Summary of the 7th annual NOREPOS workshop
Hurdalsjøen, 20 - 21 September 2012

written by Kristin Holvik

This year's workshop was organized by the Oslo group and the venue was Hurdalsjøen Hotel and Conference Center in Akershus. Twenty-seven researchers from across Norway interested in epidemiologic osteoporosis research met for two days and discussed research results and future plans. Professor Karl Michaëlsson from Uppsala University participated as invited guest speaker. As always, the purposes of the workshop were to share results of ongoing research in NOREPOS, to network across study sites, and to conceive new ideas and research questions.

Thursday, 20 September

Haakon Meyer welcomed this year's participants to the workshop. The participants each presented themselves.

Grethe Tell gave a brief overview of the history and scope of NOREPOS and the health studies included. She described the ongoing project: "Hip fractures: Predictors, incidence and survival", the collection of hip fractures from all hospitals in Norway 1994-2008 constituting the NOREPOS hip fracture database, and new grant applications that are currently under consideration. It was emphasized that the NOREPOS network is intended to be a source of data that anyone who are interested are welcome to join and make use of.

Karl Michaëlsson gave an invited lecture about epidemiologic studies on osteoporosis and fractures in Sweden. He presented the Swedish national registries and quality registries that contain population data and health data which may be used for research. He presented research from his own environment in Uppsala, including the Swedish Mammography Cohort and the Uppsala Longitudinal Study of Adult Men. They study osteoporosis, fractures, and mortality as endpoints using various designs. Their research questions are related to heritability and genetic variation, as well as lifestyle factors such as diet and physical activity. In particular, twin studies using the large Swedish Twin Registry provide opportunities to studying the influence of lifestyle factors while accounting for heritability.
Points that were advocated were
   - the need for validation of register data, that seem to overestimate events
   - the need for change of focus to studying fall risk rather than just bone mineral density, as the frailest with more comorbidities will not visit a DXA machine
   - the need for including clinical risk factors in the assessment of fracture risk, as most fractures occur in those with a non-osteoporotic T-score

Cecilie Dahl talked about her PhD project concerning the relation of drinking water composition to risk of osteoporosis and fractures. As well as having a very high fracture incidence, Norway has a special drinking water composition, with only 11-15% groundwater, having a low calcium concentration and a low pH. She presented results from her first paper showing that pH in drinking water was associated with risk of self-reported forearm fractures, and from her second paper concerning the effects of toxic metals cadmium, lead, and aluminum on hip fracture, using the NOREPOS hip fracture database. She also presented some preliminary results from her third manuscript concerning a possible protective effect of magnesium, calcium, and pH on hip fracture.

Kristin Holvik presented results from her current Post Doc research project about vitamin D, vitamin A, and risk of hip fractures, using baseline examination data and blood samples from four health studies and hip fracture follow-up data from the local fracture registries in Tromsø, Nord-Trøndelag, Hordaland, and Oslo, in a case-cohort design. Vitamin A intake is very high in Norway, and the research question is whether a potential harmful effect of vitamin A on bone could interact with a protective effect of vitamin D.

Tone Omsland reviewed the collection and quality assurance of the national NOREPOS hip fracture database, and its validation against local hip fracture registries in Tromsø and Oslo. There has been a decline in total hip fracture incidence in both men and women in Norway in the period 1999-2008, but the number of hip fractures is unchanged due to the increasing ageing population. She also presented her studies of mortality after hip fracture according to degree of urbanization, and the risk of a second hip fracture in a competing risk-analysis. She is currently applying for an extension of the NOREPOS hip fracture database up to and including 2012 with data from the Norwegian Patient Register.

Nina Emaus presented results concerning risk of subsequent fractures based on data from the Tromsø study, ongoing work in cooperation with Post Doc Luai Ahmed. 27,000 participants in Tromsø IV have now been followed for 15 years with regard to fractures. Questions that are addressed are: What type of subsequent fracture do patients suffer according to type of first fracture; how long does the increased risk last; is the risk different in men and women, or in younger and older persons?

Friday, 21 September

Today, short presentations were given from various ongoing epidemiologic research projects within osteoporosis and fractures in Norway.

Ellen Apalset talked about IFN-gamma induced inflammation and kynurenines in relation to bone density in the Hordaland Health Study.

Anne Johanne Søgaard presented the associations between body mass index, waist hip ratio, and risk of hip fracture using baseline data from Cohort of Norway and outcome data from the NOREPOS hip fracture database.

Trine Finnes showed associations between the bone formation marker procollagen type 1 amino-terminal propeptide in serum and hip fracture in elderly women, based on data from HUBRO and HUSK in a case-cohort design.

Mari Hoff described her planned Post Doc project concerning forearm fractures. She will use data from the fracture register in Nord-Trøndelag Health Trust, the HUNT 1-3 studies, as well as the Norwegian Prescription Database to answer questions about treatment and subsequent fractures.

Arnulf Langhammer talked about the HUNT Databank which now includes more than 120,000 persons screened at least once in the HUNT studies. He presented some results from the recently published non-participation study in HUNT 3 showing that patients with chronic diseases were underrepresented in the health study. He also presented some results about the relationship between chronic obstructive pulmonary disease and osteoporosis in HUNT 3.

Svanhild Waterloo talked about health-related quality of life in patients with vertebral fractures. There was a clear relationship between self-reported back pain and health-related quality of life (according to EQ-5D) in women who had experienced a vertebral fracture, but not in men. Interestingly, she also found that persons without osteoporosis as measured by DXA who reported osteoporosis had poorer health-related quality of life than those who had osteoporosis according to DXA but reported no osteoporosis.

Anne Winther presented her recently initiated PhD project, using data from Fit Futures 1, a health study in adolescents in Tromsø carried out in eight upper secondary schools in 2010/11. The study had a high response rate of 92% and included interviews, questionnaires, anthropometric measures, DXA measurements, and blood samples collected at the University Hospital of Northern Norway in collaboration with the University of Tromsø. She presented results of BMD in femoral neck according to age.

Haakon Meyer gave a brief overview lecture about the impact of antiresorptive treatment on hip fracture rates, based on calculations done by Helene Devold who completed her dissertation this spring. If assuming that: a) alendronate reduces the risk of hip fracture by 40% (RR 0.6) as concluded in the recent Cochrane review, b) that half of the hip fracture patients have osteoporosis, c) that all osteoporosis patients receive treatment, and d) that compliance is 100%, it was estimated that alendronate would lead to a 20% reduction in number of hip fractures. If half of the patients would adhere to the treatment, the estimated reduction would be 10%. However, according to previously estimated figures by e.g. Johnell, only 24% of osteoporosis patients receive treatment. Using this number, the expected reduction in number of fractures on a population level would be 3.5%. Ragnhild Støen et al. recently suggested that about one-third of the reduction in hip fracture rates in women 70-79 years in Oslo could be attributed to medical treatment (Osteoporos Int 2012; 23: 2527-34). In conclusion, the majority of the reduction in fracture incidence is thus far unexplained.

Finally, **Karl Michaëlsson** summed up and gave advice for how to further make advantage of the existing data in NOREPOS.
His advice were:
-   One message per scientific paper
-   Analyse your data thoroughly: twist and turn the data
-   Perform sensitivity analyses
-   Big is beautiful, but quality is also important: Validation
-   Quality in exposure as important as quality in outcome
-   More studies about physical activity and fracture risk – with and without adjustment for BMD
-   Use the Norwegian cohorts to study fracture prediction based on clinical risk factors
-   Use repeated measurements, study changes
-   Focus on causal inference; draw DAGs (recommended website: www.DAGitty.net)
-   Focus on falls and comorbidity
-   Intervention study with factorial design on medication and fall prevention
-   Study the association between alpha-tocopherol and hip fracture risk

Participants were encouraged to ask questions to Michaëlsson. **Grethe Tell** and **Nina Emaus** led the discussion where the purpose was to formulate specific objectives and to form groups related to the suggested topics. This could be writing groups or groups for discussing topics or developing specific projects within the NOREPOS collaboration.