyabean (genistein)
Prostate Cancer Chemoprevention with GTE

High grade prostate intra epithelial neoplasia: 30% prostate ca w/in year
GTE given (75.7% catechins; confirmed) 600 mg/d or placebo
60 pts treated for 1 year
No sig ADE’s, QOL scales for BPH sx improved as well

Aged Garlic Extract & Colon Polyps

- 51 pts w/colorectal adenomas; Polyps > 5 cm removed & remainder observed
- AGE high dose (2.4 ml/d) vs. low dose (0.16 ml/d)- 6 capsules/day for 12 months
- Colonsocopy @ 0, 6, 12 months
- Results:
  - 37 subjects completed the study
  - Number of adenoma: incr. control; decr. Trx
  - Change in total size of adenomas similar
  - One carcinoma in control patient

Tanaka S et al. J Nutr 2006; 821S-826S.
Effect of Aged Garlic Extract: Changes in the number and total size of adenomas in the subjects who completed the study

A aged Garlic Extract & Polyps: Changes in the number and total size of adenomas in subjects who had adenomas at the beginning of the study (baseline)


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Black Cohosh & Breast Cancer

• 136 breast cancer pts after surgery, radiation & adjuvant chemotherapy (age 35-50); Groups equivalent for tumor stage & therapy
• Open label trial
• Tamoxifen +/- BCE (Klimadynon)20 mg/d
• Assessment: HF number & severity
• Outcome (1 yr):
  – 50% patients free of hot flashes
  – Severe hot flashes (24% BCE vs 74% Us care)
  – No significant ADE occurred in either group

Black Cohosh & Breast Protection

- Retrospective case-control study of incident breast cancer cases and controls
- 1,214 incident breast cancer cases identified & 949 interviewed
- 1,524 controls completed the interview
- 10-20% of pts reported use of hormone-related supplements (HRS); African American slightly more likely to use
- Wide variety of products used including: red clover, BC, Ginseng, DHEA, soy etc.
- BCE assoc w/ reduced risk of breast ca (adjusted OR 0.39, CI:0.22-0.70)

Rebbeck et al. Int J Cancer 2007; 120:1523-28
Take Home Messages

- Anticipate that many survivors are using DS
- Ask about use in a manner to encourage disclosure
- Encourage lifestyle modification FIRST
- Cancer diagnosis constitutes a teachable moment
- Although evidence of benefit for many vitamins is not clear, neither is the evidence for harm
- Consider targeted therapies in individual patients
- Consider assessing VD levels
“Something from the supplement cart?”
Summary & Questions