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Nitrate in drinking water and colorectal cancer

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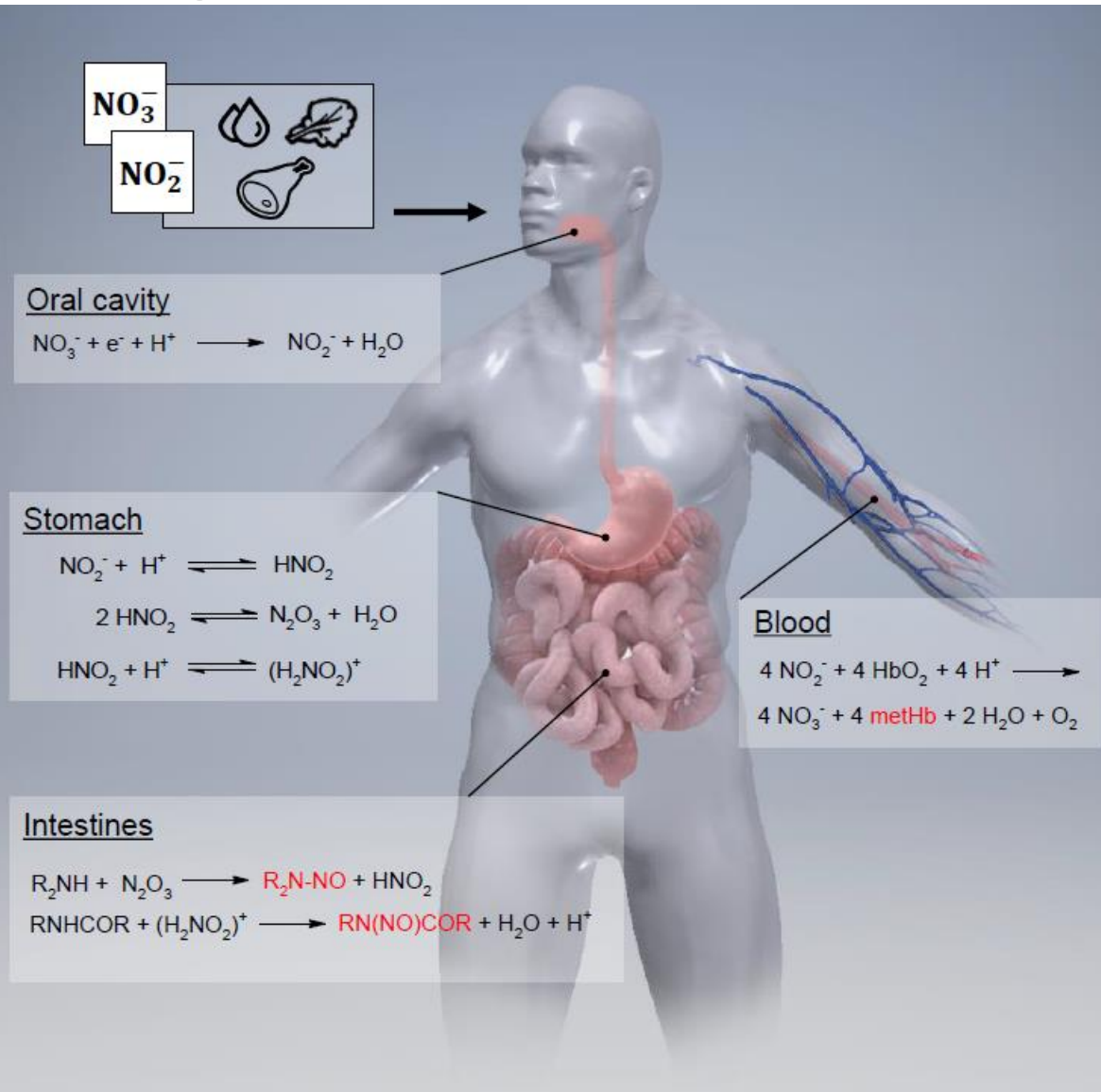
Geological Survey of Denmark and Greenland
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Centre for Integrated Register-based Research, Aarhus University
National Centre for Register-based Research, Aarhus University

dNmark conference, 27 June 2017





Endogenous Nitrosation



Drinking water standard: 50 mg/L

protects infants from methemoglobinemia

Chronic effects?

- NOCs are animal/human carcinogens

IARC group 2A

probably carcinogenic to humans under conditions that result in endogenous nitrosation

Ward et al. (2005), IARC (2010,2016),
Mirvish et al. (1998), Møller et al. (1989)

Colorectal Cancer



Established risk factors

- red/processed meat intake
- smoking
- alcohol intake
- physical inactivity
- obesity

NORDCAN (2016), Giovannucci (2001)
Giovannucci et al. (1995), Larsson & Wolk (2007)
Cho et al. (2004), Aune et al. (2013)



Epidemiologic Studies Nitrate & CRC

Ecologic studies

Gulis et al. (2002): increased risk CRC >20 mg/L

Case-control studies

De Roos et al. (2003): susceptible groups (low vitamin C/high red meat intake):
≈ 2-fold increased risk for colon cancer at >22 mg/L for >10 years

McElroy et al. (2008): increased risk for proximal colon cancer, no overall association

Espejo-Herrera et al. (2016): ≈ 1.5-fold increased risk for colon cancer >4.3 mg/L,
rectum cancer >8.6 mg/L

Challenge:
study size
retrospective exposure estimation
private wells

Cohort studies

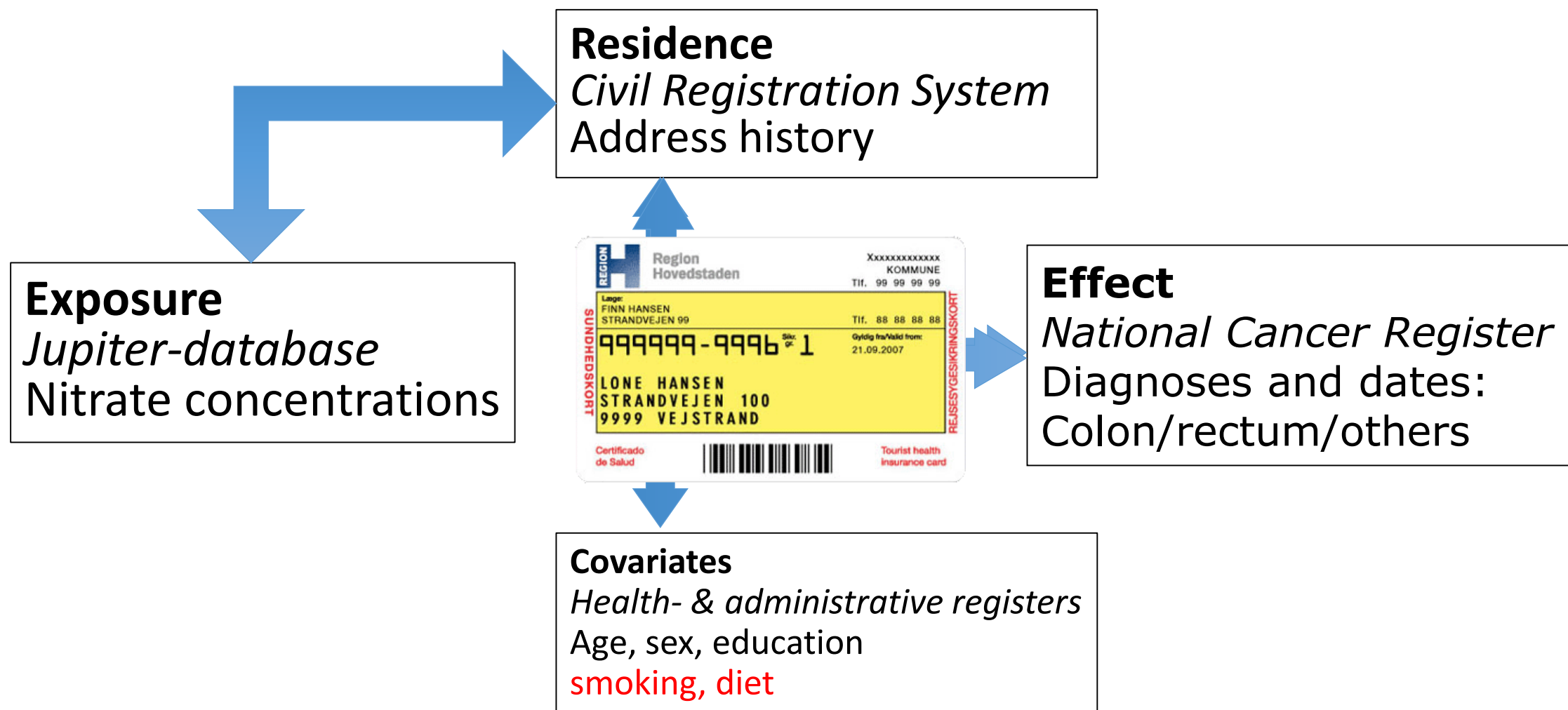
Weyer et al. (2001): no clear association with colon cancer, inverse association with
rectum cancer

METHODS



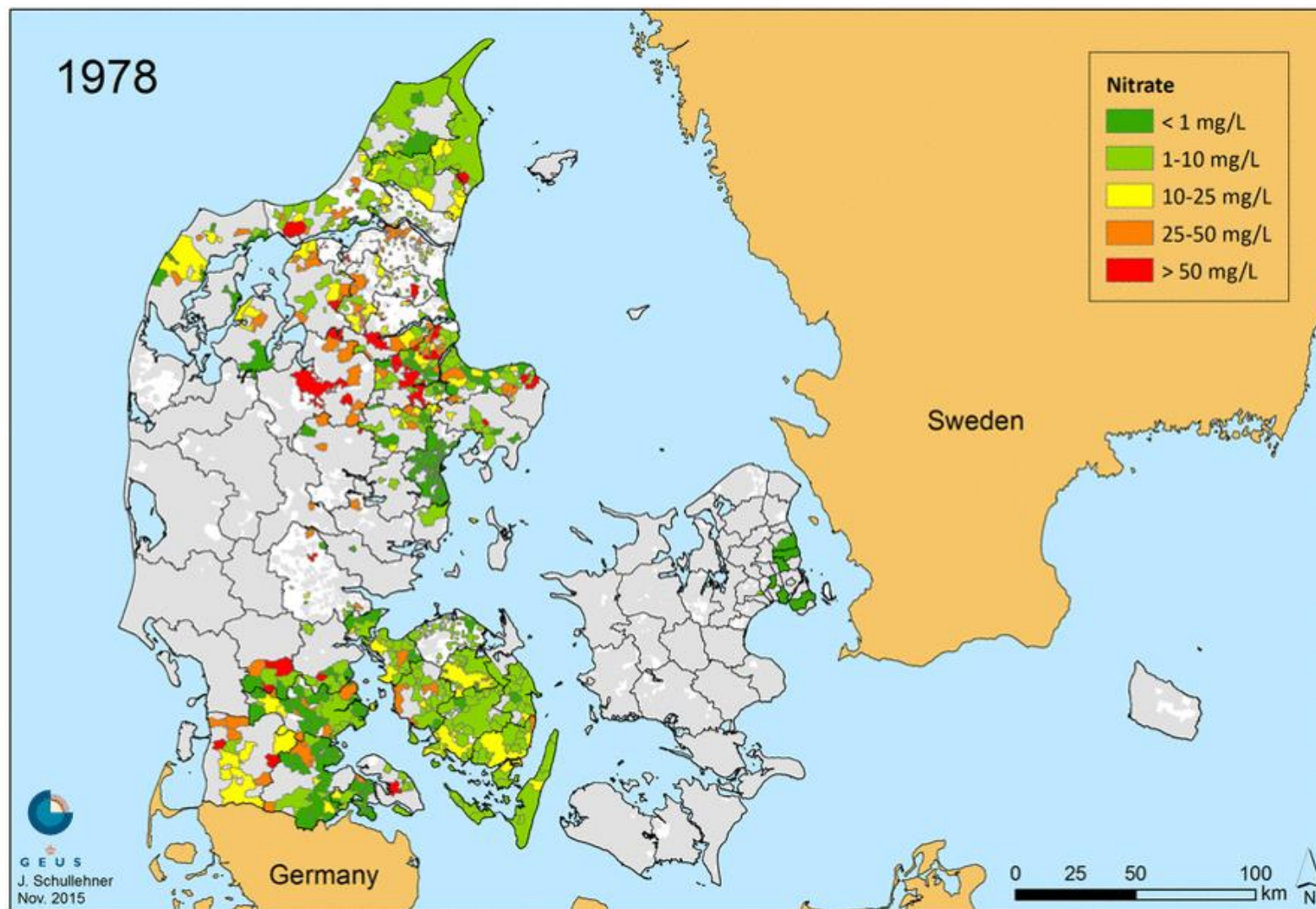


Register-based Cohort Study





Nitrate in Public Water Supply Areas



Supplementary Figure 1: Nitrate concentrations in the water supply areas, 1978-2013.

For every person:
Residence between 1978 – 2012
→ known exposure to nitrate level



7,342,450,927

Study Population

All residents of Denmark

Exposure

average nitrate concentration between age 20-35

Covariates

age, sex, calendar year, other cancer diagnosis, socio-economic status

Follow-up

from age 35 until cancer diagnosis / death / end of study

Cox-PH model

1.7 million individuals, 5944 colorectal cancer cases

RESULTS





Nitrate in Drinking Water and Colorectal Cancer

Drinking water nitrate more than
9.25 mg/l

15% (7%-24%) increased risk
of colorectal cancer compared to
< 1.27 mg/l

Preliminary results – under review

DISCUSSION





Nitrate in Drinking Water and colorectal cancer

One of few epidemiological studies

Positive association between nitrate in drinking water and **colorectal cancer, colon cancer, and rectal cancer**

Observed effect **far below** the current drinking water standard of 50 mg/l

Consistent with results from Spanish-Italian study from 2016

Sensitivity analyses show **robust results**



Strengths

- Population-based
 - Largest study population/ number of cases
 - High validity and completeness of register data
 - Prospective data collection
 - **Exposure assessment**
 - Based on longitudinal data from water sample analysis by certified labs
 - maximal physical boundaries of a waterworks
 - Inclusion of private wells
 - High spatial and temporal resolution
- Most detailed dataset available on nitrate exposure from drinking water



Limitations

Lack of individual-level data of

- Other sources of nitrate/nitrite/NOCs
- Diet, smoking, BMI, physical activity...
- Modulators of endogenous nitrosation

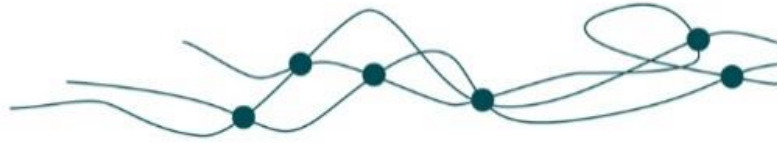
Private wells: nitrate ↑ knowledge ↓

Acknowledgements

Co-authors

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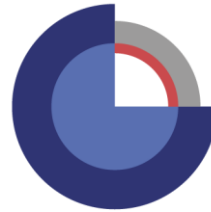
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Thank you for your attention



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