Nutrition and gastrointestinal cancer: An update of the epidemiological evidence

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Epidemiology of colorectal cancer

- Third most common cancer type
- Incidence
  1.4 million new cases diagnosed in 2012
- Mortality
  694,000 deaths in 2012

Total Number and Percentage of New Cases Diagnosed per Year, Worldwide

Ferlay et al. Int J Can 2014
Epidemiology of colorectal cancer

- 54% of colorectal cancer cases occur in developed countries.
- More deaths (52%) in the less developed regions
- Increase by 60% by 2030
  - 2.2 million new cases
  - 1.1 million deaths
Nutrition and cancer promoting mechanisms

Food and nutrition

Carcinogenesis
N-ntroso compounds
Heterocyclic amines

Apoptosis
Vitamin A
B vitamins

DNA repair

Metabolism
Obesity
Metabolic syndrome

Differentiation
Polyphenols
N-3 PUFA

Inflammation and immunity
Selenium
Zinc
Antioxidants

Folate
Objective

To review the meta-epidemiological evidence on the role of nutrition (including body composition) in colorectal cancer in order to identify potential targets for nutritional chemoprevention.
Methods

- Umbrella review of evidence

- An online literature search
  - MEDLINE, ISI Web of Science and Scopus

- Studies published in English (up to June 2017)

- Inclusion criteria:
  - Systematic literature reviews (SLRs) and meta-analyses (MAs) of observational studies
  - Most updated reviews and meta-analyses
## Nutrition and colorectal cancer

### Food, Nutrition, Physical Activity and Cancers of the Colon and the Rectum 2011

<table>
<thead>
<tr>
<th>DECREASES RISK</th>
<th>INCREASES RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Convincing</strong></td>
<td>Physical activity(^{1,2})</td>
</tr>
<tr>
<td></td>
<td>Foods containing dietary fibre(^3)</td>
</tr>
<tr>
<td></td>
<td>Red meat(^4,5)</td>
</tr>
<tr>
<td></td>
<td>Processed meat(^4,6)</td>
</tr>
<tr>
<td></td>
<td>Alcoholic drinks (men)(^7)</td>
</tr>
<tr>
<td></td>
<td>Body fatness</td>
</tr>
<tr>
<td></td>
<td>Abdominal fatness</td>
</tr>
<tr>
<td></td>
<td>Adult attained height(^8)</td>
</tr>
<tr>
<td><strong>Probable</strong></td>
<td>Garlic</td>
</tr>
<tr>
<td></td>
<td>Milk(^9)</td>
</tr>
<tr>
<td></td>
<td>Calcium(^{10})</td>
</tr>
<tr>
<td><strong>Substantial effect on risk unlikely</strong></td>
<td>None identified</td>
</tr>
</tbody>
</table>

1. Physical activity of all types: occupational, household, transport and recreational.
2. The Panel judges that the evidence for colon cancer is convincing. No conclusion was drawn for rectal cancer.
3. Includes both foods naturally containing the constituent and foods which have the constituent added. Dietary fibre is contained in plant foods.
4. Although red and processed meats contain iron, the general category of ‘foods containing iron’ comprises many other foods, including those of plant origin.
5. The term ‘red meat’ refers to beef, pork, lamb, and goat from domesticated animals.
6. The term ‘processed meat’ refers to meats preserved by smoking, curing, or salting, or addition of chemical preservatives.
7. The judgements for men and women are different because there are fewer data for women. For colorectal and colon cancers the effect appears stronger in men than in women.
8. Adult attained height is unlikely directly to modify the risk of cancer. It is a marker for genetic, environmental, hormonal, and also nutritional factors affecting growth during the period from preconception to completion of linear growth (see chapter 6.2.13 – Second Expert Report).
9. Milk from cows. Most data are from high-income populations, where calcium can be taken to be a marker for milk/dairy consumption. The Panel judges that a higher intake of dietary calcium is one way in which milk could have a protective effect.
10. The evidence is derived from studies using supplements at a dose of 1200mg/day.
Red and processed meat

- **Meta-analysis**
  - 13 prospective studies

- **Main results**
  - 14% risk increase in colorectal cancer for every 100 g/day increase of total red and processed meats
  - Non-linear association
  - Above 140 g/day, the risk increase is less pronounced.

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<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Subgroup</th>
<th>RR (95% CI) per 100g/day increase</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chen</td>
<td>1996</td>
<td>Male</td>
<td>1.11 (0.76, 1.63)</td>
<td>4.18</td>
</tr>
<tr>
<td>Pietinen</td>
<td>1999</td>
<td>Male</td>
<td>1.05 (0.74, 1.49)</td>
<td>4.86</td>
</tr>
<tr>
<td>Flood</td>
<td>2003</td>
<td>Female</td>
<td>1.14 (0.74, 1.75)</td>
<td>3.41</td>
</tr>
<tr>
<td>Lin</td>
<td>2004</td>
<td>Female</td>
<td>0.73 (0.55, 0.99)</td>
<td>6.13</td>
</tr>
<tr>
<td>Larsson</td>
<td>2006</td>
<td>Female</td>
<td>1.20 (0.99, 1.45)</td>
<td>10.58</td>
</tr>
<tr>
<td>Norat</td>
<td>2005</td>
<td>Mixed</td>
<td>1.25 (1.10, 1.42)</td>
<td>14.65</td>
</tr>
<tr>
<td>Berndt</td>
<td>2006</td>
<td>Mixed</td>
<td>1.38 (0.84, 2.28)</td>
<td>2.64</td>
</tr>
<tr>
<td>Cross</td>
<td>2007</td>
<td>Mixed</td>
<td>1.31 (1.20, 1.44)</td>
<td>17.51</td>
</tr>
<tr>
<td>Kabat</td>
<td>2007</td>
<td>Female</td>
<td>1.12 (0.60, 2.09)</td>
<td>1.77</td>
</tr>
<tr>
<td>Fung</td>
<td>2010</td>
<td>Female</td>
<td>1.10 (0.99, 1.22)</td>
<td>16.80</td>
</tr>
<tr>
<td>Fung</td>
<td>2010</td>
<td>Male</td>
<td>1.07 (0.97, 1.17)</td>
<td>17.43</td>
</tr>
<tr>
<td>Subtotal</td>
<td>(%-squared = 56.2%, p = 0.011)</td>
<td></td>
<td>1.14 (1.04, 1.24)</td>
<td>100.00</td>
</tr>
<tr>
<td>Colon cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Willett</td>
<td>1990</td>
<td>Female</td>
<td>1.57 (1.08, 2.29)</td>
<td>8.10</td>
</tr>
<tr>
<td>Boatlick</td>
<td>1994</td>
<td>Female</td>
<td>0.97 (0.74, 1.25)</td>
<td>12.41</td>
</tr>
<tr>
<td>Giovannucci</td>
<td>1994</td>
<td>Male</td>
<td>1.73 (1.25, 2.39)</td>
<td>9.86</td>
</tr>
<tr>
<td>Chao</td>
<td>2005</td>
<td>Mixed</td>
<td>1.12 (0.93, 1.35)</td>
<td>16.18</td>
</tr>
<tr>
<td>Larsson</td>
<td>2005</td>
<td>Female</td>
<td>1.54 (1.22, 1.95)</td>
<td>13.65</td>
</tr>
<tr>
<td>Norat</td>
<td>2005</td>
<td>Mixed</td>
<td>1.26 (1.07, 1.48)</td>
<td>17.59</td>
</tr>
<tr>
<td>Kabat</td>
<td>2007</td>
<td>Female</td>
<td>0.61 (0.29, 1.28)</td>
<td>2.76</td>
</tr>
<tr>
<td>Cross</td>
<td>2010</td>
<td>Mixed</td>
<td>1.20 (1.05, 1.37)</td>
<td>19.46</td>
</tr>
<tr>
<td>Subtotal</td>
<td>(%-squared = 59.6%, p = 0.015)</td>
<td></td>
<td>1.25 (1.10, 1.43)</td>
<td>100.00</td>
</tr>
<tr>
<td>Rectal cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chao</td>
<td>2005</td>
<td>Mixed</td>
<td>1.33 (0.98, 1.80)</td>
<td>20.12</td>
</tr>
<tr>
<td>Larsson</td>
<td>2005</td>
<td>Female</td>
<td>1.28 (0.75, 2.21)</td>
<td>7.20</td>
</tr>
<tr>
<td>Norat</td>
<td>2006</td>
<td>Mixed</td>
<td>1.22 (0.99, 1.51)</td>
<td>34.63</td>
</tr>
<tr>
<td>Kabat</td>
<td>2007</td>
<td>Female</td>
<td>4.27 (1.42, 12.77)</td>
<td>1.86</td>
</tr>
<tr>
<td>Cross</td>
<td>2010</td>
<td>Mixed</td>
<td>1.31 (1.07, 1.61)</td>
<td>36.18</td>
</tr>
<tr>
<td>Subtotal</td>
<td>(%-squared = 18.2%, p = 0.299)</td>
<td></td>
<td>1.31 (1.13, 1.52)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis

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Meta-analyses of red and processed meat consumption and the risk of colorectal cancer

Chan D et al. Plos One 2011

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Non-linear dose-response meta-analysis
Poultry and colorectal cancer

- Meta-analysis
  - 16 studies
  - 11% lower risk for the highest versus lowest category of intake

Dose–response analysis between poultry intake and colorectal cancer

Meta-analysis of poultry intake and the risk of colorectal cancer


Meta-analysis of poultry intake and the risk of colorectal cancer

Heme iron

Meta-analysis
- 7 prospective studies

Main results
- 14% risk increase in colorectal cancer for high versus low heme iron intake
Alcohol and colorectal cancer

**Meta-analysis**
- 18 prospective studies

**Main results**
- 21% higher risk for moderate alcohol drinking
- 52% higher risk for heavy (≥4 drinks/day) alcohol drinking compared to occasional drinking
- 7%, 38%, and 82% higher risk for 10, 50, and 100 g/day of alcohol, respectively

![Dose-response meta-analysis of alcohol consumption](image)

**Meta-analysis of alcohol consumption (heavy versus occasional drinkers) and the risk of colorectal cancer**

**Lifetime alcohol**

### Meta-analysis of alcohol consumption measured during lifetime/over time and colorectal cancer

<table>
<thead>
<tr>
<th>First author, Year</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cohort</strong></td>
<td></td>
</tr>
<tr>
<td>Ferrari, 2007*</td>
<td>2.02 (1.51, 2.70)</td>
</tr>
<tr>
<td>Thygesen, 2008</td>
<td>1.59 (1.06, 2.38)</td>
</tr>
<tr>
<td>Subtotal (I²-squared = 0.0%, p = 0.346)</td>
<td>1.88 (1.47, 2.36)</td>
</tr>
<tr>
<td><strong>Case-control</strong></td>
<td></td>
</tr>
<tr>
<td>Williams, 1977</td>
<td>1.31 (0.88, 1.96)</td>
</tr>
<tr>
<td>Kune, 1987</td>
<td>1.20 (0.90, 1.59)</td>
</tr>
<tr>
<td>Freudenheim, 1990</td>
<td>1.83 (1.25, 2.68)</td>
</tr>
<tr>
<td>Riboli, 1981</td>
<td>1.35 (0.89, 2.06)</td>
</tr>
<tr>
<td>Benedetti, 2009</td>
<td>1.32 (1.01, 1.74)</td>
</tr>
<tr>
<td>Subtotal (I²-squared = 0.0%, p = 0.533)</td>
<td>1.35 (1.17, 1.57)</td>
</tr>
<tr>
<td><strong>Overall</strong> (I²-squared = 33.5%, p = 0.172)</td>
<td>1.49 (1.27, 1.74)</td>
</tr>
</tbody>
</table>

Relative risk (highest vs lowest intake category)

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**Meta-analysis of alcohol consumption measured during lifetime/over time and colorectal cancer**

Jayasekara et al. Alcohol and Alcoholism 2016

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Obesity and colorectal cancer

Meta-analysis

- 41 studies on general obesity
- 13 studies on central obesity

Main results

- 33% higher risk for the obese vs. normal category of BMI
- 45% for the highest vs. lowest category of WC

Meta-analysis of general abdominal obesity (waist circumference) and the risk of colorectal cancer

Ma Plos One 2013
NuGOweek 2017 Varna, Bulgaria
Weight gain and colorectal cancer

Meta-analysis
- 18 prospective studies

Main results
- 22% higher risk for high body weight gain (midpoint: 15.2 kg) compared with stable weight

Meta-analysis of weight gain in adult life and the risk of colorectal cancer

Schlesinger S, Aleksandrova K et al. Obes Rev 2013

NuGOweek 2017 Varna, Bulgaria
Physical activity and colorectal cancer

- Meta-analysis
  - 28 cohort

- Main results
  - 17% lower risk for high vs. low physical activity
  - Similar results for men and women

Wollin K et al. Br J Can 2009

Meta-analysis of physical activity and colon cancer: cohort studies

Wollin K et al. Br J Can 2009
Dietary fibre

Metanalysis
- 21 prospective studies

Main results
- Inverse association between intake of dietary fibre, cereal fibre, and whole grains
- No significant evidence for fibre from fruit, vegetables, or legumes.

Meta-analysis of dietary fibre types and the risk of colorectal cancer

Aune D et al. BMJ 2011
Fruits and vegetables intake and colorectal cancer risk

- Meta-analysis
  - 19 prospective cohort studies

- Main results
  - 8% lower risk for high vs. low intake
  - Non-linear association
  - Greatest reduction in risk when increasing intake from very low levels

Dose-response analysis of fruits and vegetables and risk of colorectal cancer


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Dairy products

Meta-analysis
- 12 cohort studies

Main results
- 19% lower risk for colon cancer the high versus low intake
- No association for rectal cancer

Total dairy products and colorectal cancer

Dose-response analysis of dairy and milk and risk of colorectal cancer

Meta-analysis of dairy products and the risk of colorectal cancer

Calcium intake and colorectal cancer risk

- Meta-analysis
  - 15 prospective cohort studies

- Main results
  - Total calcium intake: 8% lower risk for each 300 mg/day increase
  - Supplementary calcium: 9% lower risk for each 300 mg/day increase

Dose-response analysis of dietary calcium and risk of colorectal cancer

**Vitamin D and colorectal cancer**

- **Meta-analysis**
  - 9 prospective cohort studies vitamin D intake
  - 9 studies on 25-hydroxyvitamin D [25(OH)D]

- **Main results**
  - 12% lower risk for highest versus lowest category reported vitamin D intake
  - 33% lower risk for blood 25(OH)D levels

A 10 ng/mL increment in blood 25(OH)D level conferred an RR of 0.74 (95% CI, 0.63 to 0.89)

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**Dose-response analysis of blood 25(OH) D levels and risk of colorectal cancer**

**Relative risks of colorectal cancer for the highest versus lowest categories of (A) vitamin D intake or (B) 25-hydroxyvitamin D [25(OH)D] blood level**

Ma Y et al. J Clin Oncol 2011
Dietary supplements

Meta-analysis
- 25 prospective cohort studies

Main results
- 8% lower risk for use versus non-use of multivitamins
- 14% lower risk for calcium supplements

Inconsistent associations: supplemental vitamin A, vitamin C, vitamin E, vitamin D, garlic and folic acid.

Summary RRs of “use-no use” meta-analyses and “highest-lowest” meta-analyses for the association of dietary supplement use and colorectal cancer risk

<table>
<thead>
<tr>
<th>Dietary supplement</th>
<th>Summary RR</th>
<th>95% CI</th>
<th>I², p heterogeneity</th>
<th>Included studies</th>
<th>Outcome¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Use-no use meta-analyses</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivitamins</td>
<td>0.92</td>
<td>0.87, 0.97</td>
<td>4.9%, p = 0.39</td>
<td>726-32</td>
<td>CRC</td>
</tr>
<tr>
<td>Multivitamins (including Pooling Project)</td>
<td>0.92</td>
<td>0.86, 0.98</td>
<td>0.0%, p = 0.43</td>
<td>1621,28,29,31</td>
<td>CRC</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>0.77</td>
<td>0.62, 0.94</td>
<td>0.0%, p = 0.76</td>
<td>233,34</td>
<td>CC</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>0.87</td>
<td>0.63, 1.21</td>
<td>77.4%, p = 0.01</td>
<td>333-35</td>
<td>CC</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>0.85</td>
<td>0.72, 1.01</td>
<td>20.0%, p = 0.29</td>
<td>533-36</td>
<td>CC</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>0.92</td>
<td>0.78, 1.09</td>
<td>53.9%, p = 0.07</td>
<td>534,37,38,40,41</td>
<td>CRC</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.86</td>
<td>0.79, 0.95</td>
<td>63.7%, p = 0.01</td>
<td>834,37,40,42-46</td>
<td>CRC</td>
</tr>
<tr>
<td>Garlic</td>
<td>1.24</td>
<td>0.99, 1.54</td>
<td>0.0%, p = 0.34</td>
<td>248,49</td>
<td>CRC</td>
</tr>
<tr>
<td><strong>Highest-lowest meta-analyses</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin A</td>
<td>0.79</td>
<td>0.62, 1.01</td>
<td>0.0%, p = 0.97</td>
<td>233,34</td>
<td>CC</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>0.85</td>
<td>0.68, 1.05</td>
<td>10.9%, p = 0.33</td>
<td>333-35</td>
<td>CC</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>0.82</td>
<td>0.67, 0.99</td>
<td>11.0%, p = 0.34</td>
<td>533-36</td>
<td>CC</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>0.87</td>
<td>0.62, 1.22</td>
<td>67.1%, p = 0.03</td>
<td>434,37,39,40</td>
<td>CRC</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.80</td>
<td>0.70, 0.92</td>
<td>49.2%, p = 0.08</td>
<td>634,37,40,42-44</td>
<td>CRC</td>
</tr>
<tr>
<td>Folic acid</td>
<td>0.88</td>
<td>0.78, 0.98</td>
<td>6.2%, p = 0.34</td>
<td>332,35,47</td>
<td>CRC</td>
</tr>
</tbody>
</table>

¹Outcomes: CC (Colorectal Cancer), CRC (Colorectal Cancer Risk)
**Micronutrients**

**Selenium**

- 12 observational studies and two clinical trials

**Zinc**

- 6 prospective cohort studies

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**Meta-analysis of selenium and the risk of colorectal cancer**

*Ordered by biospecimen type (serum/plasma and toenail samples) and by selenium concentrations within each biospecimen type*

**Takata Y et al. CEBP 2011**

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**Meta-analysis of zinc and risk of colorectal cancer**

**Qiao & Feng Can Causes Control 2013**

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One-carbon metabolic pathway

**Vitamin B6**
- 9 studies on vitamin B6 intake
- 4 studies on blood PLP levels

**Vitamin B12**
- 17 observational studies (incl 5 cohort studies)

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Meta-analysis of vitamin B6 intake or blood PLP Level and risk of colorectal cancer

Larsson S, Orsin N & Yolk A et al. JAMA 2010

Meta-analysis of vitamin B12 intake and risk of colorectal cancer

Sun NH et al. Public Health Nutrition 2015

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Summary

- High body fatness (central adiposity): major risk factor for colorectal cancer

- Other established factors
  - alcohol, red and processed meat intake
  - whole grain intake

- Potential for chemoprevention through optimising micronutrient intakes:
  i.e. calcium, vitamin D, vitamin B6 and B12, zinc and selenium

- However, more data from randomised control trials would be needed
Outlook

- Further research focus on
  - Complex dietary patterns & lifestyles
  - Micronutrients with chemopreventive potential
  - Targeted prevention via modulation of cancer-related biomarkers

- Prevention focus on
  - Complex lifestyle recommendations
  - Patient education about nutritional risks and benefits (i.e. processed meat)
  - Identification of high-risk individuals
  - Empowerment for behaviour changes
Combined impact of nutritional factors

<table>
<thead>
<tr>
<th>Lifestyle factor</th>
<th>Index points</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overweight and obesity</td>
<td>0</td>
<td>Overweight or obese: BMI 25 kg/m² or waist circumference 94 cm for men and 80 cm for women</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Healthy weight: BMI 18 to 25 kg/m² or waist circumference &lt;94 for men cm and &lt;80 for women</td>
</tr>
<tr>
<td>Physical activity</td>
<td>0</td>
<td>Low and very low physical activity: sedentary or standing occupation and recreational METs ≤57 for men and METs ≤82 for women</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>High and very high physical activity: manual or heavy manual occupation and recreational METs &gt;57 for men and METs &gt;82 for women</td>
</tr>
<tr>
<td>Smoking</td>
<td>0</td>
<td>Smoking: current smokers</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Non-smoking: never or former smokers</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>0</td>
<td>Heavy alcohol consumption: not adherent to alcohol consumption recommendations of WCRF/AICR (2007) [15] for two standard drinks a day (&gt;24 g/day) for men and one standard drink a day (&gt;12 g/day) for women</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Limited alcohol consumption: adherent to alcohol consumption recommendations of WCRF/AICR (2007) [15,16] for two standard drinks a day (&gt;24 g/day) for men and one standard drink a day (&gt;12 g/day) for women</td>
</tr>
<tr>
<td>Diet quality</td>
<td>0</td>
<td>Unhealthy diet quality: 0 to 4 points of the diet index of colorectal cancer related foods</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Healthy diet quality: 5 to 8 points of the diet index of colorectal cancer related foods</td>
</tr>
</tbody>
</table>

Based on data from 350 000 men and women in the EPIC cohort

Number of lifestyle factors

P-trend < 0.0001

Aleksandrova K et al. BMC Medicine 2014

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THANK YOU FOR YOUR ATTENTION!
Biomarkers of Obesity

Adipose tissue
- Established relationship with insulin resistance
- Play a role in the regulation of insulin signaling and action

Source of inflammation

Adipocytokines
- Leptin
- Adiponectin
- IL-6
- TNFalpha
- Free fatty acids
- Resistin

Does obesity drive these changes in hormones or do hormones drive changes in body shape, weight, and adiposity?
Biomarkers of Obesity: Data from the EPIC cohort

Multivariable-adjusted RRs associated with an increase in continuous log-transformed biomarker concentrations.

Models are stratified for EPIC center, age, sex, fasting status, date of blood collection, and adjusted for smoking status, education, alcohol, physical activity, red and processed meat, fish and shellfish, fruits and vegetables, body mass index and waist circumference.

Percent change in the association between abdominal obesity and colon cancer with adjustment for biomarkers.
## Evidence matrix

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In partnership with

- American Institute for Cancer Research
- World Cancer Research Fund
- Wereld Kanker Onderzoek Fonds
- World Cancer Research Fund

NuGOweek 2017 Varna, Bulgaria
Whole grains and colorectal cancer

- **Meta-analysis**
  - 6 studies

- **Main results**
  - 10% reduction in risk of colorectal cancer for each 10 g/day intake of total dietary fibre and cereal fibre
  - 20% reduction for each three servings (90 g/day) of whole grain daily

![Meta-analysis of whole grains and the risk of colorectal cancer](image.png)

Aune D et al. BMJ 2011