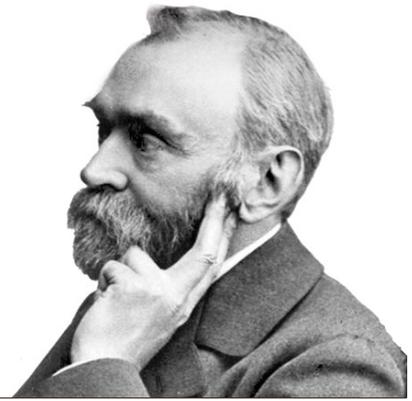


Örebro University's **NOBEL DAY FESTIVITIES**



BOOK OF ABSTRACTS

7 December 2023

Örebro University, **School of Health Sciences** and
School of Medical Sciences, Örebro Sweden.



Title: Örebro University's Nobel Day Festivities, Book of abstracts, 2023.

Publisher: Örebro University, 2023, www.oru.se/nobeldayfestivities

Editor: Caroline Larsson.

Örebro University's Nobel Day Festivities Committee:

Fredrik Alm, Ulrika Fernberg, Ina Johansson, Ashok Kumawat, Caroline Larsson, Tatiana Marques and Annika Söderman.

ISBN: 978-91-87789-92-2 (pdf).

Preface

The “Nobel Day Festivities” were established 2009 by Allan Sirsjö and Nikolaos Venizelos, researchers within Biomedicine, Department of Clinical Medicine (now School of Health Sciences and School of 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 honour this day by organizing research activities and festivities.

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!

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Otsu and Chan-Vese methods compared in thyroid active volume segmentation with Monte Carlo generated SPECT

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Background/Objective: The Otsu method and the Chan-Vese model are proven to perform well in determining organ volumes; this study aimed to compare their performance regarding segmentation of active thyroid gland volumes, by varying the parameters: gland volume, activity concentration, activity concentration heterogeneity and background activity concentration.

Method: Computed tomography was performed on three playdough thyroid phantoms (20, 35 and 50 ml). Image data were separated into playdough and water, based on Hounsfield values. Sixty single photon emission computed tomography (SPECT) projections were simulated by Monte Carlo method with Technetium-99m. Linear combinations of SPECT images were made, generating 12 volume and background combinations: each with both homogeneous thyroid activity concentration and three hotspots of different relative activity concentrations (48 SPECT volumes in total). The relative background levels chosen were 5%, 10%, 15% and 20% of phantom activity concentration and hotspot activities 100% (homogeneous case) 150%, 200% and 250%. Poisson noise (coefficient of variation of 0.8 at a 20% background level, scattering excluded) was added before Monte Carlo based SPECT reconstruction by the Sahlgrenska Academy reconstruction code (SARec). Otsu's threshold selection method and the Chan-Vese model for active contours without edges were applied for segmentation; the results were evaluated concerning relative volume, mean absolute error and standard deviation per thyroid volume, as well as dice similarity coefficient.

Result: Both methods segment the images well and deviate similarly from true volumes. They both slightly overestimate small volumes and underestimate large ones. Different background levels affect the two methods similarly as well. However, Chan-Vese deviates less and paired t-testing showed significant difference between distributions of dice similarity coefficients ($p < 0.01$).

Conclusion: Our investigations indicate that Chan-Vese performs better and is slightly more robust, albeit more challenging to implement and use clinically, than Otsu. There is a trade-off between performance and user-friendliness.

The association between depression and pain-related functioning among youth with musculoskeletal pain. A longitudinal study.

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Background/Objective: Chronic or recurrent pain and psychological distress are highly prevalent among adolescents globally. Nearly one in four adolescents report neck/shoulder pain. 45% of the girls and 28% of the boys also report co-occurring depressive symptoms. Chronic pain can result in negative consequences on functioning in various domains of life. There is some evidence that depression and pain-related functioning correlate. However, uncertainty remains on how they relate to one another. Theoretically, according to the fear avoidance model, depressive symptoms may be interpreted as consequences of pain-related functioning as well as pain-related functioning may be interpreted as affected by depressive symptoms. Earlier studies are cross-sectional, which does not enable analysing temporal relationships. Therefore, the aim of this study was to further analyse the temporal association between depression and pain-related functioning in daily life in adolescents with musculoskeletal pain.

Method: This is a longitudinal survey study, Three-cities study, including youth in 18 lower secondary schools in three cities in mid-Sweden. A subsample of data from youth in 7th grade, who reported musculoskeletal pain once a week, or more, during the last six months is used (n=617). The survey was filled in by the youth, in the classroom, once every year until 9th grade. Depressive symptoms were assessed with Center for Epidemiology Studies Depression Child (CESD-C). Functioning was assessed with three questions, assigning problems in school, leisure activities and contact with friends due to pain (answer: no, partially, yes). Four cross panel regression models were estimated to find the best fitting model for the association between depression and functioning across time: Autoregressive (the basic model); Depression predicting functioning; Functioning predicting depression; A bidirectional model where depression predicted functioning and functioning predicted depression. Gender was entered as a covariate.

Result: Analyses showed that depression and pain-related functioning were correlated across time. The model where depression predicted pain-related functioning provided the best model fit.

Conclusion: In this cohort of youth with recurrent musculoskeletal pain from the general population, depressive symptoms had a larger impact on future pain-related functioning than pain-related functioning had on the development of depressive symptoms. This supports a theoretical model where depressive symptoms drive pain-related functioning more than the other way around, which stress the importance of screening for depression in adolescents with chronic pain. In addition, targeting depressive symptoms might be essential in affecting pain and its functional consequences.

Comparative Analysis of Gastrointestinal and Faecal Microbiota

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Background/Objective: The accuracy of faecal samples in representing the human gastrointestinal microbiota remains a subject of debate. While rodent studies have reported substantial differences between faecal samples and internal gastrointestinal content, human studies have yielded contradictory findings. Our study aims to address this by comparing internal gastrointestinal content and faecal samples.

Method: We enrolled ten healthy adult participants and collected a total of 141 samples, employing 16S rRNA sequencing (V3-V4) to analyse taxonomic composition.

Result: Within our dataset, we observed robust intra-individual stability across various gut locations and sample types, with minimal variations overshadowed by inter-individual differences. Shannon alpha diversity index exhibited only slight variations between sample types and locations, while there was otherwise a notable general similarity between faecal samples and internal gastrointestinal content.

Conclusion: These findings support the use of faecal samples as reliable indicators of gastrointestinal microbiota, aligning with theoretical expectations.

Parents to new-born infants rated parent-delivered pain management as significantly meaningful during venepuncture

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Background/Objective: Parents express great readiness to actively deliver comfort for their infant during painful procedures. Previous research shows evidence for the efficacy of skin-to-skin contact and breastfeeding, preferably in combination. Live parental lullaby singing combined with skin-to-skin contact and breastfeeding has not previously been investigated during painful procedures. Parents as pain management in Swedish neonatal care (SWEpap), is a cutting-edge interdisciplinary multi-center study with mixed methods. The randomized controlled trial investigates the efficacy of combined parent-delivered pain management compared with standard care during routine blood sampling of healthy newborn infants.

Method: The aim of this analysis was to investigate how meaningful the parents experienced providing procedural pain management to their newborn infant in the three treatment groups; standard care with glucose, skin-to-skin contact, or a combination of skin-to-skin contact, breastfeeding (if applicable) and live parental lullaby singing. The parents rated the meaningfulness of the various conditions on a 100 mm visual analogue scale (VAS) from “not meaningful” on the left end point, up to “most possible meaningful” on the right end point of the scale. The parents were also asked to comment on how they experienced providing pain management.

Result: A total number of 151 newborn infants with at least one parent, participated in this analysis. The mean VAS-ratings for meaningfulness were 82.1 for standard care with glucose, 89.5 for skin-to-skin contact, and 88.9 for combined interventions with live parental lullaby singing, breastfeeding and skin-to-skin contact. The ratings for parent-delivered pain-alleviation were significantly higher than for standard care ($p=0.036$). Parents in all groups expressed that it was meaningful to provide pain-relief and participate in the pain management of their newborn infant.

Conclusion: Parents found it meaningful to provide parent-delivered pain-alleviating interventions with skin-to-skin contact, breastfeeding and live parental lullaby singing during painful procedures in postnatal care. The parents stated that they will continue using these methods in future painful situations.

Efficacy of *Lactobacillus rhamnosus* in novel micro-encapsulated Vs free-probiotic powder form to affect brain functional connectivity

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This project was partially funded by AnaBio Technologies, Cork, Ireland.

Background/Objective: The abundance and diversity of microbial species residing in the gut can influence the brain's biochemistry and structure through the **gut-brain axis**. Aging is a natural process that comes with physiological, but also lifestyle changes including diet, exercise, and socializing, relevant to this axis. Manipulation of the microbiota-gut-brain axis through **probiotic supplementation** has been shown to impact cognitive function and mental health, though little has been known about its impact on healthy older adults. Hence, this study involves a 3-arm, 6-week probiotic intervention in healthy, community dwelling, older adults (ages 60-80) that consumed a placebo, or a probiotic strain of *Lactobacillus rhamnosus* either in a free-probiotic or a novel micro-encapsulated powder form. This novel form can potentially elevate the probiotic's chance of survival in the stomach to reach the small intestine more efficiently. Our primary aim was to compare alterations in brain functional connectivity during resting state between the three groups among other markers of cognitive function, mental and gut health .

Method: We used Functional Magnetic Resonance Imaging (fMRI) to measure structural and resting-state functional connectivity changes in the brain. Other measurements were also performed in relation to changes in brain structure and concentration of certain neurotransmitters in the striatum; immune function and gut barrier integrity in blood; gut microbiota composition and their metabolites in fecal samples; as well as assessing cognitive, mental health and physical activity status.

Result: Our results include data analysis concerning the participants' anthropometric/demographic information, Food Frequency Questionnaire (FFQ), physical activity questionnaire (IPAQ), adverse events and the Gastrointestinal Symptom Rating Scale (GSRS). Moreover, we present some preliminary data from fMRI scans preprocessing as well as characterization of immune cell populations via FACS flow cytometry.

Conclusion: This study sheds light on whether the two different forms of the same probiotic could differentially affect the gut-brain axis in healthy older adults, and if they could potentially improve their current cognitive and mental well-being, among other markers of immune system and gastrointestinal health.

Adults' Experience of Suicidality - A Reflective Lifeworld Research

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Background/Objective: The relationship between suicidal ideation and suicidal actions is not convincingly linear which may be a reason why measuring suicidal thoughts/ideation has failed to predict imminent suicide risk. Previous research has led to a number of theories and statistical risk factors, which are to some extent incongruent with qualitative research findings regarding survivors' experiences. Therefore it is important to extend the knowledge and understanding in how people experience suicidality. What does it mean to be suicidal? The aim of this study was to illuminate the lived experience of suicidality among adults who survived a suicide attempt.

Method: Four men and three women aged between 18 and 54, with a variety of psychiatric diagnosis were interviewed with life-world interviews. All interviews started with the (only) predetermined question "You recently attempted suicide, can you tell me about that?". The interviews were audio recorded, transcribed verbatim and analysed with Reflective Lifeworld Research including phenomenological meaning analyse. All authors participated in the analyses, where preunderstanding and prejudice was consistently bridled. Three out of seven interviews are so far analysed, and preliminary findings are presented below.

Result: The informants describe the time just before the suicide attempt as filled with mental pain impossible to endure. At the same time they were firmly convinced that the condition was impossible to alleviate. Suicidality was experienced as a process driven by losses of values, safety and contexts combined with triggering factors that gradually increased over time. Finally, they found themselves entangled in excruciating mental pain with no hope of recovering, no value for themselves or others and total failure of own set life goals. They saw no point in seeking help since nothing or no one could ease their suffering. Due to bad experiences or assumptions, they felt distrusted by the care and the thought of inpatient care were frightening: *"that is, if I were to be admitted, I would be locked in a room and have to feel this! To have no way out. It is the most horrible thing I could imagine"*. According to the informants experiences, killing oneself was the only reasonable course of action.

Conclusion: Findings are similar with entrapment which has shown promising predictive values, more research in this topic is urgently needed. There may be other decisive factors than suicide thoughts, ideation or planning that drives a person to suicide. Risk assessment based on statistical risk factors may also contain variables that has its origin in lived experience of suicidality. Reluctance to seek care in relation to suicidality needs further research.

Loss of tolerance toward microbial antigens due to genetic environmental risk factors differs with age at Crohn's disease diagnosis

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Background/Objective: Loss of tolerance to microbial antigens is common in preclinical Crohn's disease, but whether this differs with age of diagnosis is largely unknown. To examine if the influence of genetic and environmental risk factors on the development of anti-microbial antibodies differs with age at diagnosis, we examined twin pairs discordant for Crohn's disease.

Method: CBir1flagellin (anti-CBir1), *Escherichia coli* outer membrane porin C (anti-OmpC), *Pseudomonas fluorescens*-related protein (anti-I2), anti-*Saccharomyces cerevisiae* antibody (ASCA) Immunoglobulin (Ig)A and ASCA IgG levels in 49 healthy twins (monozygotic n=18, dizygotic n=31) were correlated with age at diagnosis of Crohn's disease of their twin siblings. The influence of subclinical inflammation, defined by inflammatory serum proteins (n=92) and faecal-calprotectin, and by Crohn's disease-associated microbial handling single-nucleotide polymorphisms (SNPs) (n=4) was assessed in relation to the anti-microbial antibodies.

Result: Overall quartile ($r=-0.35$, $p=0.01$) and scaled sum ($r=-0.33$, $p=0.02$) levels of microbial antibodies in the healthy twin siblings inversely correlated with age at diagnosis in the twin with Crohn's disease. Significant correlations were also observed for the individual antibodies; anti-CBir1 ($r=-0.41$, $p=0.003$) and anti-OmpC ($r=-0.33$, $p=0.02$). After stratification by zygosity, results only remained significant in monozygotic pairs. Serum inflammatory protein, faecal-calprotectin and microbial handling SNPs correlated not with anti-microbial antibody levels.

Conclusion: In preclinical Crohn's disease, loss of tolerance toward microbial antigens due to genetic and environmental risk factors inversely correlates with age at diagnosis and is independent of the presence of subclinical inflammation. The difference across age seems to be mainly explained by genetic predisposition.

Cerebral Blood Flow in Cognitive Impairment: A Systematic Review and Meta-Analysis of Transcranial Doppler Studies

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Background/Objective: Reduced cerebral blood flow has been associated with cognitive decline and incident dementia, with oxidative stress and reduced beta-amyloid clearance as possible mechanisms for neurodegeneration. Transcranial doppler sonography is a non invasive tool for measuring cerebrovascular hemodynamics, including mean cerebral blood flow velocity. A systematic review and meta-analysis was performed to study mean cerebral blood flow velocity in the middle cerebral artery in persons with mild cognitive impairment and dementia compared to cognitively normal elderly.

Method: We searched Pubmed, Embase, Cochrane Library, Epistemonikos, PsychINFO, and CINAHL according to the Preferred Reporting Items for Systematic Reviews and Meta Analyses guidelines. In total, 33439 titles and abstracts were screened, 86 articles were reviewed in full text, and 35 were included.

Result: Mean cerebral blood flow velocity in the middle cerebral artery was significantly lower in Alzheimer's disease (mean difference = 8.42; 95% confidence interval, -10.56 to -6.28), vascular dementia (mean difference = 11.75; 95% confidence interval, -14.68 to -8.82) and mild cognitive impairment (mean difference = 4.19; 95% confidence interval, -5.52 to -2.85) compared to cognitively normal elderly, see figures 1 – 3. Reduction in blood flow was equally pronounced in Alzheimer's disease and vascular dementia (mean difference = 2.79; 95% confidence interval, -0.78 to 6.35).

Conclusion: Cerebral blood flow velocity is reduced in Alzheimer's disease, vascular dementia and MCI, with more pronounced disturbances in dementia.

Interferon gamma alters glutamine metabolic pathways in human aortic smooth muscle cells

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Background/Objective: Cells within atherosclerotic lesions have a higher glutamine demand than cells in healthy vessel although glutaminase, the enzyme converting glutamine to glutamate, is significantly downregulated in human carotid lesions (1-3). This may suggest rewiring of glutamine metabolic pathways in atherosclerotic lesions, caused by infiltrating immune cells and or their cytokines. Here we aimed at exploring the enzymes and transporters involved in glutamine metabolism in human carotid atherosclerotic tissues and aortic smooth muscle cells(hAoSMCs) exposed to interferon gamma.

Method: Protein and mRNA from interferon gamma-treated hAoSMCs were subjected to Western blot or qRT-PCR for quantification of key enzymes and transporters involved in glutamine metabolism. H2DCFDA probe was utilized for detection of intracellular reactive oxygen species using flow cytometry. The expression of these enzymes and transporters was also evaluated in human carotid lesions (GEO accession: GSE43292).

Result: Interferon-treated hAoSMCs display a significantly lower expression of glutaminase followed by an increase in the expression of glutamine transporters, glutamine synthetase and glutamine-fructose-6-phosphate transaminase-1 (GFPT1). The level of ROS and the expression of enzymes involved in *de novo* synthesis of glutathione are elevated in interferon-treated cells. A similar expression pattern for these genes, except for GFPT1, is also evident in human carotid lesions where glutaminase mRNA shows a strong positive correlation with SMC markers and a strong negative correlation with macrophage markers.

Conclusion: Glutamine metabolism is disrupted in human carotid lesions and interferon gamma alters glutamine metabolism in hAoSMCs, which may favor the production of UDP-GlcNAc and reactive oxygen species.

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Development of a novel live-attenuated Tick-born encephalitis vaccine by adapting the Langat virus platform

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Background/Objective: The incidence of Tick-born encephalitis cases showed a remarkable elevation in recent years and currently available vaccines have a burdensome immunization schedule along with poor immunogenicity in the elderly, which may contribute to observed vaccine failures. As a part of the Developvaccines@oru project, our aim is to develop a novel TBE vaccine that could provide improved immunogenicity using fewer doses. Our strategy is to induce an immune response at possible sites of virus infection by a live-attenuated vaccine based on Langat virus (LGTV).

Method: Our strategy is to induce an immune response at possible sites of virus infection by a modified live attenuated vaccine based on Langat virus (LGTV). Infectious clones of Langat virus (LGTV IC) are created followed by the generation of modified LGTV IC as potential attenuated virus. Then, we compare them with the LGTV TP21 lab strain using cell based and animal models.

Result: DNA-based LGTV IC were successfully created in our laboratory and confirmed by RT-qPCR, western blot, and next generation sequencing. We performed a pre-pilot study in mice to evaluate immunogenicity of LGTV IC and compared it to the LGTV TP21 lab strain. ELISA results indicated similar levels of TBEV cross-reactive antibodies in the serum of mice after LGTV TP21 and LGTV IC infection. Moreover, both LGTV strains showed a viraemia peak at 2 days post infection, yet LGTV IC showed slightly lower viraemia than LGTV TP21. The T lymphocytes, isolated from infected mice spleens, revealed weak Interferon gamma and Interleukin-2 response after stimulation with TBEV peptides. However, the cellular responses were higher in LGTV TP21 compared to LGTV IC infected mice. The health status assessment suggested that intramuscular administration of both strains was well tolerated in mice. Notably, mice infected with LGTV IC presented a comparatively reduced body weight. Besides, to attenuate LGTV IC further, modifications were introduced as sets of individual or combined mutations within NS3, NS5 and/or 3' non-coding region (3' NCR) of LGTV genome (Table 1). The LGTV IC mutants were successfully rescued after transfection in HEK 293 cells and confirmed by LGTV specific RT-qPCR.

Conclusion: Mice immunization with LGTV (TP21 or infectious clone) generates humoral immune response that may protect against TBEV infection. However, cellular immune response requires further evaluation and understanding. Developing new TBEV vaccine using modified attenuated LGTV infectious clone seems promising, but it requires further in-vitro and in-vivo investigation.

High-risk HPV and cervical dysplasia in intrauterine device users and controls

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Background/Objective: Intrauterine devices (IUDs) are common contraceptive methods for women globally, and both the copper-containing IUD and the hormonal IUD, are highly effective in preventing pregnancy, but their side effects, positive as well as negative, differ. A meta-analysis published in 2017 found that women who reported ever use of an IUD were less likely to develop cervical cancer (OR 0.64; 95% CI 0.53-0.77), but this meta-analysis was unable to examine the influence of IUD type. The mechanisms behind this is unclear. It is speculated that the insertion of IUD induce a cellular immune response that might clear HPV infections and preinvasive lesions, and that the copper-containing IUD is associated with a higher clearance rate compared with the hormonal IUD.

In the HPV based screening programme for cervical cancer in the Region Örebro County, Sweden, the participating women report the use of contraceptive methods at the time of the screening. This provides a unique opportunity to analyse HPV status and cervical dysplasia in relation to contraceptive method.

The objective of this study was to examine the prevalence of high-risk human papillomavirus and cervical dysplasia, and the clearance rate of HPV infections, in users of different kinds of IUDs and other contraceptive methods.

Method: A cross-sectional register-based study was performed that included all women aged 30–49 years who participated in the screening programme for cervical cancer in Region Örebro County in 2017–2018. Data on contraception from their screening records was paired with the HPV test results, eventual cytological and histological follow-up tests and subsequent HPV test.

Result: The odds for an HPV-positive screening test were not significantly different in users of copper-containing IUD compared to women with no reported use of contraception (aOR 1.01; 95% CI 0.81–1.27). Use of hormonal IUD and hormonal contraception were associated with higher odds for HPV infection when adjusted for age (aOR 1.21; 95% CI 1.04–1.41, aOR 1.41; 95% CI 1.22–1.63, respectively). The odds for histological HSIL+ were significantly higher among women using hormonal contraception, aOR 1.56 (1.13–2.16 95% CI) or hormonal IUD, aOR 1.45 (1.02–2.06 95% CI), but not in women using copper-containing IUD. No significant differences were found in HPV clearance rates in different contraception groups. No data on condom use, number of sexual partners, smoking or other risk factors were available.

Conclusion: Hormonal IUD and hormonal contraception were associated with a higher prevalence of HPV infections and histological HSIL+ compared to no reported use of contraception or use of copper-containing IUD.

Lifetime healthcare expenditures across socioeconomic groups in Sweden

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Background/Objective: Individuals of lower socioeconomic status generally have higher healthcare expenditures than individuals of higher socioeconomic status. However, little is known about how expenditures are distributed across socioeconomic groups over a lifetime, once accounting for differences in life expectancy. This study describes how lifetime healthcare expenditures are distributed across age, sex, and socioeconomic groups in Sweden while adjusting for differences in life expectancy.

Method: Healthcare utilization from 2016 were linked to demographic and socioeconomic data for a random sample of individuals aged 20 and above in the four largest Swedish regions (n=440,659). Mortality data were used to estimate income- and sex-specific survival rates. Expected lifetime healthcare expenditures were estimated by combining survival rates with mean healthcare expenditures over age, by sex, and income quintile.

Result: We find that expected lifetime healthcare expenditures are highest among the first (lowest) income quintile despite their evident lower life expectancy. Expected lifetime expenditures were 17.9% (16.8%) higher in the first income quintile compared to the fifth (highest) quintile for women (men). Individuals in the first income quintile had higher expected lifetime expenditures for all care categories except for primary care.

Conclusion: We conclude that despite a lower life expectancy, the quintile of the lowest socioeconomic status still had higher lifetime healthcare expenditures.

The effect of plant-based protein on surrogate markers of health - A dietary intervention study

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Background/Objective: Plant protein was shown to have a lower impact on the climate in comparison to animal protein influencing a transition towards a plant-based diet in our society. However, its lower protein quality and digestibility result in lower bioavailability and higher microbial proteolytic fermentation in the colon. Data on the health effects of metabolites produced during proteolytic fermentation is contradictory, highlighting the need for well-controlled interventions using plant-based proteins. Hence, the aim of this intervention study was to investigate the effect of isolated pea protein (IPP) on health by assessing several surrogate and inflammatory markers in blood and stool samples.

Method: Twenty-nine healthy participants (20-42 years) completed the study which included one study visit per week over a period of 8 weeks.

On study visit 1-3, participants handed in fecal samples, and study visits 4-8 additionally included the collection of fasting blood samples. Directly after study visit 4, participants started to supplement IPP daily for 4 weeks with weekly increasing amounts (0.25g/kg BW/day, 0.5g/kg BW/day, 0.75g/kg BW/day, 1g/kg BW/day). Questionnaires evaluating lifestyle and health (weekly), 24h food diaries (3x/week), body composition measurements (5x/study), and 24h urine samples (5x/study) were used to assess if participants kept the same lifestyle and diet during the study and if they were compliant with the intervention.

Data on blood and fecal markers was analyzed in GraphPad Prism using a mixed-effects analysis including multiple comparisons. In all analyses, values from each intervention visit (visit 5-8) were compared to supplementation's baseline (visit 4).

Result: Preliminary statistical analyses of blood markers showed no significant differences for C-reactive protein, glucose, insulin, HDL, LDL, and cholesterol. Comparisons regarding triglycerides, however, resulted in significant differences between visit 5 and 4 as well as visit 6 and 4. In line with the increasing amount of protein supplementation, blood urea values steadily increased from visit 4 to 8 and differed significantly when comparing visit 8 to baseline, indicating participant's compliance with the intervention.

Moreover, levels of fecal calprotectin – a marker of intestinal inflammation – significantly increased with the increasing amount of protein supplementation.

Conclusion: Our preliminary results indicate that supplementing IPP may affect intestinal inflammation in healthy participants. Effects on triglycerides might be influenced by individual dietary changes during the intervention period, therefore further analyses regarding possible lifestyle changes will be conducted to complement and verify these results.

Perceptions of quality of care in the oncological outpatient setting - Focus groups with health care staff

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Background/Objective: Studying the health care staffs' perception is of importance to both staff and management since it can lead to improved working environment, by highlighting potential problem areas. Previous research has shown that health care staffs' preferences might differ from what the patients consider important. Identifying possible differences and similarities enables for improvement work with positive effects on the patient care.

This study is part of a larger project, with the aim of developing an instrument, based on patient participation and with a 'staff module', to measure quality of care within the oncological outpatient setting, something that is lacking today. Therefore, the aim of this specific study is to describe how health care staff within the oncological outpatient setting perceive the concept quality of care.

Method: By using a purposive sampling and a phenomenographic approach, four focus group discussions were held, with 20 participants from the health care staff, from oncological outpatient settings in four hospitals, in four different counties in Sweden. Each group consisted of five participants, and each group met for a single session. The group discussions were audio-recorded and transcribed verbatim. Data collection was carried out from January to March 2023. Analysis was performed using a phenomenographic approach in four steps.

Result: Two descriptive categories emerged from the data; 'The professional's personal ability for good care' and 'The structural conditions for good care', consisting of eight conceptions. Results show that health care staff generally perceive quality of care as a non-neutral concept and describes the concept in terms of enablers and hinderers that contributes to the type of care they wish to offer.

Conclusion: According to health care staff, quality of care within the oncological outpatient setting is relying on organisational structure in combination with a professional and personal care.

Knowledge about what health care staff believes constitutes quality of care should be highly valuable to policy makers and hospital management. When combined with the patient perspective it also provides a wider perspective to the concept quality of care as an entity.

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Combined p-values of baseline variables of randomized controlled trials published in 2022 indicate non-randomness beyond chance

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Background/Objective:

Background: Randomized controlled trials (RCTs) are crucial for the evaluation of interventions. This, however, requires that the randomization is carried out correctly. The anesthesiologist Carlisle has developed a method to test whether the baseline variables of an RCT could reasonably originate from a true randomization, assuming the p-values are uniformly distributed. In a study from 2017, based on 5087 RCTs from 8 medical journals, 5.6% more RCTs than expected had a combined p-value >0.95 or $p < 0.05$ [1].

Objectives: Apply Carlisle's method to a sample of recent RCTs, and compare the findings to Carlisle's results.

Method: A sample of 1075 RCTs, published February 2022, indexed with the MeSH term 'Randomized Controlled Trial' in MEDLINE, were checked for eligibility. The inclusion criteria were primary/secondary analyses of RCTs providing number of participants, mean and standard deviation or standard error, of baseline variables. Carlisle's method adopts Monte Carlo simulation, ANOVA and t-test to get p-values of baseline variables, and Stouffer's method combines them for comparison to a uniform distribution, using R software. A smaller combined p-value indicate that the groups are similar; larger indicate that they are dissimilar.

Result: 568 RCTs were included and 6,326 baseline variables were extracted. The proportion of p-values within $p > 0.95$ or $p < 0.05$, $p < 0.01$ or $p < 0.00001$ was 23.8%, 4.5% and 0.4% respectively, i.e. 2.4, 4.5 and 400 times larger than would be expected by chance (10%, 1% respectively 0.001%).

Possible non-randomness was more common in this sample compared to Carlisle's with the arbitrary limit of $0.95 < p < 0.05$, about the same for $p < 0.01$ and less common for the extreme limit $p < 0.00001$ (15.6%, 4.1% respectively 1.3%) [1].

Conclusion: The findings of this study on more recent RCTs indicate that a larger proportion are associated with non-randomness than expected by chance. The findings are not completely in accordance with Carlisle's results. Reasons for this can only be speculated about at this time. Nevertheless, Carlisle's method seems to be a promising statistical tool for systematic reviews, and the evaluation of RCTs.

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Automated Oxygen treatment in Daily Life of patients with COPD - a pilot study

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Background/Objective: “Automated oxygen titration” is a new technology which could give patients on home oxygen the opportunity of personalized oxygen treatment, during for example physical activity. Automated oxygen has never been tested in a real life setting in the patient’s home.

The object of this study was to test a setup in the home of patients with COPD with automated oxygen titration and continuous flow regulation up to 8 liters a minute (l/min).

Method: In a pilot design an electronic device, able to automatically titrate the oxygen flow between 0.6 and 8 l/min, was connected to the oxygen concentrator in the patients’ home. The patients wore a wrist pulse oximeter, connected via Bluetooth to the device. The oxygen flow was regulated based on the oxygen saturation (SpO₂) targeted to be 90-94%.

Result: Two male patients with COPD with a usual fixed oxygen flow of two l/min for patient 1 and one l/min for patient 2 wore the pulse oximeter for four days and thus received automated oxygen titration. 266 000 paired observations of SpO₂ and oxygen flow were sent to the database (a cloud solution) for each patient. The high-flow concentrator reached a maximum flow of 6.7 l/min. SpO₂ was within target in more than 85% of the time. Oxygen flow was median 1.3 l/min (2.5-97.5 % percentile: 1.0-5.9 l/min) for patient 1 and median 0.6 l/min (0.5-6.7 l/min) for patient 2.

Conclusion: It seems feasible to regulate oxygen flow from 0.6-6.7 l/min in a home setting, but it requires large concentrators and continues adjustments in oxygen flow with up to 3 times more oxygen than the usual oxygen flow. The pilot study underlies our approach in a larger crossover feasibility study.

Keywords: Chronic Obstructive Pulmonary Disease (COPD), Long term oxygen treatment (LTOT), Physiotherapy, Activities of Daily Living (ADL), O2matic HOT.

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Increased proportion of circulating neutrophils with impaired phagocytosis capacity in patients with peripheral arterial disease

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Background/Objective: Peripheral arterial disease (PAD) is a clinical manifestation of atherosclerosis, affecting arteries in the leg. Based on their symptoms and severity, PAD patients are characterized into three sub-groups: asymptomatic, intermittent claudication (IC) and critical limb ischemia (CLI) (1,2). Despite its high prevalence, PAD remains under diagnosed and the role of immune cells in PAD pathophysiology remains poorly understood.

Aim: In this study, we characterized the innate immune responses in PAD-IC patients compared to healthy controls.

Method: Blood samples were collected from 22 patients with PAD (IC) and 48 healthy controls, to assess the phenotype of monocytes and neutrophils by using 10-colour flow cytometry. Phagocytosis assay was performed with labelled *E.coli* particles and intracellular reactive oxygen species (ROS) production with DCF fluorescence. Mann-Whitney U non-parametrical test was used for statistical comparison between PAD patients and healthy controls.

Result: A significant higher proportion of leukocytes ($p=0.01$) and a moderate higher proportion of neutrophils ($p=0.06$) was observed in PAD-IC patients compared to healthy controls, whereas monocyte subsets showed no significant differences. Interestingly, neutrophils showed a significantly impaired phagocytosis capability ($p=0.004$), reduced expression of myeloperoxidase (MPO) ($p=0.001$) and a moderate reduced level of intracellular ROS production in PAD-IC patients compared to healthy controls.

Conclusion: Taken together these results, suggest that PAD-IC patients have an increased proportion of leukocytes. Further there is moderate increase of neutrophils in circulation that have an impaired phagocytic capacity compared to healthy controls.

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Development of a web-survey for assessment bowel and bladder function in children who are toilet trained during infancy

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Background/Objective: Functional bowel and bladder disorders, including conditions like constipation and urinary incontinence, are prevalent among children. It is crucial to acknowledge that self-reported bowel and bladder symptoms can be inconsistent and unreliable. Therefore, robust assessment tools are essential for accurately evaluating the impact of interventions and monitoring changes over time. The ROME Foundation offers diagnostic criteria for functional gastrointestinal disorders, while the International Children's Continence Society (ICCS) provides criteria for functional bladder disorders. It is worth noting that the validity of these assessment tools may be influenced when applied in the context of complex research studies. The impact of infant toilet training on the prevalence of childhood bowel and bladder disorders has not previously been investigated. Our research group has launched the BABITT study (Bowel And Bladder function in Infant Toilet Training), a randomized controlled intervention study to investigate whether infant toilet training initiated during the first year of life reduces the prevalence of functional gastrointestinal and urinary tract disorders up to 4 years of age. The aim of this study was to construct a questionnaire, assessing bowel and bladder function in children who are toilet trained during infancy and evaluate content validity as well as feasibility in the BABITT study setting.

Method: In three consecutive steps, a web-based questionnaire was developed. In step 1, the questionnaire was outlined based on literature review and consensus panel discussions. In step 2, the questionnaire was validated in two assessment rounds by the content validity index method. In step 3, a pilot phase allowed for assessment of feasibility in the clinical study setting.

Result: As the ROME foundation and ICCS display paramount positions in scientific literature for the fields bowel and bladder disorders respectively, these frame works were in step 1, chosen to underpin the main outcomes of the intervention study. After the final assessment round in step 2, the I-CVI ranged from 0.88-1.00 in most items in all domains for both relevance and simplicity. Generally significant improvement between rounds and somewhat higher scores on relevance than simplicity, emphasizing revisions of the simplicity aspect of the items in the questionnaire. In the pilot phase, step 3, feasibility parameters to assess respondent burden was analysed. Response rate was 95% at 2 months and acceptability of the intervention was satisfactory.

Conclusion: A web-based questionnaire for assessment of parent-reported bladder and bowel function in children who are toilet trained during infancy was developed. The BABITT questionnaire emerged as valid and feasible in its context.

The role of periodontitis and periodontal bacteria in development of dementia

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Background/Objective: So far, the research focusing on the characteristic abnormal protein structures for Alzheimer's disease, amyloid-beta (A β) and phosphorylated tau neurofibrillary tangles (p-TauNFTs) in the brain, has not resulted in clinically useful treatments. An infectious etiology to AD has been proposed and periodontitis/periodontal bacteria have been highlighted as a risk factor for dementia and AD (1-3). Our aim is to investigate an association between periodontitis, presence of periodontal bacteria (*P. gingivalis*) and their virulence factors in cerebrospinal fluid (CSF) with cognitive decline and dementia diagnosis using a retrospective cohort.

Method: Out of patients investigated for cognitive impairment at the Memory Clinic, Department of Geriatric Medicine, USÖ, 120 patients were included based on available CSF sample stored in the biobank and sufficient medical and dental records. Bacterial DNA in CSF was analyzed using RT-qPCR, virulence factors (gingipains) and antibodies with ELISA and inflammatory proteins using OLINK proteomics. Dental and medical records will be evaluated.

Result: Antibodies against, as well as gingipains from, *P. gingivalis* was identified and quantified in CSF. Association analysis between OLINK proteomics and *P. gingivalis* antibodies/gingipains showed that there are correlations between *P. gingivalis* antibodies/gingipains and inflammation markers in CSF. No *P. gingivalis* DNA could be identified in CSF.

Conclusion: Our preliminary findings show that antibodies against *P. gingivalis* and gingipains are present in CSF. We have also found correlation between the antibodies/gingipains and inflammation markers in the CSF. Hence, the next step is to evaluate these findings to periodontal disease and dementia status.

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Can prediction models aid in the process of selecting treatment for hyperthyroidism?

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Background/Objective: Hyperthyroidism (HT) is treated with antithyroid drugs (ATD), radioactive iodine (RAI), or surgery. Previous studies have demonstrated that patients who undergo repeated treatment without remission have impaired quality of life 6-10 years after diagnosis. This study aimed to evaluate predictive machine learning models as a means of support in selecting treatment for HT.

Method: The study is based on a dataset of 2916 de novo HT patients diagnosed between 2003-2005, who later were invited to participate in a 6-10 year follow-up study. This dataset was pre-processed following the standard traditional procedure for representing and preparing data for learning algorithms. Additionally, Large Language Models (LLM) were assessed as an alternative to conventional pre-processing by encoding medical records into sentence embeddings. Subsequently, we trained and evaluated various regression models to predict the probability of a successful treatment based on nine features (Age, Sex, Diagnosis, thyroid-stimulating hormone receptor antibodies (TRAb-levels), T4-levels, TRAb (reference), TRAb (corrected), TRAb (positive), Thyroid-associated Ophthalmopathy (TAO)).

Result: Two different multi-output regression models were trained and evaluated for each pre-processed dataset: Gradient-Boosting (GB) and Random Forest (RF). Root Mean Squared Error (RMSE) and the coefficient of determination, R² score, were measured for evaluation metrics. The best performance was reported for RF trained on the traditionally pre-processed dataset, with an RMSE of 0.1764 and an R² score of 0.1460. The differences between both evaluated models were, however, negligible. The differences in results between both assessed data preparation approaches were likewise negligible.

Conclusion: This study show promising results in using prediction models for assessing the probability of successful treatment in individual patients. Nevertheless, further investigation is necessary regarding the choice of prediction models and how the data are prepared and represented.

Perceptions of interprofessional team collaboration among professionals working in the Occupational Health Service

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Background/Objective: In Occupational Health Service (OHS), the goal is to enable solutions of complex issues related to health and exposures that could cause unhealth in different work environments. Interprofessional team collaboration (ITC) among the professionals in OHS is therefore crucial when giving service to customers and their employees. The aim of the study was to describe and compare perceptions relating to ITC among the professionals in OHS in Sweden.

Method: Data were collected with a questionnaire including the instrument AITCS-SII (OHS) and one open-ended question. The AITCS-SII(OHS) is measuring team members' perception of ITC and the integration of customer and customer employees as part of the team and is adjusted for the Occupational Health (OH) context. The instrument is measuring ITC in the three subscales: cooperation, partnership and coordination. The questionnaire was sent to 1,923 professionals at different OHS in Sweden. Descriptive and analytic analyzes were performed. The free-text related to ITC were analyzed with deductive qualitative content analysis.

Result: Professionals like physicians, registered nurses, safety and health engineers, physiotherapists/ergonomists and behavioural scientists/psychologists from different OHS in Sweden responded on the questionnaire (response rate n = 472, 24%). Out of the 472 professionals that responded to the questionnaire, 456 are included in the analysis. Most of the professionals, 76%, were working in the private sector and 91% were permanently employed. Education in Occupational Safety & Health differed between the professionals. The result shows a significant difference in self-rated ITC between professionals in OHS in Sweden. All professionals reported high mean values on items related to openness, honesty and trust in the subscale cooperation. In the subscale coordination all professionals reported ITC to be less adequate than in cooperation and partnership. The result also shows that the professionals estimate ITC different depending on if the own organization is intern, private or public. The professionals gave a range of descriptions of their perception of ITC in their text response to the open-ended question. Eight out of 52 responded that there was no teamwork at their workplace.

Conclusion: To summarize the findings; registered nurses, physicians, ergonomists and physiotherapists have a similar perception of ITC in the Swedish OH context. These professionals perceived ITC to be more adequate than did safety and health engineers, psychologists and behavioural scientists. Overall, psychologists and behavioural scientists perceived ITC to be less adequate compared with the other professionals. The professionals employed by private OH providers perceived ITC to be more adequate than did public OH providers. To develop ITC further within the OH context, future studies need to explore what enables and supports ITC.

Daily assisted toilet training in healthy infants and functional gastrointestinal disorders (BABITT): a randomised, intervention study

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Background/Objective: Delayed start of toilet training is suggested to contribute to functional gastrointestinal disorders in children. This study aims to evaluate if parent assisted infant toilet training can reduce the prevalence of these disorders during infancy.

Method: This randomised, parallel group, open label, controlled, intervention study recruited healthy infants at six Child Health Care Centers in Sweden. Infants were randomly assigned (1:1) by computer, stratified by sex, in permuted blocks, to start assisted infant toilet training at 0-2 months or at 9-11 months of age (i.e. control group). The intervention group received oral and written information and were encouraged to practice at least once a day, 5-7 days per week. Parents answered validated web-based questionnaires at 2, 3, 6 and 9 months of age.

The primary outcome measure was the compound period prevalence of functional gastrointestinal disorders (infant colic, infant dyschezia and/or functional constipation, defined by ROME IV criteria) up to 9 months of age. Primary analyses were made on complete cases using logistic regression according to intention-to-treat (ITT) principle in models including group allocation and sex. The study is registered at ClinicalTrials.gov (NCT04 082689).

Result: 293 infants (141 females, 48%) were randomly assigned at median age of 34 days (range 9-71) between April 18th 2019 and September 24th 2021 ($n=147$ intervention group; $n=146$ control group). There was no difference in the total period prevalence of functional gastrointestinal disorders between the intervention group and the control group (55.0% vs 56.5%, difference 1.6% [95% CI -10.1 to 13.2]; $p=0.7918$, (ITT with complete cases $n=138$ vs $n=142$)). Per-protocol analysis ($n=63$ vs $n=120$) was not significant ($p=0.8598$). 59.5% reported intervention adherence.

Conclusion: Daily assisted infant toilet training, at a low dose, do not reduce the prevalence of functional gastrointestinal disorders during infancy. Long-term effects are being evaluated in the ongoing study up to 4 years of age.

Estrogen alters the virulence of Uropathogenic E. coli

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Background/Objective: Urinary tract infection (UTI) is one of the most common bacterial infections in humans and the main etiology is uropathogenic E. coli (UPEC). UTIs mainly affect women and they experience a high risk of recurrence (1). Menopausal women have higher occurrences of UTI due to decreased levels of estrogen. There is a strong clinical association between estradiol levels and development of UPEC-mediated UTI (2). However, we do not know if the direct effects of estradiol on UPEC virulence could partially explain the association between estrogen levels and UPEC-mediated UTI. Our objective is to evaluate the modulatory effects of estradiol on the in vivo virulence of uropathogenic E. coli.

Method: The UPEC strain CFT073 was grown in presence or absence of estradiol (300 pg/ml) statically at 37°C for 24 hours. Estradiol was washed away prior to infecting the mice. Anesthetized C57BL/6 female mice (age 7–9 weeks) were instilled with 1) PBS 2) CFT073 at 1×10^8 CFU/mouse 3) estrogen primed-CFT073 at 1×10^8 CFU into the bladder through a soft polyethylene catheter. At 24 h post-infection, urine and blood samples was collected. The bladder and kidneys was extracted, evaluated, and homogenized and plated on agar for CFU counting. The phenotype UPEC virulence expression of type-1 fimbriae, P-fimbriae and hemolysin was also evaluated in presence or absence of estradiol.

Result: We found that the estradiol primed-CFT073 group colonized the bladder and kidneys less than the CFT073 group. We also found that estradiol primed-CFT073 caused less intracellular colonization of the bladder, kidneys and spleen compared to the CFT073 group. In addition, estradiol primed-CFT073 decreased severe bladder inflammation and increased survival 24 h post infection. Next, we evaluated key UPEC virulence factors to understand our in vivo findings. We found that estradiol priming suppressed type-1 fimbriae, P-fimbriae and hemolysin expression compared to CFT073.

Conclusion: Our preliminary findings show that estradiol suppresses key UPEC virulence factors, which decreased the severity of a UPEC mediated UTI in vivo. Understanding how estrogen from the human host affects the virulence of UPEC may be a new frontier in the fight against UTI. If we can elucidate how UPEC senses its environment and mobilizes its virulence, we may inhibit this activation and dampen or completely prevent the infection.

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Home phototherapy for hyperbilirubinemia in neonates – an unblinded multicentre randomised controlled trial

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Background/Objective: The aim of this study was to assess whether home phototherapy is a safe alternative to hospital treatment.

Method: This was a randomised controlled, multicentre, trial in which term newborns with a total serum bilirubin of 300-400 µmol/ were randomized to either home phototherapy or conventional in-hospital phototherapy.

The outcome measurements were parent-infant bonding, stress and measurements of safety and feasibility. A descriptive qualitative study based on interviews was performed as well as a health economic analysis.

Result: 147 patients were recruited from 6 hospitals, Results showed no difference between groups in the safety and feasibility outcomes. Parents in the intervention group had better scores on bonding and lower levels of stress. The interviews showed that parents felt secure at home. The cost per patient was €337 for home phototherapy compared with €1156 for the hospital alternative indicating average cost savings of €819 or 71% per patient.

Conclusion: Home phototherapy can be considered a safe and feasible alternative to hospital care for well selected patients. It improves bonding and stress for parents and reduces health care costs. Since the first publication from this study was published home phototherapy is now recommended by the American Academy of Pediatrics as an alternative to hospital care for patients with uncomplicated hyperbilirubinemia.

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Aberrant immune checkpoint expression in T cells of patients with peripheral artery disease

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Background/Objective: Immune checkpoint (IC) molecules are crucial in regulating the immune response towards antigens. The increased occurrence of cardiovascular events following treatment with IC inhibitors suggests a potential role for ICs in promoting atherosclerosis formation. This study aims to investigate whether IC expression and function is aberrant in patients with peripheral artery disease (PAD), a type of (cardio)vascular disease in the elderly population which is caused by atherosclerosis.

Method: IC expression was analysed by flow cytometry in T cells of healthy controls (HCs, n=22) and PAD patients (n=13). Among the analysed ICs were the co-stimulatory ICs CD28 and Glucocorticoid-Induced TNFR-Related (GITR) protein. The co-inhibitory ICs included programmed-death 1 (PD-1), T cell immunoglobulin and mucin domain-containing protein 3 (TIM3), B and T lymphocyte attenuator (BTLA) and Lymphocyte activation gene 3 (LAG-3). In addition, soluble forms of these ICs were assessed using a LUMINEX multiplex assay in a pilot study including 16 HCs and 9 PAD patients. Finally, cytokine production capacity was assessed in a subset of patients and HCs (n=3) to assess whether T cells expressing co-inhibitory ICs were exhausted.

Result: Among CD4⁺ T cells of PAD patients, there was a higher frequency of cells expressing TIM3 and GITR than in HCs. CD8⁺ T cells had a higher frequency of LAG-3⁺ cells in PAD patients than in HCs. The frequencies of the other ICs were not different among T cells of PAD patients and HCs. Soluble levels of TIM3, GITR and LAG-3 were not different between PAD patients and HCs. In contrast, PAD patients had elevated soluble levels of BTLA compared to HCs. As TIM3⁺CD4⁺ T cells are most often considered to be exhausted, we investigated whether the increased expression of TIM3 on CD4⁺ T cells in PAD patients indeed meant that they would be unresponsive upon stimulation. Preliminary data indicated that CD4⁺TIM3⁺ T cells from both HCs and PAD patients had a low capacity to produce IFN- γ , IL-17A, TNF- α and IL-10.

Conclusion: Our data show that CD4⁺ T cells in PAD patients have increased expression of TIM3 and GITR and CD8⁺ T cells had increased LAG-3 expression. The soluble levels of these checkpoints remain unaffected. GITR is upregulated on T cells upon TCR stimulation and could therefore be expected to be higher in PAD patients in which continuous TCR stimulation is likely. The TIM3⁺CD4⁺ T cells seem to be exhausted, as shown by low cytokine production capacity in both HCs and PAD patients. An increased frequency of TIM3⁺CD4⁺ T cells in PAD could therefore be caused by the prolonged inflammatory state of the patients. LAG-3 is also a known exhaustion marker and could indicate exhaustion of CD8⁺ T cells in PAD as well.

The effect of a GnRH analogue injection on the circulating levels of kisspeptin-1 in girls with suspected central precocious puberty

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Background/Objective: Kisspeptin stimulates the GnRH neurons in hypothalamus initiating puberty. It is not known whether GnRH inhibits kisspeptin secretion by negative feedback and possible correlations between kisspeptin and other hormones important for the onset of puberty, are not yet fully clarified.

Method: Thirteen girls with suspected central precocious puberty performed an adjusted GnRH stimulation test twice, placebo-controlled in a randomized order. Blood was sampled 0, 30, 60, 90, 120 and 150 min after the iv injection (Relefact LHRH vs. saline). The protease inhibitor AEBSF was added to each sampling tube (final concentration 2 mg/ml). An ELISA kit from LifeSpan BioSciences, Inc. (No LS-F8231) was used for the analyses of Kisspeptin-1 levels. The levels of ghrelin, estradiol, Luteinizing Hormone (LH), Follicle-Stimulating Hormone (FSH), insulin and glucose were analyzed, as well, to study potential correlations to kisspeptin.

Result: The median Kisspeptin-1 level at baseline was 39 pg/ml (0.1 – 221.3). The areas-under-the curve (AUC) for Kisspeptin-1 levels did not differ significantly after the GnRH and placebo injections. We did not find any significant correlations between the levels of kisspeptin and ghrelin, estradiol, LH, FSH, or insulin but we could see a positive correlation between kisspeptin-1 and glucose levels (ρ 0.63, $p=0.021$).

Conclusion: The levels of kisspeptin in girls with suspected central precocious puberty were not affected by the effect of GnRH analogue during a GnRH stimulation test, compared to placebo, indicating the absence of a negative feedback mechanism. A positive correlation between kisspeptin and glucose was observed, in accordance with previous findings, suggesting a possible association between kisspeptin and metabolic factors, even if a correlation to insulin was not observed here.

Challenging Prior Conclusions: Differential Regulation of ACE2 in Inflammatory Bowel Disease

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Background/Objective: Intestinal fibrosis poses a therapeutic challenge in inflammatory bowel disease (IBD). Recent evidence suggests a critical role of the renin-angiotensin system (RAS) in modulating both inflammation and fibrosis in IBD. For example, a negative correlation between the activity of Angiotensin Converting Enzyme 2 (ACE2), which is an important player in the alternative RAS pathway, and mucosal fibrosis was observed (1). Previous studies have shown differential ACE2 gene expression in the inflamed and normal mucosal tissue in patients with IBD compared to controls. Here, we aim to investigate ACE2 in relation to IBD and inflammation on protein level.

Method: Newly diagnosed patients with IBD (n=160), symptomatic, non-IBD controls (n=83), and healthy controls (n=44) within the Swedish inception cohort for IBD (SIC IBD) were included. Normalized protein expression (NPX) values of ACE2 were measured using proximity extension methodology (OLINK Proteomics, Uppsala, Sweden) (2). Kruskal-Wallis test was used to compare ACE2 NPX values across groups, followed by Dunn's post hoc test. P-values < 0.05 were considered significant.

Result: In ileal tissue, relative ACE2 protein expression was higher in macroscopically inflamed biopsies versus non-inflamed biopsies from patients with Crohn's disease (p < 0.001). Conversely, in colonic tissue of patients with ulcerative colitis, inflamed biopsies showed lower ACE2 estimates compared to non-inflamed biopsies from symptomatic controls (p = 0.01), but not compared to non-inflamed biopsies of healthy controls (p > 0.05).

Conclusion: We assessed ACE2 protein expression in biopsies from mostly treatment-naive patients. Our observed results on protein level do not align with previously published results from gene expression data, which may have biological or methodological explanations.

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Validation of a handheld single-lead ECG algorithm for atrial fibrillation detection after coronary revascularization

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Background/Objective: Atrial fibrillation (AF) is a rapidly increasing global public health concern entailing a high risk for ischemic stroke that can largely be avoided with anticoagulation therapy. AF is often underdiagnosed and there is a need for a reliable method of detection in individuals with additional risk factors for stroke such as coronary artery disease. We aimed to validate an automatic rhythm interpretation algorithm in thumb ECG in subjects with recent coronary revascularization.

Method: Thumb ECG, a patient-operated handheld single-lead ECG recording device with an automatic interpretation algorithm, was performed three times daily for a month after coronary revascularization and 2-week periods 3, 12, and 24 months post-procedure. The detection of AF by the automatic algorithm on subject and single-strip ECG level was compared to manual interpretation.

Result: 48,308 of 30 s thumb ECG recordings from 255 subjects (mean 212 ± 3.5 recordings per subject) were retrieved from a database (AF 47 subjects/655 recordings; non-AF 208 subjects/47,653 recordings). The algorithm sensitivity at subject level was 100%, specificity 11.2%, positive predictive value (PPV) 20.2%, and negative predictive value (NPV) 100%. At the single-strip ECG level, sensitivity was 87.6%, specificity 94.0%, PPV 16.8%, and NPV 99.8%. The most common reasons for false positive results were technical disturbance and frequent ectopic beats.

Conclusion: The automatic interpretation algorithm in a handheld thumb ECG device can rule out AF in patients recently undergoing coronary revascularization with high accuracy, but manual confirmation is needed to confirm the diagnose of AF because of high false positive rates.

Charting of patients receiving specialized palliative home care being transported to hospital near death - A national registry study

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Background/Objective: Many patients receiving palliative home care wish to die at home, even when symptoms intensify and the disease progresses. Despite this, numerous of patients die in hospital, showing a discrepancy between the desired place of death and the actual place of death.

The aim in this study was to map the occurrence of patients receiving specialized palliative home care that are transported to hospital near death in Sweden.

Method: A national retrospective cross-sectional study based on data collected from the Swedish Register of Palliative Care. Patients ≥ 18 years of age enrolled in specialized palliative home care with dates of death 2015 11 01 – 2022 10 31 were included ($n=39,698$). Descriptive statistics were used to compare patients who were transported to hospital and died there within seven days of arrival, with patients who were not transported or transported earlier than seven days from time of death.

Result: Of the total study population, 7,383 patients were identified as dying in hospital/other care unit within 7 days of transport from specialized palliative home care. The majority (74%) were admitted to a specialized palliative care unit, 23% to a non-specialized palliative care unit and 3% to additional care units. It was most common for patients to die 1-2 days after arriving at the hospital. No clinical relevance differences were noted regarding sex, age, or diagnosis when comparing transported patients with non-transported patients, whereas the transported patients had more frequent dyspnea (31% vs. 23%, $p < 0.001$) and anxiety (60% vs. 57%, $p < 0.001$). Presence of several simultaneous symptoms (confusion/anxiety, pain/severe pain, dyspnea/respiratory secretion) was significantly more common in the transported group (27% vs. 25%).

Conclusion: Many patients enrolled in specialized palliative home care are transported and die in hospital. Most of these patients die 1-2 days after arrival. The patients have complex symptoms and not all patients are admitted to a specialized palliative care unit. Some common denominators, such as symptoms and symptom burden, can be noted in the patients who are transported, but more studies are necessary to identify the causal relationship that these transports take place.

Age-related immunomorphological changes in rat testes in diabetes mellitus

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Background/Objective: The most urgent global medical and social challenge is diabetes mellitus (DM) due to the relentless growth of the disease and its complications. The global prevalence of DM among children and adolescents is dramatically increasing [1]. DM can result in male infertility [2]. Testicular dysfunction in adult-onset DM is well studied, while the effects of DM on the functional development of the testes in children remain unclear.

Therefore, the objective of our study was to assess the effect of streptozotocin-induced DM (SDM) on rat testicular immunomorphology both in the peripubertal period and adulthood.

Method: A total of 40 (20 rats of different ages) 6- and 2-month-old rats were examined. Group I (experimental) comprised 20 animals who were administered a single intraperitoneal streptozotocin injection at a dose of 6 mg/100 g (6-month-old rats) and 7 mg/100 g (2-month-old rats); Group II (control) included 20 animals. Samples were collected on the 28th and 56th days of the experiment.

Result: In 6-month-old rats, on the 56th day of SDM, a decrease in the proliferative activity of spermatogenic epithelium (Ki-67), a 1.7-fold decrease in apoptosis intensity, a 1.6 decrease in the number of WT1-positive Sertoli cells, and a 1.5-fold decrease in the AR-immunoreactive area of the seminiferous tubules were observed (in all cases $p < 0.05$). The response of 2-month-old rats to hyperglycemia was similar; however, they maintained apoptotic activity and androgen receptor (AR) expression longer (at least until the 56th day). The processes of testes maturation continued, manifested by an uneven asynchronous decrease Ki-67, a decrease in caspase-3, and high levels of AR-immunoreactive area of the seminiferous tubules.

Conclusion: According to our findings, SDM results in pronounced degenerative and atrophic changes in the testes of 6-month-old rats. In contrast, in 2-month-old rats with SDM, the processes of testes maturation continue.

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