Whole-grain and fibre intake and colorectal cancer
new results from the HELGA and EPIC cohorts

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Colorectal cancer

- Third most common cancer in the world (1.2 million cases in 2008)
- 10-fold higher in developed countries compared to developing countries

**Risk factors:**
- Western lifestyle (≈40%)
- Hormonal factors
- Familial adenomatous polyposis (FAP)
- Hereditary nonpolyposis colorectal cancer (HNPCC/Lynch syndrome)
- ...?
### Change from "probable" to "convincing"

| FOOD, NUTRITION, PHYSICAL ACTIVITY AND CANCERS OF THE COLON AND THE RECTUM 2011 |
|----------------------------------------|----------------------------------------|
| **DECREASES RISK**                     | **INCREASES RISK**                     |
| Convincing                             |                                        |
| Physical activity\(^1,2\)             | Red meat\(^4,5\)                      |
| Foods containing dietary fibre\(^3\)  | Processed meat\(^4,6\)               |
|                                        | Alcoholic drinks (men)\(^7\)         |
|                                        | Body fatness                         |
|                                        | Abdominal fatness                    |
|                                        | Adult attained height\(^8\)          |
| Probable                               |                                        |
| Garlic                                 | Alcoholic drinks (women)\(^7\)       |
| Milk\(^9\)                             |                                        |
| Calcium\(^10\)                         |                                        |
Recent meta-analysis

Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies

BMC open access

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Aune et al., BMJ, 2011
Compounds in whole grains

Bran:
- B vitamins
- Phytochemicals
- Protein
- Dietary fiber

Endosperm:
- Protein
- Carbohydrates

Germ:
- B vitamins
- Polyunsaturated FA
- Phytochemicals
- Vitamin E
- Minerals
Colorectal cancer
Studies on fibre and whole grains

Intake of dietary fiber, especially from cereal foods, is associated with lower incidence of colon cancer in the HELGA cohort

Intake of whole grains from different cereal and food sources and incidence of colorectal cancer in the Scandinavian HELGA cohort

Plasma alkylresorcinols, biomarkers of whole-grain wheat and rye intake, and incidence of colorectal cancer

Helga Cancer Cohort Research Center, Copenhagen, Denmark; Aarhus University, Aarhus, Denmark; Aalborg University, Aalborg, Denmark; University of Southern Denmark, Odense, Denmark; Danish Cancer Society, Copenhagen, Denmark; Department of Public Health, University of Copenhagen, Copenhagen, Denmark; University of Southern Denmark, Odense, Denmark; Danish Cancer Society, Copenhagen, Denmark; Department of Public Health, University of Copenhagen, Copenhagen, Denmark; University of Southern Denmark, Odense, Denmark; Danish Cancer Society, Copenhagen, Denmark; Department of Public Health, University of Copenhagen, Copenhagen, Denmark; University of Southern Denmark, Odense, Denmark; Danish Cancer Society, Copenhagen, Denmark; Department of Public Health, University of Copenhagen, Copenhagen, Denmark; University of Southern Denmark, Odense, Denmark; Danish Cancer Society, Copenhagen, Denmark; Department of Public Health, University of Copenhagen, Copenhagen, Denmark; University of Southern Denmark, Odense, Denmark; Danish Cancer Society, Copenhagen, Denmark; Department of Public Health, University of Copenhagen, Copenhagen, Denmark; University of Southern Denmark, Odense, Denmark.
The EPIC and HELGA cohorts

The HELGA cohort \((n \ 120 \ 000)\):
- The Norwegian Women and Cancer Study \((n \ 37 \ 000)\)
- The Northern Sweden Health and Disease Study \((n \ 26 \ 000)\)
- The Danish Diet, Cancer and Health Cohort Study \((n \ 57 \ 000)\)

European Prospective Investigation into Cancer and Nutrition (EPIC) cohort \((n \ 500 \ 000)\)
- 23 centres in 10 European countries
HELGA: Exposure and outcome

Outcome:
- ~ 1200 colorectal cancer cases
- ~ 12 y follow-up

Exposures:
- Calculated intake of dietary fiber
- Sources of fiber
- Whole-grain products
Fibre intake in the HELGA cohort

<table>
<thead>
<tr>
<th>Intake (g/day)</th>
<th>Men Median (5–95)</th>
<th>Women Median (5–95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetable fibre</td>
<td>3 (0–8)</td>
<td>3 (1–8)</td>
</tr>
<tr>
<td>Fruit fibre</td>
<td>2 (0–8)</td>
<td>3 (0–9)</td>
</tr>
<tr>
<td>Potato fibre</td>
<td>3 (1–6)</td>
<td>2 (0–4)</td>
</tr>
<tr>
<td>Cereal fibre</td>
<td>13 (5–25)</td>
<td>11 (5–20)</td>
</tr>
<tr>
<td>Total fiber</td>
<td>22 (10–38)</td>
<td>20 (10–34)</td>
</tr>
</tbody>
</table>
Total dietary fibre and colorectal cancer

Men

Women
Fibre from different sources and colorectal cancer
Cereal fibre (men)
Conclusion

• Dietary fibre was found associated to colon cancer incidence in the HELGA cohort

• The association was only statistical significant for cereal fibre

• The association was strongest and most consistent among men

• A tendency towards strongest effect for distal colon cancer
Intake of whole grains from different cereal and food sources and incidence of colorectal cancer in the Scandinavian HELGA cohort


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Abstract

Purpose: A high intake of whole grains has been associated with a lower incidence of colorectal cancer, but the studies are based on associations with whole grains from different cereal and food sources, and little has addressed these separately. The objective of this study was to investigate the association between whole grains and colorectal cancer. Methods: We used data from the large population-based Stockholm cohort HELGA consisting of 10,000.

Results: Electronic supplementary material - The online version of this article (doi:10.1007/s10552-013-0155-x) contains supplementary material.

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Introduction

Colorectal cancer is the third most common cancer worldwide. In 2008, it was diagnosed in 1.2 million people. 3] Whole grains are rich in dietary fibers, phytochemicals, and other active substances that have beneficial health effects. [4] In contrast, refined cereals contain complex carbohydrates, which have been eliminated. It
Calculated whole-grain intake

- **Norway**: Median intake (g/day) for Men is significantly higher than for Women.
- **Sweden**: Median intake (g/day) for Men is considerably higher than for Women.
- **Denmark**: Median intake (g/day) for Men is higher than for Women, but not as significantly as in Norway and Sweden.
- **USA**: Median intake (g/day) for Men is lower compared to Men in other countries, and Women's intake is lower as well.
Whole-grain product intake (g product/day) and incidence of colorectal cancer

Incidence rate ratio

Whole-grain product intake quartiles
Conclusion

- **Intake of whole grains associated with lower incidence of colorectal cancer**
- The association was only significant for *whole-grain products* and not for total *whole-grain intake (g/day)*
- Wheat was the only cereal type that alone was associated with colorectal cancer incidence
- No apparent difference depending on colorectal cancer sub-site
Exposure measurement – Whole grains

- Most cohort studies have no or low quality information on whole grain intake.

- Especially difficult, because it is difficult to know how much whole grain the products contain.
Alkylresorcinols - biomarkers

- Alkylresorcinols are only present in bran and whole grains
- Not destroyed during food processing
- Well absorbed in humans
  - After absorption, transported in lipoprotein fractions and in erythrocyte membranes and may be distributed and stored in some tissue, especially adipose tissue
- Validated (measured in plasma) both in intervention and cohort studies
  - Intra-class correlation coefficient = 0.88–0.90
  - Dietary assessment vs. plasma alkylresorcinol: \( r = 0.25–0.57 \)
Alkylresorcinols and colorectal cancer

- Plasma levels of alkylresorcinols and risk of colorectal cancer
- Nested case-control design
- 1550 colorectal cancer cases and 1550 controls from 10 European countries (total cohort, n=500 000)
Alkylresorcinols and colorectal cancer - methods

- **Matching**
  Colorectal cancer cases were matched to controls (1:1) by:
  - Age, gender, study center, time of blood collection, fasting status, menopausal status, use of HRT/oral contraceptives

- **Laboratory analysis**
  - Alkylresorcinols, 5 different homologues (C17:0, C19:0, C21:0, C23:0, C25:0)
  - Measured in plasma samples using GC-MS

- **Statistical analysis**
  Conditional Logistic Regression
Take home message

- Increasing evidence that dietary fibre is associated with decreased risk of colon cancer
- This association may – to a high degree – be linked to WG as a fibre source and maybe other constituents of WG
- No clear difference in association by whole-grain source
- Maybe some differences by colon sub-site (left side)?
- Should WG be classified as protective?
Acknowledgements: