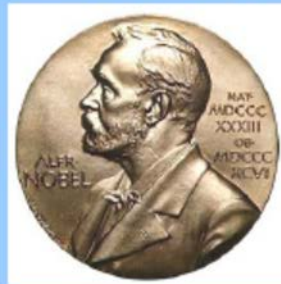


2014

# Book of Abstracts 2014



## Nobel Day Festivities 10<sup>th</sup> of December 2014



Traditionally, on 10<sup>th</sup> of December, the anniversary of Alfred Nobel's death, is awarded the Nobel Prize in Physiology or Medicine. School of Health and Medical Sciences shows attention to this day by organizing own research activities and festivities.

School of Health and Medical Sciences  
Örebro University  
10<sup>th</sup> of December 2014

**Program Committee:**

Professors; Nikolaos Venizelos, Allan Sirsjö, Olle Ljungqvist,  
Annica Kihlgren, Magnus Grenegård, Claes Möller, Berth Danemark  
Charli Eriksson, Christer Ericsson, Fawzi Kadi



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Book of abstracts, Nobel Day's Festivities 10<sup>th</sup> of December 2014  
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## **Preface**

The "**Nobel Day Festivities**" were established 2009 by Biomedicine, Department of Clinical Medicine, School of Health and Medical Sciences at Örebro University, and is organized traditionally every year in order to notice the anniversary of Alfred Nobel's death (10th of December) with scientific activities including poster presentations and selected oral presentations by doctoral students, which are documented in this "*Book of abstracts*". Nobel day's activities are open and scheduled so that all students and personnel can attend the scientific activities.

We warmly welcome you to enjoy all the good science that will be presented at Nobel Day.

### **The Organizers**

Nikolaos Venizelos, Professor em. (Chair)  
Allan Sirsjö, Professor (Biomedicine)  
Olle Ljungqvist, Professor (Surgery)  
Annica Kihlgren, Assoc. Professor (Care Sciences)  
Magnus Grenegård, Professor (Medicine)  
Claes Möller, Professor (Disability Science)  
Berth Danemark, Professor (Disability Science)  
Charli Eriksson, Professor (Public Health Sciences)  
Christer Ericsson Professor (Sport Sciences)  
Fawzi Kadi, Professor (Sport Sciences)

### Beliefs of what contributes to and counteracts Optimal Functionality from the perspective of older adults

**Samal Algilani<sup>1</sup>, Karin Blomberg<sup>1</sup>, Lina Östlund-Lagerström<sup>1,2</sup>, Annica Kihlgren<sup>1</sup>**

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<sup>2</sup>Nutrition Gut Brain Interactions Research Centre. School of Health and Medical Sciences, Örebro University, Örebro, Sweden

**Objective:** Exploring the concept of Optimal Functionality (OF), the first step was a literature review indicating that OF is a concept with a holistic approach based on three major themes; body-related factors, self-related factors and external factors; each major theme comprised three aspects. Each aspect contained several factors, all contributing or counteracting for experiencing OF (1). In the review of OF it was concluded that the majority of the articles had a quantitative approach and there were few articles with a qualitative design. Hence, the aim of this study was to further explore and develop the concept of Optimal Functionality from the perspective of older adults.

**Methods:** Focus group discussions (FGDs) were chosen as data collection method in order to expand and obtain as rich information as possible about the concept of OF. Six FGDs were conducted with three groups of older adults; senior orienteers who still exercise and compete, older adults in ordinary housing without assistance and older adults living in retirement-homes receiving assistance from nurse-assistants. Analysis is ongoing of the FGDs by deductive content analysis according to Elo & Kyngäs.

**Preliminary results:** Preliminary findings show new additions to the factors contributing and also counteracting experiences of OF. Contributing factors were relaxation, personal accomplishment and good social relations. Counteracting factors were shame and negative views of ageing among others.

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### Validity and test-retest reliability of the internet version of Children Hand-use Experience Questionnaire (CHEQ) for children with unilateral cerebral palsy

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**Objective:** To confirm validity of the internet version of Children Hand-use Experience Questionnaire (CHEQ) with 1-4 rating scale by testing i) the four-point rating scale and ii) the internal validity, and to investigate the test-retest reliability.

**Methods:** Data was collected for 242 children with unilateral CP from six countries (age mean= 9y, 10m, SD= 3y, 5m). For 20 children from study sample were included in retest with 7-14 days period. Validity tested by Rasch analysis using WINSTEPS 3.80 based on Rating scale model (1), each subscale was analyzed separately. Test-retest reliability was tested by Intraclass correlation (ICC).

**Results:** Average measures and step difficulties were in order and increased monotonically, and the distance between adjacent thresholds was within the recommended range. The CHEQ subscales showed good uni-dimensionality as the items' standardized residuals were distributed randomly in the first principal-component analysis of residuals. The test the reliability of the three subscales varied from 0.89 to 0.92, the separation between individuals was 2.91 to 3.44, and for 2,52-3.46 activities. INFIT MnSq and ZStd were acceptable for most activities. One activity did not fit and was therefore removed. Test-retest reliability was high for all three scales; ICC for efficiency in the hand grip / support was= 0.91, for the duration= 0.88 and for the feeling of discomfort= 0.91.

**Conclusion:** The 4-point scale indicated a good validity and CHEQ meets most of the criteria for a valid rating scale instrument. Test-retest reliability indicating that CHEQ is reliable and useful for children with unilateral CP.

#### References

1. Wright B, Mok M. *An Overview of the Family of Rasch Measurement Models*. In: Smith EV J, RM S, editors. *Introduction to Rasch Measurement*. Maple Grove, Minnesota: JAM Press; 2004.

### **Community Verbal Autopsy of Maternal and Neonatal Deaths in Bangladesh: Experiences and Lesson Learnt**

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<sup>1</sup>Department of Public Health Science, School of Health and Medical Sciences, Örebro University, Örebro, Sweden

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*\*Presenting Author*

**Objectives:** To know the process of community verbal autopsy of maternal and neonatal deaths and explore the lesson learnt and challenges in conduction at the community level.

**Methods:** A document review was done to know the process of development of instruments, guideline and conduction of VA. Qualitative information collected though focus group discussions, in-depth interviews and observation of 100 maternal and neonatal VAs during 2010-2012 in four districts of Bangladesh.

**Results:** The VA tool developed though an adaptation of different national and international tools, a number of technical and professional expert groups meeting organized to finalize the process considering country context. Health Inspector, Assistant Health Inspector or Family planning inspector were responsible to conduct the death review after a death notified though MPDR system. The community people accepted, welcomed VA and provided information. The autopsy explored social barriers; factors related to death and also find out signs and symptoms which helped to assign causes. However, the autopsy is required to perform within 21days of a death event otherwise many information may lost due to recall errors.

**Conclusions:** Verbal autopsy of maternal and neonatal deaths is possible and useful to perform in the community. It indentifies social and medical causes of death in a non-blaming approach. The people are ready to provide information to the government health staff and findings are guide the local health mangers and planners to take appropriate action plan at the district to improve maternal and newborn health services in Bangladesh.

### Facility death review of Maternal and Neonatal Deaths in the district and upazila health facilities: Experiences and Lesson Learnt

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*\*Presenting Author*

**Objectives:** To know the process of Facility Death Review (FDR) in maternal and newborn deaths and explore the lesson learnt and challenges in conduction at the district and upazila health facilities in Bangladesh.

**Methods:** Process documentation of development FDR was reviewed. Qualitative information collected though focus group discussions, in-depth interviews and observation of 50 maternal and 100 neonatal FDRs during 2010-2012 in four districts of Bangladesh.

**Results:** The FDR tool developed though an adaptation of different national and international tools, a number of technical and professional expert groups meeting organized to finalize the process. Senior Staff nurses at the district facilities were responsible to conduct death review after a death notified. Nurses were collected death related information from the patient's record and recall, specially other health care providers who delivered services during the patient's illness or before death. Doctors were also provided their support in cause assignment of death in FDR. However, during the conduction of FDR, facilities found scarcity of patient's record and due to high admission rate of patient irrespective of bed numbers at the district; quality of services faced challenges.

**Conclusions:** Facility death review of maternal and neonatal deaths is possible and useful to perform in district facilities. It identifies not only the medical causes of deaths but also explore gaps and challenges in the facility to recover. The findings of FDR helpful to the local health mangers and planners to take appropriate action plan to improve quality of services at the district facilities in Bangladesh.

### Preventing maternal and newborn deaths in Bangladesh: Experiences from Maternal and Neonatal Death Review (MNDR) system

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\**Presenting Author*

**Objective:** The objective of the study is to explore why mothers and neonates are still dying in the rural community of Bangladesh.

**Methods:** Under the Maternal and Neonatal Death review (MNDR) system of joint GoB- UN Maternal Newborn Health (MNH) Initiatives in Bangladesh [1], we have reviewed purposively selected 100 verbal autopsies of maternal and neonatal deaths and performed case studies of each those deaths.

**Results:** We have found that mothers had received antenatal care but in majority of the cases who died deliveries were performed at home by the traditional birth attendant (TBA) and relatives. Families made delayed in decisions making, waited until the TBA tried to deliver and manage the post-delivery complications. Transport facilities still one of the key factor for hard to reach areas, we have found a number of mothers died in the road or in boat.

In addition, in neonatal death cases, most of the neonate died within first six hours. However, the family members practiced to bring their newborn to nearby village doctors or traditional healers for treatment during critical situations.

We have also explored that the rural community have a number of misperception within the families, lack of knowledge on birth planning and understanding on maternal complications and neonatal danger signs which triggered death process.

**Conclusions:** Delivery conducted by the untrained people and followed by delays in the community are the foremost barriers in the rural community which requires urgent remedial actions which could avert a number of maternal and neonatal deaths in Bangladesh.

#### References:

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### Stress resilience and physical fitness in adolescence and risk of coronary heart disease in middle age

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**Objective:** Exposure to psychosocial stress has been identified as a possible risk factor for coronary heart disease (CHD). The relationship of stress resilience in adolescence with subsequent risk of CHD is less investigated. Our objective was to assess this and the possible mediating role of physical fitness.

**Methods:** In this register-based cohort study, 237 980 males born between 1952 and 1956 were followed from 1987 to 2010 using information from Swedish registers. Stress resilience was measured at a compulsory military conscription examination using a semi-structured interview with a psychologist, and physical fitness was assessed using an ergometric cycle test. Some 10 581 diagnoses of CHD were identified. Cox regression estimated the association of stress resilience with CHD, with adjustment for established cardiovascular risk factors.

**Results:** Low stress resilience was associated with increased risk of CHD. The association remained after adjusting for physical fitness and other potential confounding and mediating factors across the life-course, with fully adjusted hazard ratios (and 95% confidence intervals) of 1.17 (1.10 to 1.25). CHD incidence rates per 1000 person-years (and 95% confidence intervals) for low, medium and high stress resilience were 1.59 (1.53 to 1.67), 1.97 (1.92 to 2.03) and 2.61(2.52 to 2.70) respectively. Higher physical fitness was inversely associated with CHD risk, however this association was attenuated by low stress resilience, as shown by stratification and interaction testing ( $p < 0.001$ ).

**Conclusions:** The association between low stress resilience in adolescence and CHD risk in middle age is likely explained in part by poorer physical fitness among those with low stress resilience. Low stress resilience appears to attenuate the benefits of physical fitness. These results provide new evidence of the role of stress resilience in determining risk of CHD and its interrelationship with physical fitness.

### Treatment of Hyperthyroidism in Sweden

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**Introduction:**The incidence of hyperthyroidism was found to be 27.1/100000 inhabitants(children included) /year in a prospective study 2003-2005 in Sweden, including approximately 40% of the entire Swedish population of 9 million inhabitants. Sweden is considered iodine sufficient. Living Patients have been followed up by a Questionnaire and we have studied treatment, cure, complications and quality of life.

**Methods:**2915 Patients of all ages, who were diagnosed with overt hyperthyroidism in the years 2003-2005, were prospectively registered in a multicenter study(cities; Malmö, Karlskrona, Göteborg, Örebro, Eskilstuna/Katrineholm, Stockholm and Uppsala) organized by the "Swedish Thyroid Study Group (Vetenskapsrådets Planeringsgrupp för Tyreoideasjukdomar). For each patient-the diagnosis (Graves' disease(GD), toxic multinodular goiter(TMG) and solitary toxic adenoma(STA)), smoking, initial treatment, occurrence of Thyroid Associated Ophthalmopathy(TAO) and demographic data were registered. The participating clinicians were specialists in medicine, endocrinology, oncology, nuclear medicine or surgery and all shared interest in thyroid diseases. 2451 living patients have been asked to participate in a follow up study. 1442(58%) patients are included in this study.

**Results:**24% have had medical treatment, without radioiodine or Surgery 47% have been treated with radioiodine 25% have been operated 4% have been treated with both radioiodine and surgery

**Conclusion:**24% of the patients in this material are cured with medical treatment. 47 % have been treated with radioiodine. 25% of the patients have been operated and 4% have had a combination of all treatment options. There are geographical differences both according incidence and treatment between the different hospitals. Further evaluation of this patient material is ongoing.

### **Presentation of the Lifestyle, Biomarkers and Atherosclerosis study (LBA study)**

**Ulrika Fernberg<sup>1</sup>, Maria Fernström<sup>1</sup>, Gabriella Eliason<sup>1</sup>, Madelene Johansson<sup>1</sup>, Liza Ljungberg<sup>1</sup>, Knut Fälkner<sup>1</sup>, Magnus Grenegård<sup>2</sup>, Allan Sirsjö<sup>1</sup>, Anita Hurtig-Wennlöf<sup>1</sup>**

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### Dental fear among children and adolescents in a multicultural population – a cross-sectional study

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**Objective:** The aim of this study was to explore dental fear (DF) in a multicultural population of child and adolescent dental patients, with background, gender, age, and socioeconomic status (SES) taken into account. A specific aim was to investigate whether the level of DF differed between patients with a Swedish background and patients with a non-Swedish background.

**Methods:** In conjunction with a routine visit to the dental clinic, 301 patients (8–19 years old) assessed their DF on the Children’s Fear Survey Schedule – Dental Subscale, using self-ratings. Following an interview protocol, patients’ and their parents’ country of birth, and parents’ education and occupation/employment were registered. An interpreter was present when needed.

**Results:** Self-rated DF was almost equal among patients coming from a non-Swedish background and patients with a Swedish background. Girls scored higher than boys and younger children scored slightly higher compared to older children, but the pattern of DF variation was inconsistent. Socioeconomic status differed between the groups with a non-Swedish vs. a Swedish background, but no impact of SES on DF was revealed. When children and adolescents with a non-Swedish vs. a Swedish background were modeled separately, female gender and younger age had an impact on DF only in the group with a Swedish background.

**Conclusions:** No differences in DF were found between children and adolescents from different cultural backgrounds (non-Swedish vs. Swedish). Dental fear variations according to gender and age were more pronounced in the group with a Swedish background compared to the group with a non-Swedish background. No impact of SES could be revealed.

\* *This paper is submitted in Acta Odontol Scand.*

## Specific non-digestible polysaccharides attenuate mast cell induced hyperpermeability in colonic biopsies mounted in Ussing chambers

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**Objective:** It is widely known that diseases such as inflammatory bowel disease and celiac disease are associated with a leaky gut, highlighting the importance of a healthy barrier function. Prebiotic substances such as non-digestible polysaccharides (NPS) have been shown to be able to improve immune function but their effect on the barrier function remains unknown. Our aim is to investigate the efficacy of specific NPS to counteract barrier disruption mediated through mast cell degranulation in colonic biopsies.

**Method:** The effect of NPS on intestinal hyperpermeability was investigated in colonic biopsies obtained from healthy volunteers. Twelve colonic biopsies per participant were mounted in Ussing chambers. The biopsies were pre-treated with NPS, either 0.5 mg/ml  $\beta$ -glucan derived from yeast or 0.1 mg/ml Arabinoxylan derived from wheat for 20 minutes prior to addition of the mast cell degranulating compound 48/80 (5 ng/ml). All substances were present throughout the whole experiment (90 min). Non-treated biopsies were used as control. FITC-dextran 4000 was used to measure paracellular permeability while horseradish peroxidase (HRP) was used as a transcellular marker.

**Results:** Intervention with C48/80 showed a trend of 2-3 times higher paracellular permeability compared to controls while pre-treatment with both 0.5 mg/ml  $\beta$ -glucan (N=2) and 0.1 mg/ml Arabinoxylan (N=6) resulted in a significant reduction ( $p=0.0087$  and  $p=0.0186$  respectively) of C48/80's effect on paracellular permeability. A similar pattern can be seen on transcellular permeability, although not significant.

**Conclusion:** Our results demonstrate that both  $\beta$ -glucan (0.5 mg/ml) and Arabinoxylan (0.1 mg/ml) can reduce C48/80 induced hyperpermeability. The results suggest that both NPS exerts part of their effect by possibly inhibiting mast cell degranulation.

### The role of IL-37 on cytokine responses downstream of TLR4 and TLR5 signaling in intestinal epithelial cells

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Microscopic colitis (MC), comprising collagenous colitis (CC) and lymphocytic colitis (LC), is characterized clinically by chronic watery diarrhea, abdominal pain, and weight loss. IL-37 (IL-1F7) is a newly described anti-inflammatory cytokine of the IL-1 family. Previously, reduced gene expression of IL-37 has been observed by our group in the colonic mucosa of MC patients, which was suggested as one of the reasons for the chronicity of the colonic inflammation. We here investigated the role of IL-37 on pro-inflammatory cytokine responses mediated by TLR4 or TLR5 signaling pathways in the Caco-2 cell line upon stimulation with LPS or flagellin following silencing of IL-37 with siRNA. Gene and protein expressions of IL-37, CXCL8, IL-1 $\beta$ , TNF, CXCL11 and CCL20 were detected using qRT-PCR and ELISA. IL-37 protein levels were significantly increased upon both LPS and flagellin stimulations. IL-37 silenced Caco-2 cells had significantly increased CXCL8, TNF and CCL20, but not IL-1 $\beta$  gene expressions upon flagellin stimulation, whereas LPS stimulation led to up regulation of CXCL8, TNF and IL-1 $\beta$  but not CXCL11 gene expressions compared to cells without siRNA transfections. Both flagellin and LPS stimulation of IL-37 silenced Caco-2 cells resulted in significantly increased CXCL8 protein levels. Altogether, this study confirmed the regulatory role of IL-37 on pro-inflammatory cytokine production following TLR4 or TLR5 stimulation, corroborating the importance of reduced IL-37 in MC patients as one of the important immunopathological factors.



### Oxytocin in serotonergic (SRI) treatment of obsessive-compulsive disorder (OCD) – Clinical response and sexual side-effects in a placebo controlled study

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**Objective:** A correlation between oxytocin levels and severity of OCD has been shown previously<sup>1</sup>. Since oxytocin and serotonin are interconnected within the brain, the effect of serotonin reuptake inhibitors (SRIs) against OCD may be exerted by interaction with oxytocinergic neurotransmission. Furthermore, decreased oxytocin has been hypothesized (based on animal studies) to mediate sexual side-effects induced by SRIs<sup>2</sup>. Here, we explored in the first human study whether oxytocin contribute to the anti-obsessive and sexual effects of SRIs.

**Methods:** In a randomized double-blind trial, comparing the anti-obsessive effect of paroxetine, clomipramine and placebo, blood samples for plasma oxytocin were taken from 36 adult patients at three time points: at baseline, after 1 and after 4 weeks' treatment. This was related to baseline OCD severity, anti-obsessive response after 12 weeks (measured by the Y-BOCS scale), and with sexual functions (rated with an ad-hoc scale).

**Results:** Baseline oxytocin correlated positively with baseline Y-BOCS ratings, replicating the previous study. An intriguing temporal pattern of oxytocin changes emerged, which was closely related to clinical response, but not to drug-placebo condition. After 4 weeks, responders had higher oxytocin levels than non-responders. Oxytocinergic reactivity (range between measurements) was higher in responders and lower in patients with autistic traits. Increase of oxytocin was associated with delayed orgasm, contrary to the hypothesis of other researchers.

**Conclusions:** Oxytocin is involved in OCD pathophysiology and SRIs contribute to oxytocinergic changes, which are involved in the clinical response of patients with OCD. It is unlikely that SRI-induced sexual side-effects could be counteracted by oxytocin treatment.

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### ***Neisseria meningitidis* activates NLRP3 inflammasome in human neutrophils.**

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**Objective:** Lipooligosaccharide (LOS) of *Neisseria meningitidis* is an endotoxin that is responsible for activation of immune cells and the release of proinflammatory cytokines. The NLRP3 inflammasome is an intracellular multi-protein complex that triggers caspase-1 mediated maturation of interleukin-1 $\beta$  (IL-1 $\beta$ ); one of the most potent mediators of inflammation and a major cytokine produced during infections. The NLRP3 inflammasome is activated by a number of microbial factors as well as danger molecules, but there are no data available regarding a role for inflammasome activation in meningococcal disease. The aim of this study was to investigate if *N. meningitidis* activates the inflammasome, and if so, the role of LOS in this activation.

**Methods:** Whole blood from healthy blood donors (n=5) was stimulated with LOS-deficient *N. meningitidis* FAM20 serogroup C *lpxA* mutant and wild-type FAM20 serogroup C for 2h. Caspase-1 activity of neutrophils was measured. Neutrophils were isolated from blood donors (n=5) and stimulated with *lpxA* mutants and wild-type FAM20 for 2h. Relative mRNA levels of NLRP3, pro-caspase-1 and proIL-1 $\beta$  were measured using RT-PCR.

**Results:** Caspase-1 activity was significantly increased ( $p= 0.001$ ) in neutrophils stimulated with wild-type FAM20 strain when compared with unstimulated neutrophils or stimulated with the *lpxA* mutant. Similarly, significant ( $p= 0.001$ ) increase in mRNA levels of NLRP3, pro-caspase-1 and pro-IL-1 $\beta$  was detected in neutrophils stimulated with wild-type FAM20, whereas non-significant increase was observed in neutrophils stimulated with the *lpxA* mutant.

**Conclusion:** LOS of *N. meningitidis* plays a major role in the up-regulation and activation of the NLRP3 inflammasome in human neutrophils.

### Flow cytometric detection of circulating endothelial progenitor cells

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**Objective:** Endothelial progenitor cells (EPC) is a rare population of cells in the circulation with the ability to form mature endothelial cells. Number of circulating EPC correlates with endothelial function and a reduced number of circulating EPC has been suggested as a marker for emerging cardiovascular disease. The aim of the current project was to set up a method for detection of circulating EPC using flow cytometry. Cells expressing the surface markers CD34 and KDR were classified as EPC.

**Methods:** Venous blood was collected from healthy volunteers between 18 and 25 years of age. Peripheral blood mononuclear cells (PBMC) were isolated by density gradient centrifugation and labeled with a FITC conjugated antibody for detection of CD34 and a PE conjugated antibody for detection of KDR. Isotype antibodies were used as controls. Flow cytometric analysis was performed in a Beckman Coulter Cytomics FC500. For each sample, 500 000 events of PBMC were collected.

**Results:** EPC (CD34+/KDR+) were detected at a number of 4-57 (mean  $35.19 \pm 2.6$ ) per 500 000 PBMC (n=26). Number of cells expressing only CD34 ranged between 50-511 (mean  $153.7 \pm 20.0$ ) per 500 000 PBMC.

**Conclusion:** Using this flow cytometric method we are able to detect circulating endothelial progenitor cells in human PBMC.

### Right ventricular dimensions and volumes estimated with echocardiography and MRI – a comparative study

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**Objective:** Two common methods for evaluating the right ventricle (RV) function are echocardiography (US) and magnetic resonance imaging (MRI). Previous studies have shown that 3D US underestimates the RV volumes compared to MRI<sup>1</sup>. This is probably due to difficulties in outlining the endocardium when using US. The aim of this study was to find out if there are differences in distance measurement of the RV comparing US and MRI images. Some of the distance measures were chosen to fit the RV described as part of an ellipsoid model (EM).

**Methods:** Twelve healthy volunteers underwent an echocardiographic examination and a subsequent MRI examination within an hour. Six distances and one area were measured by two observers in the images from each modality. The distance measurements were then used to calculate RV stroke volumes (RVS<sub>V</sub>) using a model of the RV approximated by an ellipsoid. The ellipsoid RVS<sub>V</sub>, RVS<sub>V<sub>MRI EM</sub></sub> and RVS<sub>V<sub>US EM</sub></sub>, were then compared to the RVS<sub>V</sub> achieved by summation of MRI short-axis (SA) stack volumes, RVS<sub>V<sub>MRI SA</sub></sub>, which is gold standard. All measurements were compared using Student's paired t-test. P<0.05 was considered to be statistically significant.

**Results:** Five of the six distance measurements and the area measurement differed significantly at the inter-modality comparison; measurements by MRI were greater than by US. When using the distances for calculation of RVS<sub>V<sub>US EM</sub></sub> the volumes were underestimated compared to RVS<sub>V<sub>MRI SA</sub></sub> (RVS<sub>V<sub>MRI SA</sub></sub>= 110 ± 20 ml, RVS<sub>V<sub>US EM observer 1</sub></sub>= 65 ± 12 ml, RVS<sub>V<sub>US EM observer 2</sub></sub>= 61 ± 12 ml). RVS<sub>V<sub>MRI EM</sub></sub> showed better agreement with RVS<sub>V<sub>MRI SA</sub></sub> (RVS<sub>V<sub>MRI EM observer 1</sub></sub>= 96 ± 20 ml, RVS<sub>V<sub>MRI EM observer 2</sub></sub>= 84 ± 21 ml).

**Conclusions:** When using US and MRI images for distance measurements of the RV there are significant differences in the results; probably due to difficulties defining the endocardial borders in the US images because of trabeculations and poorer image quality. This issue may also affect the results when estimating RV volumes by 3D US, as well as when calculating ditto by 2D US, as compared to MRI.

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### Whole Genome Microarray of Bone Marrow Fibroblasts from Myeloproliferative Neoplasms Reveals Downregulation of Interferon Signaling and Immunity Pathways

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In primary myelofibrosis and in fibrotic stages of other myeloproliferative neoplasms (MPN), normal hematopoiesis in the bone marrow is gradually replaced by fibroblast-produced extracellular matrix. Recent gene expression profiling studies on whole blood have demonstrated that human leukocyte antigen (HLA) class I and II and related genes are downregulated in MPN. Because fibroblasts have immunomodulatory functions, the observed whole blood alterations in antigen presentation pathways may partly be caused by changes in gene expression of fibroblasts in the bone marrow stroma. The aim of this study was to explore if transcriptional deregulation of immunity pathways could be observed in bone marrow fibroblasts in MPN patients. Bone marrow stromal cells from 12 MPN patients and 8 healthy controls were expanded and cultured. Six patients had primary myelofibrosis, three had essential thrombocythemia, and three had polycythemia vera. Quantitative global gene expression microarray was performed on the fibroblasts, and results were compared between MPN patients and controls after standardization. A set of 277 genes with differential expression in MPN (fold change >1.5, *P*-value <0.1) was further analyzed by Ingenuity Pathway Analysis. In canonical pathway analysis, interferon (IFN) signaling, communication between innate and adaptive immune cells, and the antigen presentation pathway were the most significant pathways in MPN, and were all downregulated. The top upstream regulators were IFN- $\gamma$ , lipopolysaccharide, and IFNA2. These results suggest that immunosuppression and inhibited IFN signaling in bone marrow stromal cells may be important factors in MPN pathogenesis, similarly to what has been reported for tumor immune escape.

**Characterization of *Porphyromonas gingivalis* interaction with human neutrophils**

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### Study of possible antifibrotic effect of IL-1 $\alpha$ on TGF- $\beta$ stimulated dermal fibroblasts

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**Objective:** Wound healing with delayed re-epithelialization as often seen in burn wounds results in scar formation. Keratinocytes have been demonstrated to down regulate the synthesis of collagen and profibrotic factors by fibroblasts. We have identified interleukin-1 $\alpha$  as the mediator of connective tissue growth factor mRNA and protein suppression in human dermal fibroblasts by keratinocytes.

The aim of this study was to further elucidate possible anti-fibrotic effect of IL-1 $\alpha$  on TGF- $\beta$  stimulated dermal fibroblasts.

**Methods:** Dermal fibroblasts were seeded in 6-well plates, cells were serum starved for 24 h, stimulated with different concentrations of TGF- $\beta$  and/or IL-1. Gene expression analysed with Q-PCR. Three different fibroblast samples were picked out to run for microarray (control, TGF- $\beta$  stim, and TGF- $\beta$ / IL-1  $\alpha$ ). 50  $\mu$ g cRNA of each sample were hybridized to Agilent SurePrint G3 Human Gene Expression 8x60K v2 Microarray, washed and scanned in Agilent Microarray Scanner. Data were corrected and normalized in Software Collection R and analyzed in Ingenuity Pathway Analysis.

**Result:** Dermal fibroblast increased CTGF gene expression in Q-PCR by 20-fold with addition of TGF- $\beta$ . IL-1 $\alpha$  suppressed TGF- $\beta$  stimulated CTGF expression in a dose dependent way, to around 20 % of maximum. The results from microarray are being statistically evaluated and are going to be analysed with IPA to look for canonical pathways in dermal fibroblasts.

**Conclusion:** We have further investigated interleukin-1 $\alpha$  inhibitory effect on TGF-beta stimulated CTGF expression. We hope that the results from microarray will generate more information, to the understanding of keratinocyte-fibroblasts interplay.

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## Effectiveness of Bivalent HPV vaccines in preventing cervical cancer-causing High-risk Human Papillomaviruses (HR-HPV) in rural African young girls

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**Objective:** To determine the effectiveness of bivalent HPV vaccine in prevention of HR-HPV infections among Ugandan girls.

**Methods:** This was a 5 years bivalent HPV 16/18 vaccine follow up study in Uganda. Cervical swabs were collected and analyzed with a HPV genotyping test, CLART<sup>®</sup> HPV2 (Genomica) which is based on consensus PCR followed by microarray for determination of genotype.

**Results:** The age range of the 393 participants which comprised of 50.4% vaccinated girls was 15-24 years and mean age was 18.57 (SD 1.39). In total, the prevalence of any HPV and that of any HR-HPV infections were 33.3% (95% CI 28.6 – 38.0) and 22.3% (95% CI 18.2 – 26.4) respectively. High-risk-HPV infections were significantly more prevalent among non-vaccinated girls than vaccinated girls (54% vs 46%,  $X^2$  5.033,  $p$  0.025, OR 1.723, 95% CI 1.068-2.781). The difference was more pronounced if HPV 16/18 only were compared (the genotypes which are the antigens in the vaccine) (90.9% vs 9.1%,  $X^2$  7.814,  $p$  0.005, OR 10.76, 95% CI 1.364-84.887). For other HR-HPV, moderate-risk-HPV and low-risk-HPV genotypes, there were no significant differences between non-vaccinated and vaccinated girls regarding their prevalence. No differences were observed in multiple HR-HPV infection rates either. The risk factors associated with HR-HPV infections among the vaccinated girls were not different from that among the non-vaccinated girls with exception of obesity and condom use.

**Conclusion:** This is the first follow up study of HPV vaccination in young girls in Africa. Our data concurs with the existing literature from other parts of the world regarding the effectiveness of bivalent HPV 16/18 vaccines in preventing HR-HPV 16/18 infections. We did not find any evidence in support of neither the theory of cross protection against other HR-HPV 16-related and HPV 18-related genotypes nor HPV type replacement after bivalent HPV vaccinations in Uganda. The role of obesity and or co-administration of nutritional interventions with HPV vaccination for adolescent girls in Africa need further research.

## A gene expression analysis of fibroblasts from patients with bipolar disorders

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**Introduction:** Bipolar Disorder is a severe, lifelong psychiatric disease characterized by abnormally elevated mood (mania) that cycle with abnormally low mood (depression). Studying such diseases with gene expression microarray experiments we emphasize on broad, biological themes, rather than on specific genes. In this direction comparative transcriptomic profiling to characterize skin fibroblasts gene expression of bipolar disorder patients compared to healthy controls has been performed.

**Methods:** Skin fibroblast cells from bipolar disorder patients (n=10) and healthy controls (n=5) have been cultured. RNA was extracted and then hybridized onto Illumina Human HT-12 v4 Expression BeadChips.

Differentially expressed genes between disease and control groups were identified by performing t-test. Fold change values were calculated for each gene. The resulting gene list was obtained by setting the p-value threshold to 0.05 and by removing genes that presented a fold change below |0.5| (in log<sub>2</sub> scale). A subset of the differentially expressed transcripts that occurred was validated by quantitative real-time PCR. In order to derive better insight into the biological processes related to the DE genes, the lists of significant genes were subjected to pathway analysis.

**Results:** We concluded to 135 overexpressed and 338 down regulated genes. The pathway analysis of the differentially expressed genes indicated pathways related with regulation of G-protein signalling pathway, phospholipid metabolism, and tyrosine and tryptophan metabolism.

**Conclusion:** Such studies characterizing pathways in fibroblasts and other non-neural cell types from bipolar disorder patients can elucidate the molecular mechanisms associated with the pathophysiology of bipolar disorder.

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## The Prevalence of lithium-associated hyperparathyroidism (LHPT) in a large Swedish population attending psychiatric out-patient units.

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**Objective:** This retrospective study determines the prevalence of lithium-associated hyperparathyroidism (LHPT) in two geographically defined, equivalent populations in Sweden, with no other selection bias. Our study included a particular focus on those few patients operated for LHPT.

**Methods:** The medical journals of all patients receiving lithium treatment were examined specifically regarding their biochemistry- calcium, parathyroid hormone (PTH), creatinine and vitamin D (25(OH)D). The condition LHPT was defined biochemically. All patient data were noted and the prevalence of the condition could thereby be calculated.

**Results:** 423 patients were included (251 ♀/172 ♂; 3:2), treated on average 13.5years (range 1-46), aged 19-92. 76 patients (18%) were identified with lithium-associated hyperparathyroidism whose median serum Calcium=2.55mmol/l and PTH=99 ng/l. A further 21% showed tendencies towards hypercalcaemia. 43% had Vitamin-D insufficiency. Only five female patients (≈1%) had undergone parathyroidectomy; age at operation ranged from 65-83yrs where the apparent surgical indication was hypercalcaemia. Pre-operative Calcium ranged from 2.66-2.92mmol/l and PTH 106-287ng/l. All but one became normocalcaemic at follow-up.

**Conclusion:** The prevalence of lithium-induced hyperparathyroidism is high and goes often undetected. Vitamin-D insufficiency is common as is polypharmacy. Surgery, for unclear reasons, has not been performed extensively, possibly because of limited knowledge of underlying pathophysiology or surgery's significance. We present standard recommendations on patient management and suggest continual, specific follow-up. Surgery should be considered with intention to improve psychiatric well-being and provide multi-organic protection. There is a clear need for a structured evaluation of the optimal surgical strategy for LHPT, preferably with a randomised study.

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### Decreased stress resilience in young men significantly increases the risk of subsequent peptic ulcer disease - a prospective study of 233 093 men in Sweden

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**Objective:** Recent studies suggest that psychosocial stress may influence the risk of peptic ulcer disease, but have not always been able to identify reliably whether stressful exposures pre-dated disease. There may be significant variation in stress resilience and thus susceptibility; and the association of stress resilience with subsequent peptic ulcer disease risk has been incompletely investigated. We assessed if stress resilience in adolescence is associated with subsequent peptic ulcer disease risk.

**Methods:** The participants comprised 233,093 men resident in Sweden, who were born between 1952-1956 and assessed for compulsory military conscription during 1969-1976, with data provided by national Swedish registers. Stress resilience was evaluated through semi-structured interviews conducted by a certified psychologist. Cox regression was used to evaluate the association between stress resilience in adolescence and the risk of peptic ulcer disease from 1985-2009, between ages 28 and 57 years, with adjustment for parental socioeconomic index, household crowding and number of siblings in childhood, as well as cognitive function and erythrocyte sedimentation rate in adolescence.

**Results:** A total of 2,259 first peptic ulcer disease diagnoses were identified. Lower stress resilience in adolescence is associated with a higher risk of peptic ulcer disease in subsequent adulthood: compared with high resilience the adjusted hazard ratios (and 95% confidence intervals) are 1.84 (1.61-2.10) and 1.23 (1.09-1.38) for low and moderate stress resilience, respectively.

**Conclusion:** Stress may be implicated in the aetiology of peptic ulcer disease and low stress resilience is a marker of risk.

### Physical fitness in adolescence and subsequent risk of inflammatory bowel disease (IBD)

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**Objective:** Physical fitness may reduce systemic inflammation levels relevant to the risk of Crohn's disease (CD) and ulcerative colitis (UC). We assessed if physical fitness in adolescence is associated with subsequent IBD, independent of prodromal disease markers.

**Methods:** Swedish registers provided information on 239,964 men who underwent military conscription assessments in late adolescence (1969 – 1976) and who were followed up to 2009 (up to age 57 years). Information included: socioeconomic conditions in childhood; and physical fitness, height, BMI and erythrocyte sedimentation rate (ESR) - a marker of systemic inflammation from adolescence. Those with IBD in adolescence were excluded. Cox regression assessed the association of physical fitness with CD (n=1,084) and UC (1,952) in separate models, with adjustment for the other characteristics.

**Results:** Low physical fitness is associated with a raised risk of CD and UC after adjustment for socioeconomic factors, with hazard ratios (95% confidence intervals) of 1.66 (1.36-2.04) and 1.29 (1.11-1.50), respectively; attenuated by further adjustment for markers of prodromal disease to 1.35 (1.09-1.69) and 1.20 (1.02-1.41), respectively. Higher inflammation (ESR) in adolescence was associated with both subsequent CD (7.44 (5.74-9.64)) and UC (2.00 (1.53-2.61)).

**Conclusion:** The inverse association of physical fitness with IBD risk is consistent with a protective role for exercise. Evidence of disease activity prior to diagnosis was already present in adolescence (raised inflammatory markers, lower BMI and reduced height). Some, or even all, of the association between fitness and IBD may be due to prodromal disease activity reducing exercise capacity and therefore fitness.

## 3D-MR based HDR brachytherapy in Cervical Cancer "Logistics and Results" - Clinical Experience at Örebro University Hospital

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**Background and Objective:** In the Department of Oncology in Örebro, we have a long and successful tradition in Brachytherapy (BT). Prior data regarding treatment of cervical cancer are published in International Journal of Oncology 2010 and in International Journal of Gynecological Cancer in 2014. In 2007 we introduced 3D-MR based HDR brachytherapy in treatment of locally advanced cervical cancer. The Interstitial Ring Applicator with a tandem is the state of art for treatment with combined intracavitary (IC) and interstitial (IS) brachytherapy. MR based optimized brachytherapy gives a significant increase in target volume coverage of extensive cervical tumors and a sparing of organs at risk using this technique.

**Methods:** A retrospective analysis was done of outcomes of patients with FIGO stage IB-IVA cervical cancer treated with primary radiation therapy with curative intent between 2007 and June 2013. Outcome measures were overall and disease-free survival, pelvic tumor control, distant metastases, and treatment related adverse events (AE).

**Results:** Today, in all 123 patients have been treated with 3D-Image-Guided Adaptive (IC/IS) BT. Ninety-four patients were analyzed. The total radiation dose was in mean 87.7 gray (Gy) and was combined with concurrent weekly chemotherapy (cisplatin) in 92% of the cases. The median follow-up time was 20 months. Primary tumor control was achieved in 97% of the Image-Guided Brachytherapy (IGBT) patients. Overall survival rate at 3 years was 58% and at 5 years 50%. Cancer-specific survival (CSS) at 3 years was 62% and at 5 years 53%. CSS was significantly ( $P < 0.01$ ) associated with D90 Brachytherapy High-Risk Clinical Target Volume (BT-HR-CTV), and also ( $P < 0.022$ ) with the D90 external beam dose + BT-HR-CTV. Pelvic recurrences were found in 2%. Eighty percent were alive more than 1 year after treatment, 18% were dead of cancer, and 2% of other diseases. Most patients had low-grade adverse events (AE). Adverse events of grade 2 occurred in 4% and AE grade 3 in 1%. Additional time in the treatment process to reach the MRI-equipment at the Department of Radiology was 17 minutes and the distance corresponded to 1 086 steps for the staff involved (Clinical feasibility; poster at ESTRO 27, 2008).

**Conclusions:** Introduction of IGBT in treatment of cervical cancer has led to significantly increased 3-year locoregional tumor control and survival rates, and reduced late morbidity. Thus, our preliminary evaluation of 3D-IGABT in Örebro showed favorable local treatment results with low and acceptable complication rate. Our prior data from before 2007 showed 11% grade3-4 AE. Combined IC/IS BT based on transvaginal ultrasonographic "preplanning" is also clinically feasible. We have shown that 3D-IGABT is clinically feasible, even when the MRI is at distance from the brachytherapy unit. Optimal applicator insertion, and a safe and consistent positioning is a precondition for the success of cervix cancer brachytherapy (BT).

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## Applications of mussel adhesive protein - development of a highly potential cell adhesive

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**Objective:** The sea mussel (*Mytilus edulis*) uses a unique mechanism to adhere to various wet and dry surfaces. One of the proteins, developed for this purpose, the mussel adhesive protein (MAP) or MEFP-1 (*Mytilus edulis* foot protein 1), was first isolated in the mid 1980's, and has been profoundly investigated. The unique properties of the protein make it potentially useful in a wide range of applications in medicine and biotechnology involving formation of adhesive bonds to tissues, cells or other molecules. In order to establish the use of MAP in healing of surgical traumas/wounds in humans, it is of great importance to study MAP as a tissue and cell adhesive. The purpose of this study was to analyze the performance of MAP as an adhesive *in vitro*, using hydrophobic plastic to which cells do not adhere readily, as a surface to test different coating strategies.

**Methods:** Immortalized human cell lines HaCaT and CHON-001 were cultured in culture flasks pre-coated with the cell adhesives; MAP, poly-D lysine, fibronectin and collagen, respectively. The effect of each adhesive on cell attachment, spreading and growth was determined and compared to cells grown on a MAP-coated surface or cultured on hydrophobic plastic without coating.

**Results:** Improved cell attachment, spreading and growth of both HaCaT and CHON-001, on hydrophobic plastic when MAP was used to coat the surface.

**Conclusions:** According to our results, the concept of developing MAP for clinical applications such as surgical procedures could be feasible.

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## Cardiac Troponin I, NT-proBNP and Galactin-3 are elevated in patients with Unrecognized Myocardial Infarction detected by cardiac magnetic resonance imaging

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**Objective:** To determine the association between levels of cardiac biomarkers and an unrecognized myocardial infarction (UMI) in patients with suspected stable coronary artery disease (CAD) with or without significant stenosis in the coronary artery supplying the infarcted area.

**Background:** UMIs are common and indicates similar future morbidity and mortality as clinically recognized myocardial infarctions.

**Methods:** A total of 234 patients (median age 65 years; 66 % men) with suspected stable CAD without previously known myocardial infarction (MI) were examined with late gadolinium enhancement magnetic resonance imaging and coronary angiography. For each patient with an UMI, the status of the coronary branch supplying the infarcted area was independently determined; a stenosis grade  $\geq 70$  % was regarded as significant. Blood samples were drawn at enrolment and high sensitivity cardiac troponin I (hs-cTnI) (Abbot), NT-proBNP (Roche) and Galectin-3 (bioMérieux) were analyzed.

**Results:** UMI was detected in 58 of the 234 patients (24.8%), 39 (67 %) of the UMIs were located in an area supplied by a coronary branch with a significant stenosis. The median levels of hs-cTnI, NT-proBNP and Galectin-3 were higher in patients with UMI compared to those without: 5.4 vs. 3.7 ng/L ( $p < 0.001$ ); 172.5 vs. 93.5 ng/L ( $p = 0.005$ ); and 11.1 vs. 10.0 ng/L ( $p = 0.028$ ), respectively. There were significant correlations between the volume of the infarcted area and hs-cTnI (Rho= 0.40;  $p = 0.002$ ) and NT-proBNP (Rho= 0.41;  $p = 0.001$ ). In a linear regression model comprising presence of UMI, age and the degree of the most severe coronary stenosis, the level of hs-cTnI was independently associated with the presence of UMI ( $p = 0.002$ ). In corresponding models, neither NT-proBNP, nor Galectin-3, was independently associated with presence of UMI.

**Conclusions:** UMIs were common among patients with suspected CAD. The presence of UMIs were associated with a significantly increased risk for future cardiac events.

### Study of the cross-talk between protein synthesis and proteasome-mediated protein degradation

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**Background and Objectives:** Protein synthesis and protein degradation are two pathways that have a crucial role in cellular and organismal survival. The balance among the processes of protein synthesis and protein degradation guarantees protein homeostasis. Proteasome and lysosome systems are the main cellular proteolytic machineries. Proteasome is a multi-catalytic enzyme complex, which is responsible for the removal of normal, abnormal, denatured or in general damaged proteins. The present study sought to investigate the cross-talk between protein synthesis and proteasome-mediated protein degradation by inhibiting protein synthesis.

**Methods:** In order to investigate the effects of protein synthesis inhibition on the functionality of the proteasome, human primary embryonic fibroblasts were treated with various inhibitors of protein synthesis and analysis of the proteasome properties were carried out. This cross-talk was also examined on organismal level by using the model organism *Caenorhabditis elegans* (*C. elegans*).

**Results:** Protein synthesis inhibition in human primary embryonic fibroblasts caused augmentation of proteasome function and assembly, with concomitant increase of the protein levels of the catalytically active subunits. On organismal level, protein synthesis inhibition increased the longevity without influencing the proteasome function.

**Conclusions:** This study gives us an insight on how the mechanisms of protein synthesis and proteasome-mediated protein degradation interact.

### Patient participation in forensic psychiatry – patients' perspective

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**Background:** Patient participation is a central concept in health care but in studies of quality in the psychiatric care the patients often rate the level of their participation as low. The concept of participation is multidimensional and complex and the meaning might depend on the context. Although the concept is described in the literature in different ways, few describe it from the patients' perspective. There are some studies of the concept from the patients' perspective in somatic care but it's not necessarily comparable with psychiatric care. No earlier studies have examined patient participation in forensic psychiatry, a setting in which the concept poses particular challenges; the care is coercive and mostly the patients have psychosocial, economic, drug related and cognitive problems besides from the psychiatric diagnose.

**Objective:** To describe patients' perceptions of the concept of participation in forensic psychiatric care.

**Design:** It is a qualitative interview study with 19 patients in forensic psychiatric care.

**Methods:** A phenomenographic approach was used in the study.

**Results:** The patients describe participation as feeling involved in planning and decision making, getting relevant information and the importance of trust and relationship with the staff. The patients also describe an adjustment to rules and the coercive care, keeping hope and motivation and to participate in activities because it leads to personal advantages, not because they necessarily want.

**Relevance:** This study is expected to give a deeper understanding of how patients in forensic care perceive the concept of participation and to give decision makers and staff important knowledge to develop forensic psychiatry.



## Tryptophan transport in cultured fibroblast cells from patients with Male Idiopathic Osteoporosis: *an in vitro* study

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**Objectives:** Serotonin is a monoamine neurotransmitter produced mainly in the gastrointestinal tract and also in platelets and Central Nervous System (CNS). The serotonin is synthesized from amino acid L-tryptophan. Over the last decade, evidence suggests that defects in the serotonin system may be etiologic of Male Idiopathic Osteoporosis (MIO). While tryptophan is the precursor of serotonin, a disturbed transport of tryptophan is implicated in serotonin synthesis. Recent study has suggested a decreased transport of tryptophan into the erythrocytes in MIO patients. However, no study has investigated the tryptophan transport kinetics parameters in the MIO patients. The aim of this study is to investigate the kinetics parameters (*Km and Vmax*) of tryptophan transport in fibroblast cells derived from MIO patients compared to age-sex matched controls.

**Methods:** Fibroblast cell lines derived from skin biopsies from 14 patients with MIO having history of osteoporotic fractures and fibroblast derived from 14 age-matched healthy controls, has been included in this study. Kinetic parameters (*Vmax and Km*) for tryptophan transport were determined by using the Lineweaver-Burke plot equation. Tryptophan transport was measured using the cluster tray method for rapid measurement of amino acid flux in adherent fibroblast cells, by using <sup>3</sup>H (5)-L-tryptophan and 12 different concentrations (5 µM to 2 mM) of unlabelled tryptophan in duplicates.

**Results:** The results of this study have shown significantly decreased Vmax ( $p = 0.012$ ) and Km ( $p = 0.002$ ) of tryptophan transport in comparison to controls.

**Conclusions:** The results of the present study indicate a decreased tryptophan transport in Male Idiopathic Osteoporosis patients; consequently the Male Idiopathic Osteoporosis patients have decreased levels of endogenous tryptophan that might reduce serotonin synthesis and the tryptophan availability at cellular level. These findings could contribute for a novel approaches for diagnosis, treatment and management strategies of Male Idiopathic Osteoporosis.

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## Cytokine response after stimulation with commensal bacteria differs in irritable bowel syndrome (PI-IBS) patients compared to healthy controls

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**Objective:** A subset of Irritable bowel syndrome (IBS) patients, denoted post-infectious IBS (PI-IBS), develop symptoms after an enteric infection. Bacterial dysbiosis and mucosal inflammation have been proposed to be involved in the pathophysiology of this entity. We aim to characterise the mucosal and faecal microbiota in PI-IBS, general IBS and healthy controls and to investigate associations between the microbiota and the mucosal immune system.

**Methods:** Mucosal biopsies and faeces were collected from 13 PI-IBS patients, 19 general IBS patients and 16 healthy controls. Global bacterial composition was determined by generating 16S rRNA amplicons that were examined by phylogenetic microarray hybridization, principal component and redundancy analysis. We correlated previously reported lymphocyte proportions with the microbiota.

**Results:** Faecal microbiota composition of PI-IBS patients differed significantly from both general IBS patients and healthy controls ( $p < 0.02$ ). Both mucosal ( $p < 0.01$ ) and faecal ( $p = 0.05$ ) microbial diversity was reduced in PI-IBS compared to healthy controls

In the intraepithelial lymphocytes the previously published proportion of CD8<sup>+</sup> CD45RA<sup>+</sup> was negatively correlated to mucosal microbial diversity ( $p < 0.005$ ). The previously published number of lamina propria lymphocytes was negatively correlated to mucosal microbial diversity ( $p < 0.05$ ). Faecal microbial diversity was significantly negatively correlated to the Hospital Anxiety and Depression scale ( $p < 0.05$ ).

**Conclusions:** We present data that distinguishes the intestinal microbiota of PI-IBS patients from that of both general IBS patients and HC. The microbial composition was significantly associated with the HADs score and alterations in lymphocyte subsets proportions.

## Inter- and intra-rater reliability of a newly developed scale, The Dyadic Interaction in Dementia Transfer Assessment Scale (DIDTAS)

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**Objective:** The objective of this study was to determine the level of inter- and intra-rater reliability of a new scale for the clinical assessment of interaction during of staff assisted transfers involving residents in dementia special care units. The Dyadic Interaction in Dementia Transfer Assessment Scale (DIDTAS) contains 17 items that rate transfer-related actions of both the caregiver and the care-receiver (i.e., care dyad) from 1 (non-optimal) to 7 (optimal). Conceptually, the DIDTAS is based on the theoretical perspectives of reciprocity produced by individual, behavioral (actions) and environmental factors presented by the Social Cognitive Theory<sup>1</sup>.

**Method:** Videos of 20 care dyads' performance in person transfers were rated by two physiotherapists on two occasions eleven days apart. Analyses were calculated with two-way random-model ANOVAs for intra-rater reliability and two-way mixed-model ANOVAs for inter-rater reliability. An "average measure" was chosen for ICC (3, 2) analyses between raters and inter-rater reliability, and a "single measure" was chosen for ICC (2, 1) analyses between test situations and intra-rater reliability.

**Result:** The results supported the overall reliability of the DIDTAS items with variations in inter-rater reliability for ICCs values between .34 and .92 and the results for intra-rater reliability varied from ICCs .56 to .92 for rater 1 and from .29 to .92 for rater 2.

**Conclusion:** This study provides initial support for inter- and intra-rater reliability of the new scale reporting on transfer-related actions during of staff supported person transfers in dementia care facilities. This in turn shows that the DIDTAS is a promising scale that can bridging the gap in this area and provide physiotherapists and occupational therapists with a new method for assessing complex transfer-related actions of dementia care dyads.

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## Possible role of the NLRP3 inflammasome in the development of human atherosclerosis and myocardial infarction

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**Objective:** The NLRP3 inflammasome is an IL-1 $\beta$  and IL-18 cytokine processing complex that is activated in inflammatory conditions. The role of the NLRP3 inflammasome in the pathogenesis of atherosclerosis and myocardial infarction (MI) is not fully understood.

**Methods:** Atherosclerotic plaques were analyzed for transcripts of the NLRP3 inflammasome, and for IL-1 $\beta$  release. The Swedish FIA cohort consisting of DNA from 555 MI patients and 1016 healthy individuals was used to determine the frequency of 5 SNPs from the downstream regulatory region of *NLRP3*.

**Results:** Expression of *NLRP3*, *ASC*, *CASP1*, *IL1B*, and *IL18* mRNA was significantly increased in atherosclerotic plaques compared to normal arteries. The expression of *NLRP3* mRNA was significantly higher in plaques of symptomatic patients when compared to asymptomatic ones. CD68 positive macrophages were observed in the same areas of atherosclerotic lesions as *NLRP3* and *ASC* expression. Cholesterol crystals and ATP induced IL-1 $\beta$  release from LPS-primed human atherosclerotic lesion plaques. The minor alleles of the variants rs4266924, rs6672995 and rs10733113 were associated with *NLRP3* mRNA levels in PBMCs and plaques but not with the risk of MI.

**Conclusions:** Our results indicate a possible role of the NLRP3 inflammasome and its genetic variants in the pathogenesis of atherosclerosis.

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## The periodontal pathogen *Porphyromonas gingivalis* regulates the expression of Angiopoietin 1 and Angiopoietin 2 in Human Aortic Smooth Muscle Cells

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**Background:** *Porphyromonas gingivalis* is a gram-negative bacterium, which has been identified as the key causative microbe for the pathogenesis of destructive chronic periodontitis. The DNA of *P. gingivalis* has been found in coronary stenotic artery plaques of myocardial infarction patients and in vitro and animal experiments support the connection between *P. gingivalis* infection and the pathogenesis of cardiovascular disease. Angiopoietin 1 (angpt1) and angiopoietin 2 (angpt2) are the ligands for Tie receptors and play important roles for vessel development. Angpts are also known to regulate inflammatory responses and contribute to possess both pro- atherosclerotic and atheroprotective effects.

**Methods:** AoSMCs were exposed to wild type (W50 and 381), gingipain mutants (E8 and K1A), and fimbriae mutants (DPG-3 and KRX-178) of *P. gingivalis* and different concentration of TNF- $\alpha$  for 24h or 48h, whereafter quantitative real-time PCR and western blot were used to study gene and protein expression of angpt1 and angpt2. The role of angpt2 on cell proliferation and migration was checked by 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide (MTT) and scratch assay, respectively.

**Results:** We found that unstimulated AoSMCs express low level of Angpt2. *P. gingivalis* (wild type, K1A, DPG3 and KRX178) and TNF- $\alpha$ , respectively, up-regulate the expression of Angpt2 in AoSMCs, so as the Angpt2 transcription factor ETS1. In contrast, Angpt1 was inhibited by *P. gingivalis* and TNF- $\alpha$ . However, the RgpA and RgpB double mutant E8 had no effect on the expression of Angpt1, Angpt2, and ETS1 in AoSMCs. Exposure to Angpt2 protein enhanced the migration of AoSMCs but had no effect on proliferation.

**Conclusions:** This study demonstrates that gingipains are crucial for *P. gingivalis* to markedly increase the expressing ratio of Angpt2/Angpt1 in AoSMCs, which corresponds to the regulatory role of angiopoietins in angiogenesis and their involvement in the development of atherosclerosis. These findings further support the association between periodontitis and cardiovascular disease.

## Senior orienteering athletes as a model of healthy ageing: a mixed-methods approach

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**Objective:** The proportion of citizens reaching old age is increasing and will in the near future consume a majority of the health care resources. It is therefore essential to facilitate health beneficial behaviour among older adults. Orienteering is an endurance-running sport, demanding considerable cognitive and physical skills of its practitioners. In this study we aimed to explore and characterize a Swedish population of senior orienteering athletes as a new model of healthy ageing.

**Methods:** The mixed-method design included quantitative and qualitative methodologies to explore the athletes (n =136, median age = 69 yrs, IQR = 67-71). Quantitative data assessed physical activity (FGAS), functional wellbeing (EQ-5D), gut health (GSRs), psychological distress (HADS) and overall health (HI). Focus group discussions were conducted as a complement to the quantitative data, exploring the individuals' views on health and physical activity.

**Results:** The vast majority of the orienteering athletes reported scores above 70% of best possible on all health measures: FGAS: 83.3% (66.7-83.3), GSRs: 95.2% (90.5-98.1), (HADS): 90.5% (83.3-95.2), EQ-5D: 85.9% (80.2-100) and HI: 86.1% (80.6- 91.7). The high perceived health and wellbeing displayed in this population were further confirmed by the FGD findings.

**Conclusion:** Senior orienteering athletes represent an excellent model of healthy ageing. Our results show that the senior orienteering athlete's choice of a healthy life-style is, besides their awareness of its long-term health benefits, mainly driven by short-term values e.g. enjoyment and passion. Thus, the importance of short-term values should be considered when introducing health interventions among the general older population.

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