

Epidemiology and risk factors of hip fractures in Norway

Examples of combining patient administrative systems,
regional health studies and national health registries

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26 November 2015

Outline

- Brief presentation of the Norwegian Institute of Public Health (NIPH)
- Tools for research and health surveillance on the population level
- Hip fractures in Norway: Examples from a research area with available high-quality individual-level national data based on large data linkages

The NIPH is one of several agencies of the central health administration of Norway



Vision: A healthier population

Our tasks are distributed on five main activities

- Health surveillance
- Research
- Advice
- Services
- Preparedness

Domain for Mental and Physical Health in the NIPH

- Health statistics
- Chronic disease epidemiology
- Pharmacoepidemiology
- Mental health
- Alcohol and drug research (from 2016)

Tools and infrastructure for research

- National health registries
- Nationwide and regional population-based health studies
 - Biologic samples, anthropometric measures, clinical examinations, questionnaire data
- Demographic data from Statistics Norway
- Biobanks and laboratory-based methods
- Information technology

National health registries

The NIPH is responsible for 9 of the 16 mandatory national health registries, covering:

- Causes of death
- Births
- Pregnancy termination
- Cardiovascular diseases
- Prescription medications
- Infectious diseases
- Infections in health institutions
- Microbial resistance to antibiotics
- Vaccination



National ID number

- All residents of Norway are allocated a personal national ID number, which they keep for life
- The ID number consists of 11 digits, of which the first six digits indicate the person's date of birth
- The ID number is the key to link individual-level data from different registers and other data sources

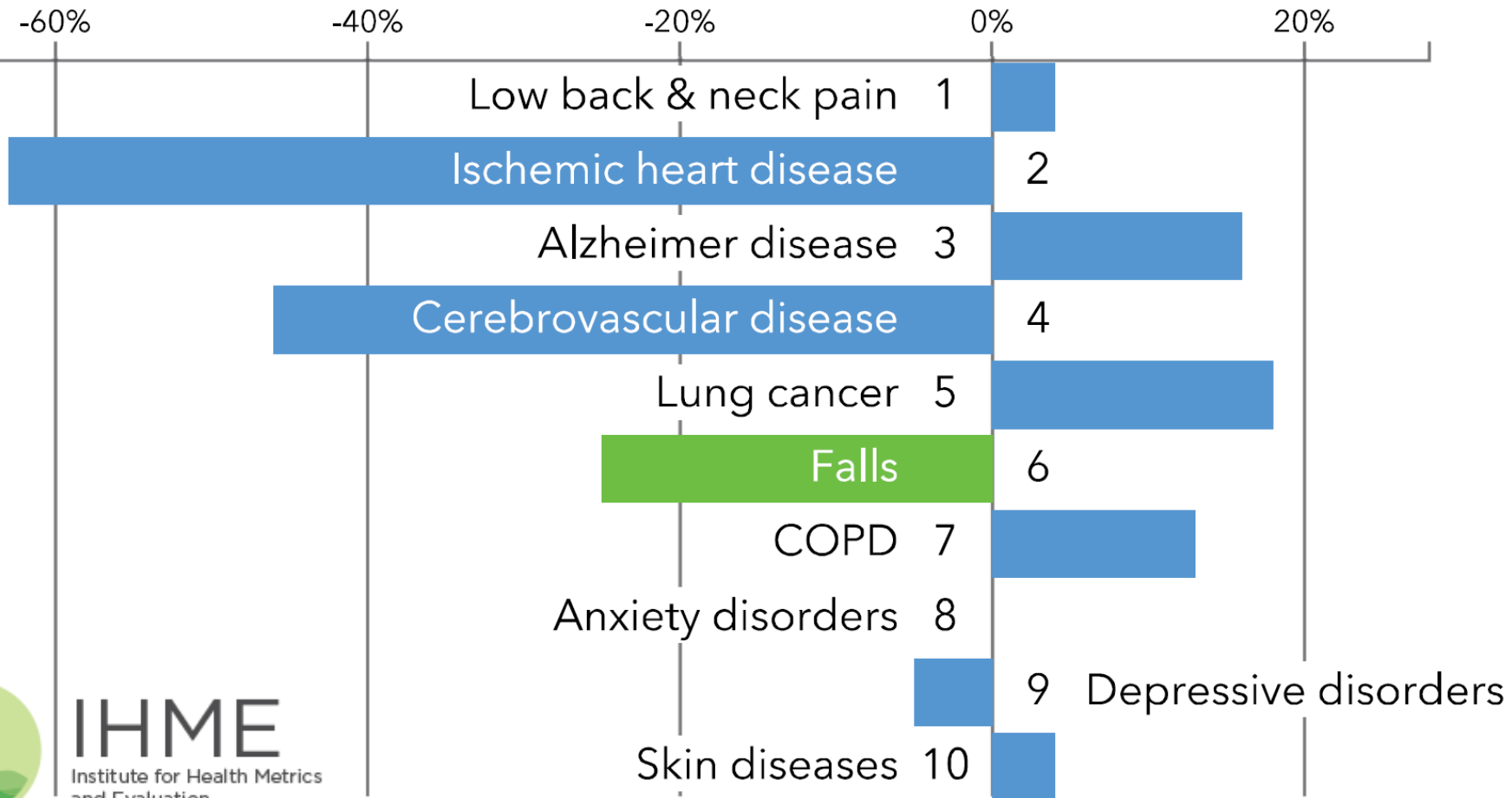


Examples from a field where we have
high-quality individual-level national
data for research and health surveillance
based on large data linkages



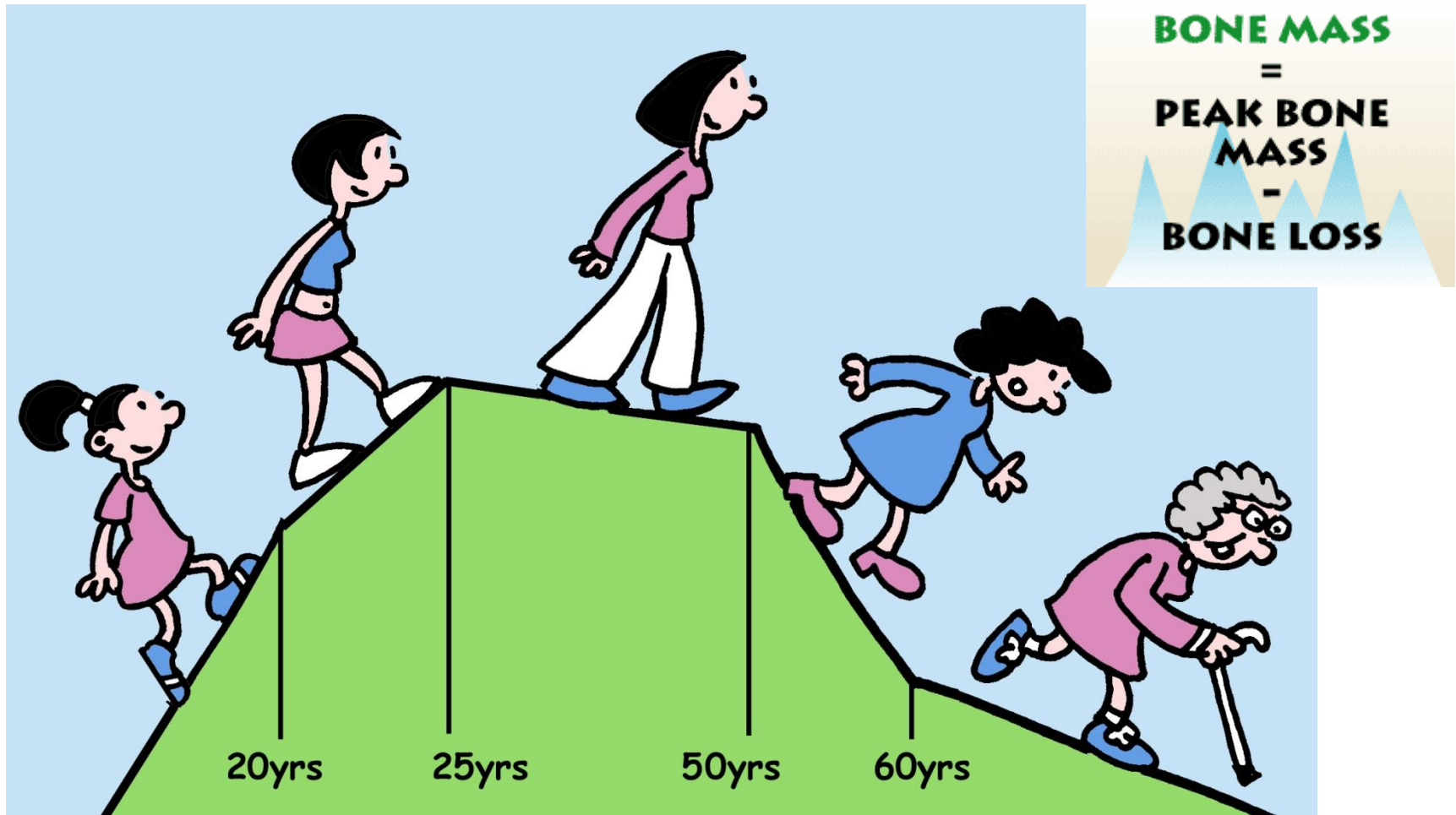
Photo: F. Frihagen, Acta Orthop Suppl 2009

Leading causes of disability-adjusted life-years (DALY) in Norway 2013



IHME
Institute for Health Metrics
and Evaluation

Bone health through life



Hip fractures

- Proximal femur fractures
- International Classification of Diseases (ICD) codes:
 - ICD-9: 820 with all subgroups
 - ICD-10: S72.0, S72.1 and S72.2



Hip fractures occur from falls combined with bone fragility

A multifactorial health problem

- Ageing
- Fall risk
- Sarcopenia; reduced muscle mass and strength
- Osteoporosis; reduced bone mass and strength
- Poor nutritional status
- Comorbidity
- Use of medications



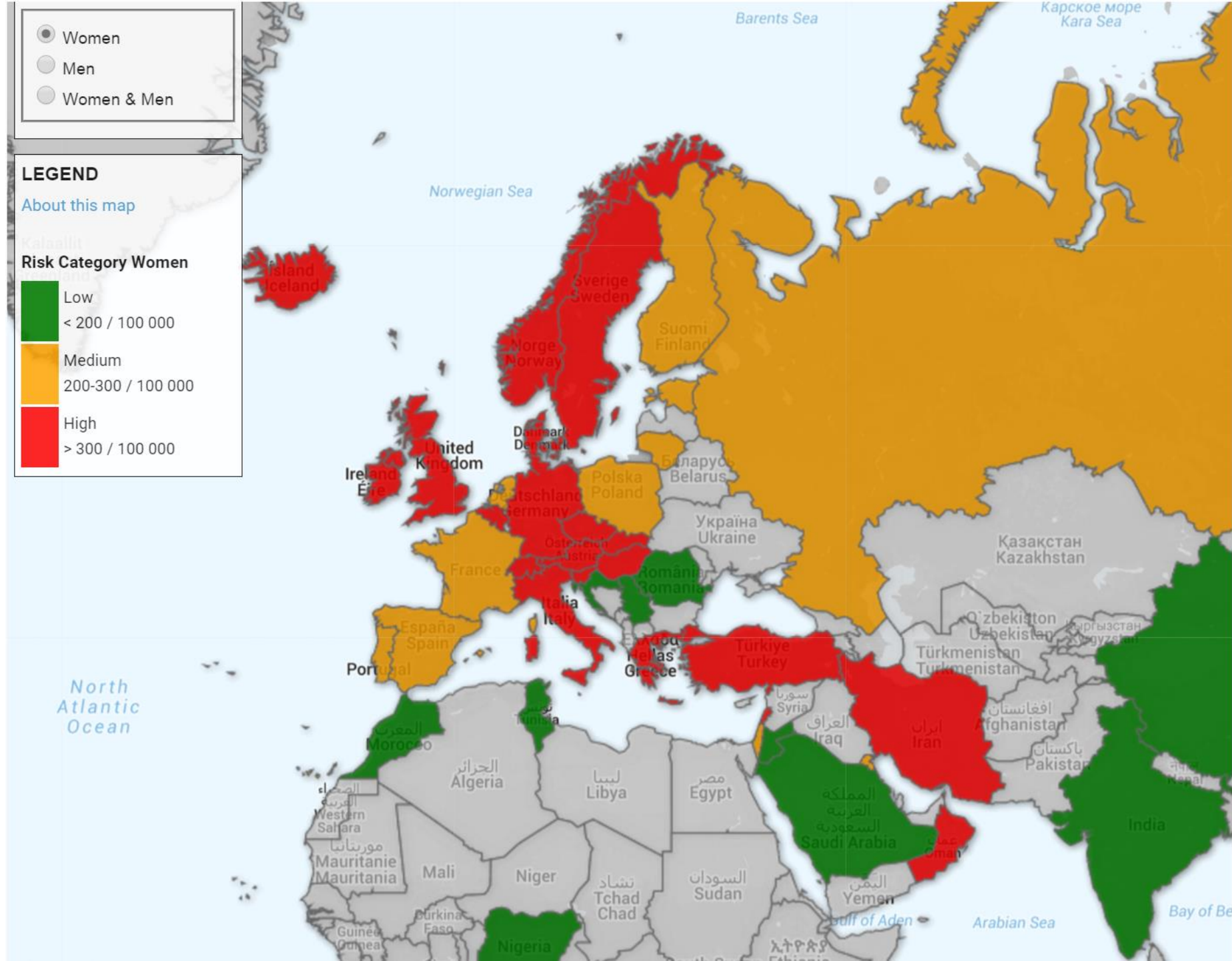
- Women
- Men
- Women & Men

LEGEND

[About this map](#)

Risk Category Women

- Low
< 200 / 100 000
- Medium
200-300 / 100 000
- High
> 300 / 100 000

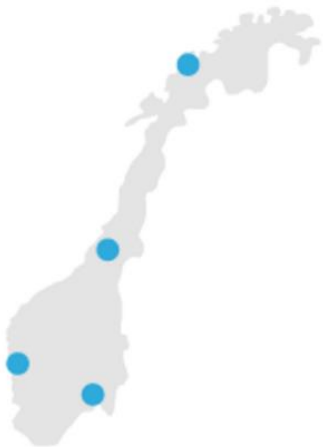




► UPCOMING EVENTS

19 November, 2015

[Phone meeting, steering group](#)
at 14:15



WELCOME TO NOREPOS



NOREPOS is an osteoporosis research collaboration

NOREPOS (Norwegian Epidemiologic Osteoporosis Studies) is a national research collaboration network of researchers from five different scientific institutions across Norway. We perform epidemiologic research in the field of osteoporosis. The collaborating institutions in NOREPOS are: University of Bergen (UiB), University of Tromsø (UiT), Norwegian University of Science and Technology (NTNU), University of Oslo (UiO), and the Norwegian Institute of Public Health (FHI). The collaboration has existed since 1997. The project is led by Professor Grethe S. Tell, Department of Public Health and Primary Health Care, University of Bergen. Eight senior researchers, two from each geographical location, constitute the

members of the [NOREPOS steering committee](#). NOREPOS received a large grant from the Research Council of Norway in 2008.

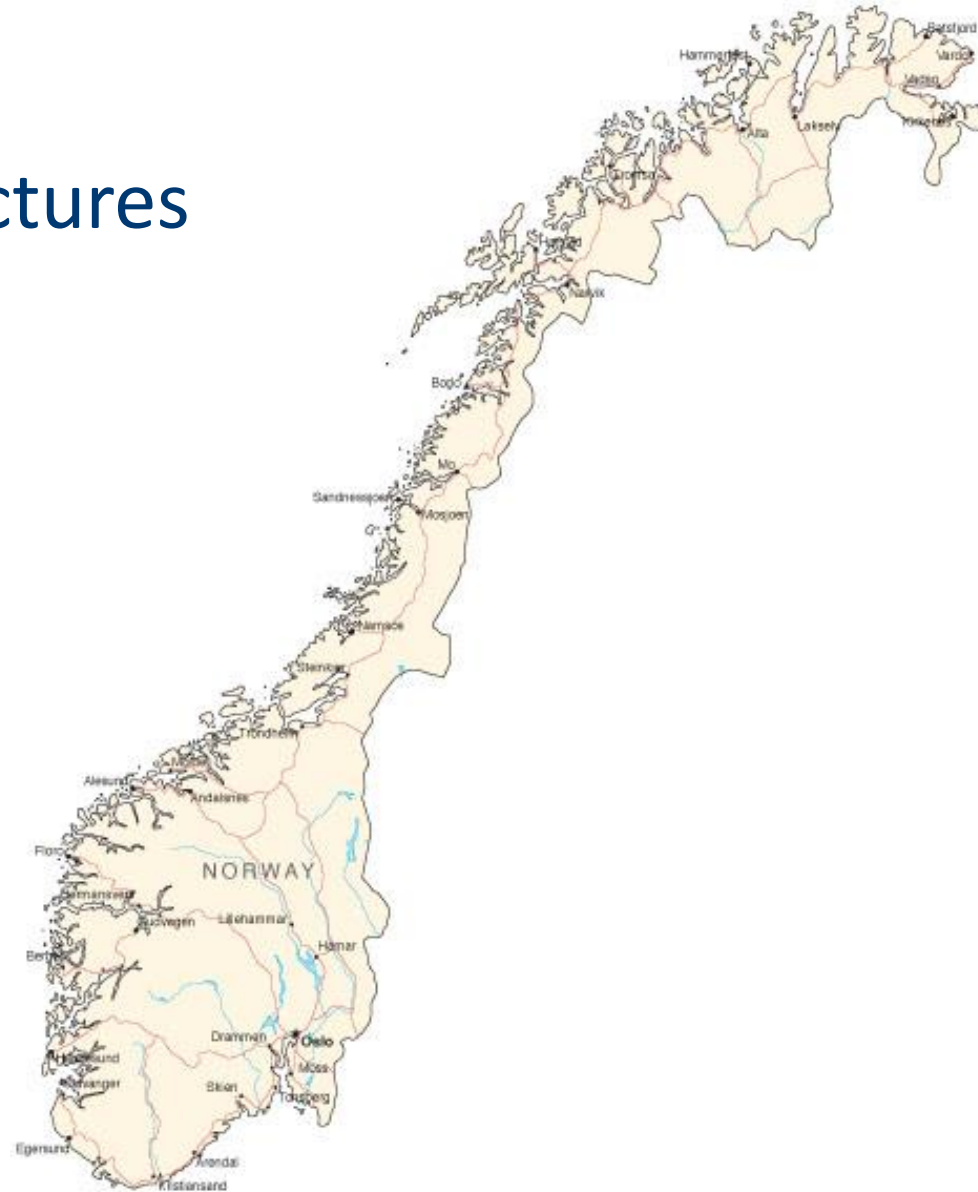
We use data sources from large population-based studies in Norway where bone mineral density measurements have been performed. Hip fractures constitute an important endpoint in our research. We have now collected all

Descriptives: Incidence

- Time trends
- Risk of subsequent fractures
- Excess mortality
- Geographic variation
- Seasonal variation

Modifiable risk factors:

- Body composition
- Drinking water quality
- Nutritional factors



Descriptive information:

- Incidence rates
- Time trends
- Geography
- Mortality

Statistics Norway

Socioeconomic,
demographic and
family data

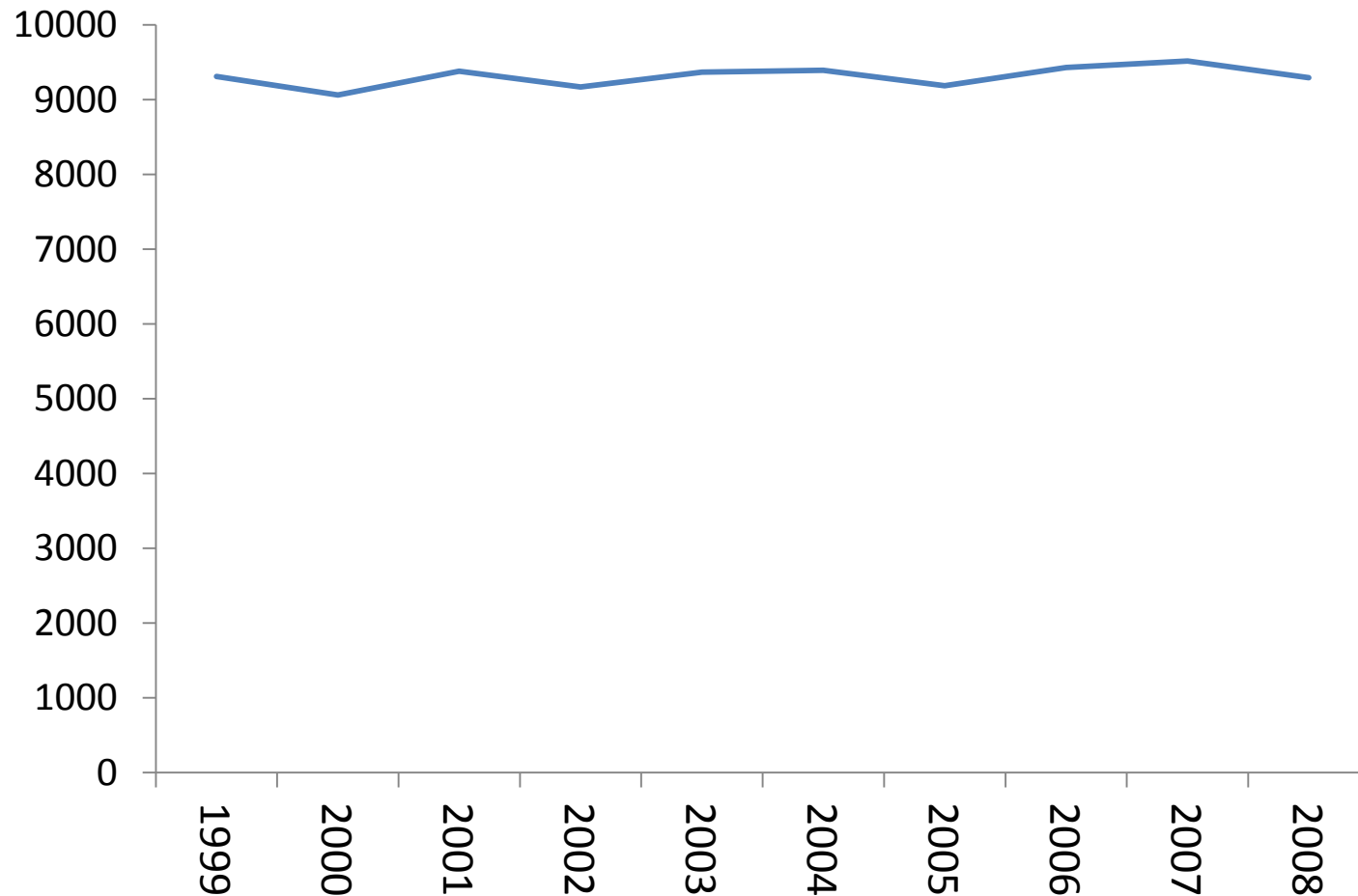
NOREPOS Hip fracture database

Hip fractures
1994-2013

Person registry

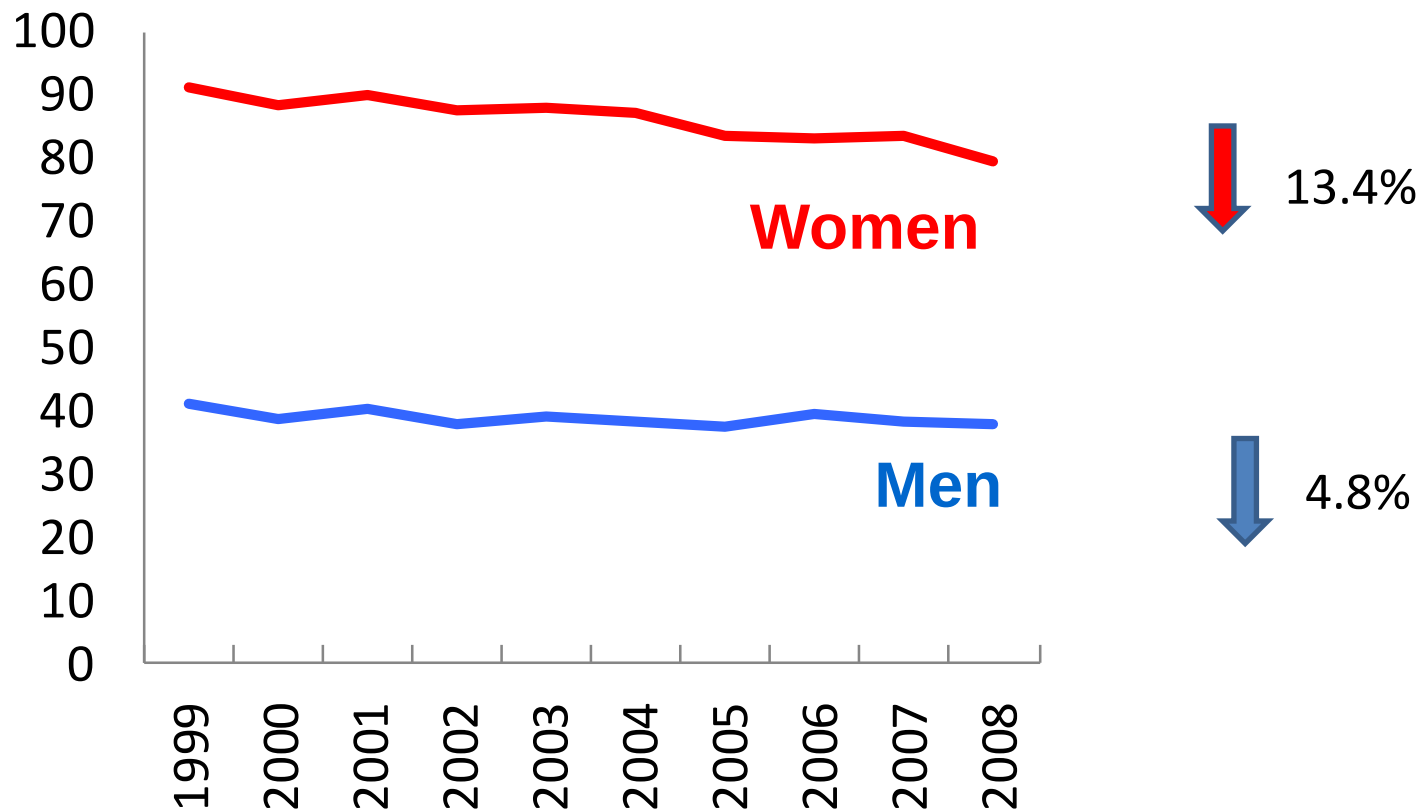
Country of birth,
date of death or
emigration

Annual number of hip fractures in Norway

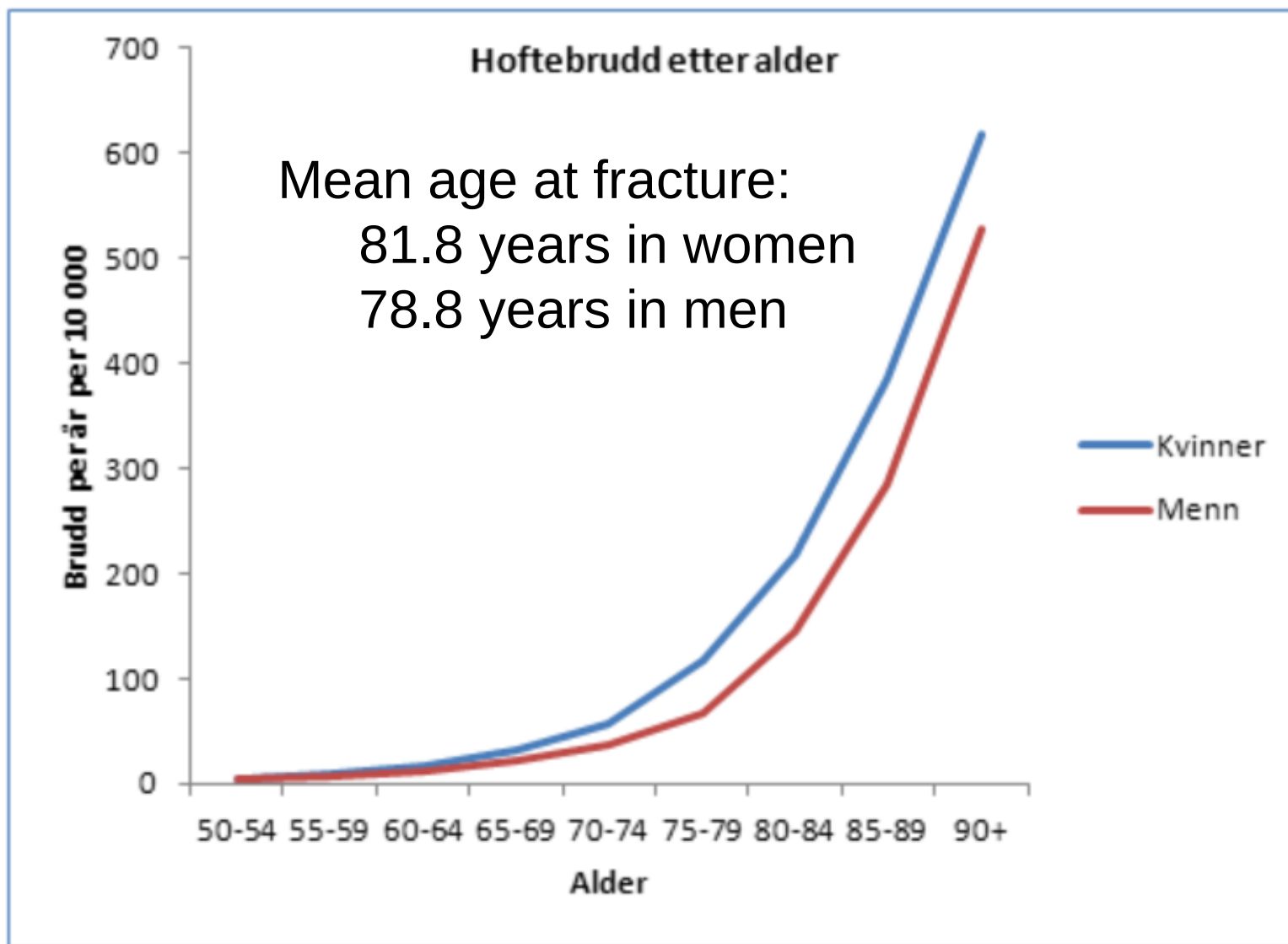


Incidence rates of hip fractures in Norway 1999-2008 (NOREPOS), age 50+

Age-standardized rates: New cases per 10,000 persons per year



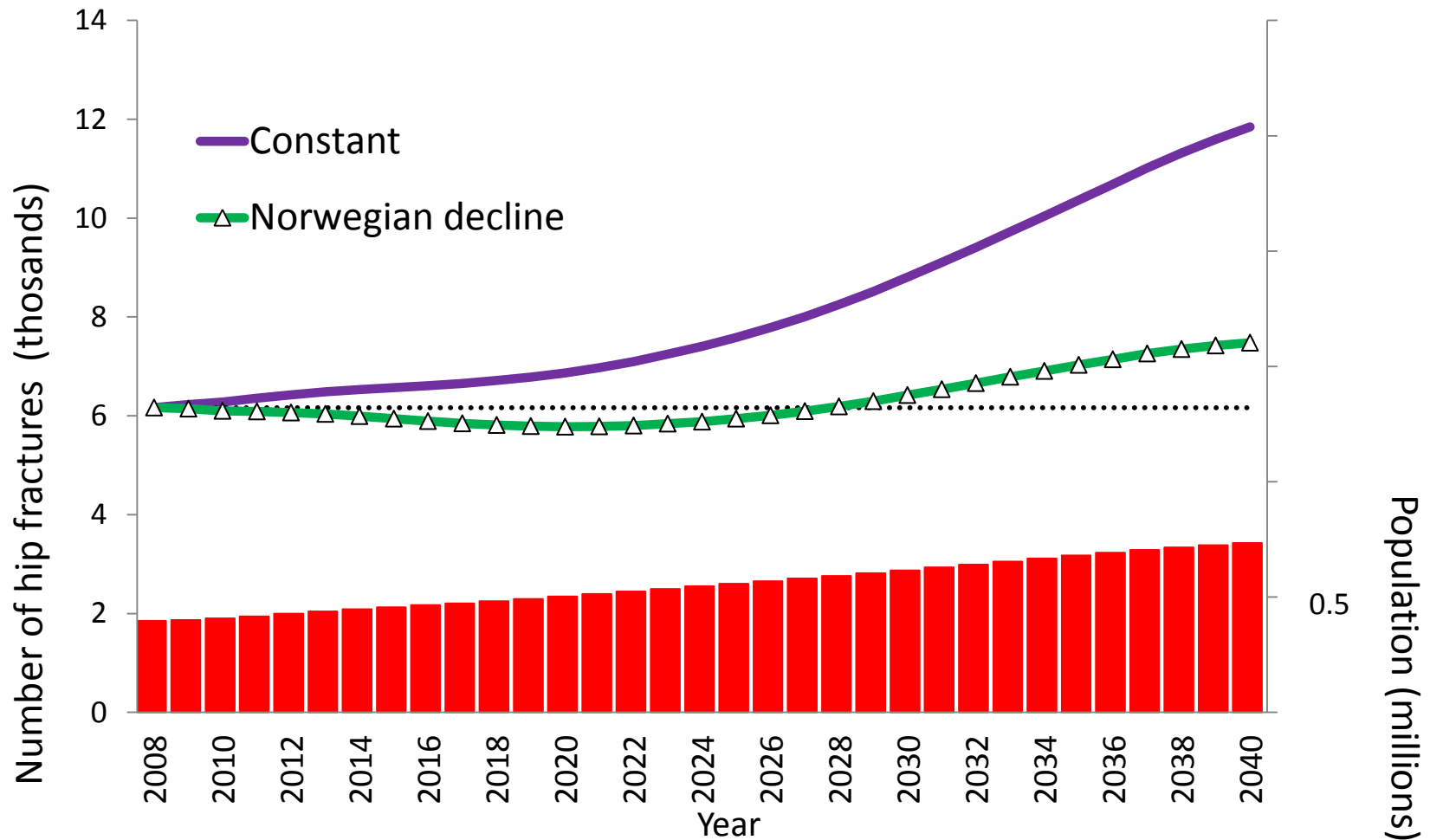
Incidence rates by age



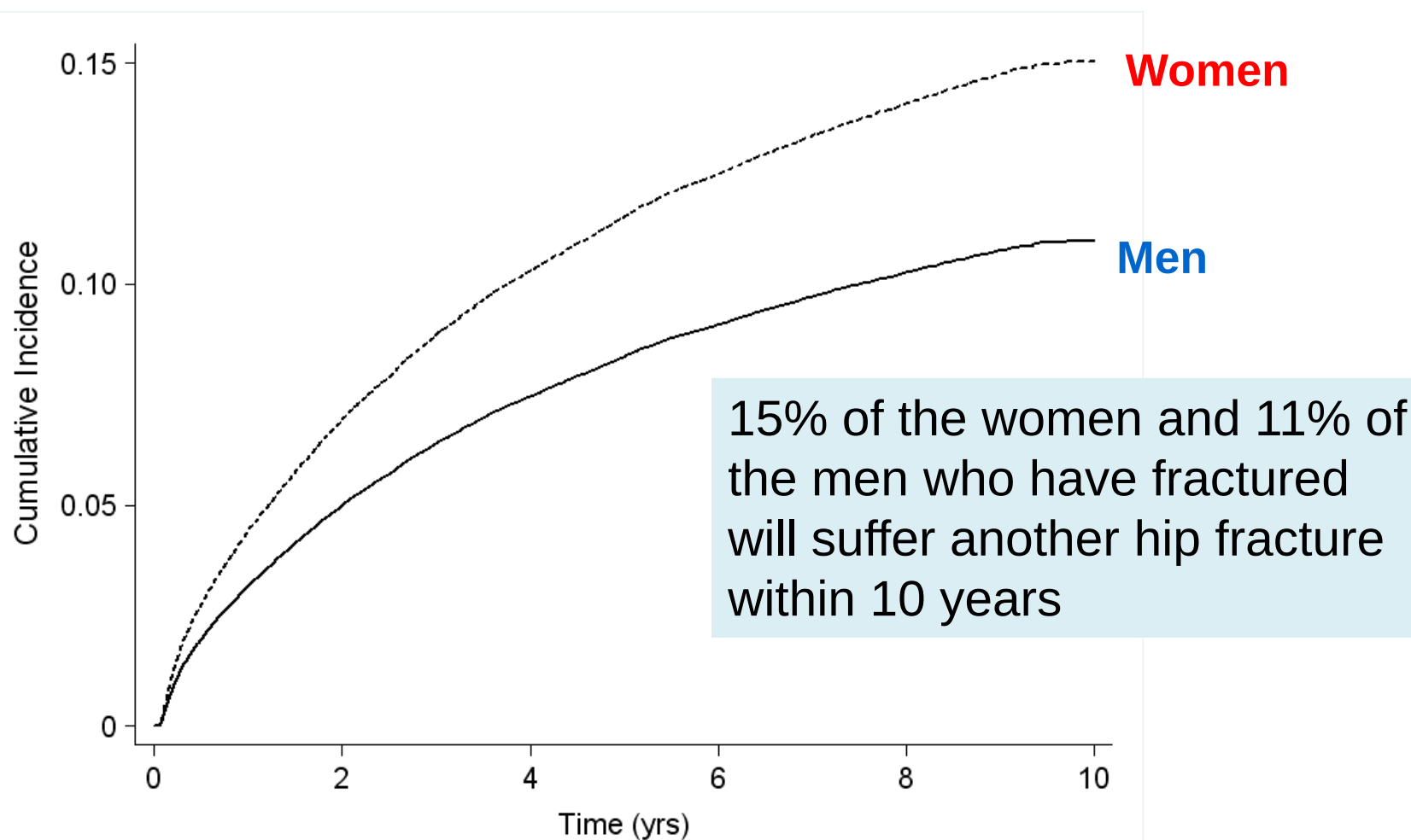
Note!
Women
Men

Forecasting the burden of hip fractures

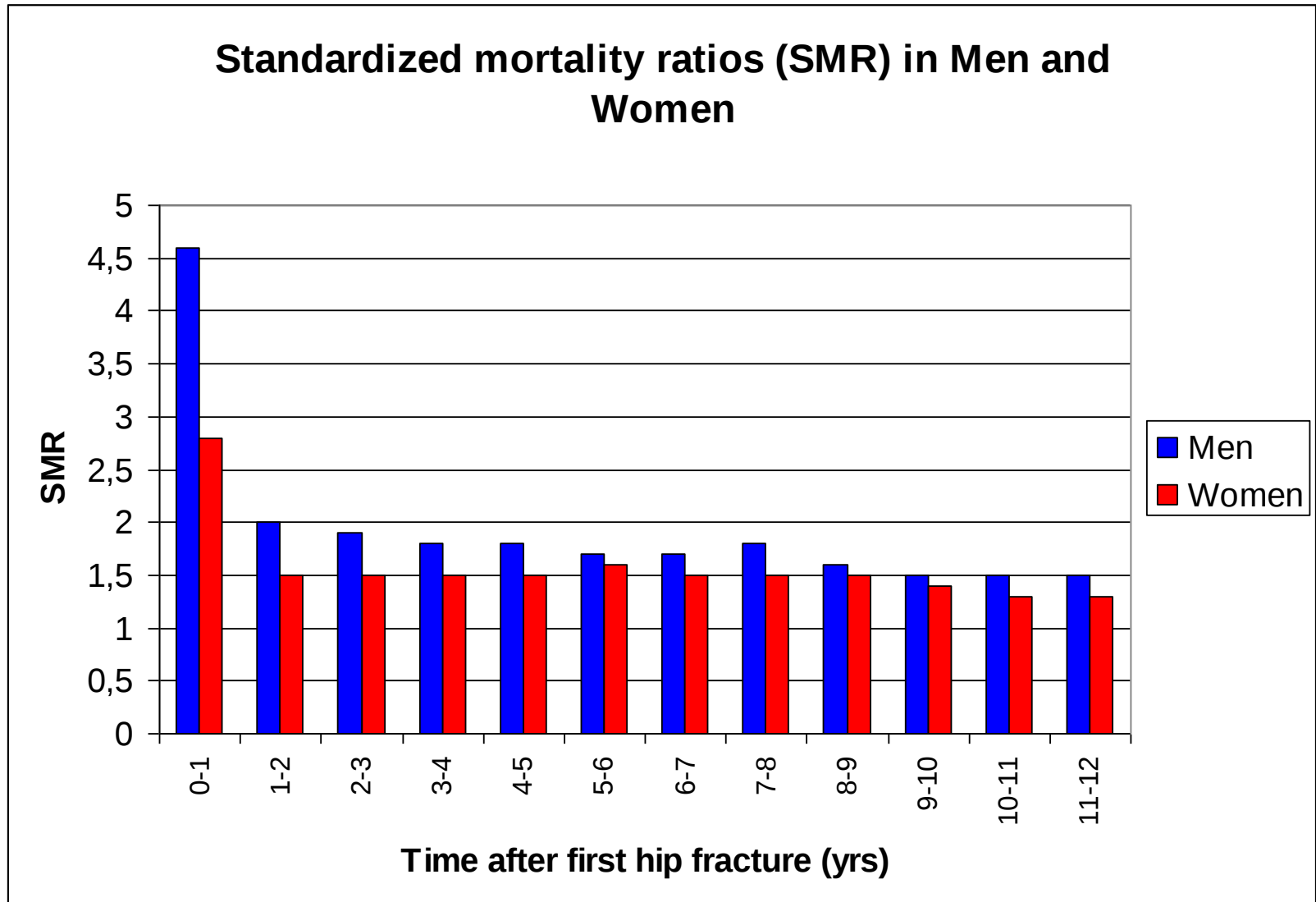
(women 65+)



Cumulative incidence of second hip fracture



Excess mortality after hip fracture



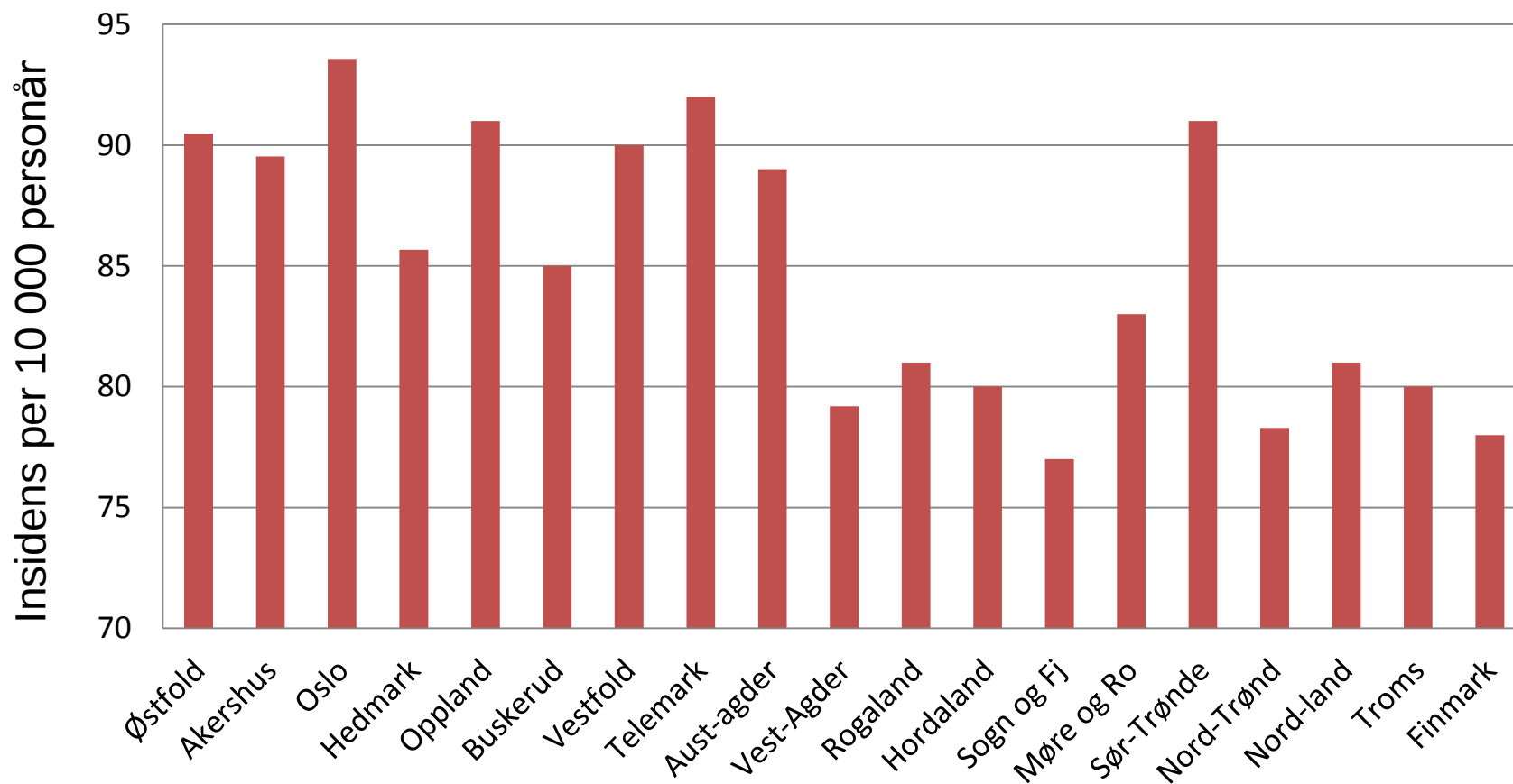
Geographic differences within Norway

1988-1989: Incidence rates in the capital Oslo were 50% higher than in the rural county Sogn og Fjordane



Standardized incidence rates of hip fracture according to county, women

Same pattern in men



Degree of urbanization

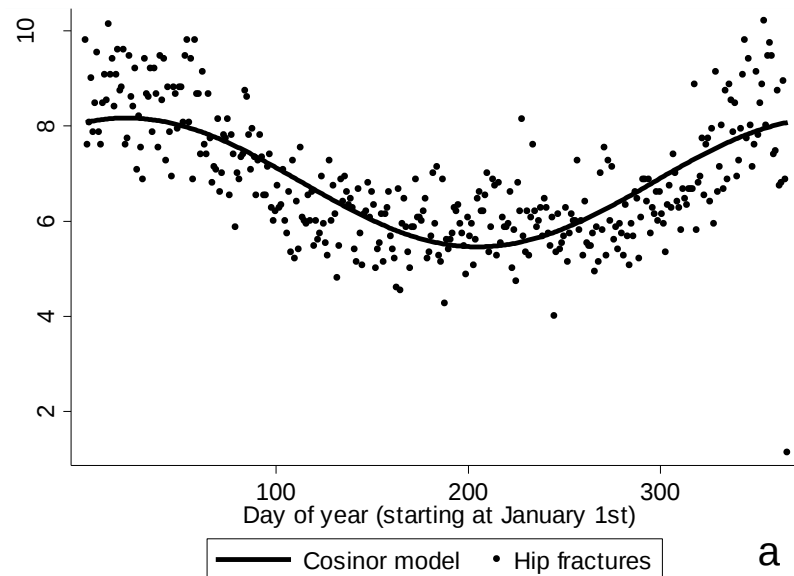
Women

	Age adjusted rate ratio	95% CI	
Rural	1,00		
Semi-rural	1,05	1,03	1,07
Urban	1,10	1,08	1,13

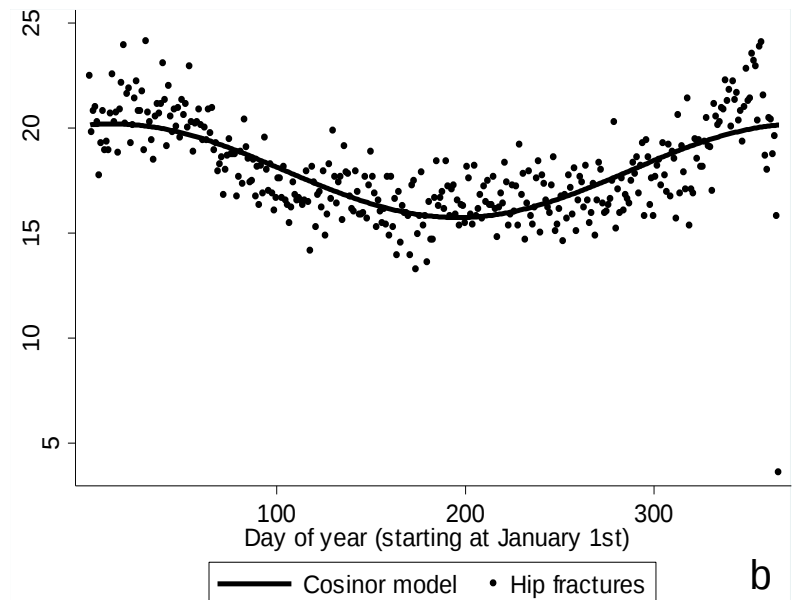


Seasonal variation: Higher risk in winter than summer

But also summer incidence is very high in Norway



Men



Women

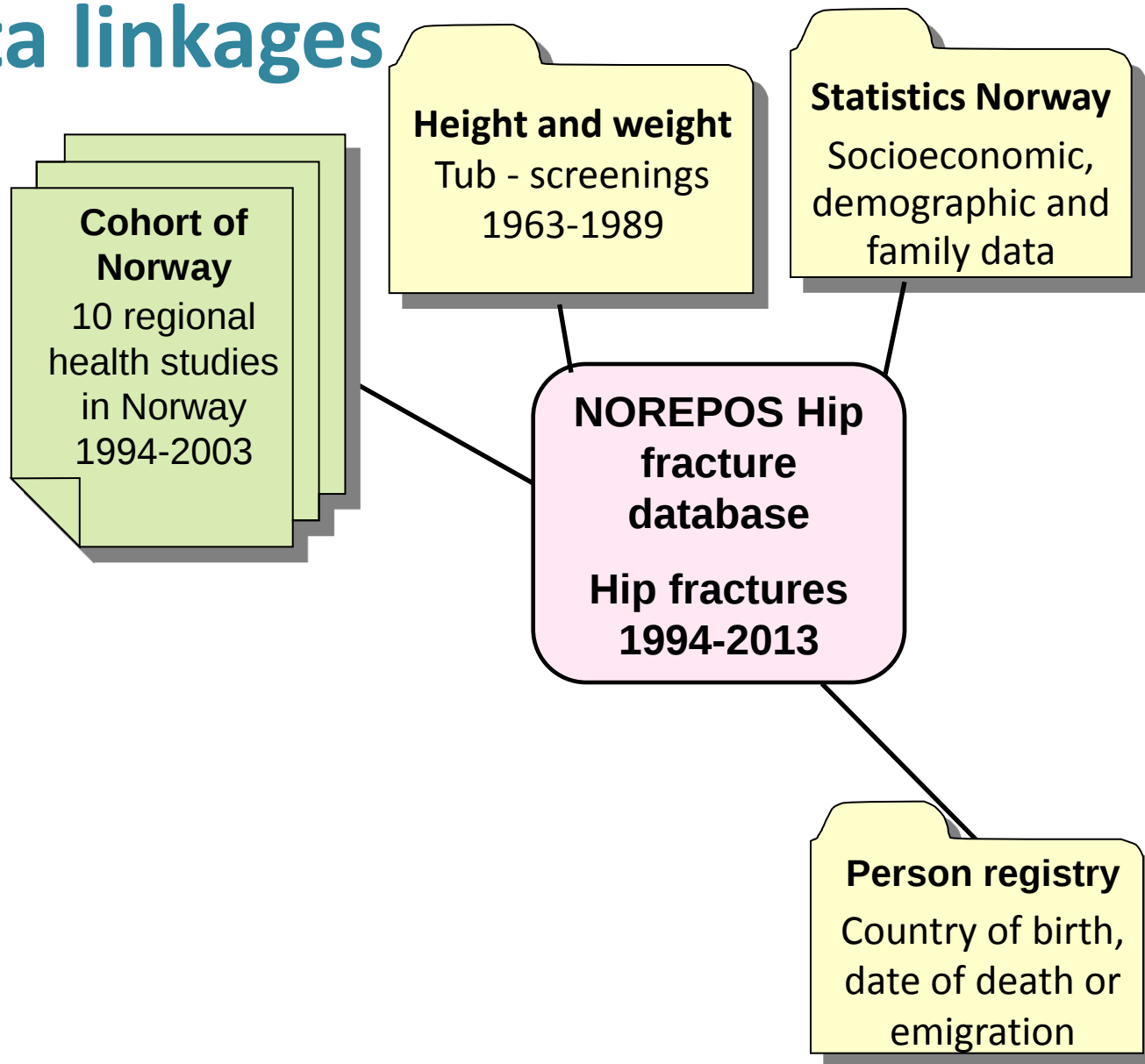
Risk factors: Body composition

Two types of anthropometric measures correlated with fat mass

- Body mass index
- Waist hip ratio

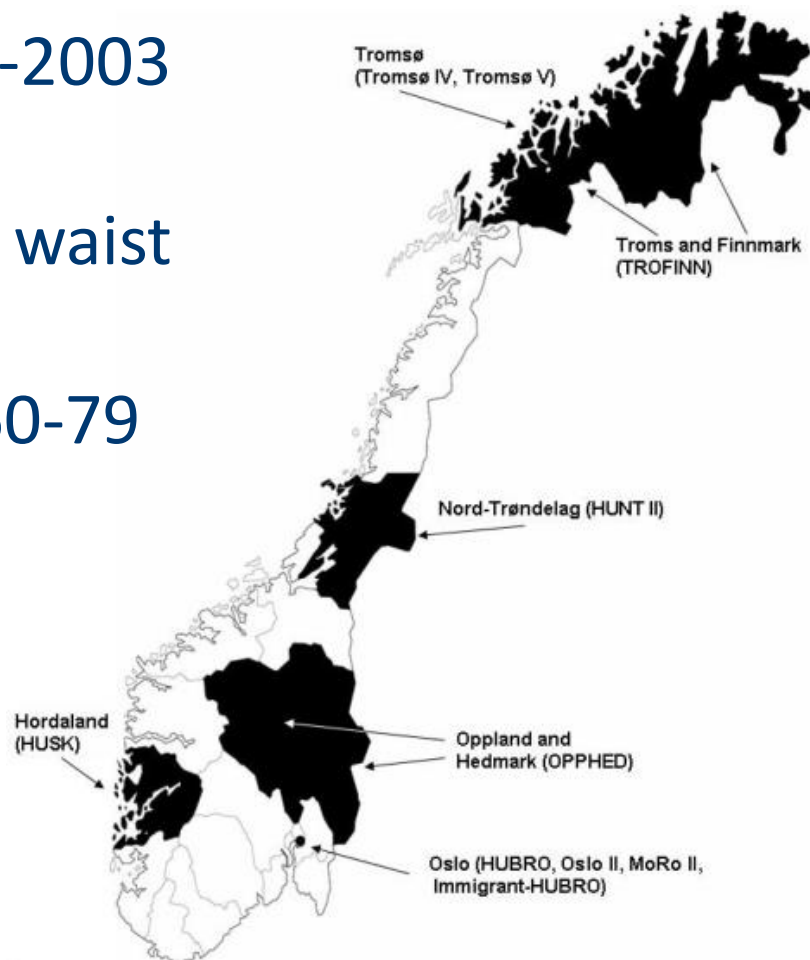


Data linkages

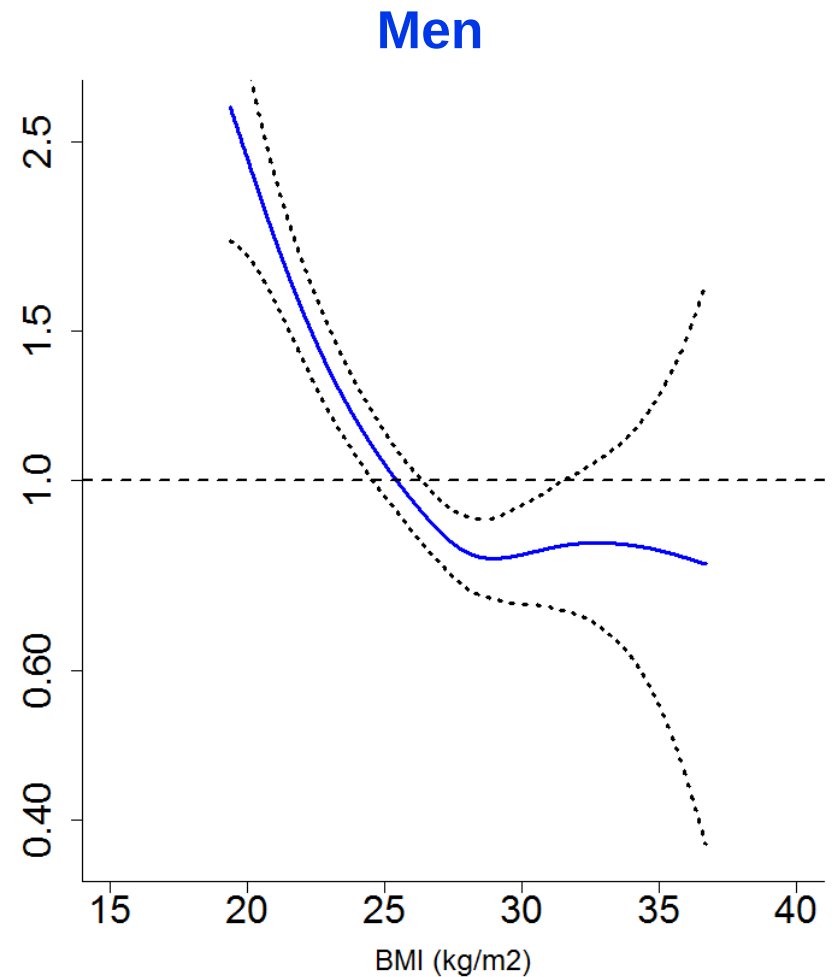
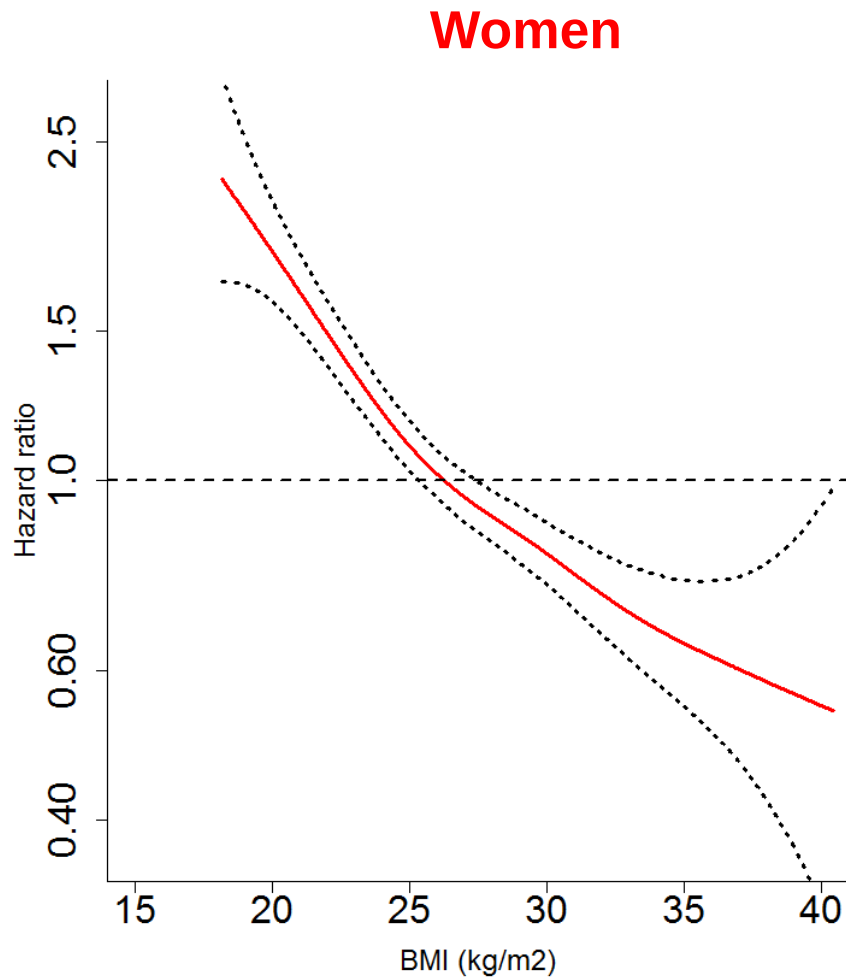


Cohort of Norway linked to hip fractures

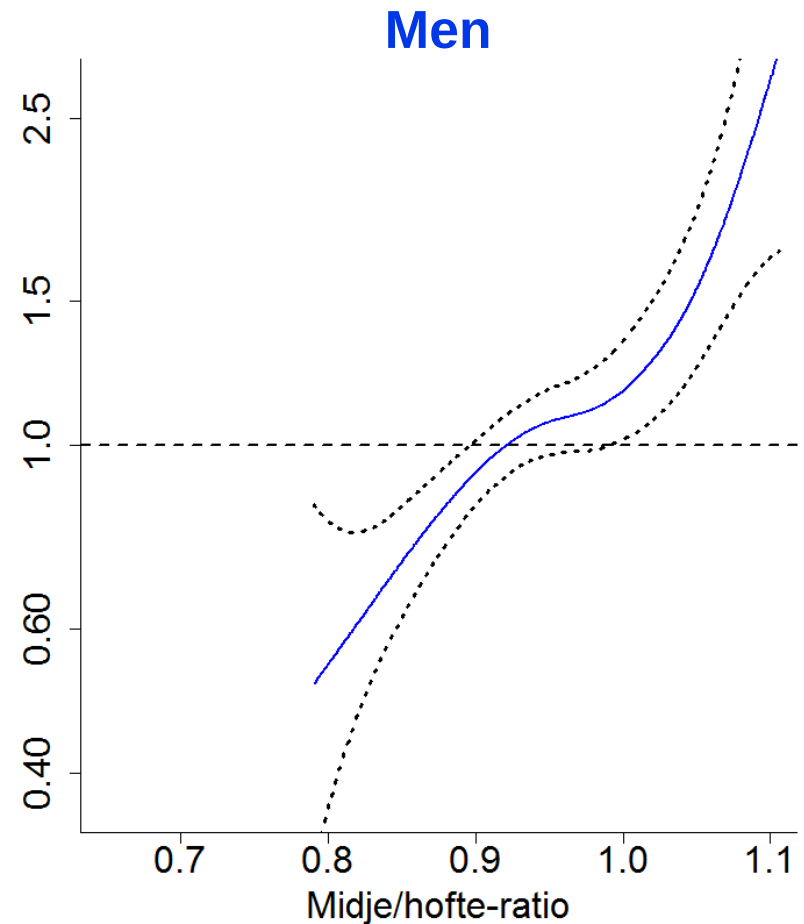
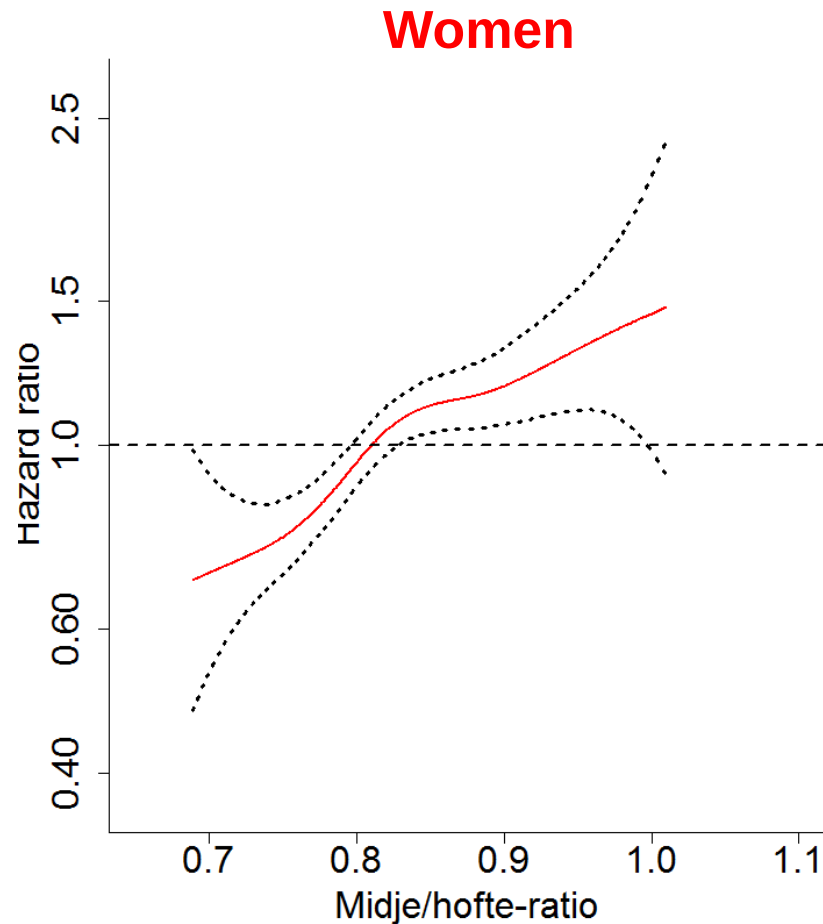
- 10 regional health studies 1994-2003
- Standardized anthropometric measurements: Height, weight, waist and hip circumference
- 43,000 men and women aged 60-79
- Followed up to 2008
 - Median 8.2 years
 - 2,400 incident hip fractures
- Cox regression



Higher body mass index is protective

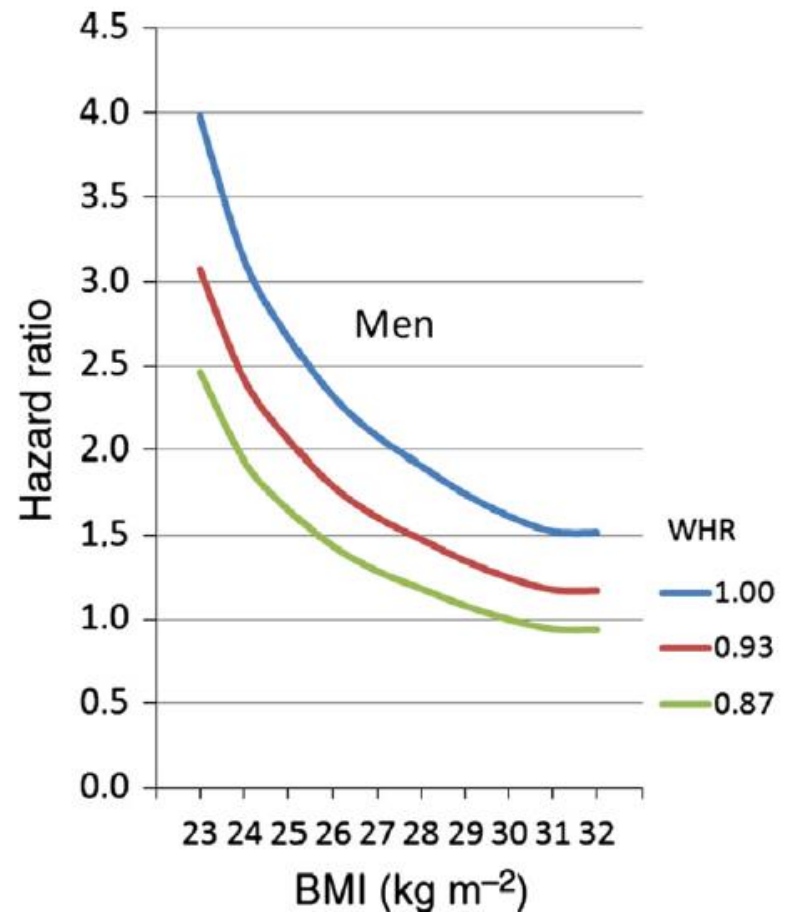
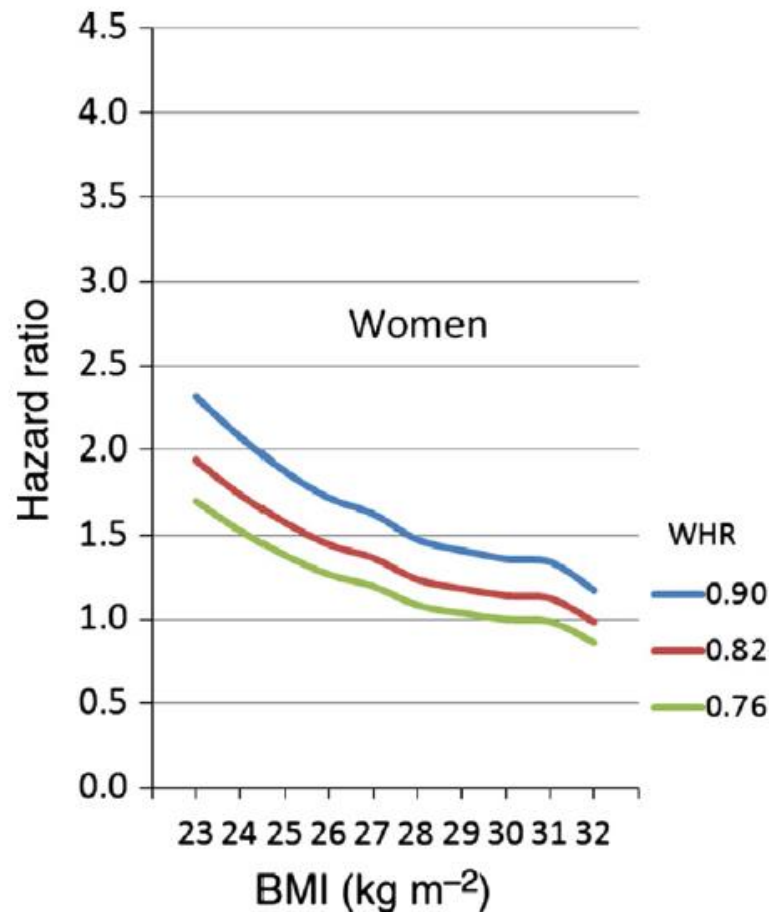


Higher waist-hip ratio is harmful



Body mass index and waist-hip ratio combined

Estimated hazard ratios for hip fracture at given levels of BMI and waist-hip ratio



Findings summarized, body composition

- The risk of hip fracture is lower with higher BMI, but this levels off at BMI about 27 kg/m² in men
- Abdominal obesity is independently associated with increased risk of hip fracture, also at lower BMI

Risk factors: Drinking water quality

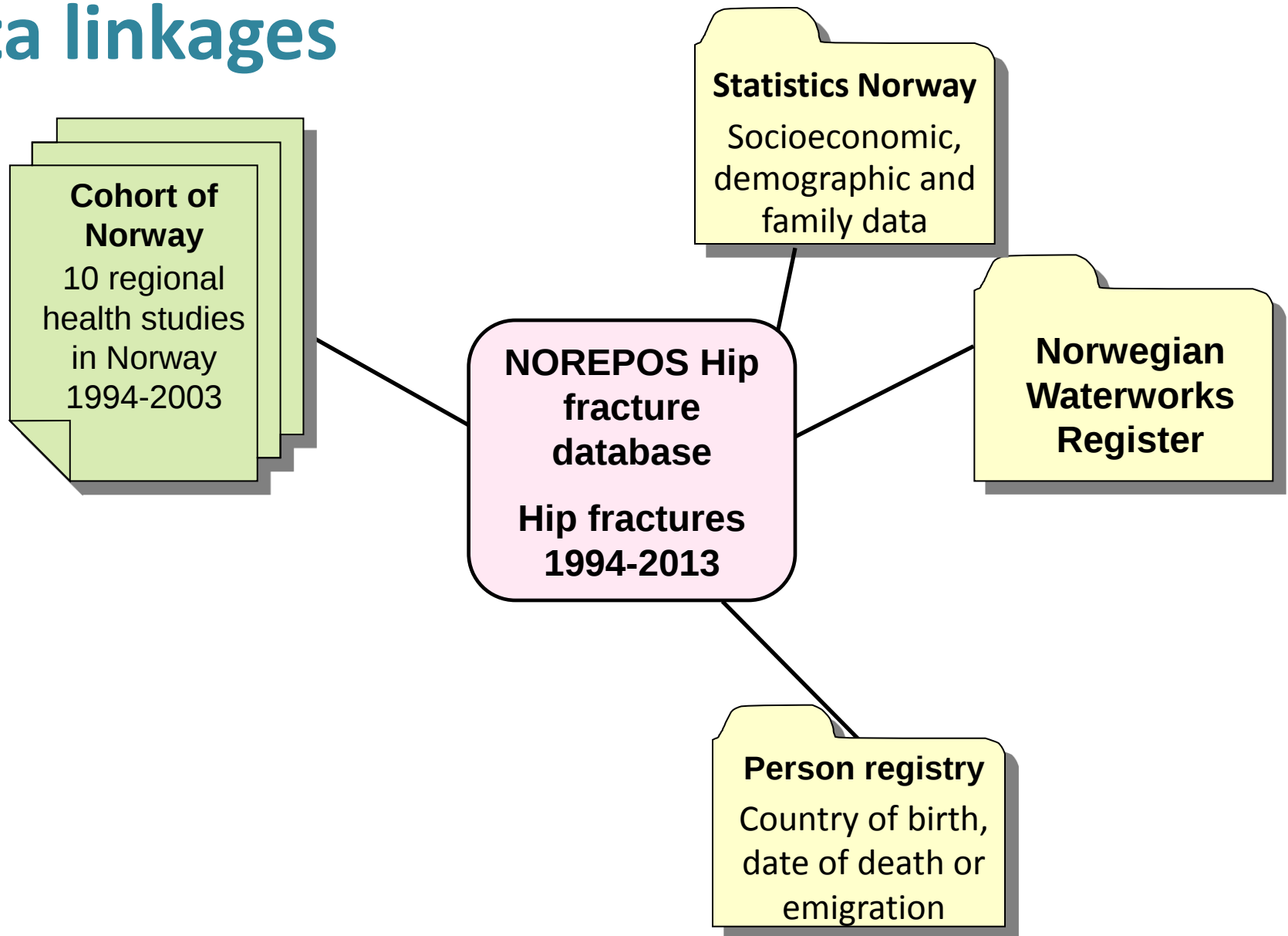
- Soft surface water >85 %
 - Low pH (rain)
 - Low in minerals
- Groundwater <15 %
 - More minerals, but lower than other European countries, and below recommendations



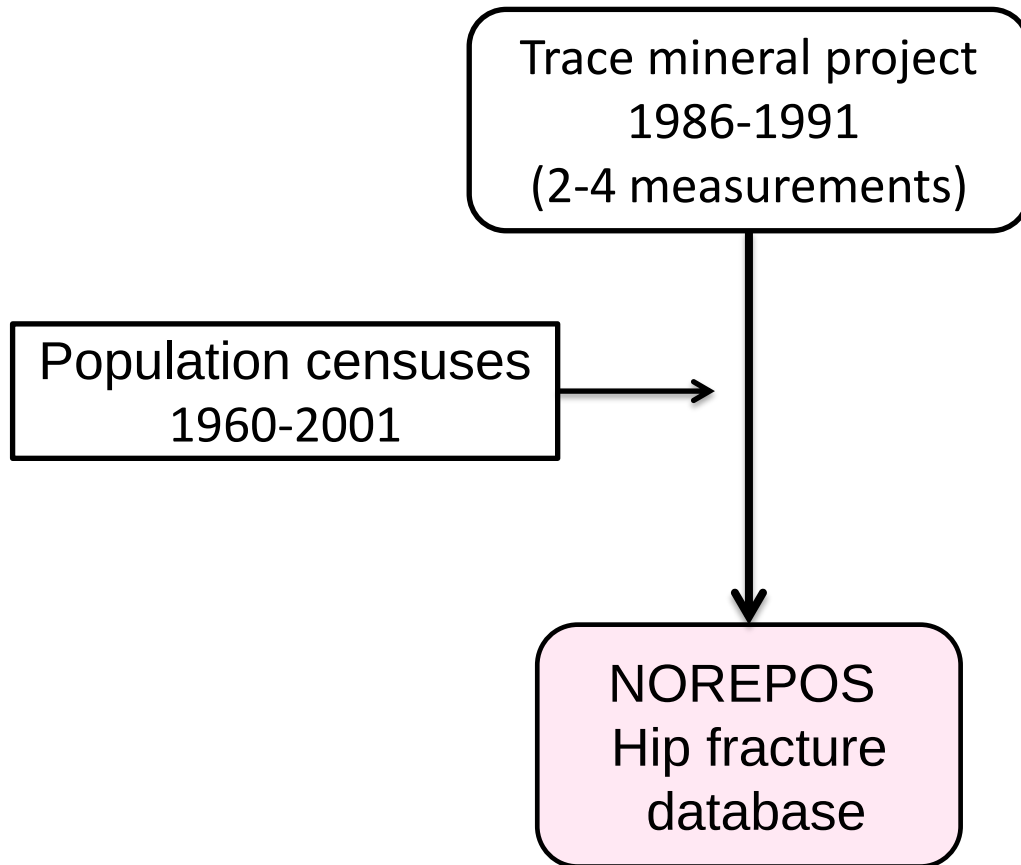
Groundwater vs. surface water in Norway:
Calcium: 14.5 vs. 3.6 mg/l
Magnesium: 2.5 vs. 0.7 mg/l

WHO:
Ca > 20 mg/l
Mg > 10 mg/l

Data linkages



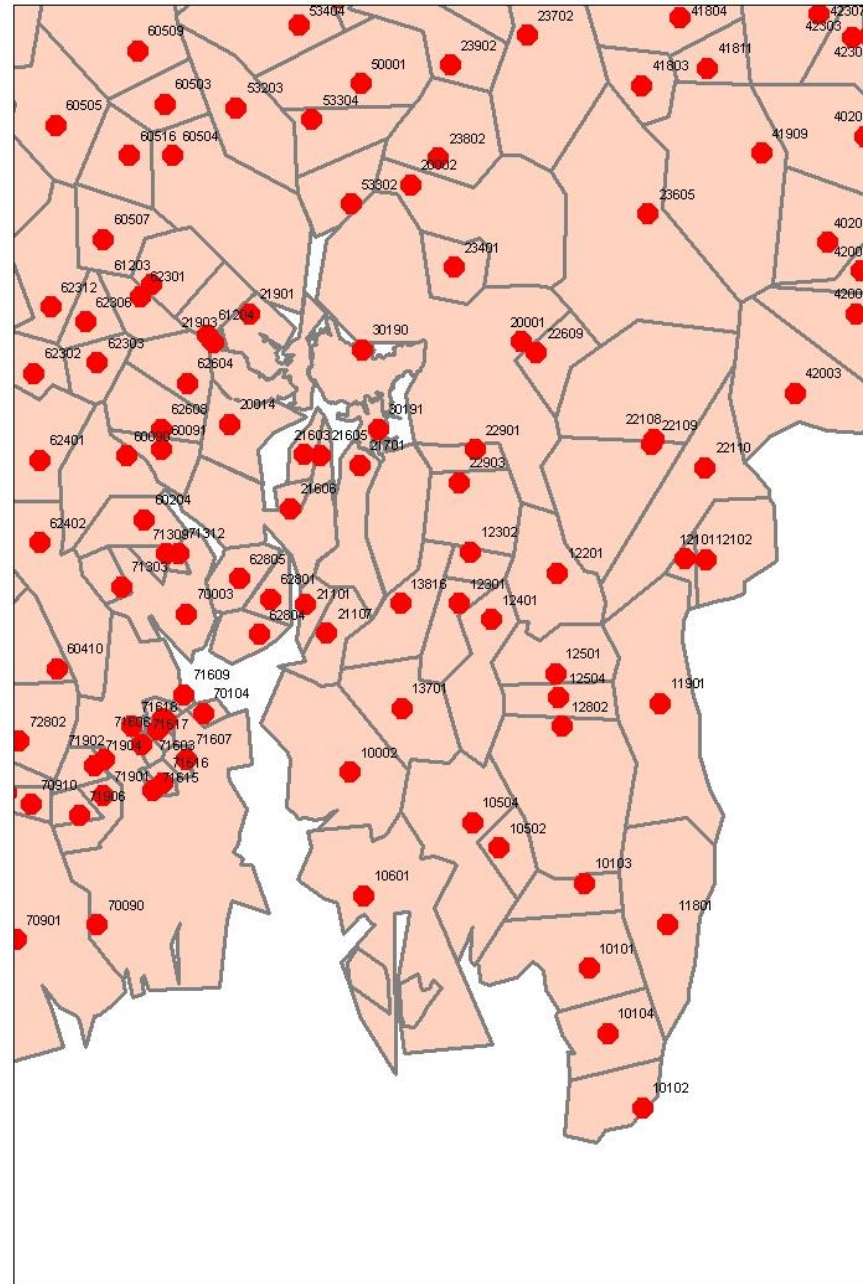
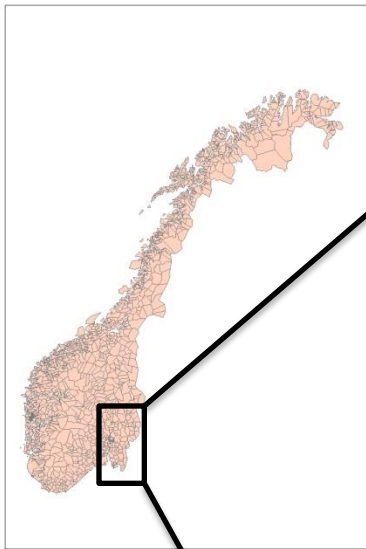
Data sources

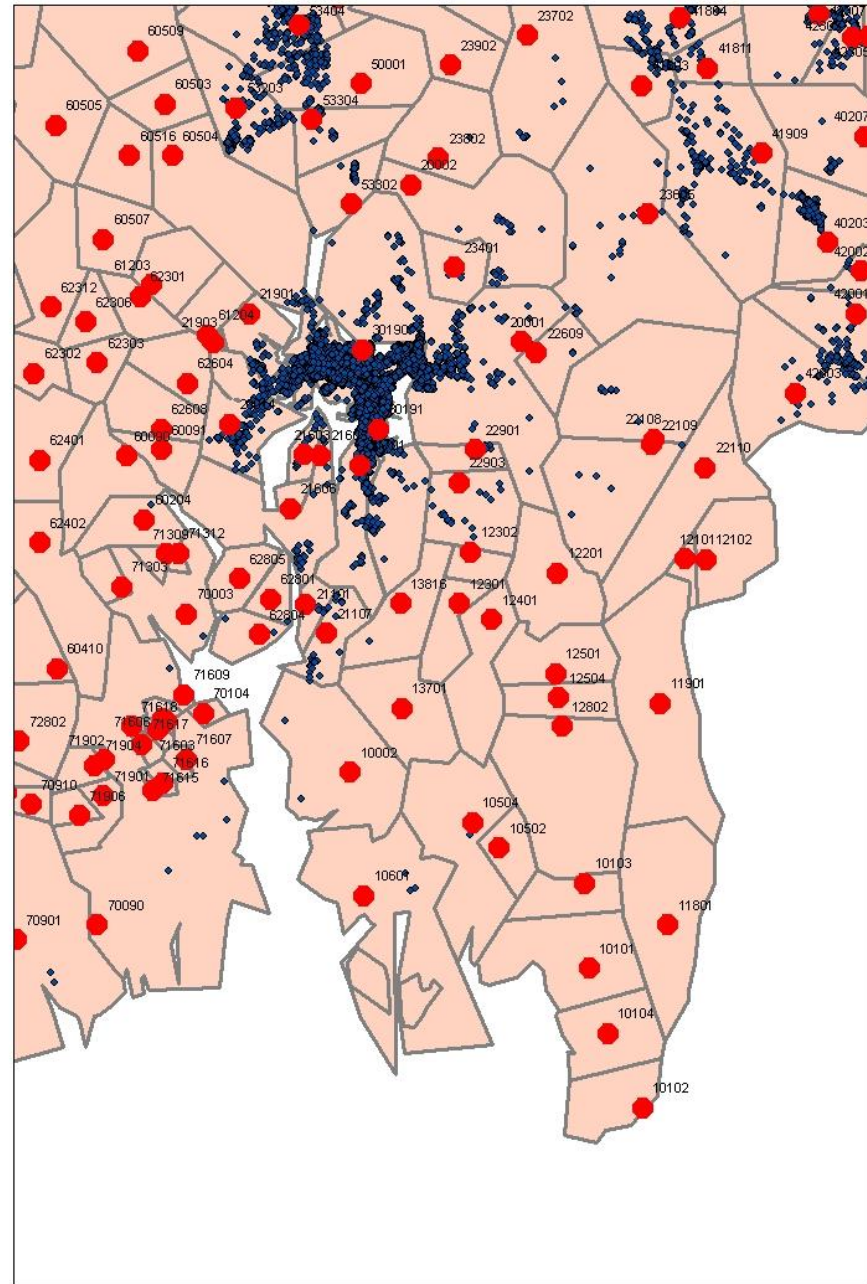
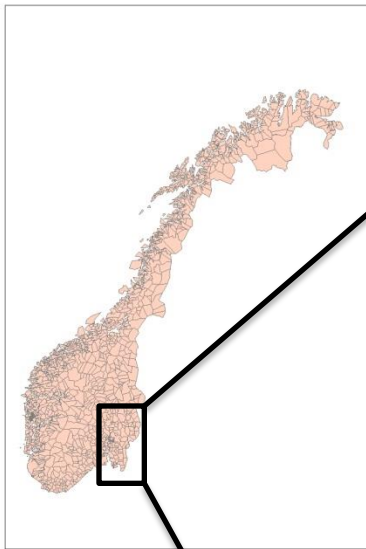


Water measurements;
area levels



Disease outcome;
individual level





Findings summarized, drinking water quality

- Slightly lower pH in drinking water (**pH 6-7**) was associated with more self-reported forearm fractures
- **Magnesium** in drinking water was associated with higher risk of hip fracture
- **Cadmium** in drinking water was associated with higher risk for hip fracture (in men)
- **Lead** in drinking water was associated with higher risk of hip fracture in the older (65-85 years)

Risk factors:

Fat-soluble vitamins: A, D, E, K

Vitamin D: Well studied but modest role in fracture prevention

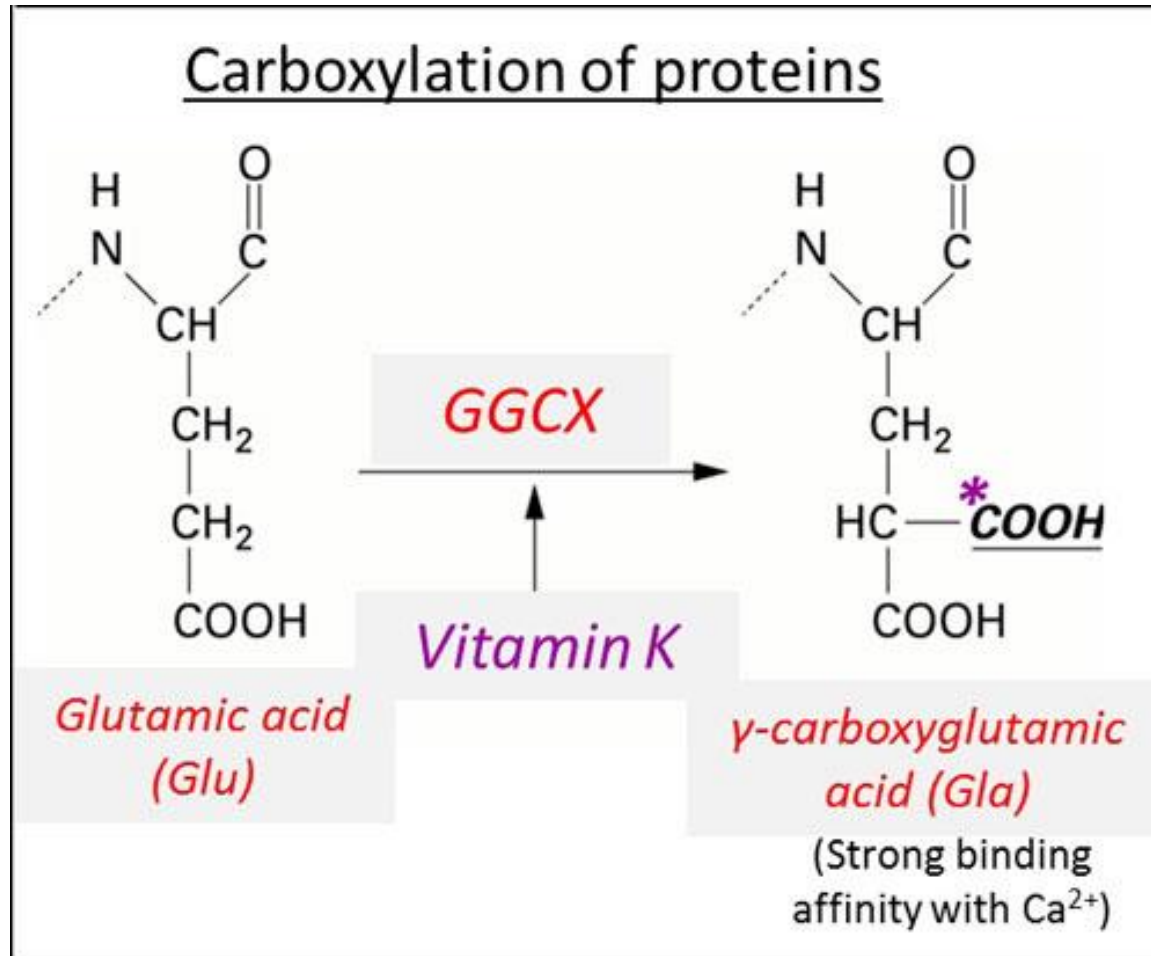
Vitamin D and vitamin D analogues for preventing fractures associated with involutional and post-menopausal osteoporosis (Review)

Avenell A, Gillespie WJ, Gillespie LD, O'Connell D



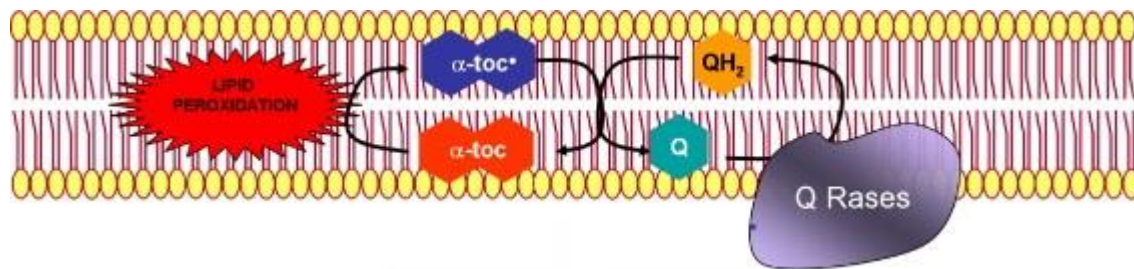
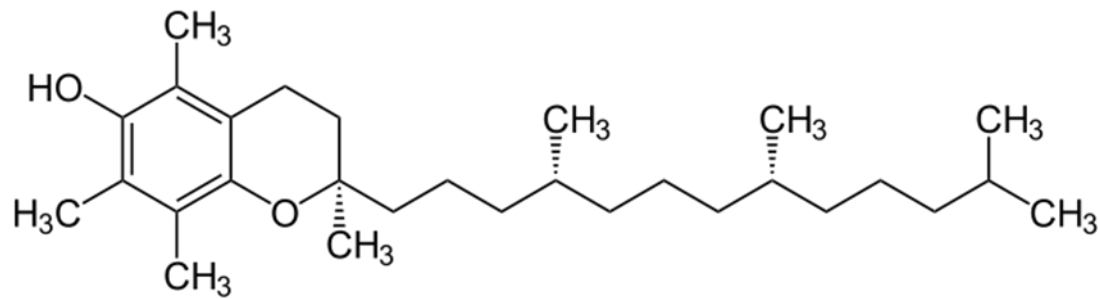
**THE COCHRANE
COLLABORATION®**

Vitamin K: Activation of mineral-carrying proteins in bone



Vitamin E (alpha-tocopherol):

Fat soluble plant substance with antioxidant capacity; possible anti-inflammatory actions also in bone



Preformed retinol (vitamin A): Harmful?

Excessive Dietary Intake of Vitamin A Is Associated with Reduced Bone Mineral Density and Increased Risk for Hip Fracture
Håkan Melhus, MD; Karl Michaëlsson, MD; Andreas Kindmark, MD; Reinhold Bergström, PhD;
Lars Holmberg, MD; Hans Mallmin, MD; Alicja Wolk, PhD; and Sverker Ljunghall, MD

Vitamin A Intake and Hip Fractures Among Postmenopausal Women

Diane Foskarmich, ScD
Vishwa Singh, PhD
Walter C. Willett, MD, DrPH
Graham A. Colditz, MD, DrPH

Context Ingestion of toxic amounts of vitamin A affects bone remodeling and can have adverse skeletal effects in animals. The possibility has been raised that long-term high vitamin A intake could contribute to fracture risk in humans.
Objective To assess the relationship between high vitamin A intake from foods and supplements and risk of hip fracture among postmenopausal women.

Serum Retinol Levels and the Risk of Fracture
Karl Michaëlsson, M.D., Hans Lithell, M.D., Bengt Vessby, M.D.,
and Håkan Melhus, M.D.

Serum Vitamin A Concentration and the Risk of Hip Fracture among Women 50 to 74 Years Old in the United States: A Prospective Analysis of the NHANES I Follow-up Study
Alexander R. Opatowsky, MD, MPH, John P. Bilezikian, MD

Although retinol has not always been associated with poor skeletal health [75], it is best to avoid cod liver oil and other concentrated fish products as sources of vitamin D due to the higher vitamin A content.

NOREPOS

Case-cohort study



Tromsø IV 1994-95



HUNT 2 1995-97



HUSK 1997-99



HUBRO 2000-2001

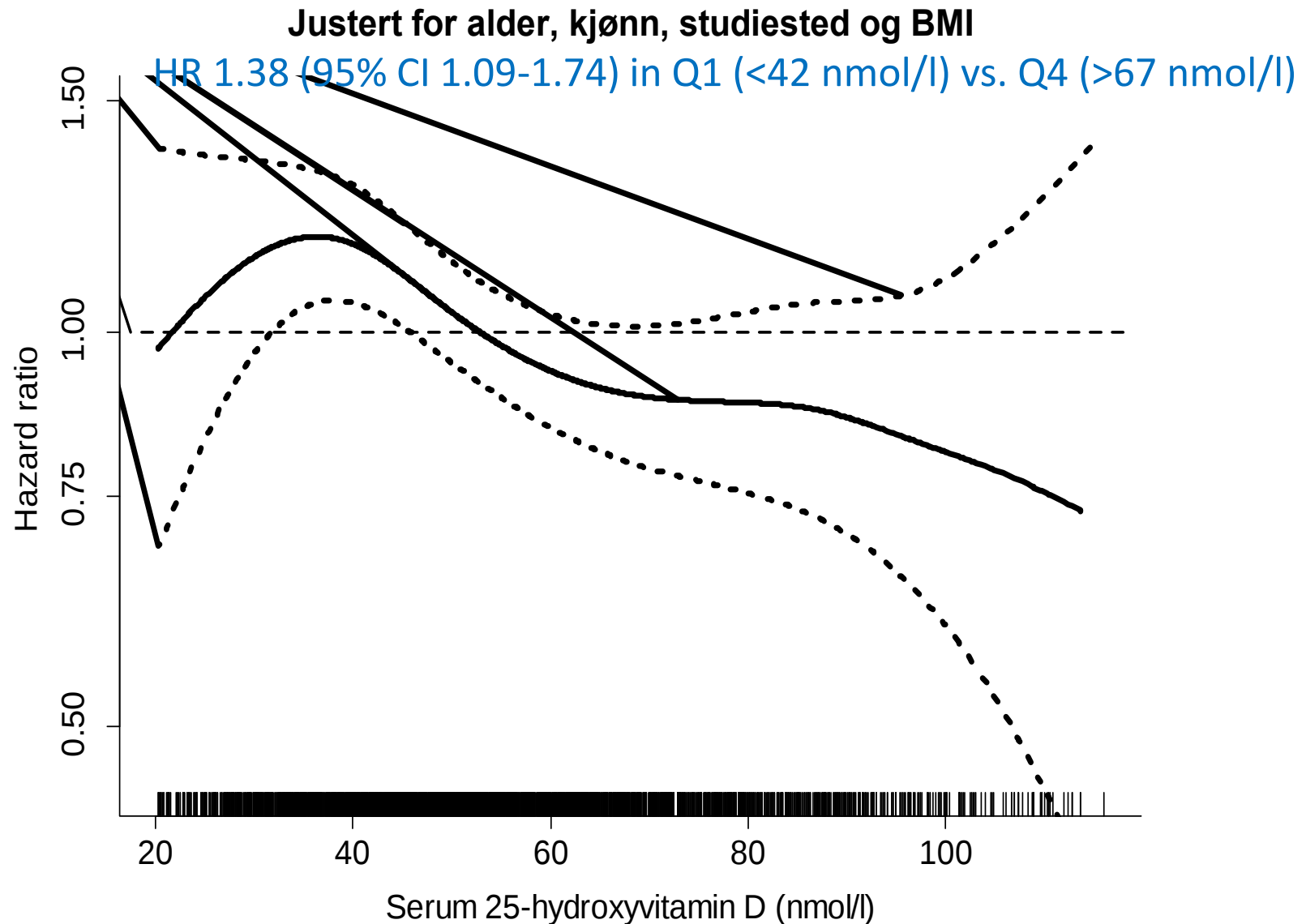


1175 hip fractures:

Vitamins A, D, E and K
in serum samples



Risk of hip fracture across serum 25-hydroxyvitamin D



Increased risk at low levels of both vitamins D and K

Table 4: Hazard ratios with 95% confidence intervals for combined groups with s-vitamin K₁ ≥ or < the median and 25(OH) D ≥ or < 50 nmol/L.

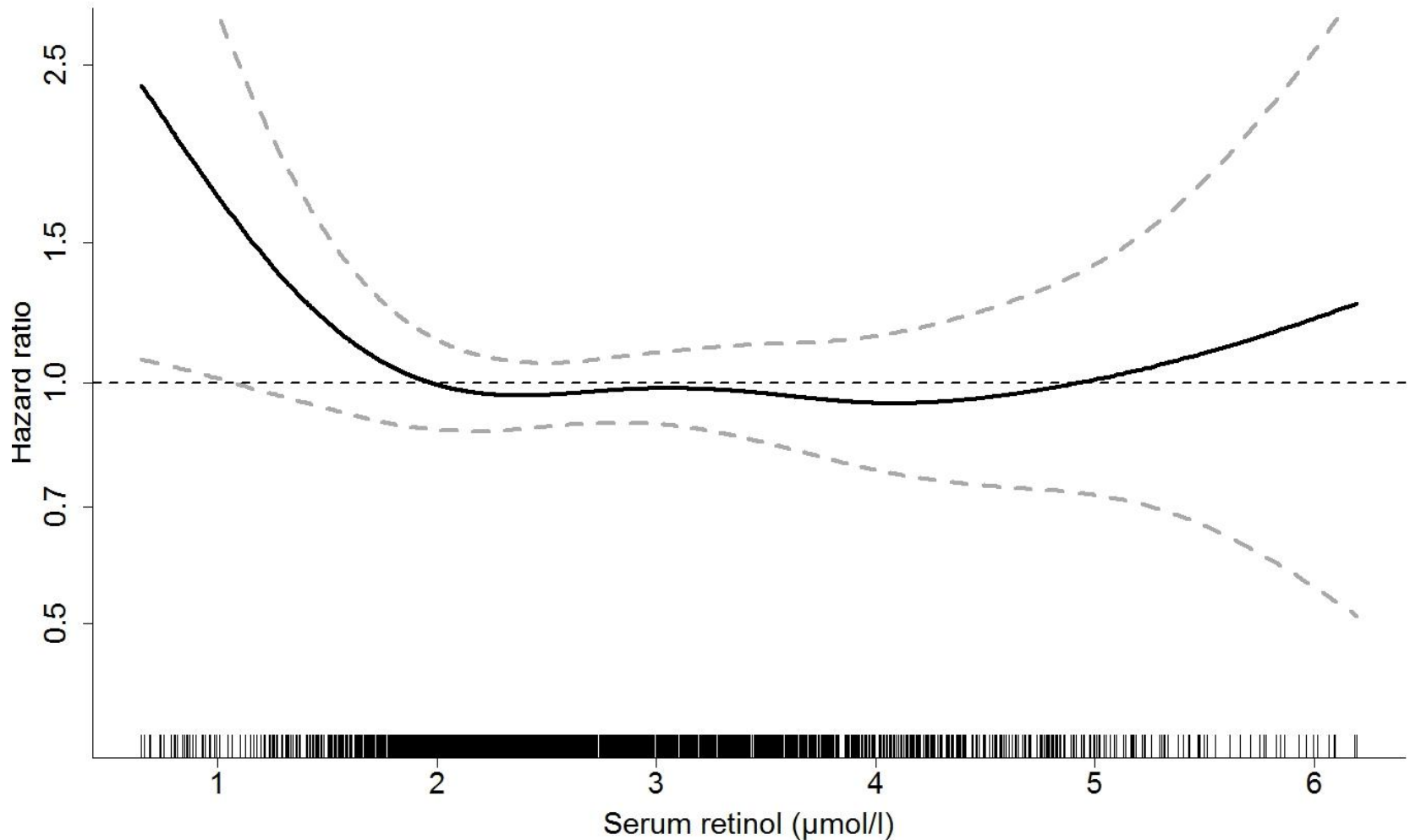
	Cases (n)	HR ^a	95% CI ^a	p ^a	HR ^b	95% CI ^b	P ^b
High K, High D	305	1	(ref)	-	1	(ref)	-
High K, Low D	201	0.97	0.76 – 1.24	0.80	1.09	0.84 – 1.42	0.50
Low K, High D	304	1.17	0.94 – 1.46	0.16	1.12	0.88 – 1.43	0.35
Low K, Low D	279	1.50	1.18 – 1.90	<0.001	1.41	1.09 – 1.82	0.009

^a) Base model (adjusted for age, sex and study site)

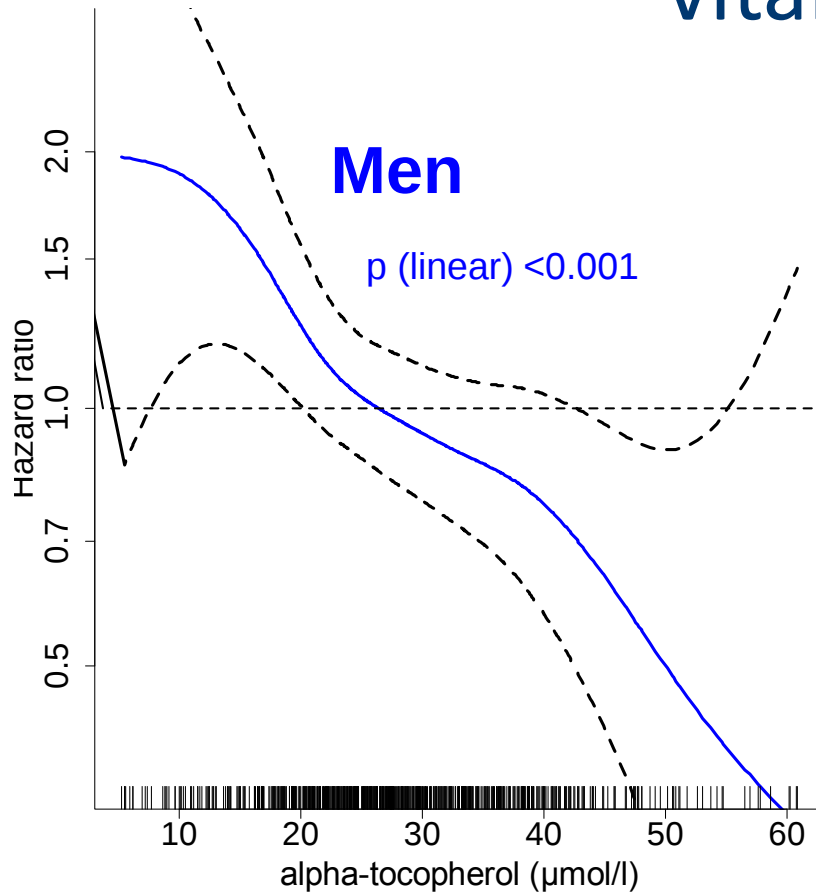
^b) Extended model, a) additionally adjusted for BMI, smoking, triglycerides and α -tocopherol

No increased risk at high retinol

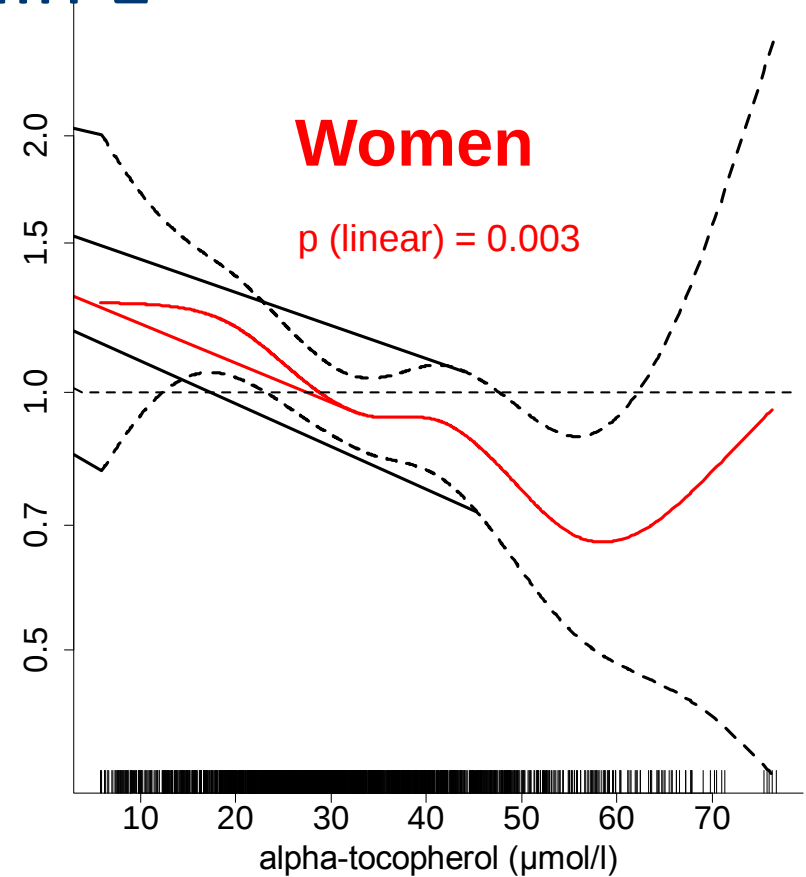
Model includes age, gender, study center, BMI, smoking, physical inactivity, self-rated health, vit. D and E



Independent strong inverse association with vitamin E



HR 1.20 (95% CI 1.02-1.42)



HR 1.10 (95% CI 1.02-1.19)

per 10 $\mu\text{mol/L}$ lower serum vitamin E

Findings summarized, vitamins

Middle and high serum concentrations of vitamin D and vitamin E (alpha-tocopherol) is associated with reduced risk of hip fracture compared to low concentrations

Contrary to expectations, high serum concentrations of vitamin A (retinol) were **not** associated with increased risk of hip fracture

Thank you for listening



City Hall Square, Oslo

Photo: John Mackey (ostimusic.com)