

**Socioeconomic status and risk of osteoporotic fractures and the use of DXA: data from the Danish population-based ROSE study**

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**Background:**

Lower socioeconomic status including income and education is known to be associated with a range of chronic conditions e.g. diabetes. The link between socioeconomic status and osteoporotic fracture is, however, more unclear. The aim of this study was to examine the relationship between socioeconomic background and the risk of osteoporotic fractures and the use of DXA-uptake that is used to diagnose osteoporosis before fractures occurs.

**Materials and methods:**

This prospective study included a cohort of 17,157 women aged 65–81 years, who participated in the risk-stratified osteoporosis strategy evaluation study (ROSE). These data were linked with information on socioeconomic background (income, education and marital status) and DXA as well as incident fractures retrieved from national registers. Competing-risk regressions analyses were performed.

**Results:**

The median follow up time was 5.0 years. A total of 4,245 women had a DXA-scan and 1,719 an osteoporotic fracture during follow up. Analyses showed that women with basic education had lower probability of DXA-scan compared to women with further or higher education (SHR: 0.83,  $P < 0.001$ , adjusted for age), while no significant differences were found with regards to marital status or income. No significant differences in the socioeconomic background and risk of fractures were found when adjusting the analyses for age.

**Conclusions:**

The study did not find differences in socioeconomic status and risk of osteoporotic fractures but demonstrated differences in the use of DXA and education level. Women with further or higher education are more often receiving a DXA-scanning, compared to women with basic school.

**Socioeconomic position and mortality from brain tumour – A Swedish national cohort study**

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**Background** To investigate associations between socioeconomic position (SEP) and mortality after brain tumour diagnosis.

**Materials and Methods** All patients diagnosed with a primary brain tumour in Sweden 1993-2010 and reported to the national cancer register were followed-up until 31st December 2015. SEP was based on education, disposable income and marital status obtained from national registers. Relative survival models were used to estimate excess hazard ratio (EHR) by SEP for glioma, glioblastoma and meningioma, separately for men and women.

**Results** Men and women with primary education had increased mortality from glioma (EHR, 1.13, 95% CI 1.04-1.24, and 1.11, 1.00-1.24) and glioblastoma (EHR 1.20, 1.07-1.35 and 1.14, 1.00-1.31 respectively) compared to those with university education. Men in the lowest income quartile had 29% and 25% higher mortality from glioma and glioblastoma compared to those in the highest quartile (EHR 1.29, 1.17-1.43 and 1.25, 1.10-1.42, respectively). Women in the lowest income quartile had higher mortality from meningioma (EHR 3.63, 1.76-7.52). Being single (EHR, men 1.15, 1.04-1.26 and women 1.21, 1.06-1.38) and widowed (EHR, men 1.30, 1.08-1.58 and women 1.14, 1.00-1.30) was associated with increased mortality from glioma. Being single was associated with increased mortality from meningioma in men (EHR 2.49, 1.42-4.36) and women (EHR 2.10, 1.18-3.73).

**Conclusions** Lower SEP is associated with increased risk for mortality from glioma and meningioma, potentially due to earlier detection in higher socioeconomic individuals. The observed inequalities highlight the need for further investigation of preventable mechanisms and promotion of better access to medical care among deprived groups.

## **Inequalities in sickness absence between Finnish and Swedish speakers in Finland: a register-based study**

Kaarina Reini, Jan Saarela

### Background

Previous research has shown that Finnish speakers in Finland have higher rates of disability pension and mortality as compared with Swedish speakers. Survey data indicate health differentials also with regard to self-reported health, and some studies even suggest differences in mental health and well-being between the two ethno-linguistic groups. Here, we examine whether they differ in the receipt of sickness benefit, which is a previously unexplored objective health measure in this context.

### Materials and methods

The individual-level data used come from the Finnish longitudinal population register. They cover the period 1987-2011, and consist of five per cent of all Finnish speakers and 20 per cent of all Swedish speakers. To estimate the likelihood of receiving sickness benefit in prime working ages, and account for multiple occurrences at the individual level over the study period, we estimate logistic regression models with generalized estimating equations.

### Results

We find that, even when we control for a number of socioeconomic and demographic background factors, Finnish-speaking men are on average 30 per cent more likely to receive sickness benefit than Swedish-speaking. In women, the difference is approximately 15 per cent. These results corroborate previous research based on other objective health measures, and are expected also from the perspective that sickness absence is a predictor of disability pension and mortality.

### Conclusion

Since sickness absence causes substantial costs for the society, these results can be utilised in policy making processes that aim to lower sickness absence rates and thus help in equalising health differences.

O4

## **Inequalities in the broken heart syndrome**

Filip Wigselius

Excess mortality after widowhood differs for men and women. Previous studies also have shown that socioeconomic status (SES) is associated with factors, e.g. access to social and other types of support, which have a bearing on the widowhood effect. I argue, that theory indicates an interaction between gender and SES. As both, the number of widows/widowers and the diversity in SES is increasing, it is necessary to examine these factors jointly.

First results using panel data of from the Swedish Panel Study of Living Conditions of the Oldest Old (SWEOLD), confirm the hypothesis that the relationship between SES and the widowhood effect differs between women and men. The widowhood effect was relatively larger among women with higher socioeconomic status among those with lower, while no differences were found among men. Analyses using Swedish total population register data will be ready in time for the NordicEpi meeting.

## **Education, Gender, and Cohort Fertility in the Nordic Countries**

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**Background:** Systematic comparisons of fertility developments based on education, gender and country context are rare.

**Data and methods:** Using harmonized register data, we compare cohort total fertility (CTF) and ultimate childlessness by gender and educational attainment for cohorts born beginning in 1940 in four Nordic countries.

**Results:** CTF has remained fairly stable in all countries. Childlessness, which had been increasing, has plateaued except in Finland. Women's negative educational gradient in relation to ultimate fertility has vanished, while men's positive gradient has persisted. The highest level of men's childlessness appears among the less educated, revealing striking educational differences. Childlessness has increased among low-educated women but not among highly educated women. The educational gradient in women's childlessness has shifted from positive to negative.

**Conclusion:** We witness both a new gender similarity and widening social inequalities in childbearing in the Nordic welfare states. Low-educated citizens of both sexes have apparently become an increasingly marginalized segment with regard to childbearing.

## **Job demand, control and social support as predictors of subsequent trajectories of depressive symptoms**

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### Background

Psychosocial working conditions such as job demands, job control and social support have been associated with depressive symptoms. However, very few studies have investigated if these work stressors predict different trajectories of depressive symptoms over time, which was the aim of this study.

### Materials and methods

We included 6679 subjects in the Swedish Longitudinal Occupational Survey of Health, who completed questionnaires bi-annually on perceived job demands, control, social support and depressive symptoms in 2006-2016. Group-based trajectory models were used to identify groups with similar development of depressive symptoms in 2010-2016. Multinomial logistic regression estimated the association between job demand, job control and social support and subsequent trajectories of depressive symptoms.

### Results

We identified six different depression trajectories including two trajectory groups with low symptoms, one small group with severe and persistent symptoms, as well as three mild/moderate trajectories. High job demands and low social support were associated with subsequent trajectories with higher symptom level compared to very low symptom level. These associations remained statistically significant after adjusting for demographic covariates and baseline depressive symptoms. Risk ratios for high job demand and low social support ranged from 1.32 to 2.51.

### Conclusion

Perceiving high job demands and low social support both seem to be associated with more unfavourable courses of depressive symptoms. The study thus suggests that interventions targeting job demands and social support may contribute to a more favourable course of depressive symptoms and improved outcome.

O7

**Pre-retirement labour market position and main-cause mortality after retirement: a longitudinal study from Finland**

Julia Klein, Jan Saarela

*The authors have chosen not to publish the abstract*

## Occupations with High All-cause Mortality in 2001-2015: The contribution of education and unemployment

### Background

There are differences in mortality among occupations. Both education and unemployment are associated with occupations and mortality.

The main aim is to examine, which are the occupations with the highest all-cause mortality, and whether these differences could be explained by education and former unemployment.

### Materials and methods

We used longitudinal individual level register based data from the registers of Statistics Finland. Study population consisted of employees aged 30-64 at the end of the year 2000. The follow-up period was 2001-2015. Analysis methods included death rates, age standardized mortality ratios and confidence intervals as well as Cox proportional hazard model.

### Results

The occupations with increased risk of death (SMR>120 and at least 10 000 person years) were mostly manual workers. The occupations with the highest risk of death were building construction labourers (SMR 183) among men and building care takers (SMR 151) among women.

Education explained max 73% of excess mortality among men and 20% among women. but especially among men in some occupations it increased the risk of death, even by 35%. Unemployment explained 3-86% among men and 0-61% among women.

On average, the adjustment of both education and unemployment explained 61% of excess mortality among men (range 17-112) and 36% (4-57%) among women. The percent was high eg. among construction industry.

### Conclusion

There are mortality differences among occupations which cannot be explained by education or unemployment. There are no clear pattern of the effect of education and unemployment on occupational mortality differences. Further studies are needed.

**Does physical inactivity modify the relationship between psychosocial work factors and depressive symptoms? Modeling the interrelationship between time-dependent exposure, moderator and outcome in longitudinal data**

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Does physical inactivity modify the relationship between psychosocial work factors and depressive symptoms? Modeling the interrelationship between time-dependent exposure, moderator and outcome with longitudinal data

**ABSTRACT**

**Background:** This study investigates whether the longitudinal associations between job strain (job demands, control) and depressive symptoms differed by physical inactivity (effect moderation).

**Materials and Methods:** The study was based on a sample of over 1300 participants in the Swedish Longitudinal Occupational Survey of Health (SLOSH). Repeated measures of job strain (demands and control), low support at work, physical inactivity, depressive symptoms and a set of time-invariant and time-varying covariates was used for the analysis. Causal effect modification on whether the effect of job strain differed by physical inactivity, was analysed using a structural nested mean model approach that combines a regression-with-residuals approach with an inverse-probability-of-treatment weighting strategy was applied, suited for time-varying exposures and moderator.

**Results:** Job strain (and particularly job demands) and low support were associated with a higher risk of subsequent depressive symptoms. The effect of work stressors varied by physical inactivity when adjusting for education, income, civil status, sex, age or smoking and drinking except for low control and low support in 2008. These results indicate that prior physical inactivity modifies the associations between job demands/strain, support and depressive symptoms. These results are likely to be more reliable than by traditional moderation analyses and clarify the temporal order between the exposure and putative moderator.

**Conclusions:** The present study gives support for the supposition that the associations between the studied psychosocial working conditions and depressive symptoms vary by prior physical inactivity.

**Keywords:** demand-control support model;depression;inverse-probability-of-treatment-weighting; physical inactivity; structural nested mean model;time-varying effect moderation

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**Shift Work and Risk of Incident Dementia: A study of two population-based cohorts**

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*The authors have chosen not to publish the abstract*

O11

**How does non-participation to the Maternal Follow-up within the Danish National Birth Cohort influence selected associations?**

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O12

## **Selection bias - a review of definitions and usage**

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### Background

The aim of this study was to identify diverging definitions and usage of the term "selection bias" in observational and interventional public health research.

### Material and methods

Definitions of the term "selection bias" in scientific literature were reviewed. Example of different usages of the term were sought for, using a combination of structured and snowball search.

### Results

The term "selection bias" was found in 10 629 abstracts and in 598 titles available in PubMed on May 12, 2017. Selection processes were in the literature generally defined and characterized with respect to 1) where the selection takes place (at population, study or analytic level), 2) the timing of the selection (into, out from or as a consequence of exposure) and 3) how results are influenced. Several, often only partially overlapping, definitions of "selection bias" were identified. Each definition was generally restricted to cover only a particular type of selection process.

### Conclusions

Understanding the full range of different sources of selection both at population and study level will be fundamental for assessing the consequences, both with respect to bias and hampered generalizability in reported exposure and intervention (e.g. treatment) effects.

O13

**Bias, bounds and sensitivity analysis for unobserved confounding when using regression imputation and double robust estimators**

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When estimating average causal effects of a treatment with observational data, scientists often rely on an assumption of no unobserved confounders. We propose a sensitivity analysis to unobserved confounders, for outcome regression imputation estimators and doubly robust estimators, based on identification bounds for the causal effect of interest. The bounds are derived from the bias of the estimators, expressed as a function of a sensitivity parameter. We describe how such bounds together with sampling variability yield an uncertainty interval with desired coverage. We are also able to contrast the size of the bias due to violation of the unconfoundedness assumption, with bias due to misspecification of the models used to explain potential outcomes. While the latter bias can in theory be made arbitrarily small with increasing sample size (assuming “sparsity”, and by increasing the flexibility of the models used), the bias due to unobserved confounding will not disappear with increasing sample size. This is illustrated through numerical experiments where bias due to moderate unobserved confounding dominates misspecification bias for typical situations in terms of sample size and modeling assumptions. Relevance to register data studies is discussed and illustrated.

**External adjustment of unmeasured confounders in a case-control study of benzodiazepines and cancer risk**

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**Background:** Previous studies have reported diverging results on the association between benzodiazepine use and cancer risk. Unmeasured confounding is a plausible explanation for discrepancies. In this study, we revisited this association by use of propensity score calibration based on external information on confounders available for a subset of the study subjects.

**Materials and methods:** We investigated the association between benzodiazepine use and cancer risk in a matched case-control study including incident cancer cases during 2002-2009 from the Danish Cancer Registry (n=94,923) and age and sex-matched (1:8) population controls (n=759,334). Long-term benzodiazepine use was defined as  $\geq 500$  defined daily doses 1-5 years prior to the index date. We implemented propensity score (PS) calibration using external information on confounders available from a survey of the Danish population. Two PS measures were used: The error-prone PS using register-based confounders and the calibrated PS based on both register- and survey-based confounders, retrieved from the Health Interview Survey.

**Results:** Register-based data showed that cancer cases had more diagnoses, higher comorbidity score and more co-medication than population controls. Survey-based data showed lower self-rated health, more self-reported diseases, more smoking, and more sedentary lifestyle among benzodiazepine users. By PS calibration, the odds ratio for benzodiazepine use and cancer overall decreased from 1.16 to 1.09 (1.00, 1.19) and for smoking-related cancers from 1.20 to 1.10 (1.00, 1.21).

**Conclusion:** Propensity score calibration moved the OR for BZRD use and cancer closer to the null, in particular for smoking-related cancers, thereby indicating that the increased risk observed in the purely register-based studies could be at least partly attributed to unmeasured confounding.

**Using fathers as a negative control to test fetal programming hypotheses**

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**Background:** Using paternal factors as negative control exposures for testing fetal programming hypotheses has become more popular in epidemiological research. However, no formal framework has hitherto been proposed for these designs, nor limitations discussed at length. We propose a framework for such research and apply it to a case study regarding fetal exposure to distress and asthma risk.

**Methods:** A causal diagram for associations of maternal (fetal) and paternal exposures with offspring outcomes is proposed, including partitioning of shared and parent-specific confounders. The case-study included data on all children born in Sweden from July 2006 to December 2008 (n=254 150). Information about childhood asthma, parental distress and covariates was obtained from the Swedish health registers. Associations between maternal and paternal distress during pregnancy and offspring asthma were assessed separately and with mutual adjustment for the other parent's distress.

**Results:** The proposed causal diagram illustrates that negative control exposure studies are useful for eliminating shared residual confounding but may continue to be biased by parent-specific residual confounding. Some of this bias can be alleviated by mutual adjustment for the other parent's exposure. Our case study found that maternal distress during pregnancy was associated with offspring asthma risk; Odds Ratio (OR) 1.32 (95% CI 1.23, 1.43). The mutually adjusted paternal distress-offspring asthma analysis indicated no evidence for residual confounding (OR 1.05 95% CI 0.97, 1.13).

**Conclusion:** Negative control models using paternal exposures can be a relatively simple extension of conventional observational studies to test the robustness of fetal programming hypotheses, but limitations need consideration.

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## **SND 2.0 – a Swedish infrastructure for sharing research data**

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Researchers in Sweden are facing a growing demand for data sharing. Sharing data increases research efficiency and the number of articles based on them. Yet, there are technical, political and legal challenges to preserving and providing access to research data. A lack of high-quality solutions often results in researchers failing to meet requirements for long-term accessibility.

The Swedish National Data Service (SND) has applied The Swedish Research Council for funding to establish SND 2.0 – a consortium\* that will address the challenges with data sharing and facilitate preservation of and access to research data from several disciplines. SND 2.0 will provide a distributed system for the Swedish research community to describe and deposit data; share data with Swedish and international researchers and discover published data. SND 2.0 will offer an advanced technical infrastructure, training, user support and standardised development of metadata.

As a national infrastructure for data sharing, SND 2.0 will be essential to Swedish research in the future. The consortium contains the competence to coordinate access to research data within a range of scientific domains, and will support, train and collaborate with local data curation professionals at in total 23 universities. Coordinated data access – whether open or controlled – has proved more successful and transparent than dispersed structures.

Fully developed, the SND 2.0 metadata register and research data repository will let researchers find and reuse well-documented, well-preserved and well-curated research data.

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## **Riksmaten Ungdom - a national dietary survey in Sweden**

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### **Background**

The aim of Riksmaten Ungdom is to provide data on diet, physical activity, nutritional status, weight status and exposure to unwanted substances from foods in Swedish children and adolescents. The information will be used as a basis for formulating recommendations on diet and physical activity and monitoring compliance to these recommendations, as well as identifying groups at risk of low nutritional status and high contaminant exposure.

### **Methods**

At least 3000 adolescents in grades 5, 8 and 2nd year at high school are recruited through schools across Sweden during the school year 2016-17. Diet is reported in a new, validated web based dietary assessment method. Participants also complete on-line questionnaires on demographics, socio-economy, health, dietary supplements, physical activity and frequencies of foods. Weight, height and physical activity (accelerometers) are measured, and blood and urine collected (1200 participants) for analyses of nutritional biomarkers and exposure to unwanted substances.

### **Results**

Preliminary results (n=2964; participation rate 69%) show that less than half of the girls and around one third of the boys report that they eat vegetables every day and that one third of the participants consume fruit every day. Furthermore (n=788) that less than half of the boys and one fifth of the girls reach the recommendation of 60 minutes of daily moderate to vigorous physical activity.

### **Conclusions**

The Riksmaten Ungdom survey will provide important national data and results on diet and physical activity and will also constitute an important basis for decision making and public health work in Sweden.

## **DOC\*X the Danish Occupational Cohort: A new open research Database on Occupational Health**

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DOC\*X is a Danish nationwide occupational cohort comprising 6.2 million people with information on labour market affiliation, industry, and job type. DOC\*X covers all work active residents in Denmark from 1970 to 2012. DOC\*X is an open research database, aiming to provide access to high quality data for both Danish and international researchers in occupational health.

DOC\*X comprises time dependent job-exposure matrices (JEMs) for various exposures according to job types and industries. DOC\*X contains JEMs on dust (organic and inorganic), biomechanical workload (lower-back, leg, arm-shoulder, lifting, working positions), psychosocial factors (emotional demands, job strain, job insecurity, ergonomic and physical demands, violence and threats) and chemical agents (formaldehyde, diesel-exhausts, organic solvents, including chlorinated).

In addition JEMs covering occupational exposure to noise, sunlight and UV-radiation are under construction.

DOC\*X also includes time dependent JEMs for five lifestyle factors (alcohol consumption, body mass index, fruit and vegetable consumption, leisure time activity, smoking) to enable adjustments in analyses.

Furthermore DOC\*X contains information on demography, retirement, mortality, hospitalisations, cancer morbidity, and other health and social security services. The amount of outcomes available varies: Mortality and cancer are virtually complete for all years, whereas other health and social security services are introduced during the period. All outcomes are drawn from nationwide registers, and have exceedingly good coverage when available.

In conclusion, the DOC\*X database gives unique possibilities to future investigations of impact of occupation on health.

More information on the DOC\*X database and access to data at [www.doc-x.dk/en/](http://www.doc-x.dk/en/)

## **Predicting major osteoporotic fracture risk by previous diagnoses: A Nationwide population- and register-based study**

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### Background:

A range of common conditions are already known to be associated with increased risk of osteoporotic fractures. However, other conditions may also be indicators of an increased risk of osteoporotic fractures. The aim of the study was to identify conditions for inclusion in predictive - as opposed to explanatory - algorithms for automated case finding of high risk individuals.

### Materials and methods:

This study included the total population of 1,294,206 women and 1,201,133 men in Denmark  $\geq 45$  years of age on January 1st 2013. All hospital diagnoses in the period 1998-2012 were used as possible exposures and major osteoporotic fractures during 2013 as outcome. Our cohort was split randomly 50-50 into a development and a validation data set for deriving and validating the predictive model. We applied forward selection on level 2 ICD-10 codes in logistic regression to develop the model adjusting for age and stratified by sex.

### Results:

In the period 1998-2012 we observed 1,564 and 1,467 different ICD-codes occurring among women and men 17,694 fractures in women and 6,716 fractures in men during 2013. After applying the selection procedure on the development set, 51 predictive baseline diagnoses in women and 59 in men were found, resulting in AUC in ROC curves of 0.7531 and 0.7599, respectively.

### Conclusions:

Our results indicate a number of previously unrecognized risk conditions, diagnoses which predict later osteoporotic fractures, and which potentially could be taken into account when identifying high risk persons for targeted assessment and potential treatment to avoid fractures.

**Intensity of leisure-time physical activity and mortality in middle-aged and older adults with ischemic heart disease, diabetes and both: the HUNT Study**

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**Background:** To assess the impact of intensity level of leisure-time physical activity (LPA) on risk for cardiovascular (CVD) and all-cause mortality in individuals with ischemic heart disease (IHD), diabetes and with both IHD and diabetes.

**Material and methods:** In a cohort of middle-aged and older adults 21751 were free from CVD, 1417 had IHD, 517 had diabetes and 157 had IHD and diabetes at baseline in the Nord-Trøndelag Health Study (1995-97). Weekly LPA was measured through questions on weekly duration of light LPA (no sweating or being out of breath) and hard LPA (sweating/out of breath). Participants were followed until 31 December 2014. CVD and all-cause mortality was determined by the Norwegian Cause of Death Registry. Adjusted cox proportional hazards models were used to estimate mortality risk.

**Results:** During the mean follow-up of 16.6 years 20.4% of the healthy, 63.2% of those with IHD, 54.5% of those with diabetes, and 70.7% of those with IHD and diabetes died. Test for trend within each group suggested a dose-relationship between intensity of LPA and mortality. Compared with healthy inactive, those with IHD reporting hard weekly PA  $\geq 3$  hours per week, and those with diabetes reporting any hard LPA per week reduced their mortality risk for CVD mortality to the same level as healthy inactive participants.

**Conclusion:** Weekly light PA reduces risk for premature death. However, weekly LPA that makes one sweat and breathless contributes to the greatest risk reduction for mortality, irrespective of being healthy or diagnosed with IHD, diabetes or both.

**End of life after stroke. A nationwide study of 42,502 deaths occurring within a year after stroke**

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**Background:** Stroke is a leading cause of death. Yet, there is very limited empirical information related to the end of life issues after stroke available in the scientific literature. The present nationwide study describes circumstances at death occurring within a year after stroke.

**Material and methods:** Datasets from three nationwide Swedish registers (the Swedish Stroke Register Riksstroke, the Palliative Care Register, and the Cause of Death Register) were linked. Basic information was available in 42,502 unselected cases of deaths within a year after stroke and more detailed information in 16,408 deaths.

**Results:** The mean age at death was 82.3 years. In the late phase after stroke (3 months to 1 year), the majority 46.3 % died in a nursing home, whereas 35.6 % died in a hospital after readmission, and 9 % at home. Eleven percent of deaths were reported as unexpected. A physician had not examined 9 % of patients dying in a nursing home and 12 % dying at home in the last month preceding death. Family members were present at 49 % of the deaths. The frequency of unattended death (neither family members nor staff present at the time of death) ranged from 5 % at home with advanced home care to 22 % in hospitals and increased markedly with.

**Conclusion:** There is considerable discordance between presumed 'good death' late after stroke (dying at home surrounded by family members) and the actual circumstances at the end of life.

## **Is the association between obesity and hip osteoarthritis explained by familial confounding? Results from the Nor-Twin OA study**

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**Objective:** To study whether familial confounding due to genetics or environmental factors explains the association between Body Mass Index (BMI) and severe hip osteoarthritis (OA).

**Design:** Data from the Norwegian Arthroplasty Registry were linked with the Norwegian Twin Registry in 2014, generating a population-based prospective cohort study of same-sex twins born 1915-60 (53.4% females). BMI was calculated from self-reported height and weight. The outcome was incident hip arthroplasty due to OA (follow-up time: 1987-2014, 424 914 person-years). We performed sex-specific co-twin control analyses of dizygotic (DZ, N=5226) and monozygotic (MZ, N=3803) twin pairs using Cox regression models and compared the findings to those of cohort analyses. A weaker/non-significant association within MZ pairs compared to the cohort association would provide evidence of familial confounding.

**Results:** The mean (SD) BMI was 22.6 (2.96), peak lifetime BMI 25.6 (2.61) and N=614 had hip surgery due to OA. In cohort analyses, BMI was significantly associated with hip OA for women and men (Hazard Ratio, HR=1.09, 95% confidence intervals, CI=1.06-1.11 and HR=1.08, 95% CI=1.04-1.12, respectively). When adjusting for familial confounding in within MZ twin analyses, the association got stronger for women (HR=1.19, 95% CI=1.05-1.36) but weaker and non-significant for men (HR=0.93, 95% CI=0.75-1.16).

**Conclusion:** The association between BMI and hip OA was likely non-causal and explained by familial confounding for men. For women, there was no evidence for familial confounding, consistent with a causal association.

**Systemic C-reactive protein levels among adults born small for gestational age**

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**Background**

The long-term health effects of being born small for gestational age (SGA) are incompletely understood. SGA neonates have elevated levels of inflammatory factors, but whether this persists into adulthood is unknown. We explored the association between blood levels of C-reactive protein (CRP) and SGA among healthy blood donors.

**Materials and methods**

Based on data on all singleton births in Denmark 1979-1993, relative birth weight was defined as small and large within gestational week, sex and birth cohort. Infants born in the 10th-90th percentile range served as reference. Birth characteristics of blood donors with information on CRP level, the Danish Blood Donor Study was linked with the Danish Medical Birth Registry on the civil registration number. We compared CRP levels between SGA and normal individuals by Gamma regression analyses. Moreover, logistic regression analysis was used to explore the association of SGA with low grade inflammation (CRP 3-9mg/L).

**Results**

CRP levels were reported in 5057 donors (55% women). The median age of cohort members was 25 years (range 18-32 years), and approximately 9% were SGA. Median CRP were 0.28 and 1.07mg/L in men and women, respectively. Adjusted for age and sex, CRP were higher in SGA compared with normal donors, 0.31mg/L, 95%CI (0.11,0.50). Adjustment for body mass index, hormonal prevention, and smoking yielded similar results. Despite increased CRP levels SGA donors were not at increased risk of low grade inflammation, OR=1.11, 95%CI (0.82,1.49).

**Conclusion**

Previously reported elevated CRP levels in infants born SGA seem to persist also into adulthood.

O24

**Body mass index measured early in life predicts future incidence of atrial fibrillation**

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*The authors have chosen not to publish the abstract*

## Parental socioeconomic status and risk of cerebral palsy in offspring

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### Background

Our aim was to investigate risk of cerebral palsy (CP) in offspring by parents' socioeconomic background.

### Materials and methods

We conducted parallel studies in Denmark and Norway using data on almost 1.3 and 2.4 million children registered in the Danish and Norwegian Birth registries, respectively. Data on all births were linked to Statistics Denmark and Norway to retrieve information on parents' education, and in Denmark also income. In Norway, the diagnoses of CP were collected from the National Insurance Scheme and the Norwegian Patient Registry, while in Denmark; the diagnoses were collected from the more detailed Cerebral Palsy Registry. Information on CP subtypes was only available in Denmark. We used log-binominal regression models to estimate relative risk (RR) of CP according to parental socioeconomic status.

### Results

Higher levels of parental educational attainment were associated with decreased risk of CP in offspring. Compared with primary education, a mother with a master degree or higher had a RR of 0.61 (95% confidence interval (CI) 0.51-0.72) for having a child with CP in Denmark and 0.67 (95% CI 0.59-0.77) in Norway. We found a similar parental educational gradient for the outcome bilateral spastic CP in the Danish cohort. The educational gradient remained stable over time in both cohorts, also after excluding pre-term born children.

### Conclusion

The decreasing risks of CP in offspring with increasing parental educational levels suggest that some of the risk factors for CP are socioeconomically mediated, implying a potential for prevention.

**Are social determinants from the earlier life course explaining health disparities across differently disadvantaged areas in northern Sweden? A decomposition analysis of neighborhood deprivation inequalities in adult somatic symptoms**

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Umeå University

**Background:** Drawing upon different strands of social epidemiological knowledge, the present study examined the contribution of individual factors from three life periods to the neighborhood deprivation gradient in self-reported somatic symptoms in a Swedish middle aged cohort.

**Materials and methods:** Self-reported information on functional somatic symptoms (FSS) and life circumstances was retrieved from 873 individuals residing in Luleå, Sweden in 1981 and who answered surveys at age 16, 21, and 42. Their neighborhood of residence at each subsequent age was collected from the Swedish registers and defined in accordance with SAMS (small-area market statistics). The concentration index (C) with the corresponding concentration curve (CC) was used to estimate the neighborhood deprivation gradient in FSS at age 42. Decomposition analyses were performed to examine the contribution of determinants from adolescent, young adulthood and mid-life to the inequality.

**Results:** The concentration index was small but significant,  $C = -0.041$  (95 % CI: -0.071, -0.011) and with a negative value suggesting that levels of FSS increased as neighborhoods became more deprived. Results from the decomposition analyses expressed themselves as a 'social chain of risk' with a reduction in the explanatory potential of factors from adolescence and young adulthood by the inclusion of adult life circumstances. For example, when only including factors from age 16, these explained about 35 percent of the inequality. In contrast, after adding determinants from age 21 and 42 their independent contribution was only 1.5 percent.

**Conclusion:** This study suggests that socioeconomic, psychosocial and demographic circumstances in adulthood may be of importance for understanding neighborhood deprivation gradient in self-reported somatic symptoms, but also that the gradient can have its roots in and be shaped by the health and living conditions people experienced throughout adolescence and young adulthood.

**Assessment of educational misclassification in register-based data on Finnish immigrants in Sweden**

Jan Saarela, Rosa Weber

In population registers, information on completed schooling is either missing or misclassified for a large share of newly arrived immigrants. It is unclear how quickly the information gets updated and whether misclassification, i.e., that the wrong level of education is recorded, biases empirical estimates. We use unique linked Swedish and Finnish register data to determine the extent of such mismeasurement. By running logistic regressions on zero earnings, we also illustrate how mismeasurement might influence the estimated effects of education on health or labour market outcomes. We find a considerable bias in estimates based on Swedish records of educational attainment during immigrants' first few years in the country. Misclassification is additionally very common even when information on educational attainment exists. These findings suggest that research and policies using recently arrived immigrants' completed schooling as a determinant of socioeconomic integration need to be interpreted with care.

O28

**Completeness of the Swedish Cancer Register regarding registration of central nervous system tumors between 1990 and 2009**

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**A framework for evaluating the quality of administrative data for research purposes**Reijo Sund<sup>1,2</sup><sup>1</sup> Centre for Research Methods, University of Helsinki<sup>2</sup> Institute of Clinical Medicine, University of Eastern Finland

The fundamental challenge with secondary data is that it is not possible to concentrate on those parts of observed reality that would be most relevant for the current research, but measurement must be based on data originally produced for some other purposes. The problems and promises of utilization of administrative data can be illustrated as a task in information communication, where the actual information must be decoded from the data and pre-knowledge using an infological equation. In order to find some shared perspective between the original and intended data utilization purposes, there is a need for a conceptual representation of each object of interest in the terms of knowledge, logical, and data components. There are two main categories of concept-data relationships: 1) the stable one where the need for additional background information is minimal; and 2) the abstracted one where the final data are a result of some intelligent transformation of available data based on the cognitive fit between the theoretically suitable and real observables. Such a framework allows and, on the other hand, insists justified and transparent evaluation of the quality of administrative data in relation to each research problem at hand. These ideas are demonstrated with pragmatic examples.

**GATHERING, POOLING AND HARMONIZING NORDIC REGISTRY DATA: EXPERIENCE FROM THE THREE NORDIC COUNTRY-WIDE RESEARCH PROGRAMME ON SOCIOECONOMIC CONSEQUENCES IN ADULT LIFE AFTER CHILDHOOD CANCER IN SCANDINAVIA (SALICCS)**

Friederike Erdmann, Maria Feychting, Laura Madanat-Harjuoja<sup>2</sup>, Nea Malila<sup>2</sup>, Mats Talbäck<sup>3</sup>, Liisa Korhonen<sup>2</sup>, Hanna Mogensen<sup>3</sup>, Anniina Tolkkinen<sup>2</sup>, Jeanette Falck Winther<sup>1</sup>

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**Background:** As a result of improving survival rates, the number of childhood cancer survivors increases continuously. Whereas a large body of evidence exists on somatic late effects in survivors, little is known about the socioeconomic and psycho-social impact of childhood cancer in long-term survivors. By applying a large cross-national registry-based population-based retrospective cohort design we investigate socioeconomic consequences in long-term survivors after childhood cancer in Denmark, Sweden and Finland, taking also the somatic and psychiatric disease burden of the survivors into account.

**Material and Methods:** App. 20,000 five-year childhood cancer (aged 0-19 years at diagnosis) survivors and five as many population comparisons are followed. Data-linkages between national cancer registries, population registries, hospital registries and Statistic bureaus of Denmark, Finland and Sweden enable us to study a broad range of outcomes related to socioeconomic and family characteristics in long-term survivors of childhood cancer.

**Results:** The most crucial challenges included (i) to obtain permission to transfer micro data between the Statistics Institutes of Denmark, Sweden and Finland, allowing to gather all medical, demographic, socioeconomic and family characteristics data at one place and to enable pooled analyses, (ii) to explore the availability, comparability and completeness of relevant variables across the three Nordic countries and (iii) to find approaches for harmonizing those variables. Further hurdles and bottlenecks will be also discussed during the presentation.

**Conclusion:** The SALiCCS cross-border cooperation demonstrates the feasibility and significance of Nordic collaborative register-based research. SALiCCS will be the largest and most comprehensive population-based investigation within this research field based on high-quality registry data.

## **Serum levels of dioxin-like polychlorinated biphenyls and risk of hypertension in a Swedish population-based longitudinal study**

Carolina Donat-Vargas<sup>1</sup>, Agneta Åkesson<sup>1</sup>, Andreas Tornevi<sup>3</sup>, Maria Wennberg<sup>3</sup>, Johan Sommar<sup>3</sup>, Hannu Kiviranta<sup>2</sup>, Panu Rantakokko<sup>2</sup>, Ingvar Bergdahl<sup>3</sup>

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### Background

Prior high global emissions of developmental-disrupting persistent chemicals like polychlorinated biphenyls (PCBs) is the reason for today's restriction on fish consumption for children and women. Cross-sectional studies report associations between PCB exposure and hypertension and experimental evidence includes the dioxin-like (DL)-PCBs' binding to the aryl hydrocarbon receptor, affecting the functions of endothelial cells. We examined the longitudinal associations between plasma levels of DL-PCBs and blood pressure (BP) and hypertension in 831 40-50 year old women and men.

### Methods

Participants in the Västerbotten Intervention Programme visited their health center twice, 10 years apart: during 1990 to 2003 (baseline) and during 2001 to 2013 (follow-up). Participant underwent a medical examination, measurement of systolic and diastolic BP and blood sampling, and completed a questionnaire on diet and lifestyle factors, PCB were measured in biobanked samples. Hypertension was defined as any of: (1) self-reported diagnosis, (2) use of antihypertensive drugs, or (3) measured systolic/diastolic BP  $\geq 140$  or  $\geq 90$  mmHg. Longitudinal analysis with repeated measures were performed using generalized estimated equations.

### Results

At baseline sampling, 49% and at follow-up 54% had hypertension. After multivariable-adjustment, including body mass index, the OR (95%CI) of hypertension was 1.50 (1.07–2.11) and the beta coefficient (mmHg) of systolic and diastolic BP were 3.03 (0.61–5.44) and 2.05 (0.67–4.44) respectively, comparing 3rd vs 1st tertile of lipid standardized DL-PCB concentrations.

### Conclusions

Increasing concentrations of DL-PCBs were consistently associated with BP levels and with hypertension risk, supporting the hypothesis that exposure to DL-PCBs is a potential cardiovascular risk factor.

O32

**Thyroid disease in a Swedish cohort exposed to PFAS: a register study**

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*The authors have chosen not to publish the abstract*

**Public water and sewage investments and the urban mortality decline: Sweden 1875-1930**

Jonas Helgertz, Martin Öennerfors

Lund University, Centre for Economic Demography

In the 19th and early 20th century Sweden, the decline in urban mortality was substantial. The urban mortality penalty, compared to the rural mortality, all but disappeared during this period. The factors behind this decline and the magnitude of their contribution, however, has not been well established in research. Making use of a newly digitised city-level dataset, this study finds that the introduction of clean water technologies (piped water/sewage and water processing) in Swedish cities had a strong impact on mortality in waterborne diseases. More specifically, whereas waterborne disease mortality declined by about ten percent as a result of piped water – regardless of processing methods – the corresponding mortality decrease from the use of advanced processing methods amounts to almost 25 percent. Using clusters of implementation sequencing, it is also found that water and sewage systems complement each other, rather than being substitutes.

This paper uses a fixed-effects model and different mortality measurements (general and disease-specific) to find associations between the implementation of water and sewage systems and mortality outcomes. The topic and results are relevant both in a historical and contemporary setting, since the urban sanitary conditions in some developing countries are comparable to those studied in this paper.

## Impacts from air pollution on health in early life – A Nordic collaboration (NordicWelfAir)

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Background: Epidemiological studies have reported negative health impact even at levels below current air quality limits, but the associations at low levels are uncertain. The Nordic region represents low exposure levels adding challenges on study power. In the NordForsk-funded NordicWelfAir study we aim to study health effects of air pollution on (i) birth outcomes and (ii) childhood asthma to evaluate (iii) the concentration-response relationship at Nordic levels and compare (iv) pure register-based approaches with existing cohorts.

Materials and methods: Combining modelled PM10, PM2.5, PM10-2.5, NO2, ozone, black carbon and metals with residential address history will be used to link exposures with the early life outcomes.

Results: This table describes the cohorts to be used and the PM2.5 levels in each country.

|    | Population recruitment                             | Scope  | Years     | Q/la | Cohort size | Mean PM2.5 (SD)(n) [ $\mu\text{g}/\text{m}^3$ ] <sup>b</sup> |
|----|--|--|-----------|------|-------------|--|
| DK | To be confirmed                                    | 11.0 (1.3)(6)                                      |           |      |             |  |
| FI | The MATEX cohort                                   | Total population (from the Medical Birth Register) | 1987-2015 | No   | 1.75 M      | 7.0 (0.9)(9)   |
| IS | To be confirmed                                    | 10.9 (5.5)(2)                                      |           |      |             |  |
| NO | The Norwegian mother and child cohort study (MoBa) | Children born in 2004 and 2005                     | 2004-2005 | Yes  | 30,000      | 9.2 (5.6)(13)  |
| SE | The Stockholm birth cohort                         | Stockholm county 2003-2013                         |           | Yes  | 252,000     | 6.1 (2.6)(9)   |

a Questionnaire or interview data availability. b EEA Airbase data from limited number of urban and suburban monitoring stations

Conclusion: The Nordic registers together with existing cohorts provide an excellent platform for cross-border Nordic co-operation and sufficient study size to investigate the effects of low exposure levels. Additionally, it allows evaluating register-only approaches against traditional cohort methods.

## **The impact of antidepressants on the disease course: a nationwide cohort study among patients diagnosed with inflammatory bowel disease**

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### Background

Depression and anxiety have shown to trigger disease relapse among patients with inflammatory bowel disease (IBD), even though the evidence is conflicting. Most studies point towards antidepressants (AD) having a beneficial effect on the disease course, however the studies are hampered by methodological limitations. This nationwide cohort study among patients with incident diagnoses of Crohn's disease (CD) and ulcerative colitis (UC) from 2000-2015 aims to examine the effect of AD on the disease course.

### Materials and methods

Data on prescription redemptions of AD and proxies of disease activity (i.e. disease course) in terms of step-up medication (corticosteroids and anti-tumor necrosis factor-alpha), IBD-related hospitalization and surgery were extracted from national population registers. Poisson regression was used to examining the effect of AD on disease course rates adjusted for age, sex, comorbidity, prior AD use, IBD subtype, diagnoses of anxiety and depression and chronic obstructive pulmonary disease.

### Results

A total of 36,964 persons with IBD (UC:70%) were included with a median age of 40 (range:0-99). Incidence rate ratio (IRR) for disease activity by AD use was 0.86 (CI:0.82-0.91) adjusted for all confounders. Stratified analyses showed an IRR of 0.77 (CI:0.70-0.85) for patients with CD and IRR=0.89 (CI:0.84-0.95) for patients with UC.

### Conclusion

In Denmark, AD users had decreased incidence of relapse among patients with IBD. The decreased incidence among AD users was most pronounced among CD compared to UC patients. These findings suggest the importance of treatment for psychiatric comorbidity as a part of IBD clinical care.

**Changes in perceived procedural justice are associated with receipt of anti-depressant medication: A study with participants from two waves of the Swedish Longitudinal Occupational Survey of Health**Viktor Persson, Loretta Platts<sup>2</sup>, Constanze Eib<sup>1,2</sup>, Claudia Bernhard-Oettel<sup>2</sup>, Constanze Leineweber<sup>2</sup><sup>1</sup> Norwich Business School<sup>2</sup> Stockholm University

Depression is one of the leading health problems in the industrialized world. Injustice at work, in particular procedural injustice, has been shown to increase the risk of depressive symptoms and other minor psychiatric disorders. However, earlier studies have mostly used a cross-sectional design and self-report measures to examine this relationship. In the current study, data from two consecutive biennial waves (2010 and 2012) of the Swedish Longitudinal Survey of Health (SLOSH) study were used to examine if perceived procedural justice at work is prospectively associated with prescriptions of anti-depressant medication. Participants answered questions about justice at work in 2010 and 2012 (N=5055) and were divided into four groups based on their perceived procedural justice at the two time points: stable low, increasing, decreasing, and stable high perceived justice. Using Cox regression and including common covariates, we studied how stability and change in perceived procedural justice over two years affected the rate of prescription of anti-depressant medication during the roughly two-year follow-up. Baseline cases were excluded to determine incident morbidity. The results showed that a decrease in perceived justice at the workplace was associated with higher rates of receipt of anti-depressants compared to people with stable high perceptions of justice (HR 1.76 (95% CI 1.16 to 2.68)). Both being female and having an insecure employment, respectively, were also associated with higher risks. In conclusion, change in perceived justice rather than low justice per se were associated with a higher risk of getting prescribed anti-depressants.

**Changes in primary health care utilization and in use of prescribed medications among Norwegian 16-18-year olds after introduction of stricter school attendance policy regulations**

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**BACKGROUND:** In August 2016, new policy regulations were enforced in Norwegian upper secondary schools (age group 16-18 years). Non-documented absence beyond 10% from any subject disqualifies from a passing grade in the subject. Only accredited health professionals can document health-related absence. We analysed rates of consultations in primary care and dispense of prescribed medications 2013-2016.

**MATERIALS AND METHODS:** Registry data on primary health care consultations and dispensed medications were available from reimbursement claims and the Norwegian Prescription Database, respectively (years 2013-2016, age group 15-18-years). We analysed data for the first semester in each school year (mid -August to mid-December) with Poisson regression and present incidence rate ratios (IRRs) with 95% confidence intervals (CIs), using 2015 as reference year.

**RESULTS:** In August 2016, there was a substantial and immediate increase in the weekly number of primary care consultations for 16-18-year-olds. No similar increase was observed for 15-year-olds or other years. The increase was strongest for respiratory infections (IRR 2.21, 95% CI: 2.17-2.25). Increased dispense rates for cough and cold preparations (IRR: 1.73 (95% KI 1.65-1.80) and for antibiotics commonly used for respiratory infections were also observed (IRR 1.22, 95% CI 1.19-1.25).

**INTERPRETATION:** Simultaneously with the introduction of new policy regulations of absence from upper secondary school, consultation rates in primary care and dispense rates of medications increased in the relevant age group. We acknowledge that we used an ecologic observational study design but still find it highly likely that the observed changes were caused by the policy shift.

**Childhood and mid-life social position and antidepressant medication: A prospective analysis using Swedish registers**

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University College London

**Background.** Childhood social position and material circumstances are associated with adult major depressive disorder, but whether childhood factors continue to be important after taking account of social position and economic circumstances in adulthood is unclear.

**Materials and methods.** Cox modelling for receipt of antidepressant prescription was performed on a register linked population of 234 128 enlisted Swedish men born in 1952–1956 to determine associations with childhood and adulthood social position and material circumstances. Childhood overcrowding, material deprivation, social group and housing tenure were obtained from the 1960 Population and Housing Census while the 1985 Census provided information about overcrowding, social class, income and marital status in adulthood. Records of antidepressants received July 2005–July 2010 were obtained from the Swedish Prescribed Drugs Register.

**Results.** Increased receipt of antidepressants in mid-life was associated with the childhood household being overcrowded, the dwelling being rented and the head of the household lacking gainful employment, but not with material deprivation. In early mid-life, individuals had a higher rate of receiving antidepressants if they were divorced, separated or single; not gainfully employed or who held a manual or non-manual occupation at a low level; and had lower incomes. Childhood and early mid-life social and demographic circumstances were associated independently with the risk of being prescribed antidepressants in late mid-life.

**Conclusion.** Factors from a range of socioeconomic domains in both childhood and adulthood were associated with receipt of antidepressant medication, suggesting that these risks accumulate over the life course.

O39

**Family, place and risk of cryptorchidism and hypospadias: a nationwide study from Sweden**

Xinjun Li

*The authors have chosen not to publish the abstract*

**Maternal Overweight and Obesity and Genital Anomalies in Male Offspring. A Population-Based Swedish Cohort Study.**

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**Background:** Overweight and obese pregnant women face higher risks of several critical birth outcomes, including an overall increased risk of congenital abnormalities. Only few studies have focused on associations between maternal overweight and the genital anomalies in boys, cryptorchidism and hypospadias, and results are inconclusive.

**Materials and Methods:** We performed a population-based cohort study and assessed the associations between maternal body mass index (BMI) in early pregnancy and occurrence of cryptorchidism and hypospadias. All live-born singleton boys born in Sweden from 1992 to 2012 were included. From the Swedish Patient Register, information on cryptorchidism and hypospadias was available. Data were analysed using Cox proportional hazards regression adjusted for potential confounders. Mediation analyses were performed to estimate how much of the association between BMI and genital anomalies were mediated through obesity-related diseases.

**Results:** Of the 1,055,705 live-born singleton boys born from 1992-2012, 6,807 (6.4 per 1,000) were diagnosed with hypospadias and 16,469 (15.6 per 1,000) were diagnosed with cryptorchidism, of which 9,768 (9.3 per 1,000) underwent corrective surgery for cryptorchidism. We observed dose-response associations between maternal BMI and hypospadias and cryptorchidism. Boys of mothers with BMI  $\geq 40$  kg/m<sup>2</sup> had the highest adjusted hazard ratios for hypospadias [HR 1.35 (95% CI 1.04;1.76)] and cryptorchidism [HR 1.25 (95% CI 1.00;1.58)]. A substantial proportion of the associations between BMI and the genital anomalies were mediated through preeclampsia.

**Conclusion:** This large register-based study adds to the current literature and indicates that the occurrence of hypospadias and cryptorchidism increase with maternal overweight and obesity severity.

## Assisted reproductive technology treatment and mortality among women

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### Background

Previous studies have reported reduced mortality among women treated with assisted reproductive technology (ART) treatment. It remains unclear whether the reduced mortality may be ascribed to selection of healthy women into ART treatment.

### Methods

Women treated with ART in public and private fertility clinics in Denmark during 1994-2009 (n=42 897) were age-matched with untreated women from the background population (n=204 514). Up to three fresh cycles of ART treatment were accessible free of charge in the public health care for women < 40 years old. In the private health care sector ART treatment was offered until female age of 45 years. Co-morbidity was obtained from hospital contacts and diagnoses. The women were followed until 31 December 2010.

### Results

During follow-up 2,041 women died. During the first two years after first treatment the risk of dying was reduced among ART treated women (HR 0.68, 95 % CI 0.63-0.74). Hereafter the difference between ART-treated and untreated women vanished and the risk did not differ significantly after 10 years (HR=0.92, 95 % CI 0.79-1.07). Further, risk of dying from external causes was halved among ART-treated women (HR=0.50, 95% CI 0.38-0.65), irrespective of time since first treatment.

### Conclusions

Data is compatible with selection of healthy women into ART treatment, even though co-morbidity did not explain the reduced mortality among ART-treated women. Behavioural adjustments associated with infertility, pregnancy planning and early parenthood are likely mechanisms explaining the reduced risk of dying among ART-treated women, from all causes as well as from external causes.

## Does lifestyle impact on the success of assisted reproduction?

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**Background:** Even though a great impact is expected, we still do not know the exact implications of preventable lifestyle factors in relation to the chance of becoming pregnant and subsequently giving birth to a child among women in fertility treatment.

**Objectives:** To examine the association between daily coffee intake, alcohol binge drinking, cigarette smoking, and the use of nicotine substitutes or addiction to nicotine on the one hand and pregnancy and live birth rate among Danish women in a Medically Assisted Reproduction (MAR)-cohort on the other.

**Methods:** A cohort study with prospectively collected exposure data, including approximately 2,000 Danish women enrolled between 2010 and 2015 during start of treatment at the Fertility Clinic, Aarhus University Hospital. Information on the different exposure variables; beverage specific average alcohol intake, number of alcohol binge episodes per month, daily coffee intake, smoking habits, use of nicotine substitution and addiction to nicotine were obtained by self-administered questionnaire before start of treatment and are available from patient-journals. Based on these data, the "Aarhus MAR-cohort" has been generated. Information on outcome variables; clinical pregnancy rate (at ultrasound scan performed at week 7-8) and live birth rate are available by linkage of data from the Fertility Clinic with data from the Danish registries. Potential confounders will be selected by use of Directed Acyclic Graphs (DAGs), and missing information will be handled using multiple imputation techniques. The association between lifestyle factors and success of assisted reproduction will be analyzed using multiple logistic regression analysis.

**Perspectives:** Intervention against lifestyle factors with known negative influence on reproductive capacity may have economic implications, but also possibility to alleviate the psychosocial and physical burden for the infertile women and couples. In contrast to other factors involved in the complex mechanism of fertilization, lifestyle factors are modifiable, thus giving couples a chance of altering their lifestyle and subsequently adding to their chance of getting pregnant.

**Epilepsy in Children Following Pandemic Influenza Infection or Pandemic Influenza Vaccination**

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**Background:** To determine whether pandemic influenza vaccination or pandemic influenza infection were associated with increased risk of epilepsy in children under 18.

**Materials and methods:** Information from Norwegian registries from 2006 through 2014 on all children under 18 years and living in Norway on October 1st, 2009 (N=1,154,113) were used in cox regression models to estimate hazard ratios (HR) for incident epilepsy after vaccination or influenza infection. A case series analysis estimated incidence rate ratios (IRRs) in several risk periods after either vaccination or influenza diagnosis.

**Results:** 572,875 children (50%) were vaccinated, while 41,811 children (3.7%) were diagnosed with influenza during the pandemic. From October 2009 through 2014, there were 3,627 new cases of epilepsy (incidence rate of 6.00 per 10,000 person-years). The risk of epilepsy was not increased after vaccination; hazard ratio (HR) 1.05, 95% confidence interval (CI); 0.92-1.20. After influenza infection, an increased risk of epilepsy was found for children 10-17 years; HR 2.47, 95% CI; 1.69-3.62, but not for those under age 10; HR; 0.59, 95% CI; 0.33-1.04. In a self-controlled case series analyses, the risk of incident epilepsy was highest the first week after an influenza diagnosis (incidence rate ratio: 7.11, 95% CI; 3.16-15.98).

**Conclusions:** Pandemic influenza vaccination was not associated with increased risk of epilepsy. Pandemic influenza infection was associated with increased risk of epilepsy in children over 10 years, but this was not the case for younger children. Concerns about pandemic vaccination causing epilepsy in children seem to be unwarranted.

O44

**Geographical patterns in acute myocardial infarction beyond the area- and individual-level sociodemographic structure: a Bayesian spatial analysis**

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*The authors have chosen not to publish the abstract*

**Indicators of regional inequalities in health and health service utilisation in Iceland**

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**Background:** With the motivation to support evidence-based spatial organization of health care we carried out three studies to explore potential regional differences in health and health service utilisation in Iceland.

**Materials and methods:** Study I used data on self-rated health from a national health survey (n=5909). Study II used data on maternal health and birth outcomes (n=40982) from a national register. Regression models were used to explore differences in I and II. Study III used data from three national registers; 1) deaths from cardiovascular disease (CVD) (n=7113), 2) individuals with CVD discharge diagnoses (n=14039) and 3) individuals with CVD contact diagnoses (n=58246). Age-standardised annual rates were calculated.

**Results:** In study I we found that residents outside the Capital Area (CA) rate their physical (aOR 1.35; 95% CI 1.23-1.50) health worse than residents in the CA. In study II we found a lower prevalence of gestational diabetes (aOR 0.68; 95% CI 0.59-0.78) and hypertension among pregnant women outside the CA. In study III, we observed higher total CVD mortality rates among women outside the CA (standardised rate ratio 1.06; 95% CI 1.05-1.07). Rates of hospital discharges and primary care contacts for CVD were increased outside the CA. The prevalence of several modifiable risk factors was higher outside the CA.

**Conclusion:** These findings reveal regional health disparities in Iceland where the more rural areas have less favourable health outcomes on a number of indicators. Future research and policy needs to identify ways to strengthen health care and health promotion outside the CA.

O46

**Tooth extractions, oral infections, and hs-C-reactive protein predict mortality in individuals with and without diabetes.**

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*The authors have chosen not to publish the abstract*

**Sex differences in treatment-seeking behavior by education and marital status before and after admission to hospital. A register-based cohort study of the Danish population aged 50+.**

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**Background:** The sex differences in treatment-seeking behavior might be of substantial importance for the widening of the sex differentials in survival after hospital admission and might explain why women enjoy better survival at all ages and regarding most causes of death. This study explores the sex differences in primary and hospital care use and how they vary with education and marital status.

**Materials and methods:** Based on a 5% random sample of the Danish population, data from the National Patient Register were linked with data of the National Health Service Register. We calculated the average number of GP contacts and hospital admissions by single years of age for the men and the women of the population aged 50+ in 1990–2011 in Denmark to compare the relative sex differences in GP contacts and hospital admissions.

**Results:** For the general population we found a consistent pattern over time: while women visit the GP consistently more often at all ages, men get more often admitted to the hospital. Further analysis will explore whether the sex differentials in GP contacts and hospital admissions vary across educational group and marital status.

**Conclusion:** The sex differences in GP contacts might play an important role in explaining the female advantage in survival. This work may shed light on vulnerable groups with respect to marital status and education as the prevention and progress of diseases and the survival after hospitalization can be substantially affected by the pattern of primary health care use.

## Stroke care on equal terms?

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Background: We aimed to identify social inequalities in Swedish stroke care and outcome.

Material and methods: This study was based on the Swedish Stroke Register (Riksstroke) 2010-2012. Riksstroke was linked with other national health registers managed by the National Board of Health and Welfare, and registers containing information on education and income managed by Statistics Sweden, using personal identification numbers. Process and outcome variables were analyzed by multiple logistic and Cox regression models, adjusting for age, sex, stroke severity, and cardiovascular risk factors.

Results: Patients with university education were more likely to arrive to hospital within 3 hours from stroke onset, OR=1.07 (95% CI: 1.01–1.13), had a higher chance of reperfusion treatment, OR=1.10, (1.00–1.21), anticoagulant treatment in patients with atrial fibrillation, OR=1.34 (1.22–1.48), and statin treatment after ischemic stroke OR=1.08 (1.02–1.15). They also had a higher survival rate, HR= 1.25 (1.16-1.28), than patients with primary school education. Patients in the highest income tertile were more likely to return to work one year after stroke, OR=1.36 (1.04-1.77), than patients in the lowest income tertile.

Conclusion: Even in a country like Sweden, where socioeconomic differences are relatively small, and where the majority of health care is publicly financed we observe social inequalities in stroke care and outcome. The socioeconomic gradients remain after adjustment for multiple potential confounders, leaving the possibility that there is an element of unconscious discrimination in stroke care.

**Socioeconomic differences in stroke survival – a mediation analysis examining the pathway through secondary prevention upon hospital discharge**

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**Background:** The aim of the study was to investigate how secondary prevention according to stroke treatment guidelines contributes to income inequalities in survival after stroke.

**Materials and methods:** The study was based on 37 760 patients registered in Riksstroke (the Swedish stroke register) with a first time ischemic stroke in 2009-2011. We used a novel approach to mediation analysis to decompose the effect of low income on case fatality 29 days-1 year after stroke into an indirect effect, mediated by treatment according to guidelines (statins, antithrombotic and hypertensive medication) at hospital discharge, and a direct effect not mediated by this intermediate variable. Results were adjusted for potential confounders such as cardiovascular risk factors, demography and other socioeconomic factors.

**Results:** Patients with incomes in the lowest tertile had a higher case fatality than patients in the upper two tertiles (11.5% vs 8.7%). Low income patients were also less likely to receive treatment according to guidelines (40.9% vs. 45.9%). After adjustment for potential confounders, low income patients were at a higher risk of dying 29 days-1 year after stroke compared to higher income patients, OR=1.118 (95% CI: 1.034-1.208). We also found a significant indirect effect due to inequalities in treatment according to guidelines at discharge, OR=1.014 (1.006-1.021).

**Conclusions:** Low income patients have a lower probability of secondary prevention according to stroke guidelines and a higher case fatality than high income patients. Inequalities in stroke case fatality is only partly mediated by differences in secondary prevention, a major part remains unexplained.

## **Socioeconomic inequalities in mortality from pancreatic cancer – A Swedish national cohort study**

Mats Talbäck, Maria Feychting, Rickard Ljung

Karolinska Institutet

**Background:** To investigate associations between socioeconomic position (SEP) and mortality after diagnosis with pancreatic cancer in a population-based national cohort.

**Methods:** Patients diagnosed with pancreatic cancer between 1993-2010 (N=13,918) and included in the Swedish national cancer register were followed-up until 31st December 2015. Indicators of SEP included education, disposable income and marital status obtained via linkage from national registers. Multivariable Cox regression was used to analyse associations between SEP and 2-year survival. Models were adjusted for age, calendar period, healthcare region and country of birth, and run separately for men and women.

**Results:** Mean age at diagnosis was 68.1 years. 12,575 (90.4%) subjects died by end of follow-up (average follow-up 4.1 months). Having a primary education (adjusted HR 1.27, 95% CI 1.18-1.36, men and HR 1.23, 1.14-1.33, women) was associated with increased mortality compared to those with tertiary (university) education. Being in the lowest income quartile (adjusted HR 1.26, 1.17-1.36, men and HR 1.21, 1.12-1.30, women) was associated with increased mortality compared to those in the highest income quartile. Associations with income showed a dose-response relationship in both sexes. Being single at diagnosis was associated with increased mortality (not married HR 1.17, 1.10-1.26, men, and HR 1.17, 1.07-1.29, women) compared to being married. Corresponding risks in those widowed at diagnosis was HR 1.26, 1.15-1.39 in men and HR 1.10, 1.03-1.17 in women.

**Conclusions:** Lower education, low income and being single at the time of diagnosis with pancreatic cancer is associated with increased mortality in men and women. This is despite the high fatality associated with pancreatic cancer.

**Metabolic factors, smoking, and bladder cancer risk in Me-Can 2.0; a pooled study using Swedish, Norwegian and Austrian cohort and registry data**

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#### Background

Bladder cancer (BCa) is a common cancer form and smoking accounts for around 50% of cases. Studies on metabolic factors and BCa risk are scarce, and the interaction with smoking remains unknown.

#### Aims

To investigate the association between metabolic factors and bladder cancer outcomes (incidence, non-invasive BCa, invasive BCa and mortality). Additionally, the study aimed to assess additive interaction between metabolic factors, smoking and risk of bladder.

#### Methods

We examined the relationship between metabolic factors (BMI, mid-blood pressure [BP, average of systolic and diastolic BP], glucose, triglycerides and cholesterol) and BCa Endpoints using detailed smoking dose data to control for confounding. Hazard ratios (HR) were corrected for random error of exposure measurements. We used relative excess risk due to interaction to determine the additive interaction between metabolic factors in quartiles and smoking status (never-/ex-/current-smoker) and BCa risk.

#### Results

BP and triglycerides showed a significant, positive relationship with BCa incidence among men, HR per SD: 1.09 (95%CI 1.02-1.17) and 1.21 (1.10-1.32) respectively. The association with BP was even stronger for BCa mortality, HR 1.25 (1.06-1.49). Furthermore, BMI among men and triglycerides among women showed a significant and positive relationship with BCa mortality, HR per SD: 0.88 (0.78-0.98) and 1.92 (1.37-2.73) respectively. No associations were significant for invasive or non-muscle invasive tumors separately. There was no significant interaction between metabolic factors, smoking and BCa risk. However, BMI was a significant risk factor among male non-smokers, HR 1.07 per quartile (1.01-1.15), but not among male current smokers, HR 1.00 per quartile (0.96-1.05).

#### Conclusion

In conclusion, BP and triglycerides were positively associated with BCa risk among men. Whilst smoking remains the strongest risk factor, high BMI is associated to bladder cancer risk among male non-smokers.

**Age-dependent associations between metabolic factors and cancer risk in Me-Can 2.0; a pooled study using Swedish, Norwegian and Austrian cohort and registry data**

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**Background:** The association between metabolic factors and cancer risk may vary by attained age, but this has not been previously systematically investigated.

**Materials and methods:** We included 813,927 individuals from six cohorts in Sweden, Norway and Austria, from which we created two random 50-50% cohorts. In the first cohort, we used Cox regression analysis with age as time-scale and tested proportional hazards assumption for body mass index (BMI), blood pressure, plasma glucose, triglycerides and cholesterol in relation to cancer risk. We tested exposures as time-dependent variables, and results with  $p < 0.05$  were additionally tested in the second cohort. A p-value below 0.05 in both cohorts was considered evident of an age-dependent association.

**Results:** As expected based on previous studies of BMI and pre- and postmenopausal breast cancer, BMI was inversely related to breast cancer risk (n cases=12,157) among younger (premenopausal) women but positively related to risk among older (postmenopausal) women. However, the association changed continuously with increasing age rather than drastically around the age of menopause. Similar and significant trends of associations were also found for triglycerides and breast cancer risk, and for BMI and triglycerides in relation to liver cancer risk among men (n cases=456).

**Conclusion:** We found age-dependent associations between BMI, triglycerides and risk of breast and liver cancer, which are unlikely to be chance findings because of the replication. The continuously changing association between BMI and breast cancer risk with increasing age may suggest that BMI interacts with other age-related factors than menopausal factors in relation to risk.

**Associations of serum 25-hydroxyvitamin D level with incidence of lung cancer and histologic types in Norwegian adults – a case-cohort analysis of The HUNT Study**

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**Background:** Previous prospective studies showed inconsistent associations of serum 25(OH)D level with lung cancer incidence. We performed for the first time a prospective case-cohort study including the largest number of lung cancer cases, aiming to explore the associations of serum 25(OH)D levels with incidence of lung cancer overall and histologic types.

**Methods:** The case-cohort study included 696 lung cancer incidence cases and 5804 individuals in the subcohort who participated in the second survey of the Nord-Trøndelag Health Study in Norway. Cox proportional hazards regression models adjusted for a case-cohort design and confounders were used to compute hazard ratios (HRs) with 95% confidence intervals (CIs) for lung cancer overall or histologic types in relation to serum 25(OH)D level.

**Results:** Compared with the 4th season-standardized quartile of 25(OH)D (median level 68 nmol/L), the 1st to 3rd quartiles were associated with a lower risk for lung cancer overall and pulmonary adenocarcinoma in particular. The HRs were 0.62 (95% CI 0.41–0.95), 0.57 (0.37–0.86), and 0.55 (0.36–0.84) for the 1st to 3rd quartiles respectively for adenocarcinoma. In addition, the associations with adenocarcinoma appeared more clearly in the overweight/obese subjects (HRs for 1st to 3rd quartiles: 0.55, 0.38 and 0.50) than in the normal weight subjects (HRs for 1st to 3rd quartiles: 1.05, 0.94 and 0.61, p for interaction=0.13).

**Conclusions:** This case-cohort study demonstrated that lower serum 25(OH)D level was associated with an approximate 40% reduced risk of pulmonary adenocarcinoma, especially in overweight/obese subjects. This implies the complex role of vitamin D on cancer development in humans.

O54

**Global trends in the incidence of esophageal squamous cell carcinoma**

Qiaoli Wang, Shaohua Xie, Jesper Lagergren

*The authors have chosen not to publish the abstract*

O55

**Does having siblings influence survival from childhood leukemia? A register-based cohort study in Sweden**

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*The authors have chosen not to publish the abstract*

O56

**Maternal diabetes and incidence of childhood cancer - A nationwide cohort study and exploratory genetic analysis**

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*The authors have chosen not to publish the abstract*

O57

**Immigrant legacy and birth weight across generations: The case of Sweden**

Siddartha Aradhya

*The authors have chosen not to publish the abstract*

**Healthy migrant effect or artifact? The impact of the gestational age estimate method on birth outcome disparities between migrants and Swedes**

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**Background:** Prior studies have shown that the offspring of migrant women have equal or lower risks of preterm births compared to those of natives (healthy migrant effect or paradox). We evaluate whether this advantage is consistent across methods of estimation of the gestational age.

**Methods:** This population-based register study includes all singleton live births occurred in Sweden (1992-2012) with information on gestational age estimated through the last menstruation period (LMP) and ultrasound (n=1,317,265). Using multinomial regression, we compare gestational age outcomes (preterm, moderate and late preterm, post-term) between migrants and natives comparing different gestational age methods. We performed sensitivity analyses using a subsample of 718,191 uncomplicated pregnancies.

**Results:** Foreign-born mothers showed lower odd ratios of delivering preterm (OR: 0.98 [95%CI:0.98,1.01]) and late preterm (OR: 0.95 [95%CI:0.92,0.98]) using ultrasound while higher risk when LMP was used instead (respectively, OR: 1.10 [95%CI:1.07,1.14] and OR: 1.09 [95%CI:1.06,1.13]). The largest differences are found among women coming from Africa and, to a lesser extent, those from Eastern Europe & Russia, and the Middle East.

**Conclusions:** Disparities in gestational age outcomes by mother's origin strongly depend on the method used to estimate gestational age. While the health advantage is partially confirmed in almost all categories of gestational age using ultrasound (except for early preterm), foreign-born mothers show worse outcomes when LMP is used instead. This finding points out that the information used might have a sensitive impact on the comparison between migrants and natives across countries and time.

**Ethnic differences in the incidence of cancer in Norway**

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**Background:** Disparities in cancer risk patterns across ethnic groups and between immigrants and native populations have been reported previously. However, since medical records in Norway do not record country of birth or origin, there has been no monitoring of cancer incidence among different immigrant groups.

**Materials and methods:** This study links data from the Cancer Registry of Norway with data from Statistics Norway to examine overall and site-specific cancer incidence rates in different immigrant groups and compare them to rates among persons born in Norway, using the age distribution from the world standard population.

**Results:** Analyses of 850 333 immigrants show that 10 334 women and 9 158 men developed cancer in the period 1990-2012. During this period, the incidence rates per 100 000 person-years were 235 for women and 267 for men. Among 4 882 955 persons born in Norway, 230 099 women and 258 333 men developed cancer during the same period, and the incidence rates were 248 for women and 298 for men. Cancer in the lung, liver, stomach, prostate, and cervix was more common in specific immigrant groups.

**Conclusion:** This study found differences in cancer incidence between immigrants and persons born in Norway. Identifying and monitoring cancer types among immigrants, that are rare in the Norwegian population, are important for early detection, and to ensure appropriate health care. Additionally, identifying lifestyle-related cancers, that are less common among immigrants, could help prevent lifestyle changes that may occur after migration.

**ADHD medication in offspring of immigrants — Does the income level of the country of parental origin matter?** Arzu Arat, Viveca

Ostberg, Bo Burstrom, Anders Hjern

## Background:

Child psychiatric treatment facilities vary greatly worldwide and are virtually nonexistent in many low-income countries. Clinical studies have shown that children from immigrant families living in Sweden received less psychiatric care than those of nativeborn parents. However, previous studies have shown a similar prevalence of ADHD in minority and majority children in Sweden and the UK. We tested the hypothesis that the consumption of child psychiatric care in immigrant families would be determined by the availability of such treatment in the parents' country of origin. Patterns of medication for attention-deficit hyperactivity disorder (ADHD) were studied as a proxy for child psychiatric care.

Methods: This was a register study of dispensed stimulant medication during 2013- 2014 in Swedish national birth cohorts from 1995-2009, 1.4 million. The children were divided by national income of the parental country of origin and whether the parents were native Swedes, European immigrants, non-European immigrants or a mixture. Logistic regression was used to calculate the odds ratios of having been dispensed at least one ADHD drug during 2013, with adjustments for gender, family status, household income and area of residence.

Results: Having parents born in low-income (OR [95% confidence interval] 0.27 [0.24- 0.29]) or middle-income (European: OR 0.23 [0.20-0.26], non-European: OR 0.39 [0.34-0.41]) countries was associated with lower ADHD treatment levels than having parents born in high-income countries (European: OR 0.60 [0.54-0.66], non-European: OR 0.68 [0.59-0.79]), when compared to children of parents born in Sweden. In families with an origin in low or middle income countries, there was no significant association between household income and ADHD medication, while in children with Swedish and mixed backgrounds high level of disposable income was associated with lower levels of ADHD medication.

Conclusion: The use of child psychiatric care by immigrant families in Sweden was largely associated with the income level of the country of origin.

Keywords: Attention-deficit hyperactivity disorder, child mental health services, health inequalities, immigrant families, income levels.

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**Racial and Ethnic Disparities in the Incidence of Esophageal Cancer in the United States, 1992-2013**

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*The authors have chosen not to publish the abstract*

## **Ethnic density, social capital and mental health in Stockholm**

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### Background

Neighbourhood socioeconomic and ethnic segregation has been a substantial characteristic of Sweden's largest cities since the introduction of large-scale State-mandated housing initiatives in the 1960s. European research has shown that for some minority groups, living among co-ethnics can protect against poor mental health, highlighting the potential role of social capital. The aim of this study is to investigate the association between own-group density and mental health for Swedish, Chilean, East African, Finnish, Iranian, Iraqi and Turkish ethnic groups, and the effect of individual and contextual social capital.

### Methods

This study used cross-sectional data from four waves of the Stockholm Public Health Cohort (n=64,399). Prevalence ratios with 95% confidence intervals were estimated for the association between own-group density—defined as the proportion of first or second generation immigrants from the same country group—and psychological distress, measured using the General Health Questionnaire-12. Social capital variables included measures of community and institutional trust and participation and were added individually to the model.

### Results

Own-group density was significantly protective against psychological distress for Swedes (PR, 95% CI: 0.91, 0.90-0.93) and East Africans (PR, 95% CI: 0.78, 0.66-0.91) whereas it was significantly detrimental for Chileans (PR, 95% CI: 2.30, 1.36-3.90). Own-group density presented no significant risk for Finnish, Iranian, Iraqi and Turkish groups. Adjustment for socioeconomic factors, as well as individual and contextual social capital variables, had little effect on the risk of psychological distress for all groups.

### Conclusions

This is the first paper to investigate the relationship between ethnic density, social capital and mental health in Sweden. The effect of neighbourhood own-group density and mental health varies between immigrant groups. Social capital did not play a role in explaining these relationships.

## **Civil status and mortality in Sweden: the role of same-sex and opposite-sex marriage formation**

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### **Background**

Lesbian, gay, and bisexual (LGB) individuals evidence higher risk for somatic and psychiatric disorders, as compared to their heterosexual peers. However, whether these risks also translate into greater mortality is not as known. We capitalized on Sweden's extensively linked databases, to investigate whether, among married persons, same-sex marriage is associated with greater mortality risk.

### **Materials and methods**

Using a population-based register design, we analyzed mortality risk among same-sex married women and men (n=11,282), as compared to different-sex married women and men (n=2,001,459) in Sweden. We selected all newly partnered or married individuals in the intervening time between January 1, 1995 - December 31, 2012. Cox regression was used to calculate adjusted relative risks (RR) of all-cause and cause-specific mortality with 95% confidence intervals (CI).

### **Results**

The mortality of women and men in same-sex marriages is higher than that of women and men in opposite-sex marriages (men: RR = 1.71, 95% CI = 1.48, 1.98; women: RR = 1.67, 95% CI = 1.27, 2.19). The mortality disadvantage for sexual-minority people holds for several broad categories of cause-specific mortality, including mortality due to neoplasms, respiratory diseases, mental and behavioral disorders, and external causes of death but not for mortality due to circulatory diseases.

### **Conclusion**

Marriage may have a protective effect for sexual minority and majority individuals alike but many of the relative health disadvantages of LGB people remains also when they married.

**Life-course socioeconomic differences and social mobility in preventable and non-preventable mortality**

Anna Johansson, Nancy Pedersen, Stefan Fors, Anna Dahl Aslan

We investigated socioeconomic differences in mortality by comparing preventable with less preventable causes of death. Participants born before 1935 from the Swedish Twin Registry (n=37 609) were included in this study. The data were linked to the Cause of Death Registry through year 2014. Preventable mortality was categorized according to indicators presented by Avoidable Mortality in the European Union (AMIEHS). Parental social class, own education, occupation and social mobility were used as separate measures of socioeconomic status. Using Cox proportional hazards models we tested association between the socioeconomic measures with total mortality, preventable mortality and non-preventable mortality. To investigate differences in early and late mortality the data were split at age 75. Adjustments for sex and birth cohort were made. The social gradient for all-cause mortality was most prominent for the adult socioeconomic measures. Mortality was higher for preventable than non-preventable mortality in all levels of the three socioeconomic measures. The social gradient was also stronger in mortality before age 75 than after, with significant risk only in the lowest two social classes. For mortality after age 75 there was a weak social gradient in non-preventable mortality, whereas it was still present in preventable mortality. This pattern was slightly stronger for males. Analyses of social mobility showed the highest mortality for life-time low SES but also for the group with downward social mobility. The social mobility patterns were more pronounced for preventable mortality but similar between males and females.

## The impact of socioeconomic factors on the health of women and children during pregnancy and after delivery

The impact of socioeconomic factors on the health of women and children during pregnancy and after delivery

### Objective

To assess the impact of socioeconomic factors on pregnancy and pregnancy outcome, with special focus on the interplay between factors like first and second generation immigrants, maternal smoking during pregnancy, maternal Body Mass Index (BMI), parental educational levels, family income levels, and the percentage of the family income coming from subsidy from society. A special interest was paid to the health during pregnancy and childbirth among women applying for asylum.

### Methods

Medical information regarding pregnancy and early infancy from 1.8 million deliveries was retrieved from the Swedish Medical Birth Register (MBR) 1997-2014, while information regarding parental country of birth, family income, and educational level was obtained from Statistics Sweden. The outcomes studied were: pregnancy complications (diabetes, gestational diabetes, pre-eclampsia), delivery mode (elective and emergency cesarean sections, vacuum extractions/forceps), infant health (Apgar scores, birth weight, birth weight z-scores, gestational age at birth, perinatal death), and maternal injuries (sphincter ruptures, post-partum bleedings). Associations were assessed using multiple logistic regression analyses. For each outcome and evaluated factor, different models were tested in which the factor in question entered as a linear continuous factor, as a second degree polynomial, or was represented divided into class variables.

### Results

Maternal educational level had significant negative association with most of the outcomes studied while the impact of paternal educational level was limited. When parental educational level was adjusted for, the impact of family income on the outcomes studied was marginal. Maternal country of origin was the most powerful risk factor studied. Women born in Africa south of Sahara, and their children, were at increased risk of almost all evaluated outcomes (pregnancy complications, poor child outcome, and post-partum complications). The risk estimates changed only marginally when adjustments for other socio-economic or maternal characteristic factors were made (e.g., the Adjusted Odds Ratios (AOR) for perinatal death compared to the children of Swedish women was AOR: 1.9 95%CI: 1.7-2.1). Women born in Middle east/north Africa also had significantly increased risks for most outcomes compared to women born in Sweden (e.g., AOR for perinatal death 1.3 95%CI: 1.2-1.4). For women (and their offspring) from foreign Asia, the risk estimates changed substantially when maternal height was adjusted for. Even after adjustment for parental country of birth, women with low education (as compared to high) were at increased risk for many of the outcomes studied (e.g., AOR for perinatal death 1.5 95%CI 1.4-1.6). For women applying for asylum, no information on maternal country of birth, educational level, or family income is available. Compared to Swedish women (and offspring) asylum seeking women were at increased risk of all outcomes studied (e.g., AOR for perinatal death 1.3 95%CI: 1.1-1.7).

### Conclusion

The magnitudes of the interactions between the studied factors were considerable, and the results must be cautiously interpreted. Nevertheless, the study clearly identified groups of women (and their children) for whom the care of the Swedish antenatal- and maternity services seem to be sub-optimal. Hopefully, the results of the current study could help the health authorities to adjust their services to achieve an equal and high quality pregnancy health care for all women.

**Neighborhoods and mortality in Sweden: A comparison between using a deprivation index at the regional and national level**

Paul Franks, Kristina Sundquist

**Background:** The association between neighborhood deprivation and mortality is well established, but knowledge about whether deprivation is best assessed regionally or nationally and how different neighborhood measures interact is scarce. The present study aims to explore if there is a difference between using a national or regional neighborhood deprivation index and whether level of urbanization or residence in the southern parts of Sweden as compared to the northern parts may modify the association between neighborhood deprivation and mortality.

**Methods:** We collected data on the entire population above 50 residing in 21 regions in Sweden the 1st of January 1990 and followed them for mortality due to all causes or coronary heart disease. The association between neighborhood deprivation and mortality was assessed using Cox-regression assuming proportional hazards with time as an underlying variable, comparing the 25% most deprived neighborhood with the 25% most affluent ones within each region using the national as well as the county-specific index. The potential interactions were also assessed.

**Results:** The choice of a national or county-specific index did not affect the estimates to a high extent despite observed differences in the median of the index between counties. The impact of neighborhood deprivation on mortality in metropolitan regions (Hazard Ratio: 1.19 (1.18-1.19)) were somewhat higher than those in the more rural southern (HR: 1.16 (1.14-1.17)) and northern regions (HR: 1.10 (1.09-1.12)).

**Conclusion:** Our data supports that choice of a national or county-specific deprivation index does not influence the results to a high extent. Furthermore, the strength of the association between neighborhood deprivation and mortality is somewhat higher in metropolitan areas as compared to more rural southern and northern areas.

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**Does Parental Death Affect Fertility? A Register-Based Study of the Effect of Parental Death on Adult Children's Childbearing Behavior in Sweden**

Johan Dahlberg

Even though fertility and mortality are two of demography's most researched topics, no prior study has examined at the micro level whether parental death influences adult children's fertility. Macro-level studies have shown that rapid increases in mortality can affect fertility rates. Parental death has also been linked to negative psychological and physical outcomes, reduced relationship quality, and making a bereaved child attach more importance to his/her family. This study applies event history techniques to Swedish multi-generation registers containing 1.5 million individuals with to micro data on mortality and fertility to investigate short-term (first birth risk) and long-term (childlessness at age 45) effects of parental death on adult children's fertility. The principal finding is that parental death during reproductive age affects children's fertility and this effect is mainly short-term. The effects differ to some degree between men and women and depend on when in the life course the bereavement happens.

## **An efficient sampling strategy for selection of biobank samples using propensity scores**

Authors (order to be decided)

Ebba Malmqvist, Jonas Björk, Lars Rylander, Anna Rignell-Hydbom

### **ABSTRACT**

#### **Background**

Overweight is an increasing public health problem and it is thus important to identify early-life risk factors. We plan a nested case-control study investigating the association between fetal exposure to endocrine disruptors and overweight in early childhood. Biobanks, organized collections of biological material from humans, are limited and costly resources, and data collection for entire cohorts from biobanks will generally neither be possible nor feasible.

#### **Objective**

The aim of this methodological study was to develop an efficient sampling strategy for case-control studies using biobank data, such that each biobank sample contributes with as much information as possible to the precision of the study results.

#### **Material and methods**

Children who visited the Child Health Care (CHC) centers in Malmö for their 4-year health examination during 1999-2005 and whose parents answered a self-administered questionnaire constituted the study cohort (n=5 853 after data cleaning and exclusion). Serum samples retrieved from Southern Sweden Maternity Cohort (SSMC) will be analyzed for levels of endocrine disrupting chemicals.

#### **Results**

The final propensity model, with smoking during pregnancy, birth weight, economic situation, type of residence and BMI of parents, yielded an area under the ROC curve of 67%. The following variables were evaluated in the propensity model: maternal smoking during pregnancy, parity, birth weight, sex of the child, parental education, economic situation, type of residence, BMI of parents, soda drinking of the child.

#### **Conclusion**

Selection of data from the biobank was stratified on sex and the propensity of being overweight (low/medium/high propensity), estimated from the final logistic regression model. Twice as many controls as cases were selected in each stratum.

## **Estimating incidence and prevalence from population registers. Example from myocardial infarction.**

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### **Abstract:**

**Background:** To illustrate how the fundamental epidemiological measures, incidence rate and prevalence proportion, can be estimated based on Swedish population registers using acute myocardial infarction (MI) as an example, together with a discussion about the analytical decisions.

**Materials and methods:** All individuals in Sweden aged 60-89 (born 1904-1954) during the study period 1994-2014 were identified through the Total Population Register. Cases of MI were defined and identified from information on hospital admissions and cause of death. Incidence rates of all-, first-, and recurrent MI were calculated together with prevalence proportions.

**Results:** The incidence rate of all-, first- and recurrent MI declined over the study period. While the incidence rates of first MI are lower for women than men, the incidence rates of recurrent MI are considerably higher but similar for men and women. The prevalence calculated with duration of disease set at 28 days also declined. This was despite improved survival from MI and increased life expectancy over the same period meaning that the decline in incidence was large enough to compensate for increased survival.

**Conclusion:** Calculating incidence and prevalence of diseases using population registers require detailed and well-reasoned definitions. The definitions will affect both the study population and the number of disease events and it is essential that the cases and the study population are defined in a coherent way. Different measures of disease occurrence contribute with different aspects of the disease panorama and a joint interpretation contributes to a thorough understanding of the disease development in a population.

**Towards non-conventional methods of designing register-based epidemiological studies: an application to pediatric research**

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**BACKGROUND:** Various epidemiological designs have been applied to investigate the causes and consequences of fetal growth restriction in register-based observational studies.

**AIMS:** This review seeks to provide an overview of several conventional designs including cohort, case-control, nested case-control, and case-cohort designs and more recently applied non-conventional designs such as family-based designs. We also discuss some practical points regarding the application and interpretation of family-based designs.

**METHODS:** Definitions of each design, the study population, the exposure and the outcome measures are briefly summarized. Examples of study designs are taken from the field of low birth weight research for illustrative purposes. Also examined are relative advantages and disadvantages of each design in terms of assumptions, potential selection and information bias, confounding, and generalizability. Kinship data linkage, statistical models, and result interpretation are discussed specific to family-based designs.

**RESULTS:** When all information is retrieved from registers, there is no evident preference of the case-control design over the cohort design for odds ratio estimations. All conventional designs included in the review are prone to bias particularly due to residual confounding. Family-based designs are able to reduce such bias and strengthen causal inference. In the field of low birth weight research, family-based designs have been able to confirm a negative association not confounded by genetic or shared environmental factors between low birth weight and the risk of asthma.

**CONCLUSIONS:** We conclude that there is a broader need for family-based design in observational research as evidenced by the meaningful contributions to the understanding of the potential causal association between low birth weight and subsequent outcomes.

## Paternal antibiotics as a negative control to confirm familial confounding between fetal exposure to antibiotics and childhood asthma

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### Background

The previously suggested association between maternal antibiotics in fetal or early life and childhood asthma may be partly explained by familial confounding such as genes and environment (1). Evaluation of paternal antibiotic exposure, as a negative control (2), could help to unravel the relationship further.

### Material and methods

All children born in Sweden to women who were pregnant between July 2005 and December 2010 (N=492 700), along with their biological fathers, were identified through the Medical Birth Register and the Multi-Generation Registry. The association between maternal and paternal antibiotic exposure from 6 months before, during, and up to 6 months after pregnancy, identified from the Swedish Prescribed Drug Register (SPDR) and asthma (defined from the SPDR and National Patient Register), was analyzed using Cox proportional hazard regression.

### Results

There was an increased risk of asthma in children 2.5 years of age, whose mothers had been exposed to antibiotics before pregnancy (adjusted hazard ratio (aHR) 1.31, 95% confidence interval (CI) 1.27-1.35); during pregnancy (1.27, 1.23-1.30); and after pregnancy (1.34, 1.30-1.38). The corresponding estimates for paternal exposure were as follows: before pregnancy aHR 1.17, 95% CI 1.12-1.21; during pregnancy 1.13, 1.09-1.17; and after pregnancy 1.19, 1.14-1.25.

### Conclusion

In this population-based study on antibiotic treatment before, during, and after pregnancy, using paternal exposure as negative control, we confirm that associations between maternal antibiotic exposure and childhood asthma are partly explained by familial confounding such

as genes and environment (3).

### References:

1. Örtqvist PMID: 28398078
2. Brew SJPH 2017
3. Örtqvist PMID: 28465011

## Timing and Duration of Childhood Economic Hardship and Early Adulthood Obstacles

Tiina Ristikari, Pasi Haapakorva, Mika Gissler

There is a vast literature demonstrating that poor socioeconomic living conditions in childhood have a long-lasting effect on different aspects of individual life trajectories. However, less is known about the effect of timing and duration of the hardship.

This study used the 1987 Finnish Birth Cohort, which includes information on all children born in Finland in 1987 (N=59,476) as well as their parents. The children are followed through their life courses using official registers until the age of 25. Finland was hit by a severe economic recession in the beginning of 1990s. The unemployment rate rose from 3.5 to 18.9 percent in a short period of time. The children in the 1987 Finnish Birth Cohort were about 4 years old when the Finnish economic crisis started to unfold.

We examined how social assistance (SA) reciprocity is related to teenage and early adulthood outcomes such as children's own SA, psychiatric in/outpatient care, criminal convictions, school dropout and teenage pregnancy. Utilizing sequence analysis, we extracted five clusters from the data: (1) no SA; (2) occasional SA; (3) occasional SA, more during early 2000's; (4) occasional SA, more during the 1990's; and (5) moderate to heavy SA throughout. Regression analyses revealed strong relationship between childhood SA and later life outcomes. In most cases a cluster with early life SA has larger OR than cluster with later childhood SA, but later childhood SA seems to have larger OR for example for psychiatric care among girls.

**Early life dietary pattern and risk of monoclonal gammopathy of undetermined significance: A population-based study**

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<sup>7</sup> Unit for Nutrition Research, University of Iceland

**Background:** All multiple myeloma (MM) cases are preceded by the premalignant state, monoclonal gammopathy of undetermined significance (MGUS). The aim of this study was to examine whether early life diet is associated with MGUS.

**Methods:** This study was based on participants from the AGES study (N=5,764, mean age 77 years). Participants gave information on frequency of intake of common foods in adolescence (14-19 yrs). All participants were screened for heavy chain MGUS and light-chain MGUS (LC-MGUS). Principal component analysis was used to extract dietary patterns and participants were ranked according to their adherence to each pattern extracted.

**Results:** A total of 575 (10.0%) MGUS cases were identified, of which 300 were heavy chain MGUS and 275 LC-MGUS. We used two dietary patterns in our analysis, an Icelandic traditional pattern, including salted/smoked meat and fish, blood or liver sausage, rye bread, and milk and a healthy pattern, including fruit and vegetables. High adherence to the Icelandic traditional pattern was inversely associated with total MGUS (odds ratio (OR) = 0.71, 95% confidence interval (CI) 0.55-0.90) and heavy chain MGUS (OR = 0.68, 95% CI 0.49-0.95). High adherence to the healthy pattern was inversely associated with LC-MGUS (OR = 0.67 95% CI 0.47-0.95).

**Conclusion:** Our findings suggest that high adherence to the traditional Icelandic diet consumed during early and mid-19th century decreases risk of MGUS later in life and high adherence to a healthy pattern decreases risk of LC-MGUS. These findings indicate that food intake during the adolescence period may alter the risk of developing MGUS.

**Survival from childhood cancer in Scandinavia: Do socioeconomic and family circumstances matter?**

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<sup>1</sup> Danish Cancer Society Research Center

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**Background:** In contrast to cancer in adults, little is still known about the role of socioeconomic and family circumstances in childhood cancer survival. Evidence of survival inequalities is accumulating, but indicating conflicting findings even within Europe.

**Material and methods:** Data from different nationwide Danish public administrative registries were linked to build a population based cohort of all children diagnosed with childhood cancer (before the age of 20) in Denmark. Kaplan-Meier curves and Cox proportional hazards models estimating hazard ratios were used to assess the impact of socioeconomic and family characteristics on survival from childhood cancer. In addition to those findings from Denmark, the evidence from the remaining Scandinavian countries will be summarized.

**Results:** Socioeconomic and family characteristics were found to be associated with survival from childhood cancers, although not consistently across cancer types and between countries. In Norway, survival was better for children with highly educated mothers and children without siblings, with findings being most pronounced for cancers predicted to encompass intense, long-lasting treatments. Also in Sweden, children with leukaemia or CNS tumours of parents with the highest education level showed better survival. For Denmark, family characteristics (parental age, cohabitation, number of siblings, birth order) tended to be more often and stronger associated with survival from different childhood cancer types than socioeconomic circumstances.

**Conclusion:** Despite free and uniform access to health care services, survival from childhood cancer is associated with some socioeconomic and family characteristics in Scandinavian children. Further research is warranted to elaborate underlying mechanisms of those survival inequalities.

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**Children's propensity to consume sugar and fat predicts regular alcohol intake in adolescence**

Lauren Lissner, Kirsten Mehlig, Leonie Bogl, Jaako Kaprio

*The authors have chosen not to publish the abstract*

**Increased 34-year risk of dementia in Swedish women with low fasting serum insulin in midlife**

Kirsten Mehlig, Leif Lapidus, Henrik Zetterberg, Cecilia Björkelund, Ingmar Skoog, Lauren Lissner

**Background:** Two previous studies (1,2) reported U-shaped associations between fasting insulin and dementia in exclusively male cohorts. The purpose of the present study is to investigate this association in a female cohort followed over 34 years, and to compare with the association between insulin and diabetes.

**Methods:** Fasting values for insulin and glucose were obtained from serum samples taken at baseline 1968. Risk of dementia was assessed by Cox proportional hazard regression mutually adjusting for tertiles of insulin and glucose, and for important covariates, and, in a second model, after censoring for incident cases of diabetes. Effects of insulin on dementia were compared to those on diabetes in a third model.

**Results:** Among 1212 women without diabetes at baseline, 142 women developed dementia before 2003. Women in the lowest tertile of insulin were at higher risk for dementia (HR 2.29, CI 1.50-3.50) compared to women in the intermediate tertile, and this was also seen for dementia without diabetes comorbidity. In contrast, the highest insulin tertile was associated with excess risk of diabetes (HR 2.04, CI 1.32, 3.17), compared to the intermediate tertile.

**Conclusions:** Our results suggest that the U-shaped relation between insulin and risk of dementia reported in men is also non-linear in non-diabetic women although the curve may be L-shaped. The association with low rather than high insulin values indicates an alternative pathway to dementia that differs from the metabolic pathway via diabetes.

1 Peila et al. *Neurology* 63, 228 (2004)

2 Rönnekaa et al. *Neurology* 71, 1065 (2008)

## Cognitive ability in young adulthood and risk of dementia in a cohort of Danish men, brothers and twins

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**Introduction:** We examined the association between cognitive ability in young adulthood and dementia in Danish men, brothers and male twins.

**Methods:** A total of 666,986 men born between 1939 and 1959 were identified for dementia diagnosis in national registries from 1969 to 2016. The association between cognitive ability from draft board examination and dementia were examined using Cox regression.

**Results:** During 44 years follow-up 6416 (0.96%) men developed dementia of which 1760 (0.26%) and 970 (0.15%) were classified as Alzheimer's and vascular dementia, respectively. Low cognitive ability was associated with an increased risk of dementia (hazard ratio per SD decrease 1.33 (95%CI=1.30-1.35) with the strongest associations for vascular dementia (hazard ratio per SD decrease 1.47 (95%CI=1.31-1.56) and a weaker for Alzheimer's disease (hazard ratio per SD decrease 1.07 (95%CI=1.03-1.13). The intra-brother and twin analyses, which account for shared family factors, showed attenuated risk estimates but with wide confidence intervals.

**Discussion:** Low cognitive ability early in life increases the risk of dementia before age 78 years. The association was partly explained by shared family factors.

**Atrial fibrillation as a predictor of cognitive decline in stroke-free subjects: The Tromsø Study**

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**Background:** Previous studies have shown an association between atrial fibrillation (AF) and cognitive decline. We aimed to investigate this association in a large longitudinal population study, and whether known risk factors for stroke modulated this association in stroke-free participants.

**Methods:** We included 4983 participants (57% women) from the 5th survey of the population based Tromsø Study (Tromsø 5, 2001), of whom 2491 participated six years later in Tromsø 6, (2007-08). Information about age, education, blood pressure, body mass index, total and high-density lipoprotein cholesterol, smoking, coffee consumption, physical activity, depression, coronary heart disease, valvular heart disease, heart failure and diabetes was obtained at baseline. AF status was recorded from hospital records. The outcome measure was change in cognitive score from Tromsø 5 to Tromsø 6, measured by the verbal memory test, the digit-symbol coding test and the tapping test.

**Results:** Mean age at baseline was 65.4 (9.6) years. The mean reduction in the tapping test scores was significantly larger in participants with AF (5.3 taps/10 sec, 95% confidence interval (CI) 3.9, 6.7) compared to those without AF (3.8 taps/10 sec, 95% CI 3.5, 4.1). The estimates were unchanged when adjusted for other risk factors and were similar for both sexes. AF was not associated with change in the digit-symbol coding or the verbal memory tests.

**Conclusion:** AF in stroke-free participants was independently associated with decline in cognitive test results as measured with the tapping test. Adjustment for cardiovascular risk factors did not affect the results.

## **Fall risk-increasing drugs and falls among older people with intellectual disability**

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**Background:** Falls is the most common cause of injury for older people in general as well as for those with intellectual disability (ID). A range of prescription drugs which are more commonly used among people with ID has been suggested to increase the risk of falls among elderly.

**Materials and methods:** Swedish national registers were used to establish a cohort of people with ID (n=7936) aged 55+ years, as well as referent cohort from the general population, one-to-one matched by sex and year of birth. Information regarding prescription of fall risk-increasing drugs (FRIDs; antidepressants, antipsychotics, anxiolytics, hypnotics and sedatives, and opioids) and health care contacts due to falls was collected from national registers.

**Results:** Compared with the general population, people with ID were more likely to be prescribed all FRIDs investigated except opioids. They were also more likely to have prescriptions of higher doses and for longer periods of time. Although people with ID were more likely than the general population to fall, the risk of falls associated with use of FRIDs was larger in the general population.

**Conclusion:** Older people with ID are prescribed more FRIDs than their age-peers in the general population. Moreover, with or without prescription of FRIDs, they have a higher risk of falls. It is important to be aware of this when prescribing drugs that increase the risk of falls further. Also, the need for the drug should be continuously re-evaluated. One way to do this is medication reviews on a regular basis.