Conference for doctoral students

24 March 2017

Book of abstracts

UNIVERSITY OF ICELAND

SCHOOL OF HEALTH SCIENCES

Contents

Birth and children

Do elite athletes experience more difficult births than untrained women?

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Background: Participation in moderate physical activity before and during pregnancy is associated with improved pregnancy outcomes and less birth complications. Less information is available on the influences of long lasting physical activity, as in competitive sports. The aim of this study was to compare delivery outcome between low and high impact elite athletes and among women who were active at a recreational level.

Methods: Retrospective observational study with a convenience sample of elite athletes and a control group of women who were moderately physically active.

The athletes competed in highest division possible, (58% for national teams). Replies from questionnaire about physical activity before first childbirth, were compared with birth register information.

Results: In all, 248 women participated. Women in the control group (n=118) exercised on average for 1.6 hours per week (SD 3.1), women competing in the low impact (n=41) vs. high impact (n=89) sports trained for 20.3 (SD 10.7) and 14.4 (SD 4.3) hours per week respectively.

Women in the high impact group had a non-significant highest rate of cesarean section (14.6%) compared with low impact athletes (7.3%) and control group (8.5%) (p=0.3). Low impact athletes had significantly higher rate of 3rd and 4th degree perineal ruptures (23.7%) when compared to high impact athletes (5.3%), ($p<0.05$) but not compared to the control group (12.1%). When adjusting for other covariates, only birthweight was associated with 3rd and 4th degree perineal ruptures.

Conclusion: Based on this sample, participation at elite level of sports does not correlate with adverse delivery outcome.

Changes in obstetric interventions among women planning a vaginal birth - A population based study

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Background: Iceland has low maternal and neonatal mortality and morbidity rates and one of the lowest cesarean section rates in the western world. However, annual reports indicate that other common obstetric interventions may be on the rise. The objective of this study was to describe temporal trends in common obstetric interventions in Iceland as well as analyse whether these may be explained by changes in socio-demographic characteristics or life-style related illness.

Methods: In this nationwide population-based study we assessed temporal changes in the use of obstetric interventions among women planning a vaginal birth in Iceland from 1995 to 2014 (N=81 465). We estimated risk ratios for labour induction, epidural analgesia, emergency cesarean section and instrumental delivery, stratified by women's parity and diagnoses of diabetes and hypertensive disorders. Models were adjusted for age, citizenship, marital and employment status, and gestational length.

Results: While obstetric interventions were more common among nulliparous than multiparous women, temporal trends were similar. Among nulliparous women labour induction rose from 8.0% to 26.1% and epidural analgesia from 37.3% to 56.9%. Emergency cesarean section and instrumental delivery prevalences changed minimally. Prevelances were 14.2% and 17.1% in 2014, respectively. When comparing 2010-2014 to 1995-1999, the relative risk of induction of labour among nulliparous women was RRa=2.00 (CI:1.85-2.17) and epidural analgesia RRa=1.40 (CI:1.34-1.47).

Conclusions: Over the study period, the prevalence of epidural analgesia and labour inductions increased while emergency cesarean section and instrumental birth prevalence rates changed minimally. Changes cannot be explained by variations in maternal socio-demographic characteristics or increased diagnoses of diabetes and hypertension.

Prevalence and predictors of negative birth experience in Iceland: A longitudinal cohort study

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Background: The prevalence of negative birth experience varies between 7-35%. Although several risk factors for a negative birth experience have been identified, little is known about if social and professional support influences the birth experience over time.

Aim: To describe low risk women's perception of their birth experience up to two years after birth, and to detect predictors of negative birth experience in particular that of women´s satisfaction with support.

Methods: A longitudinal cohort study was conducted with a convenience sample of pregnant women from 26 community health care centers. Data was gathered using questionnaires at 16th week of pregnancy (T1, n=1111), at five to six months (T2, n=765) and 18-24 months after birth (T3, n=657). Information about socio-demographic factors, reproductive history, birth outcomes, social and midwifery support, depressive symptoms and birth experience was collected. Binary logistic regression analysis was performed in order to examine predictors of negative birth experience at T2 and T3.

Results: The prevalence of negative birth experience was 5% at T2 and 5.7% at T3. Women who were not satisfied with midwifery support in pregnancy and during birth were more likely to have negative birth experience than women who were satisfied with midwifery support at T2. Being a student, any operative birth and perception of prolonged birth predicted negative birth experience at T2 and T3.

Conclusions: Perception of negative birth experience was relatively stable during the study period. Perceived support from midwives during pregnancy, labour and birth has a significant impact on women´s perception of their birth experience.

Emotion Dysregulation and the Development of Disruptive Behavior Disorders and Comorbid Problems in School-aged Children: A longitudinal study

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Recent literature has implicated deficits in emotion regulation in the development of disruptive behavior problems. However, the precise nature of the relationship between emotion dysregulation and the development of disruptive behavior disorders is still unidentified and more research in this area is called for. This project is one of the first longitudinal studies where emotion dysregulation is studied in relation to the development of symptoms of disruptive behavior disorders, ADHD and comorbid problems.

The 2010 and 2011 birth cohort in the capital region of Iceland will be followed for four years to assess the trajectories of emotion regulation and psychopathology as well as whether emotion dysregulation in preschool can predict the development of certain disorders. Prevalence, comorbidity and the developmental course of symptoms will also be assessed in relation to various background variables. The objective is to track the development of both emotion dysregulation and emerging symptoms of psychopathology from the age of 5 to 9.

The scientific value of the study will be added knowledge about the nature of the relationship between emotion regulation and the development of disruptive behavior disorders and comorbid conditions. The project can also provide an evidence-based platform for screening protocols for preschool children.

In this presentation the preliminary results among children in the 2010 cohort will be discussed. The prevalence of emotion dysregulation will be assessed and the relationship to both behavior problems and various demographic variables explored.

Investigating and establishing treatment fidelity in parent- managed treatment studies

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Introduction: Researchers are becoming increasingly aware of the fact that without proper documentation and measurements of fidelity there are huge difficulties in determining whether outcomes, positive or negative, are due to the treatment or the result of other factors. Failed implementation is a common reason for failed outcomes.

Objectives: Provide a systematic review of the role of fidelity within studies of parent-based treatments for stuttering. Evaluate fidelity measurement in parents based stuttering treatments. Define a tool to measure the basic fidelity components.

Method: Out of 384 abstracts examined, twenty-nine empirical studies, published between the years 1981 – 2015 were reviewed. All studies involve parent implementation for children aged 2 – 12 years. The aspects measured were based on their reporting of dosage, adherence, quality and responsiveness for both the clinicians and for the parents.

Results: At the clinician's level 75.8% of the studies report on dosage, 17.2% report on adherence/quality and 44.8% report on responsiveness. At the parental level only 17.2% of the studies report on dosage, 34.5% report on adherence/quality and 41% of the studies report on responsiveness. When looking at each study independently the range of reporting on fidelity was from zero reporting on any of the elements up to a study that reported on all the elements.

Conclusions: Reporting on fidelity when testing a treatment is very important but quite difficult. There needs to be some standardized measurement procedures that are used when testing treatments. This becomes even more crucial when parents carry out the treatment.

Cancer

Proton-pump inhibitors and cancer: A study proposal

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Background: Proton pumps of the v-ATPase type are normally not expressed in the plasma membrane. However, they are expressed in the plasma membrane of certain cancer cells where they might contribute to the acidification of the tumor microenvironment. Proton pump inhibitors (PPIs) are pro-drugs that become active in acidic environments and are able to bind to the v-ATPase and inhibit acid secretion. PPIs are one of the most widely prescribed drugs and their use has been steadily increasing since for several years. The study described here is the first phase of a larger project that intends to examine possible associations between PPI drugs and cancer risk, progression and survival.

Objective: The objective of this study is to examine the possible association between exposure to PPI drugs and cancer risk.

Methods: This is a nationwide population-based cohort study where data from Population Registers Iceland, the National Medicines Registry and the Icelandic Cancer Registry will be linked via personal identification numbers. We compare the risk of a first-time cancer diagnosis among individuals previously exposed to PPI drugs to first-time cancer risk among those unexposed to PPI drugs.

Significance: The potential importance of dysregulated pH gradients in cancer is now a growing field of research with as of yet limited or no clinical impact. By determining whether commonly used antacids, that affect the physiological regulation of pH, could influence cancer risk, progression and survival, the findings of the proposed project may be of major relevance for the management of cancer and have a therapeutic impact.

Survival in Multiple Myeloma 1973-2013: Results from a Population-Based Study

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Background: The introduction of novel treatment agents has had a positive effect on survival in Multiple myeloma (MM). The aim of the study was to define the survival of all patients with MM in Sweden in the years 1973 to 2013 and to relate the survival pattern to trends in treatment strategies.

Methods: Patients diagnosed with MM in the period from January, 1973 to December 31st, 2013 were identified from the Swedish Cancer Registry. Relative survival ratios (RSRs) were used to provide a measure of excess mortality of MM patients compared to a comparable group from the general population. RSRs with 95% CIs were found for one-, 5- and 10- years for four calendar periods; 1973-1982, 1983-1992, 1993-2002 and 2003-2013 and furthermore for five age categories.

Results: A total of 21.465 patients with MM were recorded in the time period. The 1-year RSR increased significantly between all calendar periods (0.69, 0.74 and 0.82, respectively). The 5-year relative survival improved in all four calendar periods, although the improvement was not significant between the two first periods (0.28, 0.31, 0.33, and 0.41, respectively). The 10-year relative survival did not improve significantly between the first three calendar periods, but increased significantly between the two last calendar periods, the RSR being 0.10, 0.12, 0.14 and 0.20, respectively. Women had a higher relative survival than men (excess mortality ratio 0.91).

Conclusion: These results suggest the increased use of novel agents in MM patients has a positive effect on survival in the whole MM patient population.

Lobectomy for non-small cell lung carcinoma: A nationwide study of short and long term survival

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Introduction: The recommended curative treatment for early stage non-small cell lung carcinoma (NSCLC) is surgical resection, with lobectomy being the treatment of choice in the majority of patients. The aim of this study was to evaluate short and long-term outcomes in all patients who underwent lobectomy for NSCLC in a whole nation during a 24-year period.

Materials and methods: The study included 489 patients with NSCLC who underwent lobectomy in Iceland in 1991-2014. Patient demographics, pTNM stage, rate of complications and 30-day mortality were registered and survival analyzed. Prognostic factors of survival were evaluated using Cox proportional hazard model.

Results: The average age was 67 yrs and 53.8% were female. The pTNM disease stage was stage I in 273 patients (55.6%), II in 146 patients (29.6%), but 74 (15.0%) were found to be stage IIIA. The rate of major complications was 4.7%; with a 30-day mortality of 0.6% (3 patients). One and 5-year overall survival was 85.0% and 49.2%, respectively; with 3-year survival improving from 48.3% to 72.3% between the periods 1991-1994 and 2011-2014 (p=0.0004). Advanced TNM-stage and age were independent negative prognostic factors of overall mortality whereas advanced calendar year and free surgical margins independently predicted improved survival.

Discussion: The short-term outcome of lobectomy for NSCLC in this study was excellent compared to other studies; reflected in the low 30-day mortality and rate of major complications. Long-term survival was acceptable and, importantly, has improved significantly during the study period.

Cancer incidence among commercial pilots

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Background: Previous studies on pilots have reported increased incidence of specific cancers, predominantly skin cancer. Workplace exposure to cosmic ionizing radiation has raised concern. This study has more precise information on cosmic radiation millisievert (mSv), longer follow-up, and larger cohort than previous studies. The aim was to study cancer incidence among commercial pilots taking cosmic radiation exposure into account.

Methods: The cohort numbered 551 Icelandic male pilots. They consisted of Icelandair pilots (flying international routes) and other pilots. Cancer incidence was obtained from the Icelandic Cancer Registry. Standardized incidence ratio (SIR), relative risk (RR), and 95% confidence interval (CI) were calculated. Various occupational exposure metrics were evaluated.

Results: The number of all cancers was 83 compared to 92 expected, yielding a SIR of 0.90 (95%CI 0.71-1.11). SIR for malignant melanoma was 3.31 (95%CI 1.33-6.81), and SIR for basal cell carcinoma of skin (BCCs) was 2.49 (95%CI 1.69-3.54). Icelandair pilots were at increased risk for all cancers (RR = 2.32, 95%CI 1.43-3.78), malignant melanoma (RR = 9.55, 95%CI 1.50-187.39), prostate cancer (RR = 2.30, 95%CI 1.02-5.31), and BCCs (RR = 3.30, 95%CI 1.52-7.80) as compared to other pilots. Employment years, cumulative air hours, and cumulative mSv up to age of 40 years showed dose-response manner of relationship with all cancers, prostate cancer, melanoma, and BCCs.

Conclusion: Commercial pilots had increased risk of prostate cancer, melanoma, and BCCs. There are indications that the time of exposure to cosmic radiation is a crucial factor. Leisure time exposure to ultraviolet radiation is an uncontrolled confounding in this study.

Sexuality and intimacy following cancer: A systematic review of couple-based interventions, synthesis and results

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Background and Purpose: Sexual problems and intimacy problems inherently entail inclusion of a partner. Only a few studies, however, address provision of couple based interventions in a clinical context; their content and the measurements used to assess their effectiveness. Therefore, the aim of this review was to describe the characteristics and effects of studies of couple-based interventions targeted to alleviate sexuality and intimacy concerns following cancer.

Methods: A systematic literature review of randomized controlled studies, quasi experimental studies and correlational pre-post studies. The Johanna Briggs Institute (JBI) reviewer's handbook guided the review process and the PRISMA statement was used to provide consistent reporting. An electronic search was conducted in PubMed, CINAHL, and PsychINFO from 2009-2016. Additional information was retrieved by scrutinizing reference lists and conducting manual searches. Two reviewers independently matched the studies with inclusion criteria and the methodological quality was assessed with JBI-MAStARI.

Results: Fourteen primary research articles were included, describing couple-based interventions relating to sexuality and/or intimacy after cancer. Mode of delivery, intensity and content of couple based interventions vary greatly between studies. Study characteristics and results are described and synthesized and recommendations made for sexual health care for cancer survivors and their partners.

Conclusion: Couple-based interventions for sexuality and intimacy remain an option in psychosexual support following cancer. To build further evidence on the effectiveness of couple-based interventions related to sexuality and intimacy concerns after cancer, continuing refinement of research methodology remains an important goal.

Effectiveness of a therapeutic conversation intervention for family members who are experiencing cancer at the end stage of the illness

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Background and Purpose: Family caregivers (FCGs) caring for a family member with advanced cancer are at risk for psychological distress and other long-term health problems. Limited evidence is available regarding effective interventions to improve caregivers´ outcomes, and few family nursing interventions have been conducted and tested in advanced cancer population. The purpose of the study was to evaluate the effectiveness of a family therapeutic conversation intervention (FAM-TCI) aimed to improve caregivers´ outcomes for home-based FCGs of a family member with advanced cancer. Also, to evaluate the effectiveness of the FAM-TCI on bereavement outcomes of FCGs where the intervention is provided before and after death of a family member.

Methods: The theoretical frameworks that guide the study are the Calgary Family Models and the Illness Beliefs Model. Caregiver outcomes; a quasi-experimental one-group pretest-posttest design. A sample of 48 home-based FCGs answered questionnaires at three time points. Three study hypotheses regarding positive outcomes of perceived emotional and cognitive support, psychological distress and caregiving burden were tested using repeated measures ANOVA. FCGs bereavement outcomes; a quasi-experimental pretest-posttest design. 50 FCGs answered questionnaires at three time points after death of a family member.

Results: In total 48 FCGs were included in the final analysis of caregivers´ outcomes. FCGs receiving the intervention reported significant improvements in perceived support ($P<.001$) and stress symptoms ($P<.05$). However, the results of appraisal of caregiving were not statistically significant. Large effect sizes (>0.14) favouring the intervention were found for perceived support. The final analysis of bereavement outcomes (intervention/control group) will be presented at the conference.

Conclusions and Implications: The results support that the FAM-TCI is an effective intervention for families caring for a family member with advanced cancer.

Genome studies

Loss of function variants in a gene segregating with mild intellectual disability

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Intellectual disability (ID) refers to a group of etiologically diverse conditions originating during the developmental period characterized by below average intellectual functioning and adaptive behavior. We have discovered three different stop gain loss of function variants, in a gene essential to neuronal development, segregating with borderline to mild intellectual disability in three unrelated pedigrees. The three mutations occurred recently and in total 13 carriers have been identified in the three families. We have analysed neuropsychological and cognitive data from family members and found that both those carriers with and without a previous diagnosis of ID show significant but general cognitive impairments (Total IQ 1.5 SD below average with performance IQ particularly affected) while non-carriers are not as impaired. This is a gene which has not been directly linked to ID before.

A rare splice donor mutation in the haptoglobin gene associates with blood lipid levels and coronary artery disease

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Introduction: The main role of haptoglobin is to bind free hemoglobin formed through the destruction of red blood cells. Studies have shown that a common copy number variant (CNV) in the haptoglobin gene (*HP*) associates with blood cholesterol levels, but the mechanism is unknown.

Materials and methods: We searched for DNA sequence variants that associate with haptoglobin levels among 13,394 genotyped Icelanders. The variants that associated significantly with haptoglobin levels were then tested for association with blood lipid levels, risk of coronary artery disease and other phenotypes in the deCODE Genetics database.

Results: We discovered a splice donor founder mutation in *HP* (NM_001126102.1:c.190+1G>C, minor allele frequency = 0.56%). This mutation occurs on the HP1 allele of the CNV in *HP* and leads to a loss of function of HP1. It associates with lower levels of haptoglobin ($P = 2.1 \times 10^{-54}$), higher levels of non-high density lipoprotein cholesterol ($\beta = 0.26$ mmol/l, $P = 2.6 \times 10^{-9}$) and greater risk of coronary artery disease (odds ratio = 1.30, 95% confidence interval: 1.10-1.54, $P = 0.0024$). We replicate the association of the HP1 allele of the CNV with lower levels of blood cholesterol and, using haplotype analysis and RNA sequencing, provide evidence of a causal relationship between HP1 and lower blood cholesterol. Furthermore, we show that the HP1 allele associates with various other quantitative biological traits.

Conclusion: We discovered a novel mutation in *HP* that associates with elevated blood cholesterol and higher risk of coronary artery disease. As this mutation causes a loss of function of the HP1 allele of the common CNV in *HP*, these data suggest a causal relationship between HP1 and lower blood cholesterol.

Polygenic risk score prediction of Tourette Syndrome using brain structures, neuropsychiatric and movement disorder phenotypes

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Tourette Syndrome (TS) is a complex childhood onset disorder which is manifested by repeated invloluntary vocal and motor tics. TS has complex inheritance pattern and lifetime prevalance of 0.3%-0.9%. So far, the identification of genetic variants confering risk of TS remains elusive. Moreover, it is still exploratory whether TS is a neuropsychiatic, movement or neurological disorder. During this study, we explored common genetic architecture of TS using external genome wide association results of brain structures, neuropsychiatric and moverment disorder phenotypes (*N*=16). To do so, we applied linkage disequalibrium based polygeneic risk score prediction and polygenic transmission disequilibrium (pTDT) models. Through this, we found that ~ 700,000 common markers significantly predicts TS explaining ~ 1% of phenotypic variance, moreover our analysis shows that TS is genetically better predicted by neurological disorder than neuropsychiatric disorder (OR =1.15).

Immunology

Adjuvants can improve vaccine responses in neonatal mice

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Immaturity of the immune system contributes to increased susceptibility to infectious diseases and poor vaccine responses during the first years of life. Antibody responses are low and transient and germinal center activation is limited due to poorly developed follicular dendritic cells, causing generation of few antibody-secreting cells (AbSCs) with limited survival. Adjuvants can be used to overcome some limitations of the neonatal immune system to induce more robust and prolonged vaccine responses. Neonatal mice were immunized with a pneumococcal conjugate vaccine Pnc1-TT or the TT carrier protein vaccine with/without the adjuvants LT-K63, MF59, IC31, Alum or CTB-CpG. Blood, spleens and bone marrow was collected at various time points after immunization. Vaccine-specific antibodies (Ab) were measured in serum with ELISA and vaccine-specific AbSCs were enumerated in spleen and bone marrow with ELISPOT assay. The adjuvants LT-K63, MF59, IC31 and Alum all induced significantly higher and prolonged vaccine-specific Ab titers compared to vaccine only, although to a different degree. These adjuvants also induced a significantly higher frequency of vaccine-specific AbSCs in spleen and bone marrow compared to vaccine only, again to a different extent. These results suggest that the adjuvants LT-K63, MF59, IC31 and Alum all induce increased germinal center activation in the spleen of neonatal mice as well as increased survival of vaccine-specific AbSCs in the bone marrow leading to improved responses to vaccination and prolonged protection.

LL-37 expression in skin and leukocytes

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Introduction: The anti-microbial peptide LL-37 is a part of the innate immune system and is over-expressed in psoriasis, both in skin and blood, and takes part in the pathogenesis of psoriasis. LL-37 has previously been shown to be expressed in several leukocyte subtypes such as B cells, NK cells, monocytes and γδ- T cells but not αβ-T cells. Psoriasis treatment in the Blue Lagoon combined with narrow-band ultra-violet B (NB-UVB) treatment has been shown to cause faster improvement than NB-UVB therapy alone as well as producing longer remission time. The aim of this research is to map out the expression of LL-37 in skin and leukocytes of psoriasis patients and healthy controls.

Material and methods: Skin samples were collected from psoriasis patients undergoing psoriasis treatment, at the start of treatment and after 6 weeks. Skin samples were sectioned and stained with fluorescence antibodies. Leukocytes were isolated and stained for flow cytometry analysis.

Results: The graded intensity of LL-37 in skin did not change after treatment but localization within the epidermal compartments was drastically altered, showing staining only along the basal membrane. Preliminary results from LL-37 expression in leukocytes in healthy controls show that many subgroups such as B cells, monocytes, granulocytes show expression and this data points to αβ T cells also being LL-37+.

Conclusions: LL-37 expression in skin confined to the basal layer is common after psoriasis treatment but not seen before treatment and LL-37 expression in leukocytes can be measured using flow cytometry.

IL-10-producing regulatory B Cells are decreased in patients with selective IgA deficiency

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Introduction: Selective IgA deficiency (IgAD) is the most common primary immune deficiency in the western world. It´s pathogenesis is largely unknown but thought to be due to a deregulation in B cell maturation.

Material and Methods: IgAD individuals and age and sex matched healthy controls (HC) where studied. Different B and T cell populations were analysed and their function after isolation assessed using FACS and Elisa.

Results: IgAD individuals demonstrated a significant defect in IgA+ B cells. In addition, IgAD individuals demonstrated a significantly lower number of transitional B cells (CD19+CD24hiCD38hi) compared to HC reflected in both their presence in peripheral blood and TLR9-CpG (ODN 2006) induced expansion. Furthermore, a significantly higher fraction of IgAD transitional B cells were IL-10+ compared to HC following CpG stimulation. Finally following extensive IgA class switching promoting cultures of isolated IgAD B cells our study model revealed a unique population of CD20+IgD-IgM-IgG-IgA- B cells being “stuck” in its differentiation pathway compared to HC. This specific defect was not due to dysfunctional iTregs from IgAD individuals since their numbers, inducibility and function was found to be normal.

Conclusions: The pathogenesis of IgAD may be related to a maturation defect of transitional cells or to antecedent maturation stages which may be related to their responses to TLR9 stimulation. The defect may be related to an IL-10 driven pathway within the transitional B cell compartment. We claim the disruption is due to proliferation without developmental progression providing us an exciting opportunity to further delineate the pathways involved.

Effect of pneumococcal vaccination on tympanic tube placement rate: A population based study

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Background: Tympanostomy tube placements (TTP) are the most common paediatric surgical procedure. Randomised controlled trials have demonstrated a reduction of TTP following pneumococcal vaccination. The 10-valent pneumococcal non-typeable *Haemophilus influenzae* Protein D-conjugate vaccine (PHiD-CV10, Synflorix) was introduced into the paediatric vaccination program in Iceland in April 2011. The aim was to evaluate the effect of the vaccination on the TTP rate in Iceland.

Methods: All children <6 years of age in Iceland were enrolled. Data on reimbursements for TTP was collected from the Icelandic National Health Insurance database for the period of 2005–2016. Individual vaccination status was extracted from the National Vaccine Register of the Directorate of Health. Cumulative proportion of vaccine eligible (VEC, 2011–2015) and vaccine ineligible (VIC, 2005–2010) cohorts receiving ≥1 TTP before the age of 3 were compared using Chi-Squared test of independence and linear trend in proportion tested using Chi-Squared Test for Trend. Incidence rate was calculated by age and calendar year.

Results: 26789 TTP were performed on 18270 children from 2005–2015. A total of 2329 children (out of 9025, 25.8%) in VEC and 6611 (out of 28023, 23.6%) in VIC received ≥1 TTP before 3 years of age. Children in VEC were significantly more likely to have undergone ≥1 TTP before 3 years of age (RR 1.09, 95%CI 1.05–1.14, p<0.00001). A significant positive linear trend in proportion was noted (p<0.00001). Overall incidence rate was significantly higher in the post-vaccine period (Mantel-Haenzel adjusted IRR 1.04, 95%CI 1.01–1.08, p=0.016).

Conclusions: Cumulative proportion and incidence of TTP increased significantly during the study period despite the added protection of PHiD-CV10. No explanation is evident. This unexpected result will be investigated further.

Reduction in Otitis Media incidence in primary health care in Iceland following PCV-10 immunisation

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Background: Pneumococcal conjugate vaccine (PCV-10) immunisation was introduced in the Icelandic childhood vaccination program in 2011, without catch-up, with a 97-98% uptake of the primary vaccine doses for birth-cohorts 2011-2014.
The aim was to determine the effect of PCV-10 immunisation on primary care visits for respiratory tract infections (RTIs) in children.

Methods: All primary care physician visits due to RTIs in children <3 years of age in Iceland, 2008-2015 were recorded. The National Vaccination Registry was used to determine if the child had been vaccinated. Children that had received ≥2 doses of any PCV were classified as vaccinated. Children previously vaccinated born in 2010 and earlier and non-vaccinated children born in 2011 and later were excluded. Repeated visits within 30 days were excluded. Birth cohorts 2008-2010 (Non-Vaccinated-Group, NVG) were compared to birth cohorts 2011 and later (Vaccinated-Group, VG). Annual incidence rates (IR) for Otitis Media (OM), pneumonia and Other RTI were compared between the groups for children <1, <2 and <3 years of age. Large sample Z test was used and incidence rate ratios (IRRs) calculated.

Results: For OM, the IRs for the NVG and the VG for children <1, <2 and <3-year-old were: 0.490 vs 0.429, 0.640 vs 0.605, 0.571 vs 0.549 respectively with IRRs: 0.877, 0.944 and 0.961. For pneumonia, the IRs were unchanged from NVG to VG for children <1, <2 and <3-year-old (0.0220 vs 0.0228, 0.0475 vs 0.0481, 0.0551 vs 0.550 respectively. For Other RTIs, the IRR for children <1 years of age was 0.914 with no change noted in other age groups.

Conclusion: A significant reduction in primary health care visits for OM in children vaccinated with PCV-10 was established. This clearly demonstrate the effect of the PCV-10 vaccination.

Bacterial Infections in Patients with Chronic Lymphocytic Leukemia

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Chronic lymphocytic leukemia (CLL) is the most common leukemia in Western countries. The median age of diagnosis is 72 years. New treatments have been introduced in recent decades with increased survival. CLL patients are exposed to serious infections, both due to immunosuppressive effects of the disease and the treatment. Our aim was to estimate the incidence of serious infections as well as its effect on survival.

Data is still preiliminary and will be better defined. Informations on patients diagnosed 1982-2013 was retrieved from well-established Swedish Registries.The cohort consisted of 18.795 patients and 53.279 controls.

Preliminary results show that admissions due to serious bacterial infections in 100 person year are 9.0 in CLL patients compared to 2.3 in controls. The difference is greatest in admissions due to sepsis and pneumonia. The incidence rises in CLL patients compared to controls more then 6 months prior to the diagnosis of CLL and is still appearant ten year after diagnosis. In a survival analysis the incidence of bacterial infections has been increasing in CLL patients in recent decades, however the survival after an infection has also increased.

Preliminary results in this large, nationwide population-based study indicate that CLL patients are more susceptible to infections compared to controls. The incidence has been increasing in recent decades, however the survival after an infection has also been increasing. Further analysis has to be done on subgroups of infections, especially in relations to immunsuppressive effects of the newer treatment.

Longitudinal studies and nutrition research

The effects of item difficulty on response behavior of longitudinal sample units

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Longitudinal sample surveys are important methodological tools for uncovering changes and/or trends in the population over time. As in every type of survey research, the respondent is an important source of error which affects the overall quality of the data. In order to minimize this error source, survey items have been written in an unambiguous and clear manner to ensure that respondents understand the items and do not find them difficult. This is particularly important in longitudinal research due to the fact that respondents are repeatedly interviewed. Off course, this is not always possible, for example when the survey deals with complex issues leading to difficulties in responding and low data quality for certain respondents. What is unclear is how unclear and difficult survey items might affect future waves of data collection in longitudinal surveys. Two possible consequences can be envisaged: 1) The respondent may decline to participate in further waves of the survey, leading to panel attrition and possible nonresponse bias; 2) The respondent may participate in future waves, while applying response styles (e.g. acquiescence or non-differentiation) in order to simplify the task of responding. This was studied using data from the LISS-panel, a high quality longitudinal internet panel from the Netherlands. The results highlight the importance of the total survey error approach in the case of longitudinal surveys and show the extent to which nonresponse bias and measurement error can be interlinked in longitudinal survey research.

Energy- and protein intake in hospitalized patients with Chronic obstructive pulmonary disease (COPD) and the association with body composition, lung function and outcomes

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Background: Low energy and protein intake has been associated with increased risk of malnutrition in outpatiens with chronic obstructive pulmonary disease (COPD). The aim was to assess energy-/protein intake of hospitalized COPD patients and to examine whether it predicts COPD severity, length of stay, readmissions within 30 days and mortality.

Methods: Subjects were COPD patients (n=99) admitted to Landspitali University Hospital during one year (March 2015- March 2016). Patients were screened for nutritional risk using a validated screening tool. Energy- and protein intake was estimated using a validated plate diagram sheet. Body composition was measured with a bioelectrical impedance analyser. Lung function was measured with spirometry.

Results: The energy-/protein intake from the hospital meals provided was lower in subjects defined at nutritional risk than those not at risk (1173 ± 358 vs. 1360 ± 360 kcal; p=0.013 and 49.0 ± 16.3 vs. 57.2 ± 16.7 g; p=0.019). However, patients at nutritional risk were provided with greater amount of oral nutritional supplements or food brought from home (194 ±151 vs. 85 ± 89 kcal; p<0.001 and 7.8 ± 6.1 vs. 3.3 ± 4.7 g; p<0.001), resulting in no difference in total energy-/protein intake. Energy-/protein intake was positively associated with measures of body composition (fat free mass index, fat mass index and body mass index), but no association was seen with outcomes.

Conclusion: Although energy-/protein intake was lower than recommended during hospitalization we found no association with outcomes. Long term studies, assessing energy-/protein intake both during hospitalization and after discharge are needed.

Infant nutrition, growth and IgE sensitization at 6 years: A longitudinal cohort

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Objectives: To compare nutrition, including age at solid food introduction and vitamin D supplements, and growth from infancy to 6 years between IgE sensitized and non-sensitized children.

Methods: In this prospective Icelandic cohort, serum-specific IgE-antibodies against food were analyzed at 6 years (cut-off sIgE≥0.35 kUA/L). Dietary information at ≤ 4 months of age was assessed using dietary recall and at 12 months and 6 years using 3-day weighed food records. Weight, length/height and head circumference was measured in infancy and at 6 years. Background variables were gathered from parental questionnaires.

Results: Out of 144 6-year-old children, 14 (10%) were IgE sensitized. At 4 months (week 17), 57% of the IgE sensitized vs. 23% non-sensitized children (p=0.006) had received solid food. From birth to 2 months, IgE sensitized compared to non-sensitized children had greater increase in weight (mean±SD; 2.2±0.4 kg vs. 1.8±0.7 kg, p=0.039) and head circumference (4.9±1.2 cm vs. 4.2±0.7 cm, p=0.017) and were more likely to be overweight or obese at 6 years (29% vs. 10%, p=0.041). At 12 months, IgE sensitized children had a lower intake of vitamin D (median (25th,75th percentiles); 3.9 µg/d (3.2,7.2) vs. 8.1 µg/d (4.4,12.3), p=0.034) and at 6 years, they were less likely to use vitamin D supplements (23% vs. 56%, p=0.026).

Conclusions: Solid food introduction prior to 4 months, a different growth pattern and less vitamin D intake was associated with increased IgE sensitization. This supports delaying solid food introduction to at least 4 months and encouraging vitamin D intake from diet or supplements.

Medicine

Acute Kidney Injury After Abdominal Surgery: Incidence, Risk Factors, and Outcome

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Background: Acute kidney injury (AKI) is a serious complication after major surgical procedures. We examined the incidence, risk factors, and mortality of patients who sustained AKI after abdominal surgery in a large population-based cohort.

Methods: All patients who underwent open and laparoscopic abdominal surgery from 2007-2014 at the University Hospital in Reykjavik were identified, their perioperative serum creatinine (SCr) measurements used to identify AKI after surgery employing the Kidney Disease: Improving Global Outcome (KDIGO) criteria. Risk factors were evaluated using multivariate logistic regression analysis and 30-day mortality compared with a propensity score–matched control group.

Results: Both pre- and postoperative SCr measurements were available for 3902 (33.8%) of surgical cases. Of these, 264 (6.8%) were complicated by AKI; 172 (4.4%), 49 (1.3%), and 43 (1.1%) were classified as KDIGO stages 1, 2 and 3, respectively. The incidence of AKI was 67.7 (99% confidence interval [CI], 57.7–78.6) per 1000 surgeries. In logistic regression analysis, independent risk factors for AKI were female sex (odds ratio [OR]=0.68; 99% CI, 0.47–0.98), hypertension (OR=1.75; 99% CI, 1.10–2.74), preoperative chronic kidney disease (OR=1.68; 99% CI, 1.12–2.50), ASA classification of IV (OR=9.48; 99% CI, 3.66–29.2) or V (OR=21.4; 99% CI, 5.28–93.6), and reoperation (OR=4.30; 99% CI, 2.36–7.70). Patients with AKI had greater 30-day mortality (18.2% vs 5.3%; $P < 0.001$) compared with propensity score–matched controls.

Conclusions: AKI is an important complication of abdominal surgery. In addition to sex, hypertension, and chronic kidney disease, ASA classification was an independent predictor of AKI. Individuals who develop AKI had substantially higher 30-day mortality.

Eye Manifestations in Adenine Phosphoribosyltransferase Deficiency (APRTd)

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Background: APRT deficiency is an autosomal recessive disorder that leads to excessive production and renal excretion of 2,8-dihydroxyadenine (DHA), causing kidney stones and crystalline nephropathy. Treatment with allopurinol or febuxostat alleviates DHA production, stone burden and kidney injury. Extrarenal manifestations have not been reported, except for one case of possible corneal deposits. The aim of this study was to characterize eye symptoms among patients with APRTd.

Methods: Records of 58 patients in the APRTd Registry of the Rare Kidney Stone Consortium were systematically reviewed. Data on eye manifestations, ophthalmologic examinations and pharmacologic therapy were collected.

Results: Twenty-seven patients, 19 females, complained of eye symptoms, the most common being irritation (n=17), photophobia (n=16), dry eyes (n=11), blurred vision (n=10) and foreign body sensation (n=10). Eleven patients underwent a thorough eye examination, of whom 8 had corneal findings, including superficial punctate keratitis, punctate epithelial erosions and corneal "deposits" which were symmetrical and central in distribution. Four additional patients had a past history of corneal defects. In all cases, eye symptoms were reported after initiation of treatment with allopurinol or febuxostat. At last follow-up, 23 patients were treated with allopurinol at a median (range) dose of 300 (200-600) mg/day, while 3 were taking febuxostat 80 mg/day. Three patients discontinued pharmacotherapy due to the eye symptoms and experienced relief within weeks.

Conclusion: Ocular manifestations are common in patients with APRTd, including signs of corneal injury and deposits, which may consist of DHA. Future studies will focus on determining the nature of the corneal deposits.

Transportation of Patients with Helicopter in Iceland – a Whole Nation Study on Outcome and Costs

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Introduction: Landspitali University Hospital (LSH) is the main hospital in Iceland and most critically ill and injured patients are transported to LSH. The emergency helicopter, run by the Icelandic Coast Guard (ICG), is an important part of the pre-hospital transport services and serves injured and ill people at sea and in remote areas. The purpose of this study was to review all flights of the emergency helicopter in Iceland in 2001-2015. Data from 2001-2012 will be presented here.

Methods: The study was a qualitative, retrospective study. Information was gathered from patient files at LSH and flight data from the ICG. The following scales were used: Revised Trauma Score (RTS), Injury Severity Score (ISS), Trauma and Injury Severity Score (TRISS), NACA score and Modified Early Warning Score (MEWS).

Results: In 2001-2012 the rescue helicopter transported 704 patients, 466 injured and 223 sick. Males were 502 (71%) and females 202 (29%). Mean age was 40.2 years. The most common diagnosis of injured patients were injuries to the head (20%) or pelvis and lower extremity (20%). RTS was 7.429 ± 1.321 and ISS was 10.5 ± 13.8. Probability of survival (TRISS) was 94,0%. The mean NACA score was 3.4 ± 1.2 for injured patients and 3.8 ± 1.0 for sick patients. The mean MEWS score was 1.5 ± 2.4.Treatment was required in 84% of transports, cardiac resuscitation 17 times and intubation 37 times.

Conclusion: Many patients requiring emergency transport with helicopter are severely injured or sick and most get treatment on board the helicopter. Further research is needed to evaluate the importance of the helicopter for patient survival.

Favorable survival after aortic valve replacement compared to the general population

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Objective: To compare the long-term survival of patients undergoing aortic valve replacement for aortic stenosis with the survival of age and gender matched Icelandic population.

Material and methods: We included 366 aortic valve replacement patients operated for aortic stenosis in Iceland between 2002 and 2011. Concomitant CABG was performed in 54% of cases. Short-term complications and 30-day mortality were analyzed. Overall survival was compared with survival of Icelanders of the same age and gender. Median follow-up was 4.7 years.

Results: Mean age was 70.1±9.8 years and 63% of the patients were males. Bioprosthesis was used in 81% of the patients and the median prosthesis size was 25±2.3 mm. The most common complications included atrial fibrillation (68%), acute kidney injury (23%) and myocardial infarction (13.6%). The 30-day mortality was 6%. Overall survival at 1 year and 5 years was 92% and 82%, respectively. There was no difference in survival between the surgical cohorts and the expected survival of Icelanders of the same age and gender (p=0.08)

Conclusions: Despite the significant rate of short-term complications, the long-term survival of patients undergoing aortic valve replacement for aortic stenosis is good compared to the general population of the same age and gender. These results confirm the importance of aortic valve replacement as an excellent treatment option for aortic stenosis, offering normalization of patients' life expectancy.

Prevalence of chronic kidney disease according to eGFR derived from standardized serum creatinine: a population-based study

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Background: Standardization of serum creatinine measurements (SCr) has improved the utility of SCr-based equations to estimate glomerular filtration rate (eGFR). The purpose of this study was to estimate the prevalence of chronic kidney disease (CKD) in Iceland based on eGFR derived from standardized SCr.

Methods: In this retrospective study, we obtained all SCr values from all clinical laboratories in Iceland for the years, 2008-2013. Information on age and sex was also obtained. Using computerized algorithms, we exclued SCr values during episodes of acute kidney injury. eGFR was calculated using the CKD-EPI equation. CKD was defined as eGFR <60 mL/min/1.73 m^2 for more than 3 months and staged according to the KDIGO classification system. Period prevalence of CKD stages 3-5 was calculated based on the population of individuals aged 18 years or above in Iceland, which numbered 245,631 on December 31, 2013.

Results: We retrieved 1,230,563 SCr values for 183,931 individuals aged 18 years and older. The median age was 60 years (range 18 – 107) and 46% were male. The age-adjusted prevalence rate per 100,000 in men was 2,881 for CKD 3A, 1,106 for CKD 3B, 343 for CKD 4, and 107 for CKD 5. In women, the age-adjusted prevalence rate per 100,000 was 3,699 for CKD 3A, 1,568 for CKD 3B, 410 for CKD 4, and 74 for CKD 5. The prevalence of CKD stages 3-5 increased with advancing age. In men from the prevalence was 18/100,000 for age 18-39 years, 799/100,000 for age 40-59 years, 6,006/100,000 for age 60-69 years, 20,858/100,000 for age 70-79 years and 43,323/100,000 in those who were 80 years of age or older. In women, the prevalence was 132/100,000; 1,206/100,000; 7,203/100,000; 22,177/100,000; and 40,479/100,000 for same age groups respectively.

Conclusions: This nationwide study, which included standardized SCr measurements and comprises a large proportion of the Icelandic population, demonstrates lower prevalence of CKD stages 3-5 compared with previous studies in Iceland.

Molecular Biology I and II

MiR-190b´s expression and methylation patterns in breast cancer subtypes

Student: **Elísabet A Frick**

Others: Ólafur A Stefánsson advisor, Stefán Sigurðsson supervisor.

Institution of student, advisor, supervisor and other co-workers: Cancer Research Laboratory

Epigenetics and microRNAs (miRNA) are important supervisory mechanisms for maintaining gene expression patterns in the cell. Differential miRNA expression is commonly shown among breast cancer subtypes, often with tumor-suppressive or oncogenic roles. Data from The Cancer Genome Atlas indicate a potential association between altered expression of miR-190b and estrogen-receptor status in breast cancer. The aim of the first part of the Ph.D study is to verify miR-190b‘s altered expression with regard to estrogen-receptor status in breast cancers and to understand if there are epigenetic mecanistics behind our findings. When processing our results we take clinical relevance into consideration, such as prognosis, tumour grading and staging along with *BRCA2* mutation status. Our methods are based on the highly sensitive taqman advanced miRNA assay (RT-qPCR) along with pyrosequencing methylation assay, in a large cohort of well annotated breast cancers to define miR-190b‘s expression and methylation status across subtypes. Our preliminary results demonstrate correlative over expression and hypomethylation of miR-190b in estrogen receptor positive breast cancers, namely Luminal A and Luminal B. Our findings furthermore indicate that miR-190b hypomethylation may be correlated to PR and Ki67 status.

Blood telomere length in Icelandic *BRCA2* mutation carriers

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Supervisor: Jórunn Erla Eyfjörð[1]

Other co-workers: Margrét Aradóttir[1], Sigríður K. Böðvarsdóttir[1], Ólafur A. Stefánsson[1]

Institutions: 1) Cancer Research Laboratory, BioMedical Center, University of Iceland

Germline mutations in the *BRCA2* gene are associated with highly increased risk of breast cancer. The BRCA2 protein plays a role in DNA repair and has been associated with telomere protection and maintenance. Dysfunctional telomere maintenance can cause excessive telomere shortening which can lead to chromosome instability, a hallmark of carcinogenesis. Telomere length (TL) has been studied as a modifying factor for various diseases, including breast cancer. Previous research on TL in *BRCA* mutation carriers has produced contradicting results.

In the first part of the project, blood TL was measured in samples from female carriers of the Icelandic *BRCA2 999del5* founder mutation (n=169), sporadic breast cancer patients (n=561) and healthy controls (n=537). Measurements were performed using a high-throughput monochrome multiplex qPCR method.

Breast cancer cases had significantly shorter TL than unaffected women, both *BRCA2* mutation carriers and non-carriers. Using only samples acquired before breast cancer diagnosis, shorter telomeres were significantly associated with breast cancer risk in *BRCA2* mutation carriers but not in non-carriers. No association was found between TL and breast cancer specific survival, subtypes or other clinical parameters.

Blood TL is predictive of breast cancer risk in *BRCA2* mutation carriers, indicating that BRCA2 has an important role in telomere maintenance, even in normal blood cells.

A Potential New Role for ALKBH3 in Double-Stranded Break Repair

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DNA repair is crucial to maintaining the health and integrity of cells. Damage that is allowed to persist within the DNA may aid in the formation of diseases such as cancer. It is therefore crucial that proteins involved in DNA repair are functional. Incidences where protein expression is impaired have been linked to disease formation. Epigenetic modification, particularly promoter methylation, can cause a downregulation of gene expression. Through database analysis we identified 5 repair proteins which undergo promoter methylation, one of which being ALKBH3. ALKBH3 is a protein responsible for the repair of a form of DNA alkylation damage, specifically 3-methylcytosine. According to The Cancer Genome Atlas, 20% of breast cancers are promoter methylated for ALKBH3. We also found this to occur in a subset of Icelandic tumor tissues. Importantly, epigenetic silencing of ALKBH3 is occurring within tumors and not the normal tissue of the same patients. Additionally, our data shows ALKBH3 is having an impact on the functionality of a key Double-Stranded Break (DSB) repair protein. Our research aims to elucidate this potential role of ALKBH3 in DSB repair and exploit the downregulation of this protein by looking for potential synthetic lethality.

Comparison of non-tumorigenic and tumorigenic breast epithelial-derived cell lines with mesenchymal phenotype

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D492 is a breast epithelial cell line with stem cell properties that can generate both luminal and myoepithelial cells and in 3D culture it forms branching terminal ductal lobular units TDLU-like structures. D492M was generated by coculture of D492 and breast endothelial cells (BRENCs) that resulted in subpopulation of cells undergoing epithelial to mesenchymal transition giving rise to D492M. D492HER2 was generated by overexpression of HER2 in D492 and this also resulted in a cell line showing EMT phenotype.

D492M is nontumorigenic while D492HER2 is highly tumorigenic. My objective is to compare these two cell lines because eventhough both cell lines show EMT phenotype, they differ in tumorigenicity.

Using transwell migration and invasion in vitro assays, proliferation assay dying with crystal violet and measuring the glucose uptake with a kit and consumption of the cells, I have found that D492HER2 migrates, invades and proliferates more than D492M, and consumes more glucose as well.

Furthermore, following the transcriptome data provided by a collaboration with Maria Perander in Tromsö, comparing D492M and D492HER2, I have confirmed by qPCR the expression of some of the most differently expressed genes. From this list, I have selected some candidates and I am working on the downregulation of the protein expression to look for associations with the differences in the behavior of the cells regarding migration and invasion, and also in the interaction with the endothelial cells of their niche.

With all these data, I try to identify the mechanisms implicated that can lead to differences in tumorigenicity between the EMT-derived from D492 cell lines.

Heterotypic interactions between endothelial and cancer cells in breast cancer progression and metastasis

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Introduction: Investigating heterotypic interactions between cancer cells and the microvasculature is important for improving our understanding of how the microenvironment supports tumor growth and facilitates metastasis.

Methods and data: D492 is a breast epithelial line with stem cell properties. D492M is a D492-derived mesenchymal but non-tumorigenic line, which underwent endothelial-induced EMT. D492HER2 was generated by overexpressing the HER2/ErbB2 oncogene in D492, is mesenchymal and shows tumorigenic properties. Here, we analyze how isogenic non-tumorigenic vs. tumorigenic breast epithelial cell lines affect their vascular niche by 2D and 3D co-culture and conditioned media treatment of human umbilical vascular endothelial cells (HUVEC).

Results: In 2D and 3D co-culture, mesenchymal D492HER2 and D492M cell-lines showed a greater physical interaction with HUVECs compared to the epithelial mother cell-line. Migration assay confirmed increased migration of D492HER2 and D492M towards HUVECs. To assess crosstalk between cancer cells and the microvasculature, conditioned media was collected from all three cell-lines. Treatment of HUVECs indicated increased 3D capillary network formation and proliferation in 2D upon D492HER2-conditioned media treatment. Conditioned media from D492HER2-induced HUVECs increased proliferation of D492 and D492HER2.

Conclusions: These data suggest that cancer cells do affect their endothelial niche and that cross-interaction with endothelial cells might be beneficial for cancer cells. Identification of candidate molecules mediating the cross-talk between endothelium and breast cancer cells could give valuable insights into a cancer-specific response of the vascular niche. To identify cancer cell-secreted factors and responsive endothelial target genes, secretome analysis and RNA sequencing of conditioned endothelial cells will be performed.

Involvement of Fas ligand and IL-6 in the pathogenesis of ischemic brain injury following perinatal asphyxia in human infants

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Aim: To determine whether inflammation contributes to neural damage in cerebral hypoxic ischemic encephalopathy (HIE) of newborn infants. We hypothesize that inflammatory cytokines are released into CSF after hypoxic insult, and that they link to apoptotic biomarkers and clinical outcome.

Methods: Levels of cytokine IL-6 and CD95/Fas ligand (FasL) were quantitated in cerebrospinal fluid (CSF) from 64 full-term infants, using enzyme immunoassay. The cohort consisted of infants with varying degree of HIE, classified as mild, moderate or severe (HIE I-III), (n=44) and control infants (n=20). Soluble CD95/Fas (sFas) was analyzed in a subsample of the cohort (n=40). Neurological assessment was performed at 18 months of age. Experiments were carried out on cultured cell lines in vitro to test the biological activity in the samples.

Results: The levels of FasL, sFas and IL-6 correlated to the degree of HIE, as well as the clinical outcome of patients. The levels were higher in CSF from patients with HIE-II and HIE-III than patients with HIE-I and controls ($p<0.0001$). Likewise, higher levels were observed in CSF samples from patients who died or had adverse outcome than patients with normal outcome or controls ($p<0.0001$). Biological activity was observed in the CSF samples on cell lines in vitro.

Conclusion: Apoptotic metabolites together with the inflammatory metabolite IL-6 are released into CSF after hypoxic insult in infants and the levels correlate to the degree of HIE symptoms. These metabolites may be useful biomarkers for estimating the extent of brain injury and predicting clinical outcome in HIE following perinatal asphyxia.

A role for MUC5B promoter polymorphism in idiopathic pulmonary fibrosis

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The MUC5B promoter (G-to-T) polymorphism is associated with idiopathic pulmonary fibrosis (IPF). In heterozygotes the T-allele is associated with a 6-8 fold increased risk of IPF and there is also an increased expression of MUC5b in the airways of carriers of this risk allele. We have previously used human basal epithelial cell lines (VA-10 and BCi-NS1.1) to model in air-liquid interphase (ALI) culture both cellular differentiation and epithelial histoarchitechture of the upper airways. Here, we have transduced these cell lines, as well as A549, with a promoter reporter construct containing the 4 kb promoter region of MUC5b with the wildtype or the T-risk allele present to gain insights into the molecular and cellular effects of IPF. We are also using CRISPR DNA-editing to engineer the T-risk allele in heterozygotes or homozygotes forms into the cell lines.

Using a bioinformatics approach, we have identified several transcription factor binding sites at the polymorphic promoter site, including a possible CEBP-beta site. Furthermore, we have seen a marked increase in MUC5B expression after induction with interleukin(IL)-13, and under these conditions there is also a marked increase in CEBP-beta expression. BCi_NS1.1 cells transduced with the T-risk allele had a 33,6% increase in luciferase signal, when compared to wild-type. This signal was further amplified to 54,21% after transiently overexpressing CEBP-beta.

Finally, we see a increased MUC5B expression in BCi-NS1 and VA-10 cells when treated with 5-azacytidine and using in vitro methylation we see that wild type MUC5B promoter reporter are more susceptible than the T-risk allele, suggesting that the region is regulated through epigenetic DNA methylation.

The mechanism of BLIMP1 mediated survival in Waldenström's macroglobulinemia

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The transcription factor B-lymphocyte induced maturation protein 1 (BLIMP1) is known to play an essential role in both normal and multiple myeloma plasma cell survival. Recent data from our group demonstrate a novel role for BLIMP1 in mediating cell survival in Waldenström's macroglobulinemia (WM). Using miRNAs, we generated stable inducible knock-downs of BLIMP1 in RPCI-WM1 and MWCL1 WM cell lines. Upon knock-down of BLIMP1, we observed an increase in apoptotic cell death in both lines. A number of pro-apoptosis genes including *XAF1* and *MAP3K5* were de-repressed following BLIMP1 knock-down, indicating a potential mechanism. Without intrinsic enzymatic activity, BLIMP1 typically acts through recruitment of epigenetic modifiers and other factors to repress transcription of its targets. Our data show the interaction of BLIMP1 with repressive histone methyltransferase EZH2 in WM cells. To explore this, we generated EZH2 miRNA knock-down lines. Using these cells, we observed EZH2 knock-down to induce apoptosis and de-repression of some of the same targets as BLIMP1. Genome-wide location analysis has demonstrated a number of additional overlapping targets. In summary, BLIMP1 appears to play a key role in the survival of WM cells, possibly through recruitment of co-repressor EZH2. Further elucidating its mechanism of action may help us to uncover novel therapeutic targets.

Northern Lights Assay of cell-free DNA (cfDNA) damage in body fluids

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Structural damage in cfDNA molecules in body fluids has been little studied. Such damage may reflect normal and abnormal cell turnover, genome instability or exposure to genotoxic agents.

We analyzed cfDNA damage in plasma, urine and saliva. Selective ion exchange chromatography allowed gentle isolation of DNA without inducing damage.

Damage in isolated DNA was assessed with the Northern Lights Assay. This assay is based on Two-Dimensional Strandness-Dependent Electrophoresis (2D-SDE) in premade microgels. Each specimen can be analyzed in sample pairs of non-digested DNA to detect single- and double-stranded breaks and *Mbo*I-digested DNA to detect other lesions. Single-stranded breaks, either nicks or gaps, were detected as horizontal streaks from uncut DNA molecules. Double-stranded breaks generated an arc in the gel. DNA molecules with interstrand crosslinks migrated as an arc behind normal dsDNA molecules. DNA with intrastrand crosslinks and bulky adducts were bent and migrated in front of that arc. Single-stranded DNA molecules, too damaged for complementary strand binding, formed a diagonal line.

Patterns of cfDNA in plasma of normal subjects showed an apoptosis pattern with single- and double-stranded breaks of nucleosomal-sized fragments. cfDNA in urine showed composite patterns of apoptosis and non-specific degradation. The most extensive damage and variable patterns were seen in saliva including prominent single-stranded breaks.

Microphthalmia associated transcription factor (MITF) regulates potassium channels in the olfactory bulb

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Microphthalmia associated transcription factor (MITF) is a basic helix-loop-helix-leucine zipper transcription factor essential for the development of melanocytes and mast cells. *Mitf* is also expressed in the glutamatergic neurons of the mouse olfactory bulb (OB), but its post-mitotic role in these neurons is unknown. As the nervous system is shaped and regulated by glutamate signaling and the appropriate response to neuronal activity is required for proper functioning of a healthy neuron, a key point of our study is to determine whether MITF determines activity-induced responses at the transcriptional level. Using the *Mitf*$^{mi\text{-}vga9}$ mutant, we have employed several methods including RNAScope, qPCR, ChIP, luciferase assays, immunofluorescence electrophysiology and behavior studies. We show an increase in the ability of distinguishing between odors in the *Mitf*$^{mi\text{-}vga9}$ mutant mouse, while its ability to detect odor remains the same. Additionally, we also observe a decrease in potassium channels sub-units using qPCR. Using ChIP-qPCR, we determined that the promoter of some of these potassium channel sub-units show a binding affinity for MITF. Interestingly, we also saw a decrease in A-current and an increase in neuronal activity in *Mitf*$^{mi\text{-}vga9}$ mutant, factors in which potassium channels play a role. We propose a model, where MITF regulates activity in the olfactory bulb, through the regulation of potassium channels in the mitral and tufted cells. Further studies are aimed at showing the the mechanism by which MITF regulates activity-dependent responses in the olfactory bulb and understand how this relates to the olfactory phenotype.

Pharmaceutial Sciences

Solubility of carbamazepine, CDs and their complexes

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Introduction: The ability of cyclodextrins (CDs) to form water-soluble complexes of poorly soluble drugs is well known and implemented in over 30 marketed drug products. Studies have shown that in solutions drug/CD complexes can precipitate at certain drug/CD ratio. The purpose of this present work is to investigate formation of aggregates of a sample drug (carbamazepine), and γCD and 2-hydroxypropyl-βCD (HPβCD).

Methods: One of the traditional approaches to estimate the mutual influence of components on their apparent solubility in drug/CD solutions is phase-solubility analysis. Also, drug permeation from aqueous solutions containing increasing concentrations of drug/CD complexes was performed.

Results: As expected HPβCD was able to solubilize carbamazepine. The phase-solubility plot gave a straight line or A_L-type profile. The results with the native γCD are more variable. The phase-solubility profile of γCD shows inflection point with negative deviation from linearity. Such behavior can be described by B_S-type profile. The same tendency was obtained from osmometry measurements.

The analysis of HPβCD flux shows that carbamazepine has insignificant effect on the HPβCD aggregation, but it affects the γCD aggregation process.

Conclusion: This is the first time that the solubility of both the drug and CD are monitored in aqueous complexation media. The sample drug had negligible effect on the HPβCD aggregation but notable effect on the γCD aggregation. Further studies will be done using Dynamic light scattering (DLS) to analyze the aggregates formed.

Effect of novel γ-cyclodextrin's derivatives on degradation of β-lactam antibiotics

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The aim was to find a cyclodextrin (CD) derivative that is able to protect β-lactam antibiotics from negative environmental factors such as catalytic degradation at physiological conditions and act as a carrier for β-lactams.

First the catalyzing effect of various CDs was investigated to reveal how CDs catalyze degradation of β-lactam antibiotics. Then effects of γ-cyclodextrin (γCD) and five γCD derivatives were evaluated. Observed first-order rate constants ($k_{obs)}$ for the β-lactam hydrolysis were determined through kinetic studies. All experiments were performed in aqueous PBS buffer solutions at pH 7.4 containing 0.5% (w/v) CD equilibrated at 37.0±0.1°C in a water bath. The initial benzylpenicillin concentration was 2.46 mM. Reversed-phase high-performance liquid chromatographic (HPLC) method was used to determine the benzylpenicillin degradation rate by the remaining drug concentration measurements.

The k_{obs} for γCD, RMγCD and HPγCD is respectively 78, 42 and 19% larger than the observed first-order rate constant for the degradation of the free drug (k_f) under the same conditions. These two derivatives and native CD have catalyzing effect. However, the k_{obs} in the presence of three novel CDs are smaller than k_f. The k_{obs} are 7 and 15% smaller for CMγCD with DS= 5.9 and 8.5 respectively, 11% for TRIMEG and up to 53% smaller for ODMCMγCD.

The effect of CDs on the degradation rate of β-lactam greatly depends of their structure. Substitution of hydroxyl groups of native γCD and its degree (DS) by another group reduces the catalytic effect and can even lead to protection of the β-lactam drug.

Effect of native and hydroxypropyl-derivatives cyclodextrins on parabens water solubility

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Purpose: The purpose of current work is to find any regularity in solubilization effect of native CDs and their hydroxypropyl-derivatives (HP-CDs) on homologous series of parabens (i.e. methyl-, ethyl, propyl- and butylparaben).

Methods: Estimation of mutual influence of components on their apparent solubility was made by phase-solubility analysis, where CD solutions and excess of solid paraben were agitated at 25°C during 48 hours Then the liquid phase was filtrated and analyzed by means of osmometry and CAD-UHPLC. Bottom phases were separated from solutions analyzed by DSC 214 Polyma (Netzsch) and melting point instrument B-540 (BÜCHI).

Results: As expected the apparent solubility of parabens increases with increasing of HP CDs concentration regardless of size of CD central cavity (A_L-type profiles).

The results with the native CDs are more variable. For propyl- and butylparaben even small amount of γCD will cause depression of the parabens' solubility displaying typical B_I – profiles. Other phase-solubility profiles (except for EtPar/α-CD and BuPar/β-CD) have inflection points with negative deviation from linearity. Such behavior can be described by A_N- and B_S-type profiles. DSC thermograms showed gradual decreasing of paraben's peak with increasing CD concentration up to complete disappearing of peak at the highest CD concentration.

Conclusions: The calculated stability constants for the paraben/CD complexes indicates that CD binding of parabens increases with increasing size of the paraben alkyl side chain as well as with increasing diameter of the central cavity (α- < β- < γ-). HP-CDs increased binding will cause increased of solubilization efficiency (positive effect) but for native CDs it will enhance negative effect.

Quantification of urinary 2,8-dihydroxyadenine by UPLC-MS/MS for clinical diagnosis and management of adenine phosphoribosyltransferase deficiency

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Adenine phosphoribosyltransferase deficiency (APRTd) results in excessive urinary excretion of poorly soluble 2,8-dihydroxyadenine (DHA), causing nephrolithiasis and chronic kidney disease. Treatment with allopurinol or febuxostat effectively reduces DHA excretion and prevents stone formation and progressive kidney disease. Thus, early diagnosis and commencement of pharmacotherapy is important. Although the characteristic round and brown urinary DHA crystals can be detected by urine microscopy, they are frequently missed or misidentified. Several cases of misidentification of DHA in kidney stone specimens have been observed with currently used techniques. Therefore, a reliable method for the diagnosis as well as therapeutic monitoring of patients with APRT deficiency is needed.

The aim of this study was to develop and optimize an ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) assay for absolute quantification of DHA in urine samples from patients with APRT deficiency. Optimization of the UPLC–MS/MS assay was performed using the chemometric approach - Design of Experiments (DoE), which offers a systematic way of varying experimental parameters that may affect the optimal setting of the method. By using a chemometric approach only a fraction of the number of experiments that would be used when changing one factor at a time (COST), is required.

Optimization of the UPLC-MS/MS quantification method was successful and future steps will be to validate the assay according to the Clinical and Laboratory Standard Institute (CLSI) guidelines. The validated UPLC-MS/MS assay will be implemented for clinical diagnosis and management of APRT deficiency.

Physical therapy and health of the elderly population

Postural control, vestibular function and plantar pressure sensation among people with fall-related wrist fractures: a case control study

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Introduction: Fall-related fractures rise significantly with increasing age. Wrist fractures may be a precursor to the more serious hip fractures. The associations of postural control, vestibular function and plantar pressure sensation with wrist fractures are not clear. The purpose of this study was to investigate whether individuals with fall-related wrist fractures have poorer postural control, vestibular function and plantar pressure sensation compared to matched controls.

Methods: A case controlled study consisting of 98 subjects aged 50-75 years having sustained a fall-related wrist fracture. Fifty healthy individuals without previous history of fall-related wrist fractures, matched according to age, gender and weekly physical activity level during the previous 12 months served as controls. Measurements included the Head-Shake test-(HST) to screen for vestibular dysfunction, Semmes-Weinstein monofilaments-(MF) to record plantar pressure sensation and the Sensory Organization Test-(SOT) for assessment of postural control.

Results: The number of fast eye beats on HST was significantly higher among subjects than controls ($p=0.037$) indicating higher incidence of vestibular dysfunction. Plantar pressure sensation was significantly poorer ($p<0.001$) among the subjects compared to controls. The SOT composite scores were lower among subjects indicating worse balance ($p < 0.001$).

Conclusions: People with fall-related wrist fractures have poorer standing and dynamic postural control, evidence of more common vestibular dysfunction and reduced pressure sensation on the soles of their feet compared to individuals with-out fall-related wrist fractures. Balance and vestibular dysfunction as well as reduced pressure sensation on the soles of the feet could be an underlying cause of fall-related wrist fractures.

Improved care at home for older people with dementia: A research plan

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Doctoral committee: Marit Kirkevold, Christine Cece, Jón Snædal, Pálmi V. Jónsson

Institutions: Margrét Guðnadóttir, PhD student at the Faculty of Nursing at University of Iceland.

Kristin Bjornsdottir, Professor at the Faculty of Nursing at University of Iceland supervises this study,

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Pálmi V. Jónsson, Professor in Geriatric Medicine at the University of Iceland and Chief of Geriatric Medicine at Landspitali University Hospital.

Abstract: Dementia will become a key public health issue in the years to come, particularly among nations where demographic aging is prominent. Results have highlighted health and financial burden placed on people with dementia and their caregivers. It is important to take action to improve the lives of people with dementia. Future research should focus on the everyday care practices families employ, including the actual physical, technological and institutional elements shaping the caregiving situations.

Aim: To enhance our knowledge and understanding of what kind of services and support individuals with dementia and their family members find helpful. Findings will be used to develop and improve community-based home care services. The study is part of an international research program, comparing the care of older people with dementia living at home.

Methods: Mixed-methods approach with ethnography, epidemiological analysis and action research. The ethnographic study aims at generating knowledge of the complexities of everyday care practices, focusing on arrangements, resources mobilised, and access to formal assistance that makes everyday life as good as possible. Data collection involves follow up on at least 10 families with an older individual living at home with dementia, organised as case studies. Each family will be visited regularly for one year. The epidemiological part of the study involves analysis of data generated using the RAI-HC instrument, analysing the health, ability, daily living and assistance provided to people with dementia living at home. The translation of knowledge into practice will employ a participatory approach (action research).

What characterize hip fracture patients in AGES part of Icelandic heart association study?

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Introduction: Among the elderly insufficient serum 25(OH)D is a strong determinant of bone health and low serum 25(OH)D has been associated with increased risk of hip fractures. However, those with insufficient serum 25(OH)D status generally also have poor health. The aim of this study was to characterize health difference between hip fracture and non-fracture according serum 25(OH)D status.

Methods: 5764 participants from the Ages gene/Environment Susceptibility (AGES)-Reykjavik study (2002-2006). At recruitment participants went through detailed clinical examination. Baseline serum 25(OH)D status as grouped according to insufficiency (<30 nmol/L), sub-optimal (≥30-50 nmol/L), sufficient (>50 -75 nmol/L) and high (>75 nmol/L) status. Bone mineral density (BMD) and other variable was used as continues.

Results: Mean age of participants were 77y range (66 to 98y) and mean serum 25(OH)D was 53.3 nmol/L (SD 24.2). Over a mean follow-up of 7.2y there were 144 and 342 hip fractures among male and female, respectively. Among both male and female hip fracture baseline BMD was far below those of non-fracture and serum 25(OH)D status was unrelated to BMD. However, in the non-hip fracture group serum 25(OH)D was positively associated with both Trabecular and Cortical BMD. Time up and go was significant higher in non-hip fracture group both with male and female. Male had higher Charlsonscore in hip fracture group but with females was no different.

Conclusions: Persons with low 25(OH)D status are likely to have worse outcome in health.

The ability of the Resident Assessment Instrument (RAI) to screen oral health, and act as guide to oral care of nursing home residents

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Introduction: Oral diseases are major public health problems and cause suffering, pain, impairment of function and reduce quality of life. To reduce health inequalities in the society, notice should be given to the vulnerable groups that report the highest prevalence of oral diseases; children, elderly and the handicapped. Residents in nursing home (NH) have complicated health issues and are functionally dependent. Studies of this population show high prevalence of untreated oral diseases, increased risk of dental caries, xerostomia, oral candidiasis and periodontitis. Daily oral hygiene and oral care (OC) are cost effective means for reducing morbidity of oral diseases and their non-oral consequences. Studies report that formal caretakers prioritise other care than oral, lack of knowledge of oral diseases and willingness to provide the service.

Methods: The study deals with data from questionnaires collected from NH residents and health personnel's, to evaluate the residents OH quality of life and to study the OC practices of staff. With qualitative method data will be analysed from interviews with NH administrators to understand their experiences related OC in this setting. The aim of this part of the study is to assess the clinical oral health (OH) of NH residents with the OH survey from WHO, and compare the results with OH variables measured with the Resident Assessment Instrument (RAI) which is used on admission to NH in Iceland. The results will be used to evaluate the validity of RAI and its ability to suggest interventions and guide to oral care.

Results: On-going study.

Temporal Relationships Between Peaks of Knee Joint Moments Associated with ACL Injury - A Cross-Sectional Study

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Purpose: Anterior cruciate ligament (ACL) injuries occur within 100 ms of initial contact of change of direction movements. The injury is a multi planar event where the valgus moment is recognized as an important risk factor. However, it is not known if the timing and magnitude of the forces during the first 100 ms of a change of direction movement are consistent with the injury mechanism.

Methods: 129 soccer and handball athletes (9-12 year old) performed 20 repetitions of a change of direction movement with 46 reflective markers being recorded using Qualisys 8 cameras at 200 hz and two AMTI force plates.

Results: All events had detectable peaks within the first 100 ms in 95% or more of trials. The temporal relationship between the variables was flexible and a high degree of variability was seen. The magnitude of the forces varied from negligible to significant. In 0.3% of trials the forces were found to coincide at the same or similar time, mimicking the proposed multi-planar event of the dynamic valgus collapse.

Discussion: A multi-planar event involving high forces around the knee is rare but possible, confirming the possibility of a dynamic valgus collapse mechanism of ACL injury. The relationship between variables is highly variable. Risk factor studies may need to perform a sub-group analysis on injured groups to account for multiple possible risk factors.

Physiotherapists' Clinical Reasoning and Decision-Making Processes when Mobilizing Patients who are Critically Ill: A Qualitative Study

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Background: Although early mobilization is widely practiced intervention for patients who are critically ill, the clinical reasoning and decision-making process used by physiotherapists to maximize its effectiveness warrants elucidation.

Purpose: The aim of this study was to investigate factors guiding physiotherapists´ clinical reasoning and decision-making processes when initiating and progressing mobilization in patients who are critically ill?

Methods: In a two phased qualitative research design, 12 physiotherapists, working in Landspitali, were observed before, during, and after a mobilization session with one patient in the Intensive Care Unit (ICU), followed by a semi-structured interview. The data was analyzed with Conventional content analysis.

Results: Six categories (Patient; ICU-context; Physiotherapist; Transfer; FITT parameters (frequency, intensity, type and time); Expected outcome) and four encompassing factors (Safety and wellbeing; Continuous assessment and intervention intertwined; Individualized and response-driven intervention; Barriers and solutions) emerged as important in guiding participants' clinical reasoning when mobilizing their patients.

Conclusions: The categories and encompassing factors identified, influenced and guided participants in their clinical reasoning and decision-making when they initiated and progressed early mobilization in the ICU. The approach was goal-oriented and tailored to each patient's needs based on moment-to-moment evaluation of responses. Knowledge of such factors not only sheds light on processes typically used by physiotherapists in mobilizing patients who are critically-ill, but also helps inform how these processes can be taught to students. The categories and factors that emerged favoured a response-driven rather than a protocol-driven approach to mobilising patients who are critically ill.

Stress and chronic pain

Women, intimate partner violence and visits to the Emergency Department.

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Background: In a 2010 study the prevalence of intimate partner violence (IPV) in Iceland was estimated 22%. Of women visiting Landspitali Emergency Department (ED), 33% had a history of IPV. According to a 1997 study, 17% of women experiencing IPV sought assistance at Landspitali's ED. Physical injuries resulting from IPV were usually minor, located on upper body and head.

Aim: To assess prevalence and nature of IPV as it appears in ED data.

Method: Data on ED visits due to violence during 2005-2014 was collected via the Nomesco registration system for external causes of injury. Information was obtained on number of visits, diagnosis, place of occurrence, survivors and perpetrator's age as well as their relationship. The woman were 18 years or older when the violence occurred. The perpetrator was the woman's current or former husband/partner/lover.

Results: The number of ED visits due to violence was 12,650. Women were 3,655 (29%), with visits due to IPV 1,284, and 2.7% were admitted. The average age of women visiting the ED as a result of IPV was 34 years. Physical injuries were usually minor, located on the upper limbs, head, face, neck and chest. Of women's visits due to IPV, 14% had visited at least once before, for the same reason.

Conclusions: IPV was 35% of all violence towards women visiting the ED, and 14% were repeated visits. Injuries were mostly located on the head and upper body.

Stressful and traumatic life events and suicidality in a population-based study: Gender specific results

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Background: Stressful life events have been associated with increased risk of various psychiatric disorders. This population-based study investigated the association between history of stressful life events and suicidality in Iceland, by demographic factors.

Methods: Women attending a cancer screening program (N=742) were invited to participate, along with a random sample of men from the capital area in Iceland (N=898). Participants answered an anonymous web-based questionnaire including questions on previous stressful and traumatic life-events (Life Stressor Checklist, LSC-R) and lifetime suicidal thoughts, self-harm and suicide attempts. We used logistic regression to evaluate the association between lifetime stressful life events and suicidality.

Results: In total, 922/1398 (66%) completed the questionnaire. The overall prevalence of lifetime suicidality was higher for men than women (17% vs. 11%). After adjusting for sociodemographic factors, the association between having experienced stressful life events and suicidality (OR 1.82, 0 .82-3.67) was not statistically significant, however, gender specific analysis revealed an association for men (OR 4.12, 1.17-27.3), but not women (OR 0.91, 0.33-3.24). In addition, we found that traumatic events, interpersonal trauma, childhood trauma and sexual trauma were strongly associated with suicidality (respectively (OR 1.64, 1.76-2.34), (OR 3.94, 2.59-6.02), (OR 5.14, 3.38-6.66) and (OR 2.27, 1.21-4.12)), and stronger for men than women.

Conclusion: Findings of this study indicate that specific traumatic life events may be associated with suicidality, even more so for men than women. By being able to identify risk groups for suicidality, e.g. by history of such traumatic events, new venues for suicide prevention may open up.

Psychological recovery after intensive care stay: outcomes of a long-term quasi-experimental study of structured nurse-led follow-up

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Objectives: To compare psychological recovery of patients receiving structured nurse-led follow-up after discharge from intensive care versus usual care.

Design: Quasi-experimental study.

Setting: Single center, university hospital, mixed intensive care patients population.

Main outcome measures: Post-traumatic stress disorder, anxiety and depression measured three and four times over 12 months after intensive care discharge. Disturbing memory of the intensive care stay and psychological reaction related to that memory (that your life was in danger, threat to physical integrity, intense fear, helplessness, horror) at three months. Mixed effect model tested difference between the groups over time and linear regression predicted post-traumatic stress at three months.

Results: The intervention group had significantly more post-traumatic stress and anxiety than the control group over the 12 months. 27% of patients from both groups had severe post-traumatic stress. Patients with post-traumatic stress at three months had disturbing memories and psychological reactions related to that memory.

Conclusion: The structured nurse-led follow-up did not improve patients' measured outcomes of psychological recovery after intensive care. The high average of patients with severe post-traumatic stress is of concern. Greater emphasis needs to be placed on disturbing memories of the intensive care stay and psychological reactions in constructing intensive care nurse-led follow-up.

Person-centred approach to the participation of patients with chronic pain in health assessment, enhanced by the phenomenologically derived assessment tool Hermes: An ethnographic study in nursing rehabilitation

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Background: Person-centred care and patient participation are central ideals in rehabilitation, requiring the development of appropriate practices. The phenomenologically derived assessment tool, Hermes was developed in response to these requirements and has been applied in three rehabilitation centres in Iceland.

Aim: To explore in what ways the use of the Hermes provides possibilities for a person-centred approach to the participation of patients with chronic pain in nursing assessment in rehabilitation.

Method: Focused ethnography was employed, informed by the theoretical approaches of person-centred care and practice developmental theories. Participants were sixteen patients with chronic pain, seven nurses and five nursing assistants on a rehabilitation ward. Data were collected by participant observation, semi-structured interviews, and review of the recordings on Hermes and ward documents. Data were analysed through the method of Charmaz.

Results: The main themes that were constructed were: Entering the patients' world; goals and strengths explored; the disrupting impacts of chronic pain on daily life discussed; and the usefulness and challenges in the use of Hermes.

Conclusion: Hermes contributed to person-centred participation of patients with chronic pain in health assessment. Furthermore, several aspects of its phenomenological groundings were supported and, in some instances, a real transfusion of phenomenological philosophy into the assessment practices was evident. Yet, some challenges emerged in the use of Hermes that stand in need of improvement.

The Lived Experience of Patients in Chronic Pain of a Rehabilitation Programme‘s Effects on Well-being and Daily Activities

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Aims: To evaluate the lived experience of patients in chronic pain of a rehabilitation programme focused on chronic pain and the programme´s effects on their well-being and daily activities.

Methods: Participants are both male and female patients in chronic pain. They attended one of three rehabilitation centres: Reykjalundur, NLFÍ Hveragerði, and Kristnes. Qualitative interviews are used which are conducted before the admission and also at least three months after the programme‘s completion and analysed according to the 12 basic steps of the Vancouver School of doing phenomenology. Data collection began in May 2016 and is ongoing.

Results: First results from ten interviews with eight participants indicate *chronic pain’s extensive effects* on well-being and daily activities such as mobility and sleep. This resulted in anxiety, depression, worries, grief, exhaustion, uncertainty, and isolation. Some were expecting to get back to work after completing the programme, even though they assumed that most likely chronic pain would be part of their lives in the future. Most of the participants experienced *valuable support from their families*. Only two participants had already completed the program and felt that they had learned some *helpful strategies* to use in their *existential struggle* with chronic pain. They also described *professional atmosphere* at the rehabilitation centre where they had received *valuable information* and *helpful treatment from various health professionals*. In rehabilitation, they met other people in similar circumstances, which they found helpful.

Conclusions: The first results indicate chronic pain’s extensive effects on well-being and daily activities.

Posters

Age comes to PCI-Cardiac catheterizations of nonagenarians during nine years

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Purpose: To evaluate indications, outcomes and success of coronary angiographies (CA) and percutaneous coronary interventions (PCI) in nonagenarians.

Methods: Information regarding all CAs and PCIs performed in nonagenarians in Sweden during 2006-2014 were registered in a nationwide all comer's registry; Swedish Coronary Angiography and Angioplasty Registry. Descriptive statistics were used to describe various parameters.

Results: During the study period 1693 nonagenarians underwent a total of 1876 CA and/or PCI. The indications for index procedures were: ST-elevation myocardial infarction for 45.5%, non ST elevation acute coronary syndromes for 34.0%, stable angina for 4.7% and other indications were 15.8%. Of all the patients 62.1% had at least a 2 vessel disease. In 67.4% (1142) of cases the index CA was followed by ad hoc PCI. Stents were used in 87.5% of the procedures and drugs eluting stents in 32.2%. Procedural success was 89.8%. Any complications after ad hoc PCI occurred in 8.1% of cases, serious bleedings in 0.7% and neurological complications in 0.6%. After PCI the 30 days' mortality was 18.1%.

Conclusions: The success of PCI in this aged population is close to the success rate for younger individuals and the complication rate is acceptable. It is however likely that these nonagenarians are a selected population of healthier individuals than other in their age group. Their mortality rate will be compared to the mortality in the general population of nonagenarians and we will look for predictors of complications in the database.

Diagnostic accuracy of qEEG recordings and novel candidate CSF biomarkers in evaluation of Alzheimer‘s disease

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Although no cure is available for Alzheimer’s disease (AD), hope is future treatments could target the disease in its earliest stages, before irreversible brain damage has occurred. Importantly, the premise for successful treatment is an early diagnosis. The main goal of this project is to evaluate the diagnostic accuracy and validity of potential novel biomarkers in AD.

The biomarkers in question are of two types, the first based on quantitative electroencephalography (qEEG) recordings and the second on measurements in cerebrospinal fluid (CSF). The qEEG-Cholinergic index, developed by the Icelandic company Mentis Cura in 2014, is intended to measure the level of cholinergic activity in the brain. Among the proteins that will be measured in CSF are markers of inflammation (Chitinase-3-like protein 1, Chitotriosidase), markers of reactive astrocytes (Glial fibrillar acidic protein, S100 calcium-binding protein B) and markers of the cholinergic signaling system (Choline acetyltransferase, Acetylcholinesterase,Butyrylcholinesterase).

The diagnostic accuracy of each potential biomarker will be evaluated, both alone and in combination with others. The association between different markers will also be tested. For example, drugs used in the treatment of AD are mainly cholinesterase inhibitors and therefore the measurements of cholinergic activity (qEEG and CSF-derived) could be very suitable for monitoring disease progression and treatment response. To further test the validity of the qEEG-Cholinergic index, association between the index and CSF cholinergic markers (in vitro measurements) will be evaluated.

As of now, about 160 participants have been recruited, thereof 51 with CSF samples.The measurement of CSF proteins started in February 2017.

Speakers