Overview

- Diet, Physical Activity and High Burden Cancers
  - Breast
  - Prostate
  - Colorectal
  - Lung

- Obesity and Cancer
BMI – Body Mass Index

- Measure of adiposity or fatness
- \( \text{BMI} = \frac{\text{kg}}{\text{m}^2} \)

<table>
<thead>
<tr>
<th>BMI (kg/m(^2))</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 18.5</td>
<td>Thin</td>
</tr>
<tr>
<td>18.5 – 24.9</td>
<td>Normal</td>
</tr>
<tr>
<td>25.0 – 29.9</td>
<td>Overweight</td>
</tr>
<tr>
<td>30.0 – 39.9</td>
<td>Obese</td>
</tr>
<tr>
<td>≥ 40</td>
<td>Morbidly Obese</td>
</tr>
</tbody>
</table>

WHO Expert Committee 1995
Breast Cancer

Most common cause of cancer among US women after skin cancer.
Second most common cause of cancer death.
Breast Cancer: Role of Diet and Energy Balance

- Adiposity
- Physical activity
- Dietary fat
- Alcohol
- Soy
- Other dietary factors
BMI and Breast Cancer Risk

- Risk varies by menopausal status
  - Premenopausal
    - Higher BMI lower risk
    - Anovulatory menstrual cycles
  - Postmenopausal
    - Higher BMI higher risk
    - Estrogen synthesis in adipose tissue
    - Stronger for ER+/PR+

Bhaskaran 2014
BMI and Breast Cancer Survival

- Obese patients have poorer prognosis
  - Overall survival
  - Breast cancer specific survival
- Association similar in pre- and post-menopausal women
- Conflicting results by tumor subtype

Widschwendter 2015

Overall Survival by BMI

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Recurrence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25.0</td>
<td>11.5%</td>
</tr>
<tr>
<td>25.0-29.9</td>
<td>14.7%</td>
</tr>
<tr>
<td>30.0-34.9</td>
<td>14.4%</td>
</tr>
<tr>
<td>35.0-39.9</td>
<td>11.9%</td>
</tr>
<tr>
<td>≥ 40</td>
<td>36.8%</td>
</tr>
</tbody>
</table>
Physical Activity and Breast Cancer Risk

- Physical Activity Reduces Breast Cancer Risk
  - 3% per 10 MET-h/wk (4 hrs leisurely walking or 1 hr running)
  - 5% per 2 hrs moderate to vigorous recreational activity

### RR for Women in Highest vs. Lowest Category of Physical Activity

<table>
<thead>
<tr>
<th>Type Activity</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recreational</td>
<td>0.89</td>
<td>0.85 – 0.92</td>
</tr>
<tr>
<td>Household</td>
<td>0.89</td>
<td>0.83 – 0.95</td>
</tr>
<tr>
<td>Occupational</td>
<td>0.90</td>
<td>0.83 – 0.97</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BMI Adjustment</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>0.89</td>
<td>0.85 – 0.93</td>
</tr>
<tr>
<td>Yes</td>
<td>0.88</td>
<td>0.85 – 0.91</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BMI Stratification</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt; 25</td>
<td>0.72</td>
<td>0.65 – 0.81</td>
</tr>
<tr>
<td>BMI ≥ 25</td>
<td>0.93</td>
<td>0.83 – 1.05</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Menopausal Status</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>0.77</td>
<td>0.72 – 0.84</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>0.88</td>
<td>0.84 – 0.92</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor Receptor</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER-/PR-</td>
<td>0.80</td>
<td>0.73 – 0.87</td>
</tr>
<tr>
<td>ER+/PR+</td>
<td>0.92</td>
<td>0.87 – 0.98</td>
</tr>
</tbody>
</table>

Wu 2013
Physical Activity and Breast Cancer – Possible Mechanisms

- Physical Activity → Ovaries
  - BMI & Abdominal Fat
    - Adrenals
      - Androgens
        - SHBG
          - Leptin
            - Adiponectin
              - TNF-α
                - IL-6
                  - CRP
                    - Physical Activity
                      - insulin
                        - C-peptide
                          - Free IGF-1
                            - Breast Cancer Risk

Lynch 2011
Dietary Fat and Breast Cancer

- Animal and ecologic studies suggest positive association of animal or saturated fat intake with breast cancer

- Prospective epidemiologic studies overall do not support an association

Rose 1986; Alexander 2010
Dietary Fat and Breast Cancer Risk
WHI Diet Trial

- **Design**
  - 48,835 postmenopausal women
  - Randomized
    - Low fat diet ($\leq 20 \%$ kcal)
    - Control group

- **Results**
  - 8 yr - HR=0.91 (0.83 -1.01)
  - 12 yr - HR=0.97 (0.89 -1.05)

- **Conclusion**
  - Evidence does not support role for adult dietary fat in breast cancer risk overall
  - Early life dietary fat may be important

Invasive Breast Cancer

Prentice 2006; Thomson 2014
Alcohol and Breast Cancer Risk

- Breast cancer risk increases by 10% per 10 gm/day ~ 1 drink
- Association similar
  - beer, wine and spirits
  - pre- and post-menopausal women
  - ER+ and ER- tumors
- Possible mechanisms
  - Hormonal
  - Acetaldehyde
  - Oxidative stress
  - DNA methylation

Collaborative Group 2002; Jung 2015

Alcohol Ingestion and Breast Cancer Risk

<table>
<thead>
<tr>
<th>RR ≥ 30 g/day vs. 0 g/day</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER+</td>
<td>1.35</td>
<td>1.23 – 1.48</td>
</tr>
<tr>
<td>ER-</td>
<td>1.28</td>
<td>1.10 – 1.49</td>
</tr>
</tbody>
</table>
Alcohol and Breast Cancer Survival

- **Overall survival**
  - Pre-diagnosis moderate drinkers better overall survival vs. non-drinkers
  - Post-diagnosis alcohol not associated

- **Breast cancer specific survival**
  - ER+ not associated with moderate pre- or post-diagnosis alcohol
  - ER- possible small benefit associated with post-diagnosis alcohol; no association pre-diagnosis
**Soy Intake and Breast Cancer Risk**

- Limited evidence for protective effect in Asian countries
- No association in Western countries

<table>
<thead>
<tr>
<th>High vs. Low Soy Intake</th>
<th>All Studies</th>
<th>Prospective Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td>95% CI</td>
</tr>
<tr>
<td><strong>Asian</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>0.59</td>
<td>0.48 – 0.69</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>0.59</td>
<td>0.44 – 0.74</td>
</tr>
<tr>
<td><strong>Western</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>0.90</td>
<td>0.77 – 1.04</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>0.92</td>
<td>0.83 – 1.00</td>
</tr>
</tbody>
</table>

Chen 2014
Other Dietary Factors and Breast Cancer Risk

- Dietary carbohydrate and fiber not associated with risk
- Inconsistent results for
  - fruits, vegetables, and meat
  - diet patterns
Advice to Reduce Breast Cancer Risk

- Maintain a healthy weight throughout life
- Engage in regular physical activity
- Limit alcohol consumption
Prostate Cancer

Most common cause of cancer among US men after skin cancer
Prostate Cancer: Role of Diet and Energy Balance

- Adiposity
- Physical activity
- Fruits and vegetables
- Antioxidant micronutrients
- Dairy
BMI and Prostate Cancer

- Risk of incident cancer differs for localized and advanced disease
  - RR per 5 kg/m² increase in BMI
    - Localized RR = 0.94 (0.91 – 0.97)
    - Advanced RR = 1.09 (1.02 – 1.16)

- Risk of fatal cancer increases with BMI
  - RR = 1.15 (1.05 – 1.25) per 5 kg/m²

- Mechanism
  - Unclear, possibly testosterone related

Discacciati 2012; Cao 2011
Physical Activity and Prostate Cancer Risk

- More physically active men at lower risk for prostate cancer
  - Association stronger for occupational activity from case-control studies, but not cohort studies
  - Vigorous activity may reduce risk of advanced disease

<table>
<thead>
<tr>
<th>Subgroups (Number of studies)</th>
<th>Pooled RR (95% CI)</th>
<th>P</th>
<th>I² (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cohort studies (24)</td>
<td>0.94 (0.91-0.98)</td>
<td>0.002</td>
<td>4.06</td>
</tr>
<tr>
<td>Case-control studies (34)</td>
<td>0.86 (0.75-0.97)</td>
<td>0.02</td>
<td>69.82</td>
</tr>
<tr>
<td>Subtotal (58)</td>
<td>0.90 (0.84-0.95)</td>
<td>0.001</td>
<td>61.65</td>
</tr>
<tr>
<td><strong>Occupational</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cohort studies (9)</td>
<td>0.91 (0.87-0.95)</td>
<td>&lt;0.001</td>
<td>0.00</td>
</tr>
<tr>
<td>Case-control studies (18)</td>
<td>0.73 (0.62-0.87)</td>
<td>&lt;0.001</td>
<td>66.42</td>
</tr>
<tr>
<td>Subtotal (27)</td>
<td>0.81 (0.73-0.91)</td>
<td>&lt;0.001</td>
<td>68.19</td>
</tr>
<tr>
<td><strong>Recreational</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cohort studies (19)</td>
<td>0.95 (0.90-1.00)</td>
<td>0.04</td>
<td>15.15</td>
</tr>
<tr>
<td>Case-control studies (15)</td>
<td>0.98 (0.85-1.14)</td>
<td>0.81</td>
<td>62.27</td>
</tr>
<tr>
<td>Subtotal (34)</td>
<td>0.95 (0.89-1.00)</td>
<td>0.07</td>
<td>43.43</td>
</tr>
</tbody>
</table>

Liu 2011
Fruits and Vegetables and Prostate Cancer Risk

- Tomatoes & tomato products

<table>
<thead>
<tr>
<th>RR of Prostate Cancer for High vs. Low Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Prostate Cancer</td>
</tr>
<tr>
<td>RR</td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Raw tomato</td>
</tr>
<tr>
<td>Cooked tomato</td>
</tr>
<tr>
<td>Dietary lycopene</td>
</tr>
<tr>
<td>Blood lycopene</td>
</tr>
</tbody>
</table>

- Other fruits not associated with risk
- Findings for vegetables mixed

Chen 2013
SELECT

Selenium and Vitamin E Cancer Prevention Trial

- 35,533 men 50+ years old and free of prostate cancer randomized
- 200 μg/day selenium and/or 400 IU/day vitamin E vs placebo
- Planned follow-up 7 - 12 years
- Early discontinuation of intervention for lack of efficacy
- Results after 7 years follow-up:

\[
\text{HR} = 1.17 \quad \text{P}<0.01 \\
\text{HR} = 1.09 \quad \text{P}=0.18 \\
\text{HR} = 1.05 \quad \text{P}=0.46
\]
Dairy and Prostate Cancer Risk

Total prostate cancer risk
- Increased – total dairy, milk (lowfat), cheese, total dietary calcium
- No association – calcium from non-dairy foods or supplements

No association advanced prostate cancer risk

<table>
<thead>
<tr>
<th></th>
<th>Total Prostate Cancer</th>
<th>Advanced Prostate Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Dairy</td>
<td>1.09</td>
<td>1.02 – 1.17</td>
</tr>
<tr>
<td>Milk</td>
<td>1.11</td>
<td>1.03 – 1.21</td>
</tr>
<tr>
<td>Cheese</td>
<td>1.07</td>
<td>1.01 – 1.13</td>
</tr>
<tr>
<td>Dietary Calcium</td>
<td>1.18</td>
<td>1.08 – 1.30</td>
</tr>
<tr>
<td>Supplements</td>
<td>1.00</td>
<td>0.95 – 1.05</td>
</tr>
</tbody>
</table>

Aune 2015
Advice to Reduce Prostate Cancer Risk

- Maintain a healthy body weight
- Be physically active
- Eat a variety of fruits and vegetables
Colorectal Cancer

Third most common cause of cancer among US men and women
Colorectal Cancer: Role of Diet and Energy Balance

- Adiposity
- Physical activity
- Red and processed meat
- Dietary fiber
- Calcium and vitamin D
- Alcohol
- Other dietary factors
BMI and Colorectal Cancer

- BMI positively associated with colon cancer risk
  - Overall 10% increase risk per 5kg/m² increase BMI
  - Association stronger in men
- BMI weak positive association with rectal cancer risk
  - Overall 4% increase risk per 5kg/m² increase BMI
- Higher BMI poorer prognosis following colorectal cancer diagnosis

Bhaskaran 2014; Campbell 2015
Physical Activity and Colorectal Cancer Risk – Cohort Studies

RR = 0.83  (95% CI = 0.78 – 0.88)
Physical Activity and Colorectal Cancer Risk

- **Significant dose response in 24 of 35 studies**
  - High vs. low intensity activity RR = 0.8
  - 1 hr/day vs. <1 hr/day moderate activity RR = 0.6

- **Type of activity**
  - Risk reduction similar for recreational and occupational physical activity
  - Inconsistent associations with walking

- **Timing of activity**
  - Consistent associations for lifetime and adult only physical activity

- **Family history**
  - Association only if no family history

- **Location**
  - Risk similar for distal and proximal colon

Wolin 2011
Increased immune function due to increased macrophages, NK cells, T cells.

Decreased inflammation due to decreased IL-6, TNF-α, PGE-2.

Decreased insulin resistance due to decreased insulin, IGF-1, C-peptide, increased IGFBP-3.

Increased vitamin D.

Physical activity leads to a decrease in body fat.

Decreased body fat leads to increased immune function.

Increased immune function decreases inflammation.

Decreased inflammation decreases insulin resistance.

Increased vitamin D decreases colorectal cancer risk.

Wolin 2011
Red and Processed Meat and Colorectal Cancer Risk

Relative Risk Colorectal Cancer - Red Meat (100 gm/day ~ 1 serving)

- Pietinen 1999 Male 0.83 (0.43, 1.61)
- Jarvinen 2001 Mixed 1.37 (0.92, 2.06)
- Tiemersma 2002 Mixed 1.69 (0.88, 3.23)
- English 2004 Mixed 1.19 (0.89, 1.58)
- Larsson 2005 Female 1.23 (0.90, 1.67)
- Norat 2005 Mixed 1.21 (1.02, 1.43)
- Lee 2009 Female 0.80 (0.52, 1.23)
- Nothlings 2009 Mixed 1.00 (0.64, 1.57)
- Subtotal (I-squared = 0.0%, p = 0.483) 1.17 (1.05, 1.31)

Relative Risk Colorectal Cancer - Processed Meat (50 gm/day ~ 1 hot dog)

- Pietinen 1999 Male 1.01 (0.80, 1.27)
- Flood 2003 Female 1.17 (0.76, 1.81)
- English 2004 Mixed 1.61 (1.12, 2.30)
- Lin 2004 Female 0.56 (0.24, 1.33)
- Larsson 2005 Female 1.13 (0.85, 1.51)
- Norat 2005 Mixed 1.15 (1.03, 1.28)
- Balder 2006 Mixed 1.21 (0.91, 1.61)
- Cross 2007 Mixed 1.26 (1.13, 1.40)
- Nothlings 2009 Mixed 1.21 (0.74, 2.00)
- Subtotal (I-squared = 12.2%, p = 0.333) 1.18 (1.10, 1.28)

Chan 2011
Red and Processed Meat and Colorectal Cancer Risk - Mechanisms

- Sulfur containing amino acids → hydrogen sulfide
  - inflammation, DNA damage, epithelial hyperproliferation

- Heme iron
  - Oxidative stress
  - Colonocyte proliferation
  - N-nitroso compounds – potent GI carcinogens

- Cooking at high temperature → mutagens
  - Heterocyclic amines
  - Polycyclic aromatic hydrocarbons

- Preservatives
  - Inorganic sulfur → hydrogen sulfide
  - Nitrates and nitrites → N-nitroso compounds
Dietary Fiber and Colorectal Cancer Risk

- **Epidemiologic studies**
  - Observational studies show overall protective effect but heterogeneous
  - 6 RCTs of fiber supplements in patients with colorectal polyps showed no benefit

- **Mechanisms**
  - Decreased stool transit time, carcinogen dilution
  - Decreased adiposity
  - Anticancer properties of bacterial fermentation products

<table>
<thead>
<tr>
<th>Source</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sources</td>
<td>0.90</td>
<td>0.86 – 0.94</td>
</tr>
<tr>
<td>Legumes</td>
<td>0.62</td>
<td>0.27 – 1.42</td>
</tr>
<tr>
<td>Cereal</td>
<td>0.90</td>
<td>0.83 – 0.97</td>
</tr>
<tr>
<td>Fruit</td>
<td>0.93</td>
<td>0.82 – 1.05</td>
</tr>
<tr>
<td>Vegetables</td>
<td>0.98</td>
<td>0.91 – 1.06</td>
</tr>
</tbody>
</table>

Aune 2011
Dairy and Colorectal Cancer Risk

- Dairy associated with lower risk of colorectal cancer
  - RR = 0.83 per 400 g/day

- Specific foods
  - High fat dairy
  - Milk

- Possible mechanisms
  - Fatty acids linoleic and butyric acid protective in animals
  - Lactoferrin
  - Calcium
  - Vitamin D

Summary RR for High vs. Low Dairy Intake

<table>
<thead>
<tr>
<th>Source</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sources</td>
<td>0.81</td>
<td>0.74 – 0.90</td>
</tr>
<tr>
<td>High fat</td>
<td>0.74</td>
<td>0.53 – 1.02</td>
</tr>
<tr>
<td>Low fat</td>
<td>0.97</td>
<td>0.74 – 1.28</td>
</tr>
<tr>
<td>Milk</td>
<td>0.83</td>
<td>0.74 – 0.93</td>
</tr>
<tr>
<td>Cheese</td>
<td>0.94</td>
<td>0.75 – 1.18</td>
</tr>
<tr>
<td>Yogurt</td>
<td>1.00</td>
<td>0.67 – 1.48</td>
</tr>
</tbody>
</table>
Calcium and Colorectal Cancer Risk

**Observational Studies**
- Colorectal cancer
  - RR = 0.92 (0.89–0.95) per 300 mg/day
- High risk adenoma (large, villous histology, dysplasia, multiplicity)
  - Non-linear
  - Compared to 550 mg/day RR = 0.77 (0.74–0.81) at 1000 mg/day

**Randomized Trials**
- Reduction adenoma recurrence in most but not all trials
- Colorectal cancer - WHI
  - Overall no effect
  - 17% reduction in non-supplement users at baseline

Keum 2014, 2015
Vitamin D and Colorectal Cancer Risk

**Observational Studies**

- Colorectal cancer
  - Diet - high vs. low vitamin D intake
    RR = 0.88 (0.80 – 0.96)
  - Blood – high vs. low 25(OH)D levels
    RR = 0.67 (0.54 – 0.80)

- Adenoma
  - Diet - high vs. low vitamin D intake
    RR = 0.89 (0.79 – 1.01)
  - Blood - RR = 0.84 (0.72 - 0.97) per 20 ng/ml increase in 25(OH)D

**Randomized Trials**

- No reduction adenoma recurrence
- Colorectal cancer - WHI
  - Overall no effect

Wei 2008; Ma 2011; Yin 2011; Cauley 2013; Baron 2015
Vitamin D and Colorectal Cancer Mortality

- Higher serum vitamin D associated with improved survival
  - Total mortality
    HR=0.91 (0.81 – 1.01) per 20 nmol/L increase 25(OH)D
  - Disease specific mortality
    HR=0.90 (0.84 – 0.97) per 20 nmol/L increase 25(OH)D

Wang 2014, 2015
Calcium, Vitamin D and Colorectal Cancer - Mechanisms

- Calcium
  - Binds to fatty acids and free bile acids
  - Decreases cell proliferation
  - Promotes cell differentiation and apoptosis
  - Inhibits oxidative DNA damage
  - Modulates signaling pathways

- Vitamin D
  - Decreases cell proliferation
  - Promotes cell differentiation and apoptosis
  - Anti-inflammatory
  - Inhibits invasion and metastasis
  - Suppresses angiogenesis
Reasons for Different Findings from Observational Studies and Trials

- Study design
- Threshold effect with high baseline intake
- Poor compliance
- Short duration of treatment or follow-up
- Anatomic site heterogeneity
- Other dietary factors
- Genetic background
Alcohol and Colorectal Cancer Risk

- Alcohol increases colorectal cancer risk 15% per 100 gm/wk ~ 10 drinks
- No difference by type of beverage

### Colorectal Cancer Risk

<table>
<thead>
<tr>
<th>Site</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>1.50</td>
<td>1.25 – 1.79</td>
</tr>
<tr>
<td>Rectum</td>
<td>1.63</td>
<td>1.35 – 1.97</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>1.73</td>
<td>1.00 – 2.98</td>
</tr>
<tr>
<td>Women</td>
<td>0.88</td>
<td>0.61 – 1.27</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Region</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>1.16</td>
<td>0.63 – 2.14</td>
</tr>
<tr>
<td>Europe</td>
<td>1.83</td>
<td>1.14 – 2.92</td>
</tr>
<tr>
<td>Asia</td>
<td>1.16</td>
<td>0.64 – 2.13</td>
</tr>
</tbody>
</table>

Moskal 2006
Advice to Reduce Colorectal Cancer Risk

• Maintain healthy body weight
• Increase intensity and duration of physical activity
• Limit intake of red and processed meats
• Consume adequate vitamin D and calcium
• Avoid excess alcohol
Lung Cancer

Second most common cause of cancer among US men and women after skin cancer

Leading cause of cancer death
Lung Cancer: Role of Diet and Energy Balance

- Adiposity
- Physical activity
- Fruits and vegetables
- Antioxidant micronutrients
BMI and Lung Cancer Risk

- Overall apparent decreased risk of lung cancer associated with higher BMI
- Smokers are leaner than non-smokers
- Among non-smokers no association of BMI with lung cancer risk
- Apparent decreased risk overall due to uncontrolled confounding by smoking

Bhaskaran 2014
Physical Activity and Lung Cancer Risk

- Physical activity associated with lower lung cancer risk
- Active vs. inactive RR = 0.87 (0.83 – 0.90)
Physical Activity and Lung Cancer – Possible Mechanisms

- Physical Activity
  - DNA Repair
  - Respiratory Ventilation
  - Immune Function
  - Chronic Inflammation
  - Growth Factors

Genetic Profile

Possible Effect Modifiers:
- Histology
- Age
- Gender
- Smoking
- BMI
- Epigenetics

Lung Cancer

Emaus 2011
Fruits and Vegetables and Lung Cancer Risk

- Lung cancer risk for high vs. low intake
  - Fruits and vegetables: RR = 0.86 (0.78 – 0.94)
  - Vegetables: RR = 0.92 (0.87 – 0.97)
  - Fruits: RR = 0.82 (0.76 – 0.89)

- Results consistent across different types fruits and vegetables

- Association non-linear, no benefit when increase intake above ~400 g/day fruits and vegetables
Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC)

- **Design**
  - 29,133 male smokers 50-69 years old randomized
  - 50 mg/day α-tocopherol, 20 mg/day β-carotene, both or placebo
  - On trial median 6.1 years

- **Lung cancer at end of trial**
  - α-tocopherol no effect on risk
  - β-carotene increased risk

- **Follow-up at 5 yrs post-intervention**
  - α-tocopherol: RR = 1.14 (0.96 – 1.35)
  - β-carotene: RR = 0.97 (0.82 – 1.15)

ATBC Study Group 1994, 2003
Advice to Reduce Lung Cancer Risk

• Avoid tobacco
• Avoid environmental radon
Summary: Ways to Reduce Risk of High Burden Cancers

- Maintain a healthy weight
- Be physically active
- Eat fruits and vegetables
- Choose whole over refined grains
- Limit consumption of red and processed meats
- Limit alcohol intake
Obesity and Cancer
Obesity Prevalence in the US
Adults (20-74 yrs)

34.9% = 78.6 million
US adults obese

CDC 2003; Ogden 2006, 2015
Obesity Prevalence in the US
Adults (20-74 yrs)

White | Black | Hispanic

% obese

CDC 2003; Ogden 2006, 2015
Prevalence of Obesity Among U.S. Adults, 2014

29.6% Maryland
Hagerstown 3rd highest US city
36.7% obese!
Prevalence of Obesity Among Maryland Adults

**Sex**
- Men: 25%
- Women: 30%

**Race**
- White: 25%
- Black: 40%
- Hispanic: 25%

BRFSS 2013, 2015
Trends in Obesity Prevalence Among Maryland Adults, 1990-2014

% Obese

Year


BRFSS 2015
BMI and Cancer Risk

Bhaskaran 2014
BMI and Cancer Risk

HR = 1.19 per 5 kg/m²
BMI and Cancer Risk

HR = 1.19 per 5 kg/m²

HR = 1.31 per 5 kg/m²
BMI and Cancer Risk

Bhaskaran 2014

HR = 1.19 per 5 kg/m²

HR = 1.62 per 5 kg/m²

HR = 1.31 per 5 kg/m²
BMI and Cancer Risk

HR=1.19 per 5 kg/m$^2$

HR=1.31 per 5 kg/m$^2$

HR=1.62 per 5 kg/m$^2$

HR=1.25 per 5 kg/m$^2$
Population Attributable Risk Due to Overweight and Obesity

- Relative risk
  - measure of strength of association

- Attributable risk
  - takes into account RR and exposure prevalence
  - estimates proportion of cases in population due to an exposure
  - important public health metric

<table>
<thead>
<tr>
<th>Site</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>11.1</td>
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<tr>
<td>Liver</td>
<td>15.6</td>
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<tr>
<td>Gall bladder</td>
<td>20.3</td>
</tr>
<tr>
<td>Breast (postmenopausal)</td>
<td>5.1</td>
</tr>
<tr>
<td>Cervix</td>
<td>7.5</td>
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<tr>
<td>Uterus</td>
<td>40.8</td>
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<tr>
<td>Ovaries</td>
<td>7.3</td>
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<tr>
<td>Kidney</td>
<td>16.6</td>
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<tr>
<td>Thyroid</td>
<td>1.9</td>
</tr>
<tr>
<td>Leukemia</td>
<td>6.3</td>
</tr>
</tbody>
</table>

Assumes 65% men and 58% women have BMI>25

Bhaskaran 2014
Cancer Diagnoses Attributable to Obesity, US

Men

15%

Women

20%
Obesity and Cancer – Possible Mechanisms

- Obesity
- Adipocytes
  - ↓ IGFBP’s
  - ↑ Free IGF-1
- IGF Axis
  - ↑ Estrogen
  - ↓ SHBG
  - ↓ Free T
- Sex Hormones
- Diet
  - ↑ Fat Intake
  - ↓ Energy Intake/Energy Expenditure
- Insulin Resistance
  - ↑ Insulin

Leptin
Adiponectin
FGF-2

↑ Inflammation

Freedland 2005
Worldwide Obesity Prevalence – Men, 2013

Ng 2014
Worldwide Obesity Prevalence – Women, 2013

B  Age-standardised prevalence of obesity (BMI ≥30 kg/m²), ages ≥20 years, women, 2013

Ng 2014
Future Directions

Research
- Mechanisms underlying obesity cancer association
- Interventions to prevent/reduce obesity

Education
- Health effects, including cancer, of overweight and obesity
- Approaches to achieve and maintain healthy weight

Workplace
- Encourage physical activity
- Provide access to healthy food choices

Public policy
- School lunch and other food assistance programs
- Nutrition labeling
- Title IX
- Built environment