Metabolic factors and prostate cancer
- preliminary results from a multi-state model

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Me-Can data overview
Prospective cohort study

Baseline (289 866 men)
- Mean age 44 year

Endpoints
- 6 922 prostate cancer cases
- 1 016 deaths due to prostate cancer

Exposure:
- BMI
- Blood pressure
- Glucose
- Cholesterol
- Triglycerides
- Metabolic syndrome score

Disease

Prospective Cohort
Research questions/methods

1. Association/Risk:

Metabolic factors /metabolic syndrome → Prostate cancer?

Method: Cox regression
Results Cox analysis:

**Figure 1a. Relative risk of prostate cancer by exposures in z-scores**

<table>
<thead>
<tr>
<th>Exposure</th>
<th>RR (CI 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>0.99 (0.96 - 1.02)</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>0.98 (0.94 - 1.03)</td>
</tr>
<tr>
<td>Glucose (log)</td>
<td>0.90 (0.82 - 0.98)</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>1.00 (0.96 - 1.04)</td>
</tr>
<tr>
<td>Triglycerides (log)</td>
<td>0.94 (0.89 - 0.99)</td>
</tr>
<tr>
<td>Composite score</td>
<td>0.96 (0.92 - 1.00)</td>
</tr>
</tbody>
</table>

**Figure 1b. Relative risk of death from prostate cancer by exposures in z-scores**

<table>
<thead>
<tr>
<th>Exposure</th>
<th>RR (CI 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.12 (1.05 - 1.21)</td>
</tr>
<tr>
<td></td>
<td>1.21 (1.08 - 1.36)</td>
</tr>
<tr>
<td></td>
<td>1.03 (0.83 - 1.28)</td>
</tr>
<tr>
<td></td>
<td>0.95 (0.86 - 1.05)</td>
</tr>
<tr>
<td></td>
<td>1.08 (0.95 - 1.23)</td>
</tr>
<tr>
<td></td>
<td>1.13 (1.02 - 1.25)</td>
</tr>
</tbody>
</table>
Research questions/methods

2. Real world scenario:

Why?
- mean age of prostate cancer=70y
- metabolic syndrome related to CVD deaths

Methods:
1. Competing risk analysis

Prostate cancer diagnosis / Death due to prostate cancer
All-cause death / Non-prostate cancer death
Censoring
1. Competing risk results: Cumulative incidence

- Cumulative mortality
- I have The metabolic syndrome
- Cumulative Incidence Prostate cancer

- Low MetS
- High MetS
- both p<0.001
2. Multi-state model (3 states)

1 Alive (disease-free)

2 Alive with prostate cancer diagnosis

3 All-cause Death

I have Prostate cancer and The metabolic syndrome

I have no cancer and normal metabolic levels
Multi-state model (4 states)

1 Alive (disease-free)

2 Alive with prostate cancer diagnosis

3 Dead (Not PC death)

4 Death due to PC

I have Prostate cancer and The metabolic syndrome

I have no cancer and normal metabolic levels
Conclusions

• Men with the metabolic syndrome and prostate cancer has highest probability of all-cause death

• BUT When removing all prostate-cancer related deaths, men with metabolic syndrome have larger probability of death

• In fact: Men with prostate cancer and normal metabolic levels have the lowest hazard of non-prostate-cancer related deaths

• NOTE: Preliminary results!
Questions?

Thank you!

Me-Can project:
Bergen, Norway: Tone Björge, Anders Engeland
Malmö, Sweden: Jonas Manjer
Copenhagen, Denmark: Tanja Stocks
Ulm, Germany: Gabriele Nagel
Innsbruck, Austria: Hanno Ulmer, Wegene Borena, Michael Erdlinger
Umeå: Pär Stattin, Håkan Jonsson, Sara Wiren, Christel Häggström
3 states Multi-state model

1 Alive (disease-free)

2 Alive with prostate cancer diagnosis

3 All-cause Death

I have The metabolic syndrome
What’s the difference?

1. Elderly population
   - Overestimation of absolute risk

2. The exposure, metabolic syndrome, is associated with early death
   - “Bias” in relative risk

References:
Berry SD, Ngo L, Samelson EJ, Kiel DP. Competing Risk of Death: An Important Consideration in Studies of Older Adults.
Competing risk approach: Fatal prostate cancer

Cumulative mortality due to other causes

Cumulative Mortality due to Prostate cancer
Cox regression models were adjusted for all single exposures and smoking, stratified for cohort, 5 categories of birth year and 5 categories of age at measurement using z-scores corrected for random errors by regression calibration.
Death due to prostate cancer (Cox)

Cox regression models were adjusted for all single exposures and smoking, stratified for cohort, 5 categories of birth year and 5 categories of age at measurement using z-scores corrected for random errors by regression calibration.