Nordic diet
and risk of cancer, type 2 diabetes and heart disease

Cecilie Kyrø
Postdoc, PhD
Danish Cancer Society Research Center
Unit of Diet, Genes and Environment (DGE)

ICDM, Seoul, Saturday September 30, 2017

Pictures: Colourbox
Conflicts of interests

I have no conflicts of interests to report in relation to this presentation
About me

• Nutritional and cancer epidemiologist
• Danish Cancer Society Research Center
• International Agency for Research on Cancer (IARC), World Health Organization (WHO)

Research - Cohort studies

➢ European cohort: *The European Prospective Investigation into Cancer and Nutrition* (EPIC) (n=500,000)
➢ Danish cohort (Danish part of EPIC): *Diet, Cancer and Health* (n=57,053)
Why study the Nordic diet?
The European Prospective Investigation into Cancer and Nutrition (EPIC)

- 500,000 European participants
  - Biological specimens from 385,000 of participants
- Baseline mid 1990’s

Riboli, E., et al. (2002), Public Health Nutr. 5(6B): 1113-1124
Regional diets – results from the EPIC cohort

<table>
<thead>
<tr>
<th>Country</th>
<th>Foods consumed ≥ 150% mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy</td>
<td>Vegetables, fruits, cereal products, vegetable oils, sauces</td>
</tr>
<tr>
<td>Greece</td>
<td>Vegetables, legumes, vegetable oils</td>
</tr>
<tr>
<td>Spain</td>
<td>Vegetables, fruits, legumes, vegetable oils, milk, eggs, fresh meat, fish</td>
</tr>
<tr>
<td>France</td>
<td>Sugar, butter, dairy products</td>
</tr>
<tr>
<td>Germany</td>
<td>Butter processed meat, coffee, juices</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>Potatoes, margarines, dairy products, processed meat, tea, coffee</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>Potatoes, cakes, sugar, margarine, butter, tea, soft drinks</td>
</tr>
<tr>
<td>Denmark</td>
<td>Sugar, margarine, tea, coffee, soft drinks, alcohol</td>
</tr>
<tr>
<td>Sweden, Norway</td>
<td>Potatoes, cakes, sugar, margarine, dairy products, coffee, soft drinks</td>
</tr>
</tbody>
</table>

Slimani et al, 2002, Public Health Nutrition
Construction of dietary index

1 point per intake above/below the sex-specific median intake

Above:
- High MUFA/SFA
- Moderate alcohol
- Legumes
- Grains (originally whole grains)
- Fruit
- Vegetables
- Dairy products (in moderation)

Below:
- Meat/meat products
Adherence to Mediterranean diet and health status: meta-analysis

Francesco Sofi, researcher in clinical nutrition,^1^2,^5^ Francesca Cesari, researcher,^1^ Rosanna Abbate, full professor of internal medicine,^1,^5^ Gian Franco Gensini, full professor of internal medicine,^3^ Alessandro Casini, associate professor of clinical nutrition^2,^4,^5^

Conclusions Greater adherence to a Mediterranean diet is associated with a significant improvement in health status, as seen by a significant reduction in overall mortality (9%), mortality from cardiovascular diseases (9%), incidence of or mortality from cancer (6%), and incidence of Parkinson's disease and Alzheimer's disease (13%). These results seem to be clinically relevant for public health, in particular for encouraging a Mediterranean-like dietary pattern for primary prevention of major chronic diseases.

Sofi et al., BMJ. 2008;337:a1344.
Mediterranean diet
- in non-mediterranean countries

• Compliance to “foreign” diet may be difficult (possible especially for lower socioeconomic status)
• Risk of replacement of healthy traditional foods with less healthy foods?
• Cultural diversity and heritage?
• Sustainability?
Healthy regional diets

Short communication
Is the term ‘Mediterranean diet’ a misnomer?

Elling Bere¹,* and Johannes Brug²
¹Faculty of Health and Sport, Serviceboks 422, University of Agder, 4604 Kristiansand, Norway:
²EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands

Conclusions: We argue that the evidence of the health-enhancing properties of the Mediterranean diet is not necessarily based on Mediterranean foods, and that we indeed do not have to eat Mediterranean foods to enjoy the health-promoting properties of the diet it represents. To maintain dietary variety, cultural diversity and heritage, as well as for environmental reasons, it seems more appropriate to promote regionally appropriate diets throughout the world – rather than a global Mediterranean diet.
Healthy Nordic foods?

- Whole grains are eaten in higher amounts in the Nordic countries than in most other western societies.

- Evidence for beneficial effects of whole grain is accumulating.

- *Does the Nordic diet contain other foods with potential health promoting effects?*

Pictures: Colourbox
Methods
Criteria for inclusion into the **Healthy Nordic Food index**

1. Originating from the Nordic nature

2. A quantitative role in the daily Nordic diet, both in the (near) past and currently

3. Ascribed beneficial health effects

4. Information obtainable

Health effects of a Nordic diet

Vitamins, antioxidants, n-3 fatty acids

CVD, inflammatory markers

Polyphenols, vitamin K, n-3 fatty acids, antioxidants, dietary fiber, carotenoids

Cancer

Phytoestrogens, dietary fibre, vitamins, minerals, antioxidants

Diabetes, CVD, colorectal cancer

Dietary fiber, Beta-carotene

Cancer

N-3 fatty acids, vitamin D, Selenium

Prevention of stroke, Reduced blood pressure, Anti-inflammatory

Vitamins, minerals, polyphenols, dietary fibers, CVD, to some extent cancer

Pictures: Colourbox
Methods
The Diet, Cancer and Health cohort

Study population:
- 57,053 men and women
- 50–64 years at baseline (1993-1997)
- Information about diet and lifestyle from questionnaires
- Biological samples (blood fractions, urine, toenail clippings, adipose tissue)
A healthy Nordic food index

Food items included:

- Rye bread
- Oatmeal
- Cabbages
- Fish
- Apples and pears
- Root vegetables
- Berries
- Shellfish
- Rapeseed oil
Foods included in the healthy Nordic food index

<table>
<thead>
<tr>
<th>Food item</th>
<th>grams per day*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fish</td>
<td>≥41/35</td>
</tr>
<tr>
<td>Root vegetables</td>
<td>≥16/29</td>
</tr>
<tr>
<td>Rye bread</td>
<td>≥63</td>
</tr>
<tr>
<td>Oatmeal</td>
<td>≥21</td>
</tr>
<tr>
<td>Apples and pears</td>
<td>≥56/71</td>
</tr>
<tr>
<td>Cabbages</td>
<td>≥15/16</td>
</tr>
</tbody>
</table>

• Intake above the sex-specific cut-off (median) = 1 point

Index with values from:
• 0 points (lowest) – 6 points (highest)

* Men/Women
Methods

Baseline
1993–1997

End of follow-up
2008-2011

57,053 men and women

- 4,126 deaths
- 1,025 colorectal cancer
- 7,366 type 2 diabetes
- 2,322 myocardial infarction

Median follow-up time: 12-15 y
RESULTS
Women

Women

![Graph showing hazard ratio for colorectal cancer and type 2 diabetes in women based on adherence points.]

Lacoppidan, Kyro et al. (2015). Nutrients 7(10): 8633-8644
Women

Lacoppidan, Kyro et al. (2015). Nutrients 7(10): 8633-8644
Women

Lacoppidan, Kyro et al. (2015). Nutrients 7(10): 8633-8644
Men

Men

Lacoppidan, Kyro et al. (2015). Nutrients 7(10): 8633-8644
Men

Lacoppidan, Kyro et al. (2015). Nutrients 7(10): 8633-8644
Men

Colorectal cancer
Type 2 diabetes
Myocardial infarction
Mortality

Poor adherence
High adherence

Lacopidan, Kyro et al. (2015). Nutrients 7(10): 8633-8644
DISCUSSION AND PERSPECTIVES
Public health relevance

- Adherence to the index seems to be associated with health!
- Lowering in risk comparable to previously reported studies of the Mediterranean food index
Food culture

- Is it easier to increase intake of well known foods than to adopt to more unfamiliar dietary habits?
- Maybe especially for those most reluctant to dietary changes?
Nordic foods for the world?

• Some of the foods relevant in worldwide perspective?
WHOLE GRAINS
What are whole grains?

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

**Endosperm:**
- Protein
- Carbohydrates

**Germ:**
- B vitamins
- Polyunsaturated fatty acids
- Phytochemicals
- Vitamin E
- Minerals
Whole grains and health
- possible mechanisms

Fermentable fiber:
- Production of SCFA – butyrate
- Anti-carcinogen
- Drop in pH → decrease in formation of secondary bile acids

Non-fermentable fiber:
- “mechanical” effects
- Faster transit time

Lignans → enterolactone

Folate – deficiency → DNA damages

Weight management?

Glucose/insulin homeostasis
Alkylresorcinols
- Biomarkers of whole-grain intake

• Phenolic lipids – found in the bran part of rye and wheat

• Unaffected by food processing

• Validated (measured in plasma) both in intervention studies and in cohort studies

  • Questionnaire vs. biomarker: $r=0.25–0.57$

![Figure 1. Structures of alkylresorcinols (ARs) commonly found in cereals.](image)
Research projects - methods

Questionnaire data
- Colorectal cancer (1100 cases)
- Myocardial infarction (2300 cases)
- Diabetes (7000 cases)
- Mortality (7800 deceased)

Biomarker
- Nested case-control design
- 1372 colorectal cases and 1372 matched controls
- The biomarker “Alkylresorcinols” analyzed using GC-MS
Whole grains and colorectal cancer

Figure 1: Dose-response meta-analysis of wholegrains intake and colorectal cancer per 90 grams per day

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Sex</th>
<th>Per 90 g/day RR (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kyrø</td>
<td>2013</td>
<td>M/W</td>
<td>0.87 (0.78, 0.96)</td>
<td>28.88</td>
</tr>
<tr>
<td>Fung</td>
<td>2010</td>
<td>M</td>
<td>0.83 (0.68, 0.97)</td>
<td>12.84</td>
</tr>
<tr>
<td>Fung</td>
<td>2010</td>
<td>W</td>
<td>0.86 (0.70, 1.06)</td>
<td>9.94</td>
</tr>
<tr>
<td>Schatzkin</td>
<td>2007</td>
<td>M/W</td>
<td>0.73 (0.63, 0.84)</td>
<td>18.19</td>
</tr>
<tr>
<td>McCarl</td>
<td>2006</td>
<td>W</td>
<td>0.79 (0.66, 0.94)</td>
<td>13.28</td>
</tr>
<tr>
<td>Larsson</td>
<td>2005</td>
<td>W</td>
<td>0.93 (0.80, 1.08)</td>
<td>16.88</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td>0.83 (0.78, 0.89)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis.
Whole grains
and risk of type 2 diabetes (men)

Kyro et al. (2017), submitted (confidential)
Whole grains
and risk of type 2 diabetes (women)

Kyro et al. (2017), submitted (confidential)
Whole grains and diabetes mortality

Aune et al. (2016), BMJ 353: i2716.
Acknowledgements

Danish Cancer Society Research Center

- Anja Olsen
- Anne Tjønneland
- Anne Kathrine Helnæs
- Vibeke Gunge
- Sandra Lacoppidan
Whole-grain intake

Kyrø & Tjønneland BMJ (2016);353:bmj.i3046