## ÖREBRO UNIVERSITY'S NOBEL DAY FESTIVITIES 2019

## ÖREBRO UNIVERSITY 9 DECEMBER 2019



Traditionally on 10 December, the anniversary of Alfred Nobel's death, the Nobel Prize in Physiology or Medicine, is awarded.

Organised and hosted by: School of Health Sciences and School of Medical Sciences acknowledge this day by organizing their own research activities and festivities.

# **BOOK OF ABSTRACTS**

School of Health Sciences and School of Medical Sciences Örebro University, Örebro, Sweden 9 December 2019

Editors: Programme Committee Simon Athlin, Åsa Berglind, Karuna Dahlberg, Camilla Ehnfors, Daniel Eklund, Cecilia Pettersson, Ignacio Rangel, Annika Rolland, Allan Sirsjö och Nikolaos Venizelos.



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### Preface

The "Nobel Day Festivities" were established 2009 by researchers within Biomedicine, Department of Clinical Medicine (now School of Health Sciences and Medical Sciences) at Örebro University.

Every year, the Nobel Prize in Physiology or Medicine is awarded on the 10th of December, the anniversary of Alfred Nobel's death. The School of Health Sciences and the School of Medical Sciences at Örebro University traditionally honor this day by organizing research activities and festivities. This year the festivities will take place on the 9th of December.

The day includes scientific activities that are open for all, such as lectures, poster presentations and selected oral presentations by doctoral students, postdocs and specially invited students. All poster presentations are documented in this Book of abstracts.

We warmly welcome you to enjoy the research that will be presented at Nobel Day Festivities 2019.

### The Committee

Editors: Programme Committee Simon Athlin, Åsa Berglind, Karuna Dahlberg, Camilla Ehnfors, Daniel Eklund, Cecilia Pettersson, Ignacio Rangel, Annika Rolland, Allan Sirsjö och Nikolaos Venizelos.

# Transcatheter aortic valve implantation for patients with aortic stenosis and concomitant ischemic heart disease: A five-year follow-up

Abawi A<sup>1</sup>, Samano N<sup>2</sup>

<sup>1</sup>Master of medicine, Örebro University <sup>2</sup>Department of cardiothoracic and vascular surgery, University Health Care Research Center, Faculty of Medicine and Health, Örebro University and Örebro University hospital, Örebro, Sweden

**Background/objectives**: Transcatheter aortic valve implantation (TAVI) is an established procedure to treat aortic stenosis (AS). This study investigates the impact of ischemic heart disease (IHD) on survival in patients undergoing TAVI. The five-year all-cause mortality stratified according to the presence or absence of IHD was the aim of this investigation.

**Methods**: Retrospective register study including all patients that underwent a TAVIprocedure 2009 to 2018. Patients were stratified according to the presence or absence of IHD. Our primary end-point was five-year all-cause mortality. Survival was analyzed using Kaplan-Meier curve. Data were acquired through the SWENTRY registry and patient files.

**Results**: A total of 264 patients were included in the study, with 139 (52.7 %) patients in the IHD group vs 125 (47.3 %) patients in the non-IHD group. Mean follow-up time was 40 ±30 months. At baseline, there was a higher proportion of males, patients with hypertension, peripheral arterial disease, left ventricular ejection fraction <50 % and, a higher EuroSCORE I in the IHD-group. Transfemoral approach was most common in both groups. No differences were noted in respect to peri- and postoperative complications. Five-year all-cause mortality was 17/38 (44.7 %) vs 18/30 (60.0 %), p = 0,232, in the IHD and non-IHD group respectively. Non-adjusted cumulative five-year survival was not significantly different between the groups (Log-Rank, p = 0,056).

**Conclusions**: In patients with severe AS undergoing TAVI, the five-year all-cause mortality was not statistically different between patients with or without IHD.

### **POSTER 2**

### Cross-cultural lay perspectives of successful aging in the oldest-old: a mixedmethods systematic review

Andreea Badache<sup>1,2</sup>, Elina Mäki-Torkko<sup>2,3</sup>

<sup>1</sup>School of Health Sciences, Örebro University, Örebro, Sweden
 <sup>2</sup>Swedish Institute of Disability Research
 <sup>3</sup>School of Medical Sciences, Örebro University, Örebro, Sweden

**Background/objectives:** Researchers have debated the meaning and use of successful aging (SA) since 1961 when Havighurst (1) started a long-lasting discussion in gerontology about what it means to age successfully. Since then, various models of SA have emerged. However, the most used definition is of Rowe and Kahn (2) which has a biomedical focus primarily. In this study, we aim to explore the views of the older adults aged 75 and above regarding successful aging through a systematic appraisal of quantitative and qualitative studies in order to supplement and compare the already existing definitions of SA identified in the literature.

**Methods:** A systematic search of the perspectives of lay people on successful aging was conducted across the following databases: PubMed, Scopus, PsychInfo, CINHAL, Scopus and Web of Science between November and December 2018. After removing the duplicates, we were left with 4131 articles to review. No language restriction was made, and all articles published until December 2018 were eligible for inclusion. We excluded non-peer reviewed articles, reviews, dissertations, cross-sectional studies, intervention studies and non-relevant articles for this study. Two independent reviewers (AB and EMT) conducted a title and abstract review to identify relevant articles for the full-text extraction and quality assessment. After the full-text assessment, we have 16 articles exploring the perspectives of the older people on SA, either through qualitative methods or surveys, to be included in the final analysis.

**Results:** We are planning a mixed-methods integrated design, where we will use a bayesian conversion approach from quantitative data to qualitative data. All the quantitative and qualitative data will be grouped, thematically synthesised and codified. The results will be presented at the conference.

### **References:**

- 1. Havighurst RJ. Successful Aging1. The Gerontologist. 1961;1(1):8-13.
- 2. Rowe JW, Kahn RL. Successful aging. The Gerontologist. 1997;37(4):433-40.

# Prevalence of attention-deficit/hyperactivity disorder in older adults: a systematic review and meta-analysis

Dobrosavljevic M1, Solares C2, Cortese S3, Andershed H2, Larsson H1

<sup>1</sup> School of Medical Sciences, Örebro University, Örebro, Sweden

<sup>2</sup> School of Law, Psychology and Social Work, Örebro University, Örebro, Sweden

<sup>3</sup> Department of Psychology, Southampton University, Southampton, The United Kingdom

**Background/objectives:** Attention-Deficit/Hyperactivity Disorder (ADHD) has been substantially investigated in children, adolescents and younger adults. However, there is, a significant knowledge gap in research of ADHD in adults older than 50, although more recent studies have indicated an increasing number of adults older than 50 in need for ADHD related health care<sup>1</sup>.

**Methods:** Using a systematic review of literature and meta-analysis of relevant studies, we aimed to investigate the prevalence of ADHD in adults aged 50 and older, separately for a) having a research diagnosis of ADHD based on a validated rating scale, b) having a clinical diagnosis of ADHD, or c) being prescribed with treatment for ADHD. We used the following electronic databases: Pubmed/Medline, Psycinfo, Web of Science and Embase, as well as manual search. Prevalence estimates were obtained with the random-effect meta-analysis.

**Results:** The pooled prevalence estimates significantly differed between groups, with 2.18% (95% CI 1.51 - 3.16) for research diagnosis based on a validated scale, .23% (95% CI .12 - .44) for clinical ADHD diagnosis, and .09% (95% CI .06 - .15) for ADHD treatment. Heterogeneity was very high across studies in all three groups.

**Conclusions:** The results indicate a substantial number of older adults with ADHD symptoms without a clinical diagnosis and a proper treatment. This poses a need for development of clinical assessment tools that are more adjusted to this age group and a better-suited care by health care providers. Further research is needed in this insufficiently recognized population of older adults.

### References

1. Torgersen T, Gjervan B, Lensing MB, et al. Optimal management of ADHD in older adults. Neuropsychiatr Dis Treat. 2016;12:79–87.

# Associations between habitual physical activity level, skeletal muscle mass and physical function in older women

Peter Edholm<sup>1</sup>, Andreas Nilsson<sup>1</sup>, Fawzi Kadi<sup>1</sup>

<sup>1</sup>Department of sport sciences, School of health Sciences, Örebro University, Örebro, Sweden

**Background/objectives:** Habitual physical activity (PA) level plays a key role for preservation of skeletal muscle mass and physical function during aging. However, to what extent present PA behaviour influences on muscle mass and physical function after past PA behaviour has been taken into account, is still unknown. Hence, it is unclear whether the influence of PA on muscle mass and physical function at old age is due to past or present PA behaviours. The aim of the current study was to investigate if present PA behaviour had a significant influence on skeletal muscle mass and physical function that was independent of past PA behaviour in older community-dwelling women.

**Method:** With institutional ethics approval 60 older women  $(67.5 \pm 1.5 \text{ years})$  were recruited to the study. An aggregated physical function score was created based on six-minute walk, squat jump and single-leg-stance balance performance. Present PA behaviour was assessed by accelerometry (Actigraph) and past leisure-time PA behaviour by the Historical Adulthood Physical Activity Questionnaire. Body composition was assessed by dual-energy x-ray absorptiometry (DEXA). Differences in physical function across tertiles of PA behaviours were analysed with factorial analysis of variance (ANOVA) with adjustment for fat mass.

**Results:** A high present PA level (mean counts per minute) was independent of past PA behaviour associated with a large muscle mass (P < 0.01) and a high physical function (P < 0.01) in older women. The effect present PA on physical function (P < 0.01) was driven by time spent in moderate-to-vigorous PA, whereas no influence was seen for time spent in sedentary behaviour. Interestingly, present PA level was associated with performance in 6-min walk and squat-jump but not single-leg-stance. This highlights that habitually PA does not influence all aspects of physical function in a uniformly pattern.

**Conclusion:** Taken together, our results supports current global health recommendations aiming to increasing PA level in order to counteract age-related decline in muscle mass and functional capacity. Moreover, as PA at old age inferred beneficial effects on muscle mass and physical function even among individuals with a past sedentary lifestyle, our results support the popular quote saying that "*it's never to late to start exercising*".

### Peritoneal bridging versus fascia closure of the defect in Intraperitoneal Onlay Mesh Repair (IPOM). A randomised controlled trial

Fathalla Ali<sup>1</sup>, Göran Wallin<sup>2</sup>, Gabriel Sandblom<sup>3,4</sup>

<sup>1</sup>Dept. of Surgery, Karlskoga Hospital, Karlskoga, Sweden.
 <sup>2</sup>Dept. of Surgery, Faculty of Medicine and Health, Örebro University, Örebro, Sweden.
 <sup>3</sup>Dept. of Clinical Science and Education Södersjukhuset, Karolinska Institutet, Stockholm, Sweden
 <sup>4</sup>Dept. of Surgery, Södersjukhuset, Stockholm, Sweden.

**Background/objectives:** Karl Leblanc first described laparoscopic ventral hernia repair (LVHR) in 1992. Simple Intraperitoneal Onlay Mesh (IPOM) Repair and IPOM with fascia closure prior to mesh placement (IPOM-plus) are the two main methods employed for laparoscopic ventral hernia repair (LVHR). Although IPOM-plus results in less post-operative seroma complications than simple IPOM, meanwhile results in more post-operative pain. The aim of this study was to test whether IPOM with peritoneal bridging causes less postoperative complications and early recovery than IPOM-plus.

**Method:** The primary outcome measure was post-operative seroma, and secondary outcome measure were post-operative pain and mobilization. The study was conducted as randomized double blind with 50 patients, randomised to IPOM-plus or IPOM with peritoneal bridging. The patients were followed-up after one week, one month, and will be followed-up for further 6 months and one year in this ongoing study. The seroma formation will be radiologically registered only for one-year follow-up, while the other follow-ups were done clinically due to ethical issues related to radiological exposure.

**Results:** The incidence of post-operative seroma was 3/25 patients in the IPOM-plus group and 0/25 in the IPOM with peritoneal bridging group at one month of follow-up (p=0.074). The mean VAS score was  $6.4\pm1.1$  vs  $2.0\pm1.2$  (p<0.05) for IPOM-plus and IPOM with peritoneal bridging respectively at one week follow-up.

**Conclusion:** IPOM with peritoneal bridging results in less post-operative seroma formation, less post-operative pain, and early recovery than IPOM-plus, but larger studies are required to test this.

### **References:**

1. LeBlanc KA: Laparoscopic incisional hernia repair: Are transfascial sutures necessary? A review of the literature. Surg Endosc 2007; 21(4): 508–513

2. Schoenmaeckers EJ, Wassenaar EB, Raymakers JT, Rakic S. Bulging of the mesh after laparoscopic repair of ventral and incisional hernias. JSLS. 2010 Oct-Dec;14(4):541

# Higher total physical activity is associated with lower arterial stiffness in Swedish, young adults – The Lifestyle, Biomarkers, and Atherosclerosis study

Fernberg Ulrika<sup>1</sup>, Fernström Maria<sup>2</sup>, Hurtig-Wennlöf Anita<sup>3</sup>

<sup>1</sup>School of Medical Sciences, Örebro University, Örebro, Sweden.

<sup>2</sup>Åstrand Laboratory of Work Physiology, The Swedish School of Sport and Health Sciences, GIH, Stockholm, Sweden

<sup>3</sup>Department of Medical Diagnostics, School of Health Sciences, Örebro University, Örebro, Sweden.

**Background/objectives:** The aims of the present study was, firstly, to present data of the physical activity (PA) pattern and time spent sedentary, in the population of Swedish, young adults. Secondly, to explore the association between PA and arterial stiffness with respect to earlier established risk factors.

**Methods:** Self-reported healthy, non-smoking, Swedish, young adults, 18-25 years old, participated in the cross- sectional Lifestyle, Biomarkers and Atherosclerosis (LBA) study. The daily PA pattern was objectively measured with an accelerometer during one week in 658 individuals. Pulse wave velocity (PWV) and augmentation index (AIx) were measured with applanation tonometry.

**Results:** Women spent significantly more time per day in light PA (LPA) (p<0.01), were less time sedentary (p<0.001), and took significantly more steps per day (p<0.05), than men. In total, 76 % of the individuals spent on average at least 30 minutes per day in the recommended moderate and vigorous PA (MVPA). Young adults without risk factors for cardiovascular diseases (CVD) had a higher level of total PA compared to the young adults with two or more risk factors. Lower arterial stiffness was associated with higher levels of total PA in both women and men.

**Conclusions:** Young adults without risk factors for CVD had a higher level of total PA compared to the young adults with two or more risk factors for future CVD. Lower arterial stiffness was associated with higher levels of total PA, and we conclude that in this age group of young adults, it is important to highlight the health enhancing possibilities of all intensities of PA on the vascular status.

### PCI in saphenous vein grafts after CABG: a review of the international literature

Ferrari G<sup>1</sup>, Geijer H<sup>2</sup>, Samano N<sup>1</sup>, Souza D<sup>1</sup>

<sup>1</sup>Department of Cardiothoracic and Vascular Surgery, Faculty of Medicine and Health, Örebro University, Örebro, Sweden. <sup>2</sup>Department of Radiology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden

**Background/objectives:** To review the international literature about the use of Percutaneous Coronary Intervention (PCI) in vena saphena magna graft after a Coronary Artery Bypass Grafting (CABG).

**Methods:** We reviewed, from three different databases, the recent international literature (published between January 1, 2000 and December 31, 2018) regarding the use of PCI in venous grafts. Two independent researchers performed the literature search, designed after a PICO model. Forty articles were selected and a quality assessment was performed.

**Results:** We noticed a high percentage of short and long-term cardiac events. The periprocedural failure rate, due to residual stenos, had a mean value around 10%. The 30-days MACE (major adverse cardiac event) had a mean value of 6-7%, with the lower rates associated with the use of embolic protection devices. The MACE rates at 1 year reported were above 10% for most reports (up to over 30%; mean 16%), with better results after the use of a drug-eluting stent (DES) instead of a bare-metal stent. The long-term MACE (2-5 years) reported was high in all studies, with values ranging between 18% and 58%, with target vessel revascularization rates between 9% and 44%. The benefits of DES no longer remain in the long term.

**Conclusions:** The percutaneous intervention of an occluded or stenosed saphenous vein graft is a challenge for the angiographer and is still associated with high rates of failure, MACE and restenosis. The key of the success of the procedure seems to be to optimize the quality of the venous graft itself.

### **References:**

- 1. Redfors, B., et al., Percutaneous Coronary Intervention of Saphenous Vein Graft. Circ Cardiovasc Interv, 2017. 10(5).
- 2. Iqbal, J., et al., Outcomes Following Primary Percutaneous Coronary Intervention in Patients With Previous Coronary Artery Bypass Surgery. Circ Cardiovasc Interv, 2016. 9(4): p. e003151.



# Impact of defunctioning stoma on long-term survival and disease recurrence following low anterior resection for rectal cancer

Soran Gadan<sup>1,2</sup>, Judith Brand<sup>2</sup>, Martin Rutegård<sup>3,4</sup>, Peter Matthiessen<sup>1,2</sup>

<sup>1</sup>Department of surgery, Colorectal unit, Örebro University Hospital, <sup>2</sup>Örebro University, School of medical sciences Örebro, Sweden <sup>3</sup>Surgical and Perioperative Sciences, Surgery, Umeå University, Umeå, Sweden <sup>4</sup>Wallenberg Centre for Molecular Medicine, Umeå University, Umeå, Sweden

**Background/objectives:** To compare the long-term oncological outcome of rectal cancer patients undergoing low anterior resection (LAR) with and without a defunctioning stoma.

**Methods:** The present study included patients who underwent low anterior resection for rectal cancer in Sweden between 1995-2010. Data were retrieved from the Swedish Colorectal Cancer Registry. Patients with cancer stage IV, non-radical resection, near-tumor perforations and tumor height >10 cm and <4 cm were excluded. After exclusions the study population consisted of 3648 patients who had undergone curative LAR, including 2269 with defunctioning stoma (DS+) and 1379 without (DS-) at the index operation. Absolute and relative risks of all-cause mortality, locoregional recurrence and distant metastasis were compared between the two groups using flexible parametric survival models to account for potential time-dependent effects.

**Results:** Patients in the DS+ group were younger, more often male and less frequently experienced an anastomotic leakage than patients in the DS- group. After adjusting for year of surgery, age, sex, tumor height, tumor stage, and neoadjuvant therapy, short-term mortality was lower in the DS+ than in the DS- group (HR at 1 year = 0.80, 95% CI = 0.67-0.95), but no difference in long-term mortality was observed. The adjusted cumulative incidence of distant metastasis and locoregional recurrence was also comparable between the two groups.

**Conclusion:** Defunctioning stoma is associated with improved short-term survival, but has no impact on long-term survival or disease recurrence in patients undergoing low anterior resection for cancer.

### What hinders and enables implementation of research results in healthcare?

Granberg A<sup>1</sup>, Matérne Marie<sup>2</sup>, Lundqvist Lars-Ove<sup>2</sup>, Duberg A<sup>2</sup>.

<sup>1</sup> Medicinsk vetenskap, inriktning Hälso och vårdvetenskap Örebro universitet
 <sup>2</sup> Universitetssjukvårdens Forskningscentrum, Region Örebro Län

**Objective:** A major challenge in healthcare is the gap between research results and implementation of the results. Despite clinical guidelines, studies show that patients do not have access to evidencebased care, or that patients receive unnecessary, and in some cases, even harmful treatment. What barriers and facilitators influence the implementation and use of new practice? The study explores what hinders and enables implementation in communities and regions by following a randomized controlled study, SWAN - specialized water dance intervention for individuals with profound intellectual and multiple disabilities.

**Methods:** Individual semi-structured interviews with 23 managers in four regions. The interviews explores managers' experience of what hinders and enables implementation. Qualitative content analysis in an inductive way was used when analyzing data.

**Results:** The analyzes of the interviews are ongoing and the results are planned to be ready for publication in spring 2020. Primary results address issues related to challenges regarding implementation, such as: time required for change, challenges to keep the change sustained over time, the importance to understand role and responsibility and also the knowledge and skills of the employees. Additional aspects that is highlighted as important in the narratives are difficulties regarding collaboration between the local, regional and national level of organizations, and also, the organizations readiness and culture for change.

**Conclusion:** This study provides an increased understanding about the complex multifaceted issues regarding implementation, and can therefore contribute to strengthen and develop efficient strategies for implementation in healthcare organizations. The findings can provide useful information for decision makers that holds potential to improve the implementation process when research turns in to reality.

# Measuring the effect of pro-inflammatory cytokines on the growth of commensal *Escherichia coli*

Samuel Hägerström<sup>1</sup>, Ignacio Rangel<sup>1</sup> and Isak Demirel<sup>1</sup>

<sup>1</sup>School of Medical Sciences, Örebro university, Örebro, Sweden

**Background/objectives:** Cytokines play a key role in coordinating the human immune system. Recent studies have shown that bacteria modulate their behaviour when exposed to cytokines. In my bachelor's thesis it was shown that *Escherichia coli* (*E. coli*) changed its growth rate when exposed to cytokines. In order to further study the effect of cytokines on *E. coli* we first need to improve the method with which we measure growth.

**Methods:** *E. coli* strain ATCC® 8739<sup>TM</sup> was exposed to the cytokines tumour necrosis factor (TNF)- $\alpha$ , interleukin (IL)-1 $\beta$ , IL-6, IL-8 and interferon (IFN)- $\gamma$  at 0.5-40 ng/ml in minimal salt media whereby growth was measured using optical density. Changes were made to the protocol improving its accuracy and precision.

**Results:** The most important change was shaking the bacteria to increase homogeneity. This together with the other improvements of the protocol increased the precision and accuracy so that 10 trials with the new protocol will be enough to achieve the same power as 150 with the old. No difference in growth was observed between the cytokine-exposed bacteria and the controls.

**Conclusion:** The improved protocol allows for testing more strains, cytokines and growth media using less resources whilst achieving greater reproducibility than the old protocol. Further testing is necessary before drawing any conclusions regarding the cytokines' effect on the growth of *E. coli*.

# IL-6 trans-signaling in vascular endothelial cells alters chemokine release to enhance lymphocyte recruitment and inhibit neutrophil trafficking

Assim Hayderi<sup>1</sup>, Mulugeta M Zegeye<sup>1,2</sup>, Ashok Kumawat<sup>1,2</sup>, Allan Sirsjö<sup>1,2</sup>, Liza U Ljungberg<sup>1,2</sup>

<sup>1</sup>Cardiovascular Research Center <sup>2</sup>School of Medical Sciences, Örebro University Sweden

**Background/objectives:** Vascular endothelium plays critical roles in both innate and adaptive immunity in addition to the homeostasis of cardiovascular system. This inner lining of blood vessels is one of the main targets of various cytokines including IL-6, a pleotropic cytokine with both anti- and pro-inflammatory properties. IL-6 signals through either the membrane bound IL-6 receptor (classic-signaling) or the soluble form of IL-6 receptor (trans-signaling), both requiring signal transducing membrane-bound gp130. Our aim was to evaluate the differences between IL-6 classic and trans-signalling in endothelial cells by looking at the protein profile of these cells after stimulation with IL-6 alone or IL-6 in combination with its soluble receptor.

**Methods:** We employed Proximity Extension Assay to analyze release of 184 proteins, which are established and exploratory biomarkers relevant in inflammatory response and cardiovascular disease, from HUVECs in response to activation of the IL-6 classic and transsignaling pathways.

**Results:** We found that IL-6 trans-signaling, but not classic-signaling, in human vascular endothelial cells significantly alters the release of 23 proteins (Cut off 1.5 fold change and BH p-value <0.05). IPA® analyses reveal that IL-6 trans-signaling in vascular endothelial cells leads to activation, migration and recruitment of lymphocytes while it inhibits vascular permeability, and binding and migration of granulocytes including neutrophils. Further, we picked the central chemokine that is involved in inhibition of granulocyte trafficking (IL-8) and demonstrated that IL-6 trans-signaling downregulates both the basal level and LPS and TNF- $\alpha$  induced IL-8 secretion from vascular endothelial cells.

**Conclusions:** Our data suggests that IL-6 trans-signaling in vascular endothelial cells induces differential regulation of proteins associated with selective recruitment of leucocytes across the endothelium.

### **References:**

Schaper F, Rose-John S. Interleukin-6: biology, signaling and strategies of blockade. Cytokine & growth factor reviews. 2015 Oct 1;26:475-87.

### Anti-inflammatory effects of novel purine analogues in aortic smooth muscle cells

Hettiarachchi U<sup>1</sup>, Paramel G<sup>2</sup>, Fotopoulou T<sup>3</sup>, Koufaki M<sup>3</sup>, Grenegård M<sup>2</sup>, Fransén K<sup>2</sup>.

<sup>1</sup>Cardiovascular Medicine Program, School of Medical Sciences, Örebro University, Sweden <sup>2</sup>Cardiovascular Research Centre, School of Medical Sciences, Örebro University, Sweden <sup>3</sup>Chemical Biology of National Hellenic Research Foundation (ICB/NHRF)

# Abstract not available Only Poster

### Postoperative agitation and delirium in children after general anesthesia -Interventions that decrease respective increase presence

Johansson Ingrid<sup>1</sup>, Johnsson Erik<sup>1</sup>

### <sup>1</sup>School of Health Sciences, Örebro University, Örebro, Sweden

**Background/objectives:** Children differ both physically and mentally from adults, which the anaesthesia nurse must take into consideration in general anesthesia in children. Postoperative agitation and delirium is not a new phenomenon but are described since the 1960. Various definitions have been used and it is hard to differ between emergence delirium and emergence agitation. Emergence delirium have been described as a disturbance in a childs awareness of and attention to his or her environment with disorientation and perceptual alterations including hypersensitivity to stimuli and hyperactive motor behavior in the immediate postanesthesia period. Between 25-80% of children are affected by postoperative agitation and delirium after general anesthesia. This can have consequences for the medical and nursing treatment, and for the wellbeing of the child and parents. The aim was to describe which interventions that decrease or increase the incidence of postoperative agitation and delirium in children after general anesthesia.

**Method:** The study was conducted as a literature review with a systematic literature search in the databases PubMed and CINAHL. After the quality control, 25 scientific studies were included, 23 studies were randomized controlled trials. The analysis and extraction of data was conducted using the PICO-model as well as Polit and Becks nine-step model.

**Results:** The result emerged from three interventions that decrease or increase the incidence of postoperative agitation and delirium. Drug delivery, anaesthetic method and nursing interventions. Drug delivery and nursing interventions proved to have a positive impact with reduced incidence on postoperative agitation and delirium in various degree. The anaesthetic method gas anaesthesia was found to have a direct negative effect with increase of the occurrence of the phenomenon.

**Conclusion:** Postoperative agitation and delirium is a common phenomenon in children after general anesthesia. A number of interventions have a negative or positive impact on the occurrence. Which drugs are administered during anaesthesia, the anaesthetic method used and the nursing interventions implemented plays a significant role. The anaesthesia staff can with knowledge of the effects of interventions create a better balance between different interventions in order to avoid children suffering from postoperative agitation and delirium.

# DNA methylation analysis in HPV-positive screening samples from women 30–69 years in the cervical cancer-screening program in Örebro, Sweden – a pilot study

Malin Kaliff<sup>1</sup>, Lovisa Bergengren<sup>2</sup>, Gisela Helenius<sup>1</sup>, Mats G Karlsson<sup>1</sup>, Gabriella Lillsunde Larsson<sup>1,3</sup>

<sup>1</sup>Dep. of Laboratory Medicine, Faculty of Medicine and Health, Örebro University, Örebro, Sweden <sup>2</sup>Dept of Women's Health, Faculty of Medicine and Health, Örebro University, Örebro, Sweden <sup>3</sup>School of Health Sciences, Örebro University, Örebro, Sweden

**Background/objectives:** In Sweden, new recommendations for cervical cancer screening has been in place since 2016, where women between the age of 30 and 69 years should be screened using HPV test and a hrHPV-positive result followed by a cytology evaluation. In the Örebro region, an mRNA- based test is used (Aptima, Hologic) for HPV primary screening where a positive or negative test result for 14 hrHPV is given. Cytology as a triage method after a HPV positive test is widely accepted and used. Other triage methods have been discussed and DNA hypermethylation analysis in certain host cell genes is one. DNA hypermethylation is suggested to be a promising molecular triage method comparable to cytology and could unlike cytology be implemented in a program with self-collected cytology sampling. The aim was to evaluate the DNA methylation state of the HPV-positive samples in the cervical cancer screening cohort and its association to the cytology- and HPV-status.

**Methods:** mRNA HPV screening- positive samples between November 2016 and April 2017 were collected (n=529), and 27 of these were analyzed in the current pilot-study. The samples was genotyped with Anyplex II HPV28 (Seegene), detecting 28 HPV genotypes. Two commercially available kits were used to analyze hypermethylation of host cell genes. The first method, QIAsure (Qiagen), evaluates methylation status of two human target genes (FAM19A4 and mir-124-2) and one control gene (ACTB). The second method, Gyntect (Oncgnostics), analyzes six human target genes (ASTN1, DLX1, ITGA4, RXFP3, SOX17, and ZNF671) and two control genes (ACHE and IDS-M).

**Results:** With QIAsure 9 of the 27 samples were positive for hypermethylation, 2 samples were invalid and 16 were negative. From analysis with GynTect 9 out of 27 samples showed positive and 18 negative results. The result concordance between the two methods was 76 % and the sensitivity of detecting cytological HSIL/CIN2+ was 63% for QIAsure and 67 % for GynTect in this pilot study. There was no statistically significant difference of hypermethylation positivity between groups of samples containing single vs. multiple number of HPV genotypes (Fishers exact test; p=0.229).

**Conclusion:** The two methods evaluated to detect hypermethylation in biobanked cervical cell samples both gave valid results and were comparable in this small pilot study. Further analysis with larger sample size is ongoing.

# The female perspective – A cross-sectional study on cancer rehabilitation needs, social stigma and quality of life in women with cancer

Jeanette Kittang<sup>1</sup>, Emma Ohlsson-Nevo<sup>2</sup>

<sup>1</sup>Faculty of Medicine and Health, Örebro University, Department of Oncology, Örebro University Hospital, Örebro, Sweden. <sup>2</sup>Faculty of Medicine and Health, Örebro University, University Health Care Research Center, Örebro, Sweden.

**Background/objectives:** Medical advances within oncology are resulting in greater nursing challenges and managing symptoms is the core of oncology nurses' role. Gynecological cancer and breast cancer has a mental connection to the female body, and may have a negative impact on the women's self esteem and quality of life. Most societies value men higher than women. Living in a society where men and women aren't equal is likely to affect women's health. Even though men and women are at risk for the same endemic diseases, women may have an increased risk due to biological and social factors which may also result in reporting symptoms different.

**Methods:** The aim of the study was to describe cancer rehabilitation needs, social stigma and quality of life in women with cancer in general and women with gynecological cancer and breast cancer in specific. The study population is adult female cancer patients living in the region of Örebro County, diagnosed with cancer during a one year period. Through the Information Network for Cancer, 521 women were identified. A cross-sectional survey study was conducted using postal questionnaires. The questionnaires used were *Cancer rehabilitation: Intervention version 2* (CRI v2), *The Stigma-related social problems scale* (SSPS), and *The European Organization for research and treatment of cancer – Quality of Life questionnaire* (EORTC QLQ-30). Data were analyzed using descriptive and analytic statistics.

**Results:** The final sample consists of 315 women, which gives a response rate of 60%. The most wanted cancer rehabilitation intervention for the entire cohort was *Information and supportive groups with people with the same diagnosis* (39%) and the second most wanted was *Individual weight training* (33%). Complexity shows that 30% of the women wanted no cancer rehabilitation intervention. 50% of the women wanted more than one rehabilitation intervention and 11% of the women wanted five different interventions. Both *Avoidance scale* and *Distress scale* were found to correlate negatively with all items of the quality of life questionnaire.

**Conclusions:** Nursing should focus on individual needs, not solely patient characteristics. Further studies need to provide knowledge on the complexity of cancer rehabilitation needs. The author welcomes gender perspective on future research.

# Dose- and time dependent changes in viability and IL-6, IL-8 and MCP-1 production in HaCaT cells exposed to cobalt. Effects of high and low calcium.

<u>Maria Klasson</u><sup>1,2,4</sup>, Magnus Lindberg<sup>1,2,3</sup>, Eva Särndahl<sup>1,2</sup>, Ing-Liss Bryngelsson<sup>4</sup>, Alexander Persson<sup>1,2</sup>

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

<sup>2</sup> Inflammatory Response and Infection Susceptibility Centre (iRiSC), Örebro University, Örebro, Sweden.

<sup>3</sup> Department of Dermatology, University Hospital Örebro, SE-701 85 Örebro, Sweden

<sup>4</sup> Department of Occupational and Environmental Medicine, University Hospital Örebro, Örebro, Sweden

**Background/objectives:** Cobalt is an important skin sensitizer and exposure of an allergen and the production of a "warning signal" are needed for sensitization. Keratinocytes are the major producers of the warning signals in the skin and they also play an important role in the regulation of inflammation due to their ability to respond to stimuli from our environment. The aim of this study is to compare effects in viability and production of cytokines/chemokines in HaCaT cells (keratinocytes) exposed to cobalt chloride grown in medium with low or high calcium concentration (the latter gives more differentiated cells).

**Methods:** HaCaT cells were exposed to different concentrations of cobalt chloride over time. Cell viability was measured with the Cell-Titer Blue Viability Assay and the production of cytokines with a bead-based immunoassay and analyzed using a flow cytometer.

**Results:** Cell viability was dose- and time dependent and a significant difference between the cells grown in high and low calcium was seen. A mixed model showed significant increase in IL-6, IL-8 and MCP-1 production over time. Increased cobalt chloride concentrations gave an increase in IL-6 and IL-8, and a corresponding decrease in MCP-1. When comparing cells grown in high and low calcium, there was only difference for IL-6.

**Conclusions:** Our results suggests that exposure to cobalt chloride triggered an alarm system in HaCaT cells and that pro-inflammatory cytokines/chemokines were secreted in a time- and dose-dependent manner. The findings indicate that the inflammatory response does not change depending on how deep the cobalt has penetrated the skin.

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# Current practice and Swedish operating theatre nurses' perioperative routines regarding saphenous vein harvesting for coronary artery bypass surgery

Hanna Larsson RN, MSc<sup>1,2</sup>, Maria Hälleberg-Nyman RN, PhD<sup>2</sup>, Örjan Friberg MD, PhD<sup>1</sup>, Karin Falk- Brynhildsen RN, PhD<sup>2</sup>

<sup>1</sup>Department of Cardiothoracic and Vascular Surgery, Örebro University Hospital, SE-701 85 Örebro, Sweden <sup>2</sup>Faculty of Health and Medicine, School of Health Sciences, Örebro University, SE-701 82 Örebro, Sweden

**Background:** Coronary artery bypass grafting (CABG) is the most common operation in cardiac surgery. Leg wound surgical site infection (SSI) remain one of the most common complications after CABG surgery. Perioperative hygiene routines play an important role to prevent SSI.

**Methods:** A prospective survey was carried out among the 119 operating theatre (OT) nurses currently working at the eight departments of cardiothoracic surgery in Sweden. Responses from all hospitals were received and the total response rate was 62/119 (52%).

**Results:** The majority of the OT nurses reported that perioperative skin disinfection was performed by an OT nurse (96.8 %) and that the skin was disinfected for about 3–5 minutes (58%). All Swedish departments of cardiothoracic surgery used Chlorhexidine 5 mg/ml in 70% ethanol and 62 % of the hospitals used tinted Chlorhexidine. Incision film or Integuseal, to prevent bacterial contamination in the wound, was almost never used on the leg (2% vs 6%). Seventy percent of the OT nurses answered that the leg was disinfected with Chlorhexidine once again before the dressing was applicated. Most often an OT nurse applicated the dressing. About half of them used a semipermeable dressing. Regarding feedback on incidence of wound infections, 45% reported that they never received feedback, 37% sometimes and 18 % reported that they received feedback on a regular basis.

**Conclusions:** Overall, the clinical routines for skin preparation and infection control is in Swedish cardiothoracic departments are concordant. The Swedish OT nurses are responsible for many infection control measures including the maintenance of an aseptic environment. However, routines for feedback and follow up on the infection incidence can be improved.

### Hyperthyroidism in children and deceased

D. Madonia<sup>1</sup>, G. Sjolin<sup>1</sup>, M. Holmberg<sup>2</sup>, O. Törring<sup>3</sup>, J. Calissendorff<sup>4</sup>, M. Lantz<sup>5</sup>, B. Hallengren<sup>5</sup>, H. Filipsson Nyström<sup>2</sup>, G. Wallin<sup>1</sup>

<sup>1</sup>Department of Surgery, Örebro University Hospital, Örebro, Sweden

<sup>2</sup>Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

<sup>3</sup>*Institution for Clinical Science and Education, Karolinska Institutet, Södersjukhuset, Sweden* 

<sup>4</sup>Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden

<sup>5</sup> Dept. of Clinical Sciences, Lund University, Lund, Sweden

**Background/objectives:** The clinical manifestations of hyperthyroidism as well as available treatments (antithyroid drug therapy (ATD), radioactive iodine (RAI) or surgery) and their efficacy are well described, however, there are few reports on long-term outcome of each treatment modality, mortality rate in elderly and outcome in children.

**Methods:** Data collection from a Swedish thyroid database TT-12, which include a span of 40% of Swedish population between years 2003-05. The reported patient cohort consisted of elderly deceased and children with hyperthyroidism, treatments options and outcomes.

**Results:** The total amount of patients reported was 2916. 10.2% of them were deceased at follow up, 2% were children. Graves's disease was present in 46% of deceased and 98% of children compared to 78% in the whole cohort. Ophthalmopathy (infiltrative and non-infiltrative) was more common among children (5% and 24%) compared to deceased (0.3 % and 3.7%) and the whole cohort (3.8% and 12%). Smoking at diagnosis was reported in 17.5% of the deceased population, in 6.8% of children in comparison to 26% in the whole cohort. Patients were treated with ATD in 25,3% of deceased and 86,4% of children compared to 45,6 % in the whole population analyzed. Treatment with RAI was adopted in 65% of deceased, in 2% of children compared to 40% of the whole cohort. Surgical treatment was used in 1,3% of deceased, in 7% of children compared to 5,5% in the whole cohort.

**Conclusion:** Graves' should be suspected in each case of hyperthyroidism in children and ophthalmopathy is a dominant clinical feature. The mean age of the deceased is higher than the whole cohort, supporting age as a risk factor for death. This also explains that RAI is more usual treatment than ATD in the deceased group. Both of these groups needs to be further studied.

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### Characterization of Calcium Homeostasis in Lithium-Treated Patients Reveals Both Hypercalcaemia and Hypocalcaemia

Adrian D. Meehan<sup>1</sup>, Maria Wedin<sup>2</sup>, Göran Wallin<sup>3</sup>, Johannes Järhult<sup>4</sup>

<sup>1</sup>Dept. of Geriatrics, Faculty of Medicine and Health, Örebro University, Örebro, Sweden.
 <sup>2</sup>Dept. of Surgery, Faculty of Medicine and Health, Örebro University, Örebro, Sweden.
 <sup>3</sup>Dept. of Surgery, Faculty of Medicine and Health, Örebro University, Örebro, Sweden.
 <sup>4</sup>Dept. of Surgery, Ryhov Hospital, Jönköping, Sweden.

**Background/objectives:** Prevalence studies demonstrate that a significant proportion of lithium-treated patients develop hypercalcaemia (3–30%). Lithium-associated hyperparathyroidism (LHPT) is poorly defined, and calcium homeostasis may be affected in a more complicated fashion than purely by elevated PTH secretion. The current study aims to examine in detail calcium homeostasis principally with regard to lithium duration.

**Methods:** Medical records of 297 lithium-treated patients (193 women, 104 men; median age 58 years) were examined, and information on gender, age, lithium treatment duration and calcium homeostasis was obtained. The median treatment duration with lithium was 16 (1.5-45) years.

**Results:** A total of 8504 calcium values were retrieved. Before initiation of lithium treatment, serum calcium was on average 2.33 mmol/l (2.02–2.60). During the treatment period, 178 patients (60%) remained normocalcaemic, 102 (34%) developed hypercalcaemia or were strongly suspected of LHPT, 17 (6%) had 3 or more intermittent episodes of hypocalcaemia. Forty-one per cent of patients with suspected or confirmed LHPT had low (<4 mmol) 24-h urine calcium levels. The success rate after 33 parathyroidectomies was 35%, hyperplasia being diagnosed in 75% of extirpated glands.

**Conclusions:** The prevalence of hypercalcaemia during lithium treatment is very high. In addition, hypocalcaemic episodes appear to occur frequently, possibly reflecting a more complicated parathyroid dysfunction than previously known. Long-term surgical results are unsatisfactory. LHPT biochemical profile is different from that of primary hyperparathyroidism and is in some ways similar to familial hypocalciuric hypercalcaemia.

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### Predictors for persistent bacteremia and death in Staphylococcus aureus bacteremia: a retrospective study from Sweden

Emelie Nilsson<sup>1</sup>, Sara Cajander<sup>2</sup>

<sup>1</sup>School of Medical Sciences, Örebro University, Örebro, Sweden <sup>2</sup>Departement of Infectious diseases, Örebro University hospital, Örebro, Sweden

**Background/objectives:** *S.aureus* bacteremia (SAB) is a heterogenous disease with prognosis ranging from uncomplicated to life-threating. Today, there are no consensus guidelines on how to manage patients with SAB. The primary aim was to assess the clinical presentation, investigation and prognosis of all-hospitably admitted patients with SAB within Region Örebro County (RÖC) during one year. The secondary aim was to evaluate Sequential Organ Failure Assessment (SOFA) score, New Early Warning Score 2 (NEWS2) and C-reactive protein (CRP) for prediction of 30-day mortality and persistent bacteremia (PB).

**Methods:** Patient-chart review was performed on all patients with growth of S.aureus in at least one blood culture (BC) sampled upon hospital-admission in RÖC during 2018. Patient characteristics, clinical assessments and outcomes were recorded.

**Results:** 115 episodes of SAB with a wide range of presentations were included. 30-day mortality was 19%. Only 49 % of patients with SAB were subjected to repeated BC sampling 48-72 h post-admission. 41 % of these had PB. Cox-regression with multivariable adjustment for age, sex and comorbidity demonstrated that elevated NEWS2 (cut-off 7) and SOFA (cut-off 2) were independently associated with higher mortality, 9.7 (95 % CI 1.3-73) and 8.8 (95 % CI 1.2-67) respectively. CRP was discriminative for development of PB, (AUC 0.76, p < 0.001).

**Conclusion:** The clinical presentation of SAB was widely heterogeneous. Elevated NEWS2 or SOFA scores were independently associated with 30-day mortality and CRP with PB.

# Treatment pattern, risk for hospitalization and mortality in elderly patients with triple-negative breast cancer

Nyström P<sup>1</sup>, Valachis A<sup>2</sup>

<sup>1</sup>School of Medical Sciences, Örebro University, Örebro, Sweden <sup>2</sup>Department of Oncology, Faculty of Medicine and Health, Örebro University, Örebro

**Background/objectives:** Triple-negative breast cancer (TNBC) has limited treatment options, as chemotherapy is the only systemic therapy. This poses a challenge in the elderly population due to the limited research done, but also the increased risk for adverse events.

**Aim:** To describe the treatment pattern, identify the risk of hospitalization and potential risk factors for hospitalization within 1 year from diagnosis, and investigate the causes of death in elderly with TNBC and possible predictors for mortality.

**Methods:** We performed a registry-based cohort study using the BCBaSe database which links cases of breast cancer from 3 Swedish healthcare regions with socioeconomic factors, hospitalizations and causes of death. Women  $\geq$  70 years old with non-metastatic TNBC, between 1/1 2007 and 31/12 2012 were chosen (n = 413). Logistic regression and Cox proportional hazards regression analyses were used.

**Results:** Age, stage and comorbidities influenced administration of chemotherapy. The risk of hospitalization overall was increased in the group receiving chemotherapy (OR 2.35, 95% CI 1.30 - 4.26) mainly due to toxicities. Chemotherapy use was not associated with either breast cancer-specific (HR 0.95, 95% CI 0.51 - 1.79) or overall survival (HR 0.72, 95% CI 0.44 - 1.18). Stage at diagnosis and comorbidities were associated with both breast cancer-specific mortality and overall mortality, whereas age was only associated with overall mortality.

**Conclusions:** In elderly TNBC patients, chemotherapy use was associated with increased risk for hospitalization within 1 year from diagnosis without improving breast cancer-specific or overall survival. No benefit regarding mortality was seen in those who were administered chemotherapy.

### **Targeting ROR-1 Receptor Tyrosine Kinase by Novel Small Molecule Inhibitors in Ovarian Cancer Cells**

<u>Mohammad Ali Okhovat<sup>1,2</sup></u>, Amine Ghaderi<sup>1</sup>, Mohammad Hojjat-Farsangi<sup>1</sup>, Anders Österborg<sup>1,3</sup>, Håkan Mellstedt<sup>1</sup>

<sup>1</sup>Department of Oncology-Pathology, Immune and Gene Therapy Lab, Cancer Center Karolinska (CCK), Karolinska University Hospital Solna and Karolinska Institute, Stockholm, Sweden. <sup>2</sup>School of Medical Sciences, Örebro University, Örebro, Sweden. <sup>3</sup>Department of Hematology, Karolinska University Hospital Solna, Stockholm, Sweden.

# Abstract not available Only Poster

# Cluster analysis and risk score calculation based on surrogate markers of vascular stiffness and vascular thickness, and their association with traditional cardiometabolic risk factors in a healthy cohort of young adults – The Lifestyle, Biomarkers and Atherosclerosis study

Pettersson-Pablo P<sup>1,2,3</sup>, Cao Y<sup>4</sup>, Nilsson TK<sup>3</sup>, Hurtig-Wennlöf A<sup>5</sup>

<sup>1</sup>Department of Laboratory Medicine, Faculty of Medicine and Health, Örebro University Hospital, Örebro, Sweden.

<sup>2</sup>School of Medicine, Faculty of Medicine and Health, Örebro University, Örebro, Sweden.
 <sup>3</sup>Department of Medical Biosciences/Clinical Chemistry, Umeå University, Umeå, Sweden.
 <sup>4</sup>Clinical Epidemiology and Biostatistics, School of Medical Sciences, Örebro University, Örebro, Sweden
 <sup>5</sup>School of Health, Faculty of Medicine and Health, Örebro University, Örebro, Sweden.

**Background/objectives:** Combining several markers of cardiovascular risk into one risk prediction model has the potential to increase its predictive power. In this study, we employed cluster analyses in a population of young subjects based on three physiological measures of vascular health. The outcome of the cluster analyses were then analyzed for their correlation with established biochemical risk factors of cardiovascular disease.

**Methods:** The arterial stiffness measures pulse-wave velocity, carotid-intima media thickness and augmentation index were measured in 834 young, healthy subjects. Three cluster analyses were employed. The subgrouping obtained from the cluster analyses were further analyzed for their association with established cardiovascular risk factors.

**Results:** The cluster analyses did not yield sufficiently distinct clustering (groups of individuals that could be categorized unequivocally as having either a healthier or unhealthier vascular structure and function). In univariate regression analyses, the three vascular health status measures were significantly associated with LDL, total cholesterol, fasting insulin, plasma glucose, body fat percentage, CRP and orosomucoid.

**Conclusions:** The cluster analyses did not yield straightforward clusters, consisting of distinct groups of progressively worsening vascular status. This could be reflective of the complexity of the atherosclerotic progression in its early stages. A vascular structure and function indicative of higher risk is detectable already in healthy, young individuals. Its relationship with the risk factors serum lipids, body composition and systemic inflammatory markers alludes to the importance of measures towards combating these risk factors in young individuals in order to stifle the atherosclerotic progression.



### The effect of faecal microbiota transfer on collagenous colitis symptoms

S. Holster<sup>1\*</sup> & J. Rode<sup>1\*</sup>, J. Bohr<sup>2</sup>, A. K. Kumawat<sup>3</sup>, E. Hultgren-Hörnqvist<sup>1</sup>, R. J. Brummer<sup>1</sup>, J. König<sup>1</sup>

 <sup>1</sup>Nutrition-Gut-Brain Interactions Research Centre, Faculty of Medicine and Health, School of Medical Sciences, Örebro University, Örebro, Sweden
 <sup>2</sup>Department of Gastroenterology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden, Örebro University Hospital, Örebro, Sweden
 <sup>3</sup>Cardiovascular Research Centre, Faculty of Medicine and Health, School of Medical Sciences, Örebro University, Örebro, Sweden

\*shared first authorship

# Abstract not available Only Poster

# Postoperative Mediastinitis by Cutibacterium acnes before and after addition of benzylpenicillin as perioperative prophylaxis

Sandström N<sup>1</sup>, Wickbom A<sup>1</sup>, Friberg Ö<sup>1</sup>.

### <sup>1</sup>Dept of Cardiothoracic and Vascular Surgery, Faculty of Medicine and Health, Örebro University, Örebro, Sweden

**Background/objectives:** Increasing evidence indicate that Cutibacterium acnes (CA) may cause deep sternal wound infections (SWI) after cardiac surgery. In Sweden, cloxacillin is recommended as the sole antibiotic prophylaxis. Cloxacillin is not optimal for prevention of CA, moreover CA are resilient to chlorhexidine. However, CA are susceptible to Benzylpenicillin. We therefore added Benzylpenicillin to our routine intraoperative prophylaxis in 2015. The aim of this study was to compare the incidence of SWI before and after addition of Benzylpenicillin

**Methods:** In his study, we included 3469 consecutive patients that underwent cardiac surgery at our centre from 2009 thru 2017. All patients were followed-up two months postoperatively. The rates of SWI that required surgical intervention and/or antibiotic treatment before and after 2015 were compared. Logistic multivariable analysis was used to adjust for potential confounders.

**Results:** The incidence of SWI that required surgical revision decreased from 4.89% to 1.78% after addition of Benzylpenicillin (p < 0.001). There was no reduction, however, in superficial SWIs that were only treated with antibiotics. Significant decrease was seen in SWIs caused by Coagulase negative staphylococci, either alone (p<0.001) or concomitant with PA (p=0.011). Addition of Benzylpenicillin remained independently associated with reduction in SWI in the multivariable analysis (OR=0.38, 95% CI=0.23-0.61)

**Conclusions:** Addition of Benzylpenicillin to routine prophylaxis was associated with a reduction in surgically treated SWI. This indicates that CA actually play an important role in SWI. Benzylpenicillin is an inexpensive, safe and ecologically attractive prophylactic antibiotic and is now included in our routine.

### Patient participation in forensic psychiatric care: The staff perspective

Selvin M<sup>1</sup>, Almqvist K<sup>2</sup>, Kjellin L<sup>1</sup>, Schröder A<sup>1,3</sup>

<sup>1</sup>University Health Care Research Center, Faculty of Medicine and Health, Örebro University, Sweden <sup>2</sup>Department for Social and Psychological studies, Karlstad University, Sweden <sup>3</sup>Department of Nursing, Faculty of Health, Care and Nursing, Norwegian U:niversity of Science and Technology (NTNU), Gjövik, Norway

**Objective:** Patient participation is a central concept in modern health care and an important factor in theories/models such as; person centered care, shared decision making and human right approaches. However, the concept of patient participation is complex. The definition is still widely defined and seems to variate depending on the context and on which perspective that is taken. Forensic psychiatric care is a specialized setting where patients generally are treated long time and often against their will. When measuring the quality of the care in this context, we know that patient participation is rated as low among both patients and staff. In an earlier study we asked patients how they perceive the concept of patient participation and to increase the understanding about the concept we also need to include other perspectives. Therefore, the aim of this study was to describe staffs' perceptions of the concept of patient participation in forensic psychiatric care.

Methods: Interviews with 19 professionals were analyzed with a phenomenographic approach.

**Results:** Staff describe patient participation as a progression. First you need to create prerequisites, then adjust after the forensic circumstances and finally use it as a way to encourage the patient to be more independent.

**Conclusions:** The findings confirm that the concept is complex but an important factor to improve in order to increase the quality of care.

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# Validation of IBD diagnoses and Montreal classification defined subgroups of the diseases in the Swedish National Patient Register

Sarita Shrestha<sup>1</sup>, Ola Olén<sup>2,3,4</sup>, Carl Eriksson<sup>5</sup>, Asa Hallqvist Everhov<sup>2,3</sup>, Par Myrelid<sup>6</sup>, - The Swibreg Study Group, Jonas F Ludvigsson<sup>7,8,9,10</sup>, Ida Schoultz<sup>1</sup>, Scott Montgomery<sup>4,11,12</sup>, Michael C Sachs<sup>2</sup>, Jonas Halfvarson<sup>5</sup>

<sup>1</sup>School of Medical Sciences, Örebro University, Örebro

<sup>2</sup>Department of Clinical Science and Education, Södersjukhuset, Karolinska Institutet, Stockholm, Sweden

<sup>3</sup>Clinical Epidemiology Unit, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden

<sup>4</sup>Department of pediatric gastroenterology and nutrition, Sachs' Children and Youth Hospital, Stockholm, Sweden

<sup>5</sup>Department of Gastroenterology, Faculty of Medicine and Health, Örebro University, SE 70182 Örebro, Sweden

<sup>6</sup> Division of surgery, Department of Clinical and Experimental Medicine, Faulty of Health Sciences, Linköping University and Department of Surgery, County Council of Östergötland Linköping, Sweden

<sup>7</sup>Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

<sup>8</sup> Department of Pediatrics, Örebro University Hospital, Örebro University, Örebro, Sweden

<sup>9</sup>Division of Epidemiology and Public Health, School of Medicine, University of Nottingham, Nottingham, UK. <sup>10</sup>Department of Medicine, Celiac Disease Center, Columbia University College of Physicians and Surgeons, New York, NY, USA

<sup>11</sup>Clinical Epidemiology and Biostatistics, School of Medical Sciences, Örebro University, Örebro <sup>12</sup>Department of Epidemiology and Public Health, University College London, London, UK

The SWIBREG Study Group:

Malin Olsson, Henrik Hjortswang, Jonas Bengtsson, Hans Strid, Marie Andersson, Susanna Jäghult, Michael Eberhardsson, Caroline Nordenvall, Jan Björk, Ulrika Fagerberg, Martin Rejler, Olof Grip.

**Background/objectives:** The Swedish National Patient Register (NPR) is considered an essential data source for research in Sweden allowing linkage with other national registers. However, whether data on International Classification of Diseases and related health problems (ICD) codes registered in the NPR can be used to predict incident diagnosis of inflammatory bowel disease (IBD) or to define subgroups of patients with prevalent Crohn's disease and ulcerative colitis is unknown.

**Methods:** Information on IBD associated ICD codes between 1966 and 2014 was retrieved from the NPR and validated against data obtained from the medical record's review. To predict types of IBD among patients with incident disease, the first two IBD-associated ICD-codes registered in the NPR were used and, ICD-codes during the 5-year period prior to the journal review for prediction of prevalent IBD and its subtypes. Positive predictive values (PPV) with 95% confidence interval were calculated.

**Results:** The accuracy was high for prediction of diagnosis of Crohn's disease and ulcerative colitis for both incident patients with PPV of 99% (95%CI: 98–100) and 97% (95%CI: 95–98) and prevalent patients with PPV of 94% (95%CI: 93–96) and PPV of 98% (95%CI: 96–99). Age at diagnosis were stratified to A1≤16 years, A2:17-40 years, A3>40 years with PPV of 95% (95%CI=93–98), 96% (95%CI=95–97) and 90% (95%CI=86–94) respectively.

**Conclusions:** The Swedish NPR is a reliable source of data to identify patients with Crohn's disease and ulcerative colitis. The register-based prediction algorithms to define age at diagnosis, complicated Crohn's disease behavior, perianal disease and disease extent had high accuracy. However, the validity was less impressive in other subtypes and it should be considered in the future studies.

# Swedish parents' experiences of their role in treatment for children with congenital limb reduction deficiency – decision making and treatment support

Lis Sjöberg<sup>1</sup>, Liselotte Hermansson<sup>1,2,3</sup>, Helen Lindner<sup>1</sup>, Carin Fredriksson<sup>1</sup>

<sup>1</sup> School of Health Sciences, Örebro University, Örebro, Sweden

<sup>2</sup> Department of Prosthetics and Orthotics, Faculty of Medicine and Health, Örebro University, Örebro, Sweden

<sup>3</sup> University Health Care Research Center, Faculty of Medicine and Health, Örebro University, Örebro, Sweden

**Objective:** Parents of children with congenital limb deficiency are facing many treatment decisions during their child the child's first years. Different treatment options are offered to suit the child's needs, i.e surgery, assistive devices or adaptations. A family centered approach, supported by Swedish legislation (Patient law, SFS 2014:821) intend to strengthen the parental role in making treatment decisions for their child. However, how do parents experience their role?

The aim of this study was to describe parent's experiences of their role in decision-making and treatment for children with congenital limb reduction deficiency.

**Method:** A descriptive, qualitative approach was used. Semi-structured interviews were conducted with parents (n=17, 12/5) of children (1-12 years of age) with upper or lower limb reduction deficiency. Data was analysed using qualitative content analysis.

**Results:** Two themes regarding the parental role appeared. *Being a decision maker for someone else* was experienced as a part of the parenthood, making the best decisions for the child in cooperation with others. *Becoming and being a (treatment) supporter* included to motivate and support the child, prepare the child for meeting people in their environment, to communicate information to the child's environment and being the "extended arm" of the health care.

**Conclusion:** Parents have a challenging role in decision-making and treatment, including many different aspects that they handle with individual approaches. In order to provide the most appropriate family centered service clinical professionals need to recognize and understand each parents' approach in the decision-making and subsequent treatment for their child.

### **TREATMENT OPTIONS FOR GRAVES' HYPERTHYROIDISM -COMPARING** A SWEDISH INDEX PATIENT COHORT WITH RESULTS FROM **INTERNATIONAL QUESTIONNAIRE STUDIES**

G. Sjolin<sup>1</sup>, M. Holmberg<sup>2</sup>, O. Törring<sup>3</sup>, J. Calissendorff<sup>4</sup>, M. Lantz<sup>5</sup>, B. Hallengren<sup>5</sup>, H. Filipsson Nyström<sup>2</sup>, G. Wallin<sup>1</sup>

<sup>1</sup>Department of surgery, Örebro University Hospital, Örebro

<sup>2</sup> Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg,

<sup>3</sup>*Institution for Clinical Science and Education, Karolinska Institutet, Södersjukhuset* 

<sup>4</sup> Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm

<sup>5</sup> Dept. of Clinical Sciences, Lund University, Lund, Sweden

Background/objectives: The treatment strategies for a 42-year old female index patient with moderate Graves' disease (GD), varies considerably according to international surveys (1-8). Higher preference for RAI treatment in USA and Middle East/Africa compared to the rest of the world were observed (2-15). Some population based studies (16-18) has confirmed these results, but comprised different patient selection through different inclusion criteria.

Methods: From a Swedish cohort of 1186 GD patients, with the same criteria used in the previous ETA and ATA surveys for the index patient (2-5) we extracted 27 women, 40-45 year old and otherwise healthy who had two children and uncomplicated GD. The choice of treatment of this subcohort was compared with the results from questionnaire studies among different Thyroid Associations worldwide. In addition, a comparison with the whole Swedish cohort was also performed.

Results: Of the 27 patient in the subcohort s who met the criteria for the index case 77.8% selected ATD, 22.2% RAI and no one underwent surgery as primary treatment. In the total Swedish cohort 65.3% received ATD and 27.3% RAI and 4,6% surgery, a distribution not significant different from the index subcohort.

**Conclusion:** To the best of our knowledge this is the first comparison between a real index patient cohort and the Thyroid Associations questionnaire surveys based on the same criteria. Treatment choice of an index patient with GD in Sweden seems to adhere to international practice according to European and Chinese surveys i.e. mainly ATD as the preferred first choice. In line with this it differs compared to US and Africa where RAI is more often used primarily (2-15).

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# Home care nurses' experiences of the Swedish Dignity Care Intervention (DCI-SWE)

Söderman, A.<sup>1</sup>, Werkander Harstäde, C.<sup>2</sup>, Hälleberg Nyman, M.<sup>1</sup>, Östlund, U.<sup>3</sup>, & Blomberg, K.<sup>1</sup>

<sup>1</sup> Faculty of Medicine and Health, School of Health Sciences, Örebro University, Örebro, Sweden <sup>2</sup> Centre for Collaborative Palliative Care, Faculty of Health and Life Sciences, Linnaeus University, Växjö, Sweden

<sup>3</sup> Centre for Research & Development, Uppsala University/Region Gävleborg, Gävle, Sweden

**Background/objectives:** Dignity is a central value for older persons' health as it concerns their wellbeing, but it can be a challenge for nurses to invest in older persons' psychosocial needs. Interventions to promote older persons' dignity are rare and those that exist need further implementation and evaluation. The Dignity Care Intervention (DCI) has been developed in Scotland to enhance dignity in persons with palliative care needs. The DCI includes the instrument "Patient Dignity Inventory", reflective questions and care actions related to a person's dignity. The nurse first measure a person's dignity related distress, and then follow up the result by communicating and planning care actions together with the person. The DCI has been adapted to the Swedish context and was tested within home care in 2017. The aim was to describe home care nurses' (HCNs) experiences of the Swedish Dignity Care Intervention (DCI-SWE).

**Method:** A qualitative design was used with focus group interviews (n=3), one individual interview, reflective diaries and field notes. Eleven HCNs participated. Data were analysed by inductive content analysis according to Elo and Kyngäs.

**Results:** The DCI-SWE gave HCNs structure and overview while providing palliative care. It also gave older persons opportunities to be seen and to express themselves. Some prerequisites for introducing DCI-SWE were found to be older persons being informed about their situation (for example about their illness), HCNs ability to hold conversations and to have uninterrupted moments with the older person. Some HCNs thought it was challenging to talk about death – but the DCI-SWE was found to develop some of the HCNs communication skills. Important resources for using DCI-SWE within the organization were found to be leadership, enough time and staff. Some improvements of DCI-SWE may be required according to HCNs responses, for example a limited text mass in the intervention. HCNs also wished for time to reflect in connection with the use of DCI-SWE.

**Conclusions:** The HCNs experienced that there is not always time for conversations with older persons, and thereby psychosocial care could be non-completed. With organizational support and training in communication, HCNs can become more comfortable in providing dignity-conserving care in the home care context. With more resources in home care, the use of DCI-SWE can be facilitated.

# The mental and physical health problems of older offenders: A systematic review and meta-analysis

Solares C.<sup>1</sup>, Dobrosavljevic M.<sup>2</sup>, Andershed H.<sup>1</sup>, Larsson H.<sup>2</sup>, Cortese S.<sup>3</sup>

<sup>1</sup>School of Law, Psychology and Social Work, Örebro University, Sweden.
 <sup>2</sup>School of Medical Sciences, Örebro University, Sweden.
 <sup>3</sup>Department of Psychology, University of Southampton, England.

**Background/objectives:** Little research has explored the health problems of older offenders. The aim of this study is to provide a comprehensive description of both Mental and Physical health problems in this population. We also aim to understand how different confounders affect the prevalence of the health problems and whether these health conditions differ to the most common health problems in older adults in the community.

**Methods:** A systematic review and meta-analysis was performed. Search was run in five databases. Publications about offenders older than 50 year old and reporting prevalence data of different health problems were included. The outcomes were any type of mental or physical health problem diagnosed using DSM or ICD criteria.

**Results:** Pool prevalences for twenty-five mental and thirty-four physical health problems were calculated. Few studies included a comparison group of older adults in the community. Older offenders showed a higher risk of having Hypertension (RR=1.16), Cardiovascular Disorders (RR=1.24), Respiratory diseases (RR=1.75), and Arthritis (RR=1.19). Heterogeneity was high (I<sup>2</sup>>75) for all the meta-analyzed outcomes. This was partially explained by the confounding effect of the country, the diagnosis assessment method and the inclusion of females or forensic patients in the samples.

**Conclusions:** Older offenders show a complex profile of mental and physical health problems and it is uncertain if they have a higher risk for negative health outcomes than older adults in the community. More research is needed controlling for different factors that may influence the health problems and including comparison groups of older adults in the community.

### Phonological development in children with otitis proneness A longitudinal study for ages 3;6 to 5;6 years

### Stålnacke, H<sup>1</sup>

<sup>1</sup>Department of health sciences, Örebro University, Örebro, Sweden

**Objective**: Children with hearing loss constitute a high-risk group for delayed language and speech development. One type of hearing loss, which occurs mainly in the early childhood years, is a conductive hearing loss, caused by fluid in the middle ear (secretory otitis media). Secretory otitis media is a consequence of an upper respiratory tract infection or an acute ear infection (acute otitis media). Acute otitis media is a common childhood disease that affects almost 80% of all children at some time before the age of five. Some children experience recurrent episodes of acute otitis media. If the child has three or more episodes of acute otitis media during a six-month period, the child is said to be prone to otitis media (Medicinska forskningsrådet, 2000). Thus, during a number of episodes of affected hearing ability, fluctuating and degraded acoustic signals are presented to the cochlea, limiting children's ability to discriminate, store and reproduce appropriate acoustic contrasts between speech sounds.

This longitudinal study focuses on the phonological development in terms of the emerging phonological system (word- and syllable-shapes, phoneme inventories), the developmental phonological processes and phonological awareness, in Swedish children with otitis-proneness.

**Method**: A total number of 43 children (25 prone to otitis media, and 21 controls) were included in the study. The children's phonological development was longitudinally investigated at ages 3;6, 4;6 and 5;6 years. Speech samples, containing a maximum of 103 words for each child, were elicited by standardized picture naming tasks (Fonemtest) at the age of 3;6 and 4;6 years. At the age of 5;6 years, results concerning phonological awareness were collected.

**Results**: The results indicate no significant group differences for either phonological production or phonological awareness. The results from a longitudinal aspect indicate some differences between the groups regarding phonological production, for example, the production of certain speech sounds and the use of certain simplification processes.

**Conclusions**: The overall findings indicates that otitis proneness before the age of 2;6 years is not an indicator for group differences in phonological development at the age of 3;6, 4;6 and 5;6 years. However, from a longitudinal perspective, 3;6 to 4;6 years, there seems to be some differences.

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# Test-retest reliability of the Assessment of Time Management Skills – Swedish version (ATMS-S)

Thorsson M<sup>1</sup>, Holmqvist Lidström K<sup>2</sup>

<sup>1</sup>School of Health Sciences, Örebro University, Örebro, Sweden <sup>2</sup>University health care research center, Faculty of Medicine and Health, Örebro University, Örebro, Sweden

**Background/objectives:** The Assessment of Time Management Skills is a self-assessment aiming to measure how clients use strategies, tools and self-awareness concerning time management skills in everyday life. The purpose of this study was to evaluate the test-retest reliability of the Swedish version of the Assessment of Time Management Skills (ATMS-S).

**Methods:** Thirty participants with neurodevelopmental disorders and difficulties in time management completed the test twice with approximately one week apart. Test-retest reliability for the ATMS-S as a whole and its three subscales was analyzed using intraclass correlation coefficients. The smallest detectable change was calculated to determine the precision of individual scores.

**Results:** The results shows overall good stability for the instrument. For the ATMS-S as a whole, the intraclass correlation coefficients were 0.734-0.932 and the coefficients of each of its three subscales ranged from 0.656 to 0.932. The smallest detectable change was 8.430 for the ATMS-S and indicates that the instrument can detect changes in individuals.

**Conclusions:** The results of this study suggest that the ATMS-S can be a useful tool for measuring time management skills in persons with neurodevelopmental disorders. Further studies are needed to validate the Swedish version of the assessment of time management skills.

### Breast milk micro-RNAs with potential immune regulating properties

Ahlberg Emelie<sup>1</sup>, Jenmalm Maria<sup>1</sup>, Tingö Lina<sup>1,2</sup>

<sup>1</sup>Department of Clinical and Experimental Medicine, Linköping University, Sweden <sup>2</sup>School of Medical Sciences, Örebro University, Örebro, Sweden

**Background/objectives:** microRNA (miRNA) are short RNA sequences that finetune protein translation by posttranscriptional modifications of mRNA. Accordingly, miRNA may be important regulators of immune-related pathways and epigenetic modifications in immune cells. miRNAs are found in various body fluids, including breastmilk (BM). BM miRNA may be transferred from mother to infant and potentially regulate development of the baby's immune system. In this study we aimed to isolate, quantify and screen for immune-related miRNAs in human BM.

**Method:** We have evaluated seven different RNA extraction kits and two different qPCRbased quantification methods to isolate miRNA from human BM. The isolation kits include six commercially available spin-column based RNA extraction kits and a kit utilizing oligonucleotide-conjugated magnetic beads. The miRNA isolates from 10 healthy lactating women four month post-delivery were subjected to single target qPCR with quantification of hsa-miR-148a-3p. In addition, samples from four of the women, collected at the same timepoint, were screened for 754 unique miRNA using TaqMan Advanced miRNA Array Cards A and B. Out of the 754 miRNAs, 60 were expressed in > 3 BM samples with a Ct < 30. Furthermore, 42 were identified as immune-related based on information available in current scientific literature and databases (*i.e.* TargetScan and miRbase). Based on this comprehensive screening we designed a customized miRNA array for quantification of immune-related human BM miRNAs in a randomized placebo-controlled (RCT) allergy prevention trial, PROOM-3. The PROOM-3 trial evaluates the effects of pre-and postnatal *Lactobacillus (L) reuteri* and omega-3 polyunsaturated fatty acid supplementation from gestational week 20 through the first year of life in 480 women and their children.

**Results:** The performance of the RNA isolation kits in BM varied. We successfully quantified hsa-miR-148a-3p by qPCR and preliminary findings from our screening of BM of 80 women included in PROOM-3 (colostrum and 3 month post-delivery) show that the interventions significantly impact BM miRNA expression. In the *L reuteri* and  $\omega$ -3 PUFA group, 16/24 miRNAs changed expression profile over time; 6/24 miRNAs changed in the  $\omega$ -3 PUFA + Placebo group, while only three miRNAs changed significantly between in the placebo + placebo treated women (all p < 0.05).

**Conclusion:** The performance variation in the isolation kits are worth taking notice of when planning RNA extractions from BM. However, miR-148a-3p was could be quantified in isolates from all kits. The preliminary findings from our RCT are promising and we are now moving further by increasing the number of women/BM samples included in the screening.

# Screening of host proteins interacting with Kunjin, Langat, Zika replication complex

Pham Tue Hung Tran<sup>1</sup>, Roger Karlsson<sup>2</sup>, Ander Karlsson<sup>2</sup>, Naveed Asghar<sup>1</sup>, Magnus Johansson<sup>1</sup>, Wessam Melik<sup>1</sup>

<sup>1</sup>School of Medical Sciences, Örebro University, Örebro, Sweden <sup>2</sup>Department of Clinical Microbiology, Sahlgrenska University Hospital, Gothenburg, Sweden; Nanoxis Consulting AB, Gothenburg, Sweden

**Background/objectives:** During infection and eclipse time, Flaviviruses induce invagination of the endoplasmic reticulum (ER) membrane to form compartments, protecting their viral replication complex. The rearrangements of ER membrane require modifications in ER membrane lipid constituents or binding of proteins to bend the membrane. Indeed, it has been implicated that both KUNV and DENV NS1, NS2A, NS4A, NS4B proteins could induce membrane remodelling. However, it is not well known whether host proteins can also participate in the formation and maintenance of these compartments. In this project, we aimed to identify host proteins interacting with Kunjin, Langat, Zika replication complex. These proteins may function for ER invagination during Flavivirus infection.

**Methods:** We used human adenocarcinoma epithelial A549 cells as a cell model, mosquitoborne Zika, Kunjin virus, and tick-borne Langat virus as virus models. After virus infections, the ER membranes from infected and non-infected cells were harvested using ultracentrifuge with a sucrose gradient. Proteins from these ERs were identified using mass spectrometry. We compared the differences between the ER proteomes to identify host candidate proteins that can cause the RC formation. To narrows the list of true candidate proteins, we attempted to enrich the RC-containing fractions by doing co-immuno precipitation, following by TMT-MS to identify and quantify the host proteins from Co-IP elutions.

**Results:** Compared to non-infected samples, we identified 168, 636, and 447 host proteins expressed in LGTV, KUNV, ZIKV infected ER, respectively. There were 73 host proteins expressed in both infected samples.

**Conclusions:** By doing proteomics analysis, we identified host proteins express during virus infection and replication. These candidates will be characterized in the future.

### Revealing new tick-borne encephalitis foci by screening antibodies in sheep milk

Amélie Wallenhammar<sup>1</sup>, Naveed Asghar<sup>1</sup>, Sezin Gunaltay<sup>1</sup>, Richard Lindqvist<sup>2</sup>, Hans Fredlund<sup>3</sup>, Åke Davidsson<sup>1</sup>, Sören Andersson<sup>1</sup>, Anna K Överby<sup>2</sup> and Magnus Johansson<sup>1</sup>

 <sup>1</sup>School of Medical Sciences, iRiSC (Inflammatory Response and Infection Susceptibility Centre), Örebro University, Sweden
 <sup>2</sup>Department of Clinical Microbiology, Laboratory for molecular infection medicine Sweden (MIMS), Umeå University, Sweden
 <sup>3</sup>Department of Laboratory Medicine, Faculty of Medicine and Health, Örebro University, Sweden

**Background/objectives**: Climate changes have increased the tick-distribution in Sweden, and the prevalence of ticks has been predicted to increase towards the northern parts of the country, increasing the risk of tick-borne zoonosis in new regions<sup>1</sup>. Tick-borne encephalitis (TBE) is the most important viral tick-borne zoonosis in Sweden as well as in Europe. TBE virus (TBEV) infection often leads to severe CNS disease, including encephalitis and severe myelitis, which may lead to paralysis and respiratory failure in humans<sup>2</sup>. TBEV and antibodies against TBEV are excreted in milk of goats, sheep and cattle and the virus can be ingested orally by consumption of non-pasteurized dairy products. Virus prevalence in questing ticks is a difficult indicator of TBE infection risk as viral RNA is rarely detected even in large sample sizes collected at known TBE endemic areas. There is hence a need for new and robust surveillance techniques to identify new TBEV risk areas at early stages.

**Methods and results:** In this study we have developed a novel strategy for identifying new TBEV foci. We have collected raw milk and colostrum samples from sheep and goats in Örebro County, Sweden. The milk samples were analyzed for the presence of TBEV antibodies by ELISA, and validated by an in-house Western Blot assay where milk samples were used as primary antibody to detect purified TBEV E-protein. By monitoring TBEV antibodies in milk we have found three novel foci in the Örebro County which also overlap with the plausible place of infection of registered human TBE cases reported during 2009-2018. Furthermore, the stability of TBEV in milk and raw milk was studied at different temperatures. Our data indicates that keeping unpasteurized milk at 4 °C will preserve the infectivity of TBEV for several days. Ticks have also been collected from areas with TBEV positive milk. We aim to extract total RNA from the sampled ticks, followed by TBEV detection by nested-PCR and next-generation sequencing.

**Conclusion:** Altogether, we here present a novel technique to reveal risk areas of tick-borne encephalitis in Sweden by detecting TBE antibodies in sheep milk. This approach is robust, reliable, and non-invasive and can accordingly be used to map TBEV "hotspots". In the TBE foci, more than 50 % of the tested animals were antibody positive. TBEV infectivity in refrigerated milk was preserved, stressing the importance of pasteurization before consumption.

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### **Bionic hands – benefit and use**

Widehammar  $C^{1,2}$ , Hiyoshi  $A^3$ , Lidström Holmqvist  $K^1$ , Lindner  $H^4$ , Hermansson  $L^{1,5}$ 

<sup>1</sup>University Health Care Research Centre, Faculty of medicine and health, Örebro University, Sweden <sup>2</sup>Dept of Peadiatrics, Faculty of Medicine and Health, Örebro University, Sweden

<sup>3</sup> Clinical Epidemiology and Biostatistics, School of Medical Sciences, Örebro University, Sweden

<sup>4</sup> School of Health Sciences, Örebro University, Sweden.

<sup>5</sup> Dept of Prosthetics and Orthotics, Faculty of Medicine and Health, Örebro University, Sweden

**Objective:** Prosthetic hands with advanced technology making it possible to perform different grasps and positions are expensive and their usefulness has been questioned. Multiple choices of grasps and positions may be useful, but are the patients able to shift between grasps in a timely manner when performing tasks, and what grasps are most useful and mostly used?

**Methods:** A single case experimental design was used. Inclusion criterions: Age >18 years, congenital or acquired amputation, previous user of a conventional myoelectric prosthesis. Five persons were assessed three times before fitting and 6 times after fitting during intensive training and follow up. Outcome measures: Canadian Occupational Performance Measure (scored 1-10, high score better performance), a modified Southampton Hand Assessment Protocol (SHAP) measured switching between grasps, and a study specific questionnaire. Visual analyses and multilevel linear regression was made.

**Result:** The occupational performance and satisfaction scores increased for all individually chosen activities by using the advanced hand. On average performance increased with 3.9 points (p<0.001) and satisfaction 4.7 points (p<0.001). Mean time for switching between grasps improved, light objects=27 seconds faster, heavy objects=48 seconds faster in the modified SHAP test. On average 7/11 grasps were used. Most useful grasps were power, tripod and key-pinch.

**Conclusion:** The advanced hand was more useful than the conventional hand for the individual chosen activities. The participants learned shifting between grasps in a timely manner, and used several grasps. A successful fitting is always a combination of the product and the training to learn how to use it.

### Immediate postoperative mobilisation after colorectal surgery: a feasibility study

Jan Stepniewski<sup>1</sup>, Rose-Marie W Thörn<sup>2</sup>, Rebecca Ahlstrand<sup>1</sup>, Hans Hjelmqvist<sup>1</sup>, Anette Forsberg<sup>2</sup>, Olle Ljungqvist<sup>3</sup>

<sup>1</sup>Department of Anaesthesiology and Intensive Care, Örebro University hospital <sup>2</sup>Department of Physiotherapy, Örebro University hospital <sup>3</sup>Department of Surgery, Örebro University Hospital

**Objective:** Early mobilisation is recommended by the Enhanced Recovery after Surgery (ERAS) guidelines. The aim of this study was to evaluate the feasibility of immediate postoperative mobilisation after elective colorectal surgery.

**Methods:** Patients undergoing elective major open and laparoscopic colorectal surgery under inhalation anesthesia were prospectively included. The patients received a mobilisation intervention by an experienced physiotherapist, starting 30 minutes after arrival in the post-anesthesia care unit (PACU). The intervention utilized the Surgical ICU Optimal Mobilization Score (SOMS), 0=no activity, 1=activity in bed, 2=sitting, 3=standing and 4=ambulation. Progress from each step to the next required a safe mobilisation including normal O<sub>2</sub> saturation, blood pressure (BP) and adequate pain control. Every half hour a mobilisation attempt was made. The level of SOMS reached during PACU stay up to 4 hours and any adverse events was assessed.

**Results:** 40 patients with mean age 65 years, 16 male and 24 female, were included. After 1 hour 11 patients (27%) could be mobilized out of bed (levels 3 and 4) and after 4 hours 30 patients (75%). Only two patients (5%) could not be mobilized (level 0) after 4 hours in PACU. No serious adverse events were observed. The most severe symptoms were; seven patients experiencing symptomatic low BP and one patient vomiting.

**Conclusions:** This study reports that 3 out of 4 patients can safely be mobilised out of bed within 4 hours of PACU-stay after major colorectal surgery. Immediate mobilisation was achieved with the support of a physiotherapist, adequate staff resources and equipment.

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### A better Understanding of Speech Perception in Noise using New Measures of Word Frequency, Neighborhood Density, Phonotactic Probability and Orthographic Transparency.

Witte, E<sup>1,2</sup>., Köbler, S<sup>1,2</sup>., Smeds, K.<sup>3</sup>, Ekeroot, J.<sup>4</sup>, Mäki-Torkko, E.<sup>5, 2</sup>

 <sup>1</sup>School of Health Sciences, Faculty of Medicine and Health, Örebro University, Örebro, SE 70182
 <sup>2</sup>Swedish Institute for Disability Research, Örebro University, Örebro, SE 70182
 <sup>3</sup>ORCA Europe, Widex A/S, Björns Trädgårdsgränd 1, Stockholm, SE 116 21
 <sup>4</sup>Department of Surgical Sciences, Section of Otorhinolaryngology, Head and Neck Surgery, Uppsala University, Uppsala, Sweden
 <sup>5</sup>School of Medical Sciences, Faculty of Medicine and Health, Örebro University, Örebro, SE 70182

**Objective:** When assessing someone's hearing, speech-in-noise testing is an important complement to other audiometric measures. When selecting linguistic stimuli for new speech-in-noise tests, various lexical factors, and their influence on the final test, need to be considered. The present study investigated which effect a set of lexical factors had on the outcome of a new Swedish phonetic perception test called the SiB-test. Specifically, the factors included were the Zipf-scale word-frequency value (Z), the Zipf-scale-weighted phonetic neighborhood density probability (PNDP), the word-minimum normalized stress and syllable structure-based phonotactic probability (SSPP), and the word-minimum grapheme-initial letter-to-pronunciation orthographic transparency (GIL2P-OT) from Witte & Köbler (2019).

**Methods:** Thirty-nine Swedish speaking adults with normal hearing or symmetric sensorineural hearing loss were each presented with 84 separate three-alternative-forced-choice auditory word discrimination trials at a signal-to-noise ratio individually adjusted as to result in approximately 60 percent correct discrimination. The response alternatives were real Swedish words, differing from each other in only one phoneme. The observational data were analyzed using multi-level logistic regression modelling with Z, PNDP, SSPP and GIL2P-OT as main effects and participant as random effect.

**Results:** The results indicate that all lexical factors had statistically significant influences upon the probability of correct trial outcome. High values of Z, PNDP and GIL2P-OT showed facilitative effects, while high SSPP, contrary to expectations, showed an inhibitory effect on word discrimination. The largest effect derived from the Z metric, which alone could affect the test results by up to 40 percentage points.

**Conclusions:** The effect of lexical measures, such as those analyzed in the present study, are highly important to consider when creating new speech perception tests.

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### Potential Applications of DNA, RNA and Protein Biomarkers in Diagnosis, Therapy and Prognosis for Colorectal Cancer: A Study from Databases to AI-Assisted Verification

Xueli Zhang <sup>1,2</sup>, Xiao-Feng Sun <sup>3</sup>, Bairong Shen <sup>2</sup>, and Hong Zhang <sup>1</sup>

<sup>1</sup> School of Medicine, Institute of Medical Sciences, Örebro University, Örebro, Sweden

<sup>2</sup> Centre for Systems Biology, Soochow University, Suzhou 215006, China

<sup>3</sup> Department of Oncology and Clinical and Experimental Medicine, Linköping University, Linköping, Sweden

**Background/objectives:** In order to find out the most valuable biomarkers and pathways for diagnosis, therapy and prognosis in colorectal cancer (CRC) we have collected the published CRC biomarkers and established a CRC biomarker database (CBD: <u>http://sysbio.suda.edu.cn/CBD/index.html</u>).

**Methods**: In this study, we analysed the single and multiple DNA, RNA and protein biomarkers as well as their positions in cancer related pathways and protein-protein interaction (PPI) networks to describe their potential applications in diagnosis, therapy and prognosis. CRC biomarkers were collected from the CBD. The RNA and protein biomarkers were matched to their corresponding DNAs by the miRDB database and the PubMed Gene database, respectively. The PPI networks were used to investigate the relationships between protein biomarkers and further detect the multiple biomarkers. The Kyoto Encyclopaedia of Genes and Genomes (KEGG) pathway enrichment analysis and Gene Ontology (GO) annotation were used to analyse biological functions of the biomarkers. AI classification techniques were utilized to further verify the significances of the multiple biomarkers in diagnosis and prognosis for CRC.

**Results:** We showed that a large number of the DNA, RNA and protein biomarkers were associated with the diagnosis, therapy and prognosis in various degrees in the CRC biomarker networks. The CRC biomarkers were closely related to the CRC initiation and progression. Moreover, the biomarkers played critical roles in cellular proliferation, apoptosis and angiogenesis and they were involved in Ras, p53 and PI3K pathways. There were overlaps among the DNA, RNA and protein biomarkers. AI classification verifications showed that the combined multiple protein biomarkers played important roles to accurate early diagnosis and predict outcome for CRC. There were several single and multiple CRC protein biomarkers, which were associated with diagnosis, therapy and prognosis in CRC. Further, AI-assisted analysis revealed that multiple biomarkers had potential applications for diagnosis and prognosis in CRC.

**Conclusion:** In this study, we showed the potential applications of the CRC biomarkers in diagnosis, therapy and prognosis for CRC. We reported that there were many single biomarkers, which were associated with the early diagnosis, better therapy and predict prognosis in CRC. However, the combinations of multiple biomarkers and pathways might play more critical roles in diagnosis, therapy and prognosis for CRC than the single biomarkers. Therefore, the applications of multiple biomarkers and pathways could provide more precise criteria as valuable tools for early diagnosis, benefiting therapy and predicting prognosis for CRC patients.

### **Regulation of vascular endothelial laminin profile by pro-inflammatory cytokines TNF-a and IL-6 trans-signaling**

Mulugeta M Zegeye<sup>1</sup>, Assim Hayderi<sub>1</sub>, Ashok Kumawat<sup>1</sup>, Allan Sirsjö<sup>1</sup>, Liza U Ljungberg<sup>1</sup>

<sup>1</sup>Cardiovascular Research Center, School of Medical Sciences, Örebro University Sweden

**Background/objectives:** Laminins (LN) are trimeric cruciform proteins that constitute the endothelial basement membrane together with other extracellular matrix proteins collagen IV, nidogens and proteoglycans. Every laminin isoform contains one of each a, b, and g chains. There are about 18 laminin isoforms identified in mammals out of which LN411, LN421, LN511 and LN521 are expressed in vascular endothelial basement membrane. Previous reports indicated that the laminin expression pattern in the vessel wall is altered due to ageing, acute myocardial injury and atherosclerotic plaque progression<sup>1,2</sup>. In this study, we aimed at investigating the role of pro-inflammatory cytokines in regulating the endothelial laminin profile and the phenotypic and secretory response of endothelial cells when cultured to different laminin isoforms.

**Methods:** We treated HUVECs with IL-6/sIL-6R and TNF-**a** and analyzed gene and protein expressions of laminin chains using qPCR and immunoblotting respectively. In addition, HUVECs were cultured on different laminin isoforms and expression of endothelial markers was analyzed using qPCR, immunofluorescence staining and immunoblotting. Moreover, the release of pro-inflammatory mediators from the supernatants was quantified using Proximity Extension Assay (Olink<sup>â</sup>, Sweden).

**Results:** We found that activation of IL-6 trans-signaling in vascular endothelial cells induces a switch in laminin expression profile from a4 to a5 dominated pattern with a slight upregulation of b1 expression. Stimulation of vascular endothelial cells with TNF-a also triggers an upregulation of b3 and g2 expression. Olink® proteomics and qPCR analyses reveal that endothelial cells, depending on the laminin isoform the cells are cultured on, differ significantly in releasing pro-inflammatory chemokines/cytokines and the expression of tight junction proteins such as Claudin-5.

**Conclusion:** Collectively, our data indicate that the laminin profile expression by endothelial cells is under inflammatory control and the laminin composition in endothelial basement membrane appears to modulate the phenotype of vascular endothelial cells.

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# The role of PEAR1 in synthetic glycopolymer induced pro-inflammatory response in human vascular endothelial cells.

### Medkhanie MA, Zegeye MM, Kardeby C, Ljungberg LU, Fälker K, Grenegård M

### Cardiovascular Research Center, School of Medical Sciences, Örebro University, Sweden.

**Objective:** Fucose-rich sulfated carbohydrates (Fucoidans), and synthetic glycopolymers have appealing wide range of bioactivities including homeostasis and immune modulation. Recently, our lab demonstrated that natural fucose-based polysaccharides and synthetic glycopolymers induce Src-and PI3K-dependent aggregation of human platelets via the Platelet Endothelial Aggregation Receptro (PEAR1) which is a membrane bound tyrosine kinase (1).

PEAR1 is also abundantly expressed by endothelial cells (ECs), and little is known about its ligand and downstream functions despite few reports on its role in negative regulation of neoangiogenesis and endothelial secretome mediated platelet aggregation (2). Hence, we aim to investigate the effect of synthetic glycopolymers on the inflammatory response of human vascular ECs, and to characterize the involvement of PEAR1 in this process.

**Methods:** This was studied via stimulating HUVECs with a sulfated a-L-fucoside-pendant glycopolymers C329 (C329) for 5 min to 48h with or without prior knockdown of PEAR1 using guided stealth siRNAs. Then we preformed immune blotting from the cells lysates to quantify pAKT<sup>ser473</sup>, and qPCR from the extracted RNA to determine gene expression.

**Results:** We show that treatment of HUVECs with C329 induces quick phosphorylation of AKT<sup>ser473</sup> that peaks after 15 minutes. Besides, C329 causes late (peaks at 24h) upregulation in the gene expressions of proinflammatory chemokines MCP-1 and CXCL-11 in HUVECs. Further, we show that knocking down PEAR1 (80% knockdown efficiency) does not seem to affect the induction of MCP1 or CXCL-11 by the C329.

**Conclusion:** Our data imply that synthetic sulfated glycopolymers provoke intracellular signalling and pro-inflammatory response in human vascular ECs, and this effect appears not to involve PEAR1. **References:** 

- 1. Kardeby C, Fälker K, Haining EJ, Criel M, Ljungberg LU, et al. (2019). Synthetic glycopolymers and natural fucoidans cause human platelet aggregation via PEAR1 and GPIbα. <u>Blood Adv</u>. 3:275-87.
- Vandenbriele C, Kauskot A, Vandersmissen I, Criel M, Geenens R, et al. (2015).
  Platelet endothelial aggregation receptor-1: a novel modifier of neoangiogenesis. <u>Cardiovasc Res</u>. 108:124-38.

LATE ABSTRACTS

# Anti-VEGF therapy improves visual acuity and macular oedema in patients with central retinal vein occlusion: A real-life study

### Karlsson K<sup>1</sup>, Karlsson N<sup>2</sup>, Westborg I<sup>3</sup>

<sup>1</sup>School of Medical Sciences, Örebro University, Örebro, Sweden
 <sup>2</sup>Department of Ophthalmology, Örebro University Hospital, Örebro, Sweden
 <sup>3</sup>Department of Ophthalmology, Uppsala University Hospital, Uppsala Sweden

**Objective:** Randomized controlled studies have demonstrated that anti-VEGF therapy improves visual outcome in central retinal vein occlusion (CRVO), but few studies have investigated the effectiveness of the treatment in clinical practice. This study aims to evaluate the effectiveness of anti-VEGF treatment in a real-world cohort of patients with CRVO, with improvement in visual acuity (VA) and central retinal thickness (CRT) as the primary outcome measurements. A secondary objective was to compare visual outcomes in patients treated with the regimens Pro Renata (PRN) and Treat-and-extend (TER).

**Methods:** This retrospective real-life study included all patients diagnosed with CRVO in Örebro County between 2016–2017 that received anti-VEGF treatment and had registered values of VA and CRT at both baseline and at 52 weeks. Data were collected from the medical record.

**Results:** 17 eyes were included in the study. Mean VA, and mean CRT was improved at 52 weeks, compared with baseline ( $p = 0.0115^*$  and  $p = 0.0001^{***}$ , respectively). The reduction of macular oedema was more profound in the TER-group compared with the PRN-group ( $p = 0.0336^*$ ). A difference in mean gain of VA was observed, in favor of patients in the TER-group, although this was not statistically significant.

**Conclusion:** This study supports the existing literature that anti-VEGF improves visual outcomes in CRVO in a real-world setting. The Treat-and-extend regime may be more effective in reducing macular oedema compared with the Pro Renata regime, but further studies are warranted to evaluate which treatment regime that is most effective for improving visual acuity.

### Title of presentation:

# Late in-the-bag intraocular lens dislocation after cataract surgery: 15 Year follow up study at USÖ

### Presenter and co-author:

1 Diedrik Svanström

2 Sven Crafoord

### Affiliation (institution, department, country)

 MB, School of Medical Sciences, Örebro University, Sweden
 MD PhD, Department of Ophtalmology, Faculty of Medicine and Health, Örebro University, Sweden

### Abstract

**Objective:** Cataract surgery, is nowadays the most common surgical procedure performed in Sweden. Late in-the-bag intraocular lens dislocation (LITBILD), occurring many years after uneventful surgery, is due to progressive zonular weakness and capsular-shrinkage. Known risk factors include among others pseudoexfoliations (PXF), high myopia and previous vitreoretinal surgery. LITBILD has been reported with an increasing frequency in recent years. Thus, there is a value in further investigating this patient group and describe related risk factors. Aim Determine the 15-year cumulative risk of LITBILD after standard cataract surgery 2003 and describe possible risk factors causing LITBILD.

**Methods:** Retrospective nested case-control study examining patients who underwent cataract surgery with phacoemulsification in 2003 at Örebro University Hospital. To locate patients within that group who sustained LITBILD ICD10 diagnosis codes relating to LITBILD covering years 2003–2018 were assessed. Each case was matched with two controls of identical sex and age.

**Results:** Patients who underwent cataract surgery 2003 had a cumulative risk of 0.6% to develop LITBILD. The LITBILD group was 9 patients out of 1499 operated with median age at LITBILD of 80 years (range 57- 82). Median time between cataract surgery and LITBILD was 134 months (range 39-167). Glaucoma before and/or after cataract surgery and high intraocular pressure before surgery were independently statistically significant risk factors for LITBILD.

**Conclusions:** We have reasons to believe that the two statistically significant risk factors are associated with pseudoexfoliation disorder which is often difficult to identify following cataract surgery due to the capsulorhexis and therefore often goes underdiagnosed.