Medicine and Health
RESEARCH DAY

ABSTRACT BOOK
12 Maj 2026

Örebro University, Faculty of Medicine and Health,
School of Health Sciences and **School of Medical Sciences**, Örebro Sweden

ÖREBRO UNIVERSITY

Preface

Dear colleagues

We are proud to present this abstract book, featuring research from the 3rd Research Day of the Faculty of Medicine and Health at Örebro University on 12 May 2026. This joint initiative by the Schools of Health Sciences and Medical Sciences highlights recent advancements across diverse research groups, reflecting strong regional, national, and international collaboration.

This collection showcases the breadth of ongoing research in medicine and health at our university. We remain committed to supporting a vibrant scientific culture, encouraging dialogue, and advancing health and medical science.

We hope you enjoy reading and feel inspired by the work presented.

Best Regards

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Dean, Faculty of Medicine and Health

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Pro-Dean, Faculty of Medicine and Health

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Cardiac spheroids as a human model for inflammation induced cardiac dysfunction

Simon Athlin, Niklas Steger, Jishamol Thazhath-Veettil, Carmine Gentile, Isak Demirel, Allan Sirsjö, Petra C Kienesberger, Anna Nordenskjöld, Geena Varghese Paramel

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Background/Objective: Inflammatory signaling is a major contributor to cardiac dysfunction in diseases such as sepsis, myocarditis, and heart failure, yet existing in vitro models lack the multicellular complexity and physiological relevance needed to accurately recapitulate human cardiac pathology.

Method: In this study, we used human cardiac spheroids, three dimensional microtissues composed of cardiomyocytes, fibroblasts, and endothelial cells to study lipopolysaccharide induced inflammation. High resolution confocal microscopy confirmed a well-organized radial distribution of cell types within the spheroids, closely resembling native cardiac tissue.

Result: Following 24 h LPS stimulation, the spheroids exhibited no significant increase in lactate dehydrogenase release, indicating preserved membrane integrity and absence of overt cytotoxicity. Nevertheless, a robust inflammatory response was observed at both transcriptional and protein levels, including significant upregulation and secretion of TLR2, IL6, TNF, CXCL8, and CCL2. Mitochondrial stress testing revealed significantly reduced basal respiration, ATP production, and maximal respiratory capacity. Functional analyses showed impaired contractility characterized by reduced beat rate, delayed time to peak contraction, and prolonged relaxation time.

Conclusion: Together, these findings demonstrate that human cardiac spheroids mount a physiologically relevant, multicellular inflammatory response that compromises both mitochondrial metabolism and mechanical performance. The model offers a powerful platform for investigating innate immune activation and for screening therapeutic interventions targeting inflammation induced cardiac dysfunction.

Chronic pain in COPD: prevalence and longitudinal associations with multimorbidity, breathlessness, emotional distress, and adverse clinical outcomes.

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Background/Objective: Chronic pain is common in patients with chronic obstructive pulmonary disease (COPD) and is linked to adverse clinical outcomes, multimorbidity and COPD symptoms, but the exact associations remain unclear. Importantly, chronic pain is underrepresented in most current clinical management guidelines. This study aimed to describe chronic pain prevalence in patients with COPD across 16 years, and its longitudinal association with mortality and respiratory-related hospital visits, multimorbidity, and COPD-related symptoms.

Method: This study included patients with COPD, with survey data sweeps in 2005 and 2012, and Swedish national register data from 2005 to 2021. The prevalence of chronic pain and mortality were described in the patients. Repeated dispensed physician-prescribed pain medication defined chronic pain. Survival analyses were used to investigate longitudinal associations among chronic pain, multimorbidity, breathlessness, emotional distress, all-cause mortality, and respiratory-related hospital visits.

Result: Chronic pain prevalence among 1071 COPD patients was 27% in 2005, 37% in 2012, and 38% in 2021. Initially, chronic pain was associated with all-cause mortality with a 72% higher hazard, compared to patients without pain. Adjustment for sociodemographic factors, breathlessness severity and multimorbidity attenuated this association to 19% (adjusted hazard ratio (adjHR) 1.19, 95% CI 1.01-1.40), although only partially. Chronic pain, breathlessness (adjHR 1.33, 95% CI 1.24-1.43), and multimorbidity (adjHR 1.44, 95% CI 1.36-1.54) were associated with all-cause mortality in fully adjusted models, and emotional distress (adjHR 1.29, 95% CI 1.20-1.38), breathlessness (adjHR 1.41, 95% CI 1.32-1.51), and multimorbidity (adjHR 1.07, 95% CI 1.01-1.13) were associated with recurrence of respiratory-related hospital visits.

Conclusion: Chronic pain was common and strongly associated with mortality in COPD patients and highlights the importance of considering chronic pain in patients with COPD. Emotional distress was associated with increased respiratory-related hospital visits but not with mortality. This emphasises the relevance of prioritising somatic COPD symptoms, more than subjective distress, in clinical decision-making. Chronic pain should be considered in COPD assessment and management, as it is associated with adverse outcomes and mortality risk in these patients.

Colonic mucosal phenotype of patients with Parkinson's disease related to gut barrier dysfunction from Akkermansia muciniphila stimulation

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Background/Objective: Many patients with Parkinson's disease (PD) suffer from gastrointestinal issues and low-grade inflammation. The evidence of a disturbed microbiota-gut-brain axis homeostasis in PD is increasing but is largely limited to associations rather than causative links. The commensal mucin-degrading bacteria *Akkermansia muciniphila* is known as a next-gen probiotic with well-documented beneficial effects on gut physiology. However, the role of *A.muc* in PD is contradictive as studies have shown increased abundance with associations to both gut barrier dysfunction and inflammation. This study aimed to elucidate the effect of live *A.muc* and its postbiotic membrane protein on colonic permeability in sigmoid biopsies taken from patients with PD and matched controls, in relation to colonic phenotype and clinical data.

Method: We recruited early-stage PD patients (n=17) from the neurology department at Örebro University Hospital, in addition to matched (age, sex, BMI) non-PD controls (n=13). All participants filled out questionnaires regarding their gut - and mental health. Biopsies from the sigmoid colon were mounted in Ussing chambers for studies of permeability. The biopsies were stimulated with either *A.muc* (10^8 cells) or AMP (7.5 ug), both with and without the addition of the barrier-disruptor Compound (C) 48/80 (10 ng/ml). Additional biopsies from PD patients and matched controls were used for immunohistochemical semi-quantification of oligomeric alpha-synuclein and ultrastructural characterisation using transmission electron microscopy.

Result: The results showed that *A.muc* increased colonic permeability in patients with PD but not in the matched controls. The postbiotic membrane protein of *A.muc* however showed barrier enhancing effects in both patients with PD and matched controls against C48/80. Colonic levels of alpha-synuclein correlated to increased permeability from *A.muc* stimulation. The colonic phenotype of a subset of PD patients showed a reduced glycocalyx barrier and indications of a low-grade inflammation.

Conclusion: We are the first to demonstrate that *A.muc* increase colonic permeability in PD patients of a specific colonic phenotype with association to thinner glycocalyx barrier, demonstrating a potential negative effect in PD patients. The postbiotic membrane protein of *A.muc* on the other hand seems to have protective barrier enhancing effects, showing therapeutic potential independent from live *A.muc* bacteria.

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 .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. 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 h. 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: Estradiol priming significantly attenuated the virulence of UPEC *in vivo*. Mice infected with estradiol-primed UPEC showed significantly lower bacterial burdens in the bladder and kidneys, together with reduced intracellular colonization of both organs compared with mice infected with untreated CFT073. Dissemination was also reduced, as fewer mice had detectable bacteria in the spleen. Consistent with these findings, estradiol-primed CFT073 caused significantly less bladder inflammation and improved host survival at 24 h. To investigate the mechanisms underlying this reduced virulence, we examined key UPEC virulence phenotypes. Estradiol priming significantly decreased type-1 fimbriae and P-fimbriae activity. Hemolysin activity was also significantly reduced. Furthermore, estradiol-treated UPEC showed decreased invasion of bladder epithelial cells and reduced bacterial motility. These findings suggest that estradiol suppresses multiple UPEC virulence factors, which may occur through modulation of bacterial two-component regulatory systems, such as PhoP/PhoQ and QseC/QseB, which are known to control UPEC virulence.

Conclusion: Our findings show that estradiol suppresses key UPEC virulence factors and reduces the severity of UPEC-mediated UTI *in vivo*. Understanding how host-derived estrogen influences UPEC virulence may open new strategies to combat UTIs.

Home-based cardiorespiratory interval training decreases post-stroke fatigue and improves cardiorespiratory fitness

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Background/Objective: Post-stroke fatigue (PSF) affects nearly half of all stroke survivors and significantly limits rehabilitation outcomes and daily functioning. PSF is a multifactorial condition, with low levels of cardiorespiratory fitness identified as a key contributing factor. As no established treatment currently exists, reduced aerobic capacity may represent an underlying mechanism of PSF, highlighting aerobic training as a potentially promising intervention.

Method: In this two–center, randomized trial we evaluated a home-based supervised cardiorespiratory interval training program (HS-CITP) in individuals with PSF (Swedish Fatigue Assessment Scale [S-FAS] ≥28) 1–7 months post-stroke. Participants were randomized (1:1) to either HS-CITP or usual care with self-directed activity following early supported discharge. The intervention consisted of 35–minute cycling sessions performed three times per week, The primary outcome was self-reported fatigue ; the secondary outcome was peak oxygen uptake post-intervention.

Result: 43 completed the post-intervention assessment (HS-CITP: n=22; control: n=21). Adherence to HS-CITP was 92%, with no adverse events. Compared with the control group, HS-CITP significantly reduced fatigue (mean between-group difference –5.35 S-FAS points; 95% CI –9.03 to –3.67; p<0.001) and improved cardiorespiratory fitness (+4.48 mL/kg/min; 95% CI 3.41–5.54; p<0.001).

Conclusion: Supervised home-based interval training significantly reduced PSF and improved cardiorespiratory fitness, with high adherence and no safety concerns. These findings support the integration of structured aerobic exercise into stroke rehabilitation and reinforce that individuals with pronounced PSF should not be excluded from supervised exercise interventions. Instead, they may particularly benefit from professional guidance combined with progressive training

Impact of a Fast-Track Diagnostic Pathway on Psychological and Physiological Stress in Men with Suspected Prostate Cancer: A Randomized Clinical Trial

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Background/Objective: The diagnostic workup for suspected prostate cancer is often emotionally distressing and may negatively affect patients' well-being. Considerable variability exists in waiting times across diagnostic pathways, yet evidence on how such delays influence psychological distress is limited. The objective of the study was to assess whether a fast-track diagnostic workup reduces psychological and physiological stress among men with suspected prostate cancer.

Method: In this study, 301 men referred for suspected prostate cancer at the Urology Department, Örebro University Hospital (Sweden), were randomized to either a fast-track diagnostic workup - aiming for the shortest possible waiting time - or usual care. Primary outcomes were patient-reported symptoms of distress (anxiety, depression, perceived stress, and sleep disruption); secondary outcomes included physiological stress markers, such as heart rate and its variability and diurnal salivary cortisol. Data were collected from randomization to 12 months after the initial specialist consultation.

Result: Men in the fast-track group had a significantly shorter waiting time to their first consultation (median 7 days) compared with the usual care group (median 35 days). Waiting for biopsy results was the most stressful period during diagnostic workup in both groups with regard to distress, anxiety and perceived stress scores. However, on average men in the fast-track showed lower psychological stress, especially for anxiety and depression, seven days after post-biopsy visit. They further showed lower anxiety, depression, perceived stress and less sleep problems a month after cancer diagnosis. Differences between groups were no longer evident 12 months after the first specialist visit. In addition, men in the fast-track showed a more favourable diurnal cortisol pattern the day before the post-biopsy visit, reflected in a larger decline from morning to lunch cortisol levels.

Conclusion: The results provide evidence of a diminished psychological and physiological stress-response in men undergoing a fast workup for suspected prostate cancer.

Overuse Symptoms, Prosthetic Use, and Self-reported Function in Patients with Upper-Limb Amputation and Congenital Differences: A Multicenter Study of 187 Patients

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Background/Objective: To map the prevalence of self-reported musculoskeletal pain, prosthesis use, function, and disability in the population of individuals with congenital upper limb difference or acquired upper limb amputation in Sweden. A second objective was to examine the association between prosthesis use and pain.

Method: The study has a cross-sectional design. The setting is a Swedish population >18 years with upper limb difference or acquired upper limb amputation. A total of 187 individuals answered a national survey, 114 with upper limb difference and 73 with acquired amputation. The response rate was 37.4%.
The main outcome measures **pain at rest and during activity** was reported on a numeric rating scale of 0-10. **Musculoskeletal pain** in the upper body was reported using a pain map. **Phantom limb pain** was reported using the present pain intensity item from the Short-Form McGill Pain Questionnaire. **Function and disability** were measured with the Pain Disability Index and the Swedish version of the Disabilities of the Arm, Shoulder and Hand questionnaire.

Result: Musculoskeletal pain at rest and during activity was common in both individuals with congenital differences and those with acquired amputations. Individuals with acquired amputations reported a high proportion of phantom pain (77%), and poorer function and more disability than those with congenital limb differences. On average, 60% reported regular use of a prosthesis. Respondents reporting regular and intensive prosthesis use tended to report lower degrees of pain both at rest and during activity.

Conclusion: Musculoskeletal pain is prevalent in individuals with limb loss, and the pain is most pronounced in shoulders and neck. There was a suggestion that prosthetic use may be associated with a reduced frequency of reported problems. Further studies, preferably randomized intervention studies, are warranted to improve outcomes in this group of patients.

Potential of starch-gelatin-based scaffolds for cartilage defect repair
- A comparison of chondrocyte growth with collagen-, hyaluronic- and chitosan-based scaffolds currently in use

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Background/Objective: Starch is a natural polymers, known for its hydrophilicity, biocompatibility, non-toxicity, cost-effectiveness, and broad availability, making it suitable for biomaterials synthesis. Another natural polymer is gelatin, valued for its affordability, biocompatibility, biodegradability, and chemical resemblance to collagen. It contains Arg-Gly-Asp (RGD)-like sequences that support cell adhesion, proliferation, migration, and differentiation. Combining these two polymers lays the foundation for a cell-friendly, resorbable and non-toxic scaffold for cartilage repair.

Method: Two variants of starch-gelatin-scaffolds and one chitosan-based scaffold were fabricated by casting and freeze-drying. The resulting materials were analyzed with respect to physicochemical and mechanical properties, cut to size, and seeded with human articular chondrocytes. Cell retention and proliferation were evaluated at 1, 14, and 42 days of culturing. Extracellular matrix production was analyzed by histo- and immunohistochemistry. Comparisons were made with that of commercially available hyaluronan- (Hyalofast®) and collagen-based (ChondroGide®) scaffolds, and synthesized chitosan hydrogels.

Result: The starch-gelatin materials exhibited highly porous structures stabilized by hydrogen bonding, with swelling behavior similar to native cartilage and favorable mechanical handling properties. Despite differences in initial cell retention, all materials except chitosan supported robust cell growth, reaching similar levels after 14 days. No significant changes were observed between 14 and 42 days with the exception of Hyalofast® showing decreased cell number. Chitosan-supported cell growth was more linear over the culture period, but resulted in only half the cell number by day 42 compared with the other materials. Without cells, Hyalofast and one variant of the starch/gelatin hydrogel degraded before day 42. starch/gelatin scaffolds showed collagen I, II, and aggrecan deposition.

Conclusion: Starch-gelatin scaffolds displayed favorable mechanical properties, supported cell growth comparable to commercial scaffolds, and promoted deposition of cartilage-specific extracellular matrix, highlighting their chondrogenic potential

Revaccination with conjugated pneumococcal vaccine improves functionality of vaccine mediated antibodies in chronic lymphocytic leukemia.

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Background/Objective: Patients with Chronic Lymphocytic Leukemia (CLL) have an increased risk of invasive pneumococcal disease and poor response to vaccination. Pneumococcal vaccination is recommended for all CLL patients however recommendations on revaccination strategies are lacking. In a previous study, we randomized treatment-naïve CLL patients (n=126) for primary immunization with a conjugated vaccine (PCV13) or a polysaccharide vaccine (PPSV23), showing a superior immune response to PCV13. Median five years after primary immunization, a revaccination study was conducted, and a control group was recruited. We aim to evaluate long term antibody functionality in CLL patients after primary immunization with PCV13 or PPSV23 followed by revaccination.

Method: Seventy-seven CLL patients were recruited , median five years after primary immunization with PCV13 (Group A, n=37) or PPSV23 (Group B, n=40). An immunocompetent control group (n=31), previously immunized was recruited. All patients and controls were revaccinated with PCV13. After eight weeks, the CLL patients received a second revaccination with either PPSV23 (Group A) or PCV13 (Group B). Antibody functionality of eight of the vaccine specific serotypes was analyzed by the Finnish Institute for Health and Welfare in Helsinki, Finland, using a multiplex opsonophagocytosis assay. Serological Protection (SP) was defined as titers ≥1:8 in >70% of the analyzed serotypes (6/8) and was statistically evaluated with mixed Poisson regression.

Result: Before revaccination, five years after primary immunization, 41% in Group A achieved SP compared to 20% in Group B (RR=2.0; 95% CI 0.9-4.2). After the first revaccination with PCV13, significantly increased proportions of patients with SP were seen in both groups (Group A: 76% Group B: 61% RR=1.2 CI 0.9-1.7). After 12 months, Group B (PCV13+PCV13), showed an improved long-term antibody functionality compared to Group A (PCV13+PPSV23) (RR=0.4; CI 0.2-0.9). The proportion of participants with SP was significantly lower before and after first revaccination in CLL patients compared to controls (30% vs. 58%; RR=0.4; CI 0.3-0.7). At 12 months, after a second revaccination in the CLL group, the difference decreased (66% vs. 81%; RR=0.8; CI 0.6-1.1).

Conclusion: Our findings support revaccination with pneumococcal conjugated vaccine in CLL patients to enhance protection against severe pneumococcal disease.

Tularemia in Region Örebro County 2019-2025

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Background/Objective: Tularemia is a vector-borne zoonotic disease caused by the bacteria *Francisella tularensis*. It predominantly infects small rodents but can cause infection in humans with different clinical manifestations depending on the route of transmission. The disease was previously primarily occurring in the northern parts of Sweden but has spread geographically and is now also occurring in the middle and south of Sweden, with known risk areas in Örebro County. Tularemia can cause outbreaks and occurs with a higher incidence some years. The objective for this project was to investigate the occurrence of tularemia over time in Region Örebro County, focusing on the geographical area of distribution and clinical manifestation.

Method: As part of the Unit for Infection Prevention and Control's responsibility to monitor infectious diseases, epidemiological data was exported from the reporting system SmiNet regarding tularemia in Region Örebro County for the years 2019-2025. Included variables were diagnosis, year, age, sex, country of infection, suspected geographical location of transmission, place of registered residence, clinical manifestation, route of transmission and referring health care unit.

Result: In total, 231 cases were reported during the observed years (15-57 cases/year). A majority of the cases were adults (average age 51, range 2-91) and a few more men than women were reported (59% and 41% respectively). Clinical manifestation was added to the form for clinical reporting in September 2021 och is therefore missing in previous cases (n=92). In the cases where clinical manifestation was reported ulceroglandular infection was most commonly registered (n=91; 39%), followed by pneumonic (n=19; 8%). Typhoidal and oropharyngeal infections occurred occasionally. In 2025 a considerably larger proportion of pneumonic cases was observed compared to previous years, 11 out of 28 cases (39%). Ten of these were men of which seven were older than 65 years of age. Tularemia occurred in all municipalities in the county, but predominantly in the municipality of Örebro (n=139; 60%). A potential geographical association was observed between cases with Örebro as the suspected geographical location of transmission and wetlands with abundant birdlife, rich plant diversity and popular paths for walking and biking (Oset, Rynningeviken, Alnängarna).

Conclusion: The geographical distribution of tularemia in the county appears stable during the observed years. Ulceroglandular infection was the most common clinical manifestation. A larger proportion of pneumonic cases was noted in 2025 compared to previous years, which indicates a need for further surveillance and analysis.

A randomized controlled trial of supervised group exercise and relaxation therapy in patients with clinical depressive and anxiety disorders

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Background/Objective: Depression and anxiety cause a significant burden on quality of life. The effect of exercise on improving depression and anxiety remains disputed because of study quality and bias. Moreover, the effect of exercise as an additional treatment to standard care is less well studied. We aimed to investigate whether supervised group exercise therapy as an add-on treatment improves depressive and anxiety symptoms more than group relaxation therapy.

Method: Individuals with a diagnosis of a major depressive episode or an anxiety disorder were recruited from outpatient psychiatry and primary care clinics in Örebro, Sweden. A total of 86 participants aged between 18 and 65 years (median=33 years; 62.8% females) were randomly assigned to an exercise (N=43) or a relaxation group (N=43). The exercise group received 36 sessions, and the relaxation group received 12 sessions during a minimum 12-week intervention. The primary outcomes were depressive symptoms measured using the Montgomery-Åsberg Depression Rating Scale (MADRS, MADRS-S) and anxiety symptoms measured using Beck's Anxiety Inventory (BAI).

Result: Depressive and anxiety symptoms improved significantly, both statistically and clinically, in both groups (MADRS: exercise from 24.5±7.4 to 15.8±8.3 points, relaxation from 22.8±6.4 to 16.6±7.8 points; MADRS-S: exercise from 27.6±7.2 to 19.6±8.1 points, relaxation from 26.3±7.1 to 18.7±9.5 points; BAI: exercise from 25.0 ±12.2 to 16.4±9.9 points, relaxation from 24.3±12.4 to 17.0±12.6 points) without a statistically significant difference between the groups. There was a significant differential attrition rate between the two groups despite great efforts to maintain compliance throughout the study.

Conclusion: Both groups demonstrated comparable and statistically significant improvements in depression and anxiety; however, limited statistical power and potential differential bias preclude reliable assessment of treatment superiority. This highlights the difficulty of maintaining compliance for therapy involving exercise in this patient group.

All-cause mortality in Graves' disease by treatment modality compared with matched controls

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Background/Objective: Graves' disease can be treated with antithyroid drugs (ATD), radioiodine (RAI), surgery, or conservative management with beta-blockers. Previous observational studies have reported differences in mortality across treatment modalities, but results have been inconsistent and the impact of treatment choice on long-term mortality remains unclear. The aim of this study was to examine all-cause mortality stratified by treatment modality in patients with Graves' disease compared with matched controls.

Method: This prospective multicenter cohort study included 2,033 adult patients with Graves' disease from a Swedish cohort of newly diagnosed hyperthyroidism recruited between 2002 and 2005. Patients were stratified by first-line treatment modality into ATD, RAI, surgery, or conservative management. Each patient was matched to 10 population-based controls by year of birth, sex, and municipality of residence. Participants were followed until death, emigration, or end of follow-up in 2021. All-cause mortality at 10 years and at end of follow-up was analyzed using Cox proportional hazards regression with matched controls as reference. Hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated in unadjusted and adjusted models including age, sex, and Charlson Comorbidity Index (CCI).

Result: At 10 years, survival was 94.2% in the ATD group, 84.5% in the RAI group, 96.7% in the surgery group, and 94.5% in the conservative management group, compared with 94.7%, 85.7%, 97.7%, and 95.0% in matched controls, respectively. Corresponding end-of-follow-up survival was 90.9%, 73.5%, 92.7%, and 85.2% in patients, versus 91.4%, 74.7%, 92.8%, and 89.0% in controls. In adjusted Cox regression, no statistically significant differences in all-cause mortality were observed for any treatment modality compared with matched controls. At end of follow-up, adjusted HRs were 1.03 (95% CI 0.83–1.27) for ATD, 1.02 (0.85–1.23) for RAI, 1.50 (0.70–3.21) for surgery, and 1.42 (0.85–2.40) for conservative management.

Conclusion: In this Swedish multicenter cohort, no clear excess all-cause mortality was observed in patients with Graves' disease across treatment modalities compared with matched controls after adjustment for age, sex, and comorbidity.

Atherosclerotic Plaque Crystals Induce Endothelial Dysfunction

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Background/Objective: Endothelial dysfunction is an early driver of atherosclerosis, yet the direct impact of endogenous crystals such as cholesterol crystals and monosodium urate on endothelial activation remains incompletely understood. In this study, we examine how crystalline stimuli modulate human umbilical vein endothelial cells function.

Method: The study assessed CC uptakes using confocal microscopy and flow cytometry, inflammatory signaling using PCR and ELISA, mitochondrial respiration using Seahorse, and neutrophil recruitment.

Result: Using dose- and time-controlled experiments, we show that CC and MSU are internalized by endothelial cells, activating NF-kB and STAT3 signaling pathways and inducing a robust pro-inflammatory cytokine profile. Notably, CC caused marked mitochondrial dysfunction, evidenced by impaired respiratory capacity and loss of membrane potential, revealing a novel bioenergetic vulnerability in endothelial cells. Both direct crystal stimulation and exposure to crystal-primed conditioned media triggered endothelial adhesion molecule expression and promoted neutrophil adhesion, indicating that soluble mediators released upon crystal stimulation can propagate vascular inflammation.

Conclusion: These findings demonstrate that crystalline stimuli are potent vascular danger signals capable of driving endothelial inflammation, mitochondrial impairment, and immune cell engagement, which are hallmarks of early atherogenesis. By elucidating these multifaceted endothelial responses, this study provides important mechanistic insights into how crystal-induced signals may contribute to vascular dysfunction and the early stages of atherogenesis.

Bladder and Bowel symptoms in relation to Toilet Training in Swedish 4-year-old Children - a population-based cross-sectional study

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Background/Objective: In high-income settings, there is a trend of increasing age for initiation and completion of toilet training. Concerns have been raised about negative effects on bladder and bowel function. There is no consensus on when toilet training should ideally begin. This study aims to describe the prevalences of bladder and bowel symptoms in Swedish 4-year-olds and possible associations with early and late initiation or completion of toilet training.

Method: A population-based cross-sectional study using a validated web-questionnaire congruent with ICCS definitions and Rome IV criteria for parent reported bladder and bowel symptoms. Prevalences of bladder and bowel symptoms were compared between groups of early/late toilet training defined as initiation before/after 18 months and completion before/after 2,5 years of age.

Result: In 436/1111 eligible children, bladder symptoms were common: urgency (72 %), urinary daytime leakage (30 %) and abnormal voiding frequency (21%). Most families (65%) initiated toilet training late and only half of the children achieved daytime dryness before 2,5 years of age. Early initiation was associated with early completion of toilet training ($p<.001$). At age 4 years, most were diaper-free during the day (410/436). Functional constipation was reported in 30% and cooccurred with bladder symptoms and stool toileting refusal. If late initiation and completion of toilet training, bladder symptoms and stool toileting refusal were more frequent. Not using the potty/toilet at pre-school was associated with functional constipation ($p<.001$) as well as stool toileting refusal ($p<.001$). Nearly one third of parents (30%) reported not receiving enough support in toilet training from pre-school staff.

Conclusion: Bladder and bowel symptoms are common among Swedish 4-year-olds. Early initiation of toilet training was highly associated with early daytime dryness. Urinary daytime leakage and stool toileting refusal at 4 years of age were more frequent when toilet training had been initiated and completed late.

Bone Morphogenetic Protein 10 and One-Year Outcomes After Open Revascularization in Symptomatic Peripheral Arterial Disease and Carotid Stenosis

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Background/Objective: Bone morphogenetic protein 10 (BMP10) has atrial-specific and vascular properties and may link atherosclerosis with cardiac disease. We evaluated whether preoperative BMP10 levels were associated with new-onset atrial fibrillation (AF), major adverse cardiovascular events (MACE), and mortality after open revascularization for symptomatic peripheral arterial disease (PAD) or carotid stenosis (CS).

Method: We enrolled patients scheduled for endarterectomy for symptomatic PAD or CS. Preoperative plasma BMP10 concentrations were measured using Luminex. Outcomes (new-onset AF, MACE, and all-cause mortality) were obtained from medical records at 1-year follow-up. Associations between BMP10 and outcomes were assessed using Cox proportional hazards regression.

Result: Of 234 enrolled patients, 210 had biomarker and one-year follow-up data available and were included in the analyses; 63% were men and 61% underwent surgery for PAD (61%). Women were generally older than men (median age 77 [IQR 7] vs. 75 [IQR 10], p=0.046) and had higher preoperative BMP10 levels (p=0.045). There were 40 patients with preoperative AF, and at 1 year follow-up, 10 patients had developed new-onset AF, 26 experienced a MACE, and 13 died.
In unadjusted Cox regression, higher BMP10 levels were associated with MACE (HR 1.01, 95% CI 1.00-1.03; p=0.047) and mortality (HR 1.03, 95% CI 1.01-1.04: p<0.001), but not with new-onset AF (HR 1.00, 95% CI 0.97-1.03; p=0.8). Associations with MACE and mortality remained significant after multivariable adjustment.

Conclusion: Higher preoperative BMP10 levels were associated with increased 1-year risk of MACE and mortality, but not new-onset AF, in patients with indication for endarterectomy for PAD or CS. Preoperative BMP10 may complement conventional risk stratification and should be validated in larger cohorts.

Children and Young People-Patient Reported Experience Measure - pilot study using the Swedish versions of the questionnaire

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Background/Objective: Using Patient Reported Experience Measures (PREM) is one way of assessing children's perspectives, for example when identifying areas for improvement in paediatric care. PREM must be validated in the relevant context and contain questions that are relevant to the target group, also when these are children. One such PREM is the English 'Children and Young People - Patient Reported Experience Measure' (CYP-PREM), which has been translated and validated in the Swedish healthcare context (Swe-CYP-PREM). The aim of the current study was to pilot the Swe-CYP-PREM questionnaire in paediatric care as a basis for future implementation.

Method: A descriptive cross-sectional design was used. The pilot study was conducted across 19 different units in four regions of central Sweden, with broad inclusion of various patient groups. Participants were asked to complete the Swe-CYP-PREM questionnaire and a study-specific questionnaire to evaluate the Swe-CYP-PREM.

Result: Of the 319 children invited, 189 completed the Swe-CYP-PREM, resulting in a response rate of 59.5%. Most were satisfied with the time it took to complete the questionnaire; no question was perceived as offensive and few incorrect answers were given. Despite predominantly positive responses, the questionnaire also captured negative experiences from healthcare visits. The open-ended questions added value to the questionnaire's closed-ended questions.

Conclusion: The Swe-CYP-PREM questionnaire is well accepted by children of various ages and can be used in clinical practice to enable children to voice their experiences after a healthcare visit.

Computational analysis of immune and oncology-related gene expression within colonic tissues in microscopic colitis

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Background/Objective: Inflammation is vital for tissue repair, but non-resolving inflammatory responses result in pathogenesis. This double-edged nature of inflammation is evident in microscopic colitis (MC) and inflammatory bowel diseases such as ulcerative colitis and Crohn's disease. Whereas UC and Crohn's colitis are linked to an increased risk of colorectal cancer (CRC), no such risk has been reported for MC. In fact, MC patients have a reduced risk of CRC compared to the general population. Immunological studies indicate a predominance of CD8+ cytotoxic T lymphocytes, effector cells essential for immunosurveillance, in MC patients relative to UC patients. The lower CRC risk in MC despite its chronic inflammatory nature suggests the presence of protective immunoregulatory mechanisms warranting further investigation. Therefore, the aim of this PhD thesis is to investigate the immunopathophysiology and mechanistic perturbations underlying MC.

Method: Formalin-fixed, paraffin-embedded colonic biopsies were obtained from 32 patients in each group: collagenous colitis (CC—a subtype of MC), UC, and non-inflamed controls. They were sequenced using the HTG-EdgeSeq targeted RNA-Seq technology comprising a Precision Immuno-Oncology Panel of 1392 immune and oncology-related genes. Differential gene expression analysis was performed in R using a linear mixed-effects model. Genes with adjusted p-values <0.05 and log fold changes >|1| were defined as significantly dysregulated and biologically relevant.

Result: In the CC group, 90 genes were upregulated compared to controls, the most upregulated being *DMBT1, NOS2, PSMB9, VSNL1, CTLA4, FOXP3* and *BATF*. Additionally, 74 genes were downregulated in CC relative to controls, among which *SMAD7, PPARD, LTK, IGFBP3* and *ABCG2* were the most significantly downregulated. Compared to UC patients, the CC group exhibited 14 upregulated genes, the most prominent being *BEX2*, *PLEKHG4*, *HMGCS2*, *ITGAE* and *CHDH*. In contrast, 54 genes were downregulated in the CC compared to the UC group, with *PFKFB3*, *ITAG5*, *MMP2*, *COL3A1*, and IRAK3 being the most downregulated.

Conclusion: Overall, MC shows increased expression of genes involved in inflammation (*NOS2*), mucosal regeneration (*DMTP1*) and barrier integrity (*HMGCS2, PLEKHG4*), enhanced CD8+ antigen presentation (*PSMB9)* and lymphocyte epithelial retention (*ITGAE*), increased regulatory T cell activity (*FOXP3*, *CTLA4*) and tumour suppression (e.g. *DMTP1, BEX2*) but also tumour progression (*BATF, PLEKHG4*) compared to non-inflamed controls and UC patients. Gene set analysis and protein-protein interactions of these genes will be performed in the next steps.

Developing QOCO - A patient-derived measure

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Background/Objective: Outpatient cancer treatment often involves long and repeated treatment cycles with multiple healthcare contact wich brings on a complex patient situation with symptoms and functional impairments. Simoultaneously, high demand, rising costs, and limited resources is highlighting the need for care improvement.
A key challenge is that quality of care is multidimensional and lacks a clear, widely accepted definition in cancer care. To improve services, we need to understand how patients perceive quality of care in oncology outpatient settings.

Method: Oncologic patients from four Swedish hospitals, receiving systemic therapy or radiotherapy, participated in the different steps of the development. A patient-derived definition of quality of care in oncology outpatient setting was formulated based on 20 individual patient interviews in the first step:
"Quality of Care in outpatient oncology is personalised, accessible, and centred on the patient's needs. It upholds dignity through respect, autonomy, honesty, and strong relationships between patients and healthcare providers. Patients feel safe and supported by skilled professionals who provide compassionate care and share responsibility for treatment decisions."
The definition was operationalised into QOCO using the iterative six-step process described by de Vet. 349 statements on quality of care were extracted from the interviews to form items. Item reduction was conducted through iterative discussions within the research group, informed by: A focus group interview with four patients, and five individual patient interviews rating 203 items for relevance and understanding and calculations of Content Validity Index (I-CVI) from ratings.

Result: The iterative process reduced the items from 349 to 203 to 84 to 48 items. Of these items, 38 had I-CVI ≥ 0.78, seven items were below the threshold and three items were added after the rating process. Of the 203 items evaluated by patients, 41 were considered difficult to understand. In the final 48-item version, nine items had previously been reported as difficult and three of these were rephrased. Items regarding children and family were moved into separate optional modules, answered only by patients with relevant experience (e.g., patients who bring children / involve family). Keywords from the definition were used to make sure all dimensions were accounted for in the measure. Those keywords were: Information, Communication, Attitude, Participation, Security and Availability. For field testing, a 5-option Likert scale, with a total sum-score was chosen.

Conclusion: QOCO is a patient-derived 48-item instrument for assessing patient-perceived quality of care in oncology outpatient settings; preliminary content validity is strong, and psychometric testing is ongoing.

Development Of A Novel Live-Attenuated Tick-Borne Encephalitis Vaccine Using The Langat Virus Platform

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Background/Objective: Tick-borne encephalitis (TBE) is a growing public health concern in Europe and Asia, driven by the increasing spread of the TBE virus (TBEV) and its tick vectors. Although current vaccines provide protection, their multi-dose schedule and reduced efficacy in the elderly contribute to occasional vaccine failures. This study aims to develop a novel TBE vaccine offering enhanced protection with fewer doses, focusing on mucosal immunization.

Method: Infectious clone of Langat virus (LGTV IC) was designed and rescued- in our laboratory. We assessed the safety and immunogenicity of the LGTV IC as a live attenuated TBE vaccine platform in a murine model. Mice were vaccinated with LGTV IC via intranasal or intramuscular routes at low or high doses. We evaluated viremia, viral presence in cerebrospinal fluid, general health, and immune responses.

Result: Intranasal immunization with LGTV IC induced strong immune responses. It elicited robust anti-TBEV IgG responses and strong TBEV NS3-specific IFNg and IL-2 production. Notably, low-dose intranasal immunization outperformed higher doses of both routes, inducing a more balanced and effective immune response. Low-dose intranasal administration was well tolerated, with no clinical signs, weight loss, or viral presence in the central nervous system. In contrast, intranasal immunization caused potential adverse effects at elevated doses.

Conclusion: These findings support LGTV IC as a promising vaccine platform for TBE, with intranasal administration emerging as a putative safe, well-tolerated, and effective needle-free alternative to intramuscular injection when given at a low dose. Ongoing efforts are focused on further attenuating LGTV IC to enhance its safety profile for future applications.

Evaluation of soluble immune checkpoint proteins as non-invasive biomarkers for urinary bladder cancer

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Background/Objective: Soluble immune checkpoint molecules (sICs) are regulatory proteins that modulate immune responses and circulate in body fluids, making them promising candidates for cancer detection. Liquid biopsies enable measurment of these markers in blood or urine and offer a less invasive alternative to cystoscopy. Quantification of sIC levels may facilitate early detection of bladder cancer (BC), potentially improving diagnostic accuracy and patient management. This study aimed to evaluate the potential of 14 sICs as non-invasive biomarkers for detection of BC.

Method: Patients were recruited from the BLAdder cancer Blood and Urine Study (BLABUS), a prospectively collected cohort of individuals with suspected BC. The study included 187 BC cases and 54 control subjects presenting with macroscopic hematuria but normal findings on cystoscopy and urography. Plasma levels of 14 sICs (CD28, GITR, CD27, TIM-3, CD137, CD152, HVEM, IDO, LAG-3, BTLA, CD80, PD-1, PD-L1, and PD-L2) were analyzed using the ProcartaPlex Human Immuno-Oncology Checkpoint Panel 1. Group differences were assessed using t-tests with Benjamini-Hochberg correction. A logistic regression-based classification model was developed to predict malignancy.

Result: Multiple sICs (TIM-3, CD28, CD137, CD152, HVEM, IDO, LAG-3, BTLA, GITR, CD80, PD-1, PD-L1, and PD-L2) showed significant differences between cases and controls ($p<0.05$). A classification model incorporating TIM-3, CD152, HVEM, IDO, LAG-3, BTLA, GITR, PD-1, PD-L1, and PD-L2 demonstrated good performance, achieving an accuracy of 83.8% (95% CI: 78.6 - 88.2). The model showed high sensitivity (98.7%) but moderate specificity (42.6%), with a positive predicitive value of 85.2% and a negative predictive value of 74.2%.

Conclusion: These findings suggest that circulating sIC levels may serve as potential diagnostic biomarkers for BC. However, further validation in independent cohorts is required to determine the clinical utility of the proposed classification model.

Extracellular vesicles as transporters of alpha-synuclein from gut to brain in Parkinson's disease

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Background/Objective: Emerging research suggest that in a subset of Parkinson's' disease (PD) patients the pathogenesis starts in the gut and spreads to the brain. Misfolded protein aggregates of alpha-synuclein (a-syn), which degenerate dopaminergic neurons in the brain, have also been found in the gut. Recent studies show that propagation of a-syn is possible via the vagal nerve that connects the gut and the brain. Studies show that vagotomy (severing the vagal nerve) leads to a reduced risk of PD. However, a risk remains, signifying the need to study other transportation routes. Extracellular vesicles (EV) are membrane-enclosed nanovesicles released by cells. They carry lipids, RNA and proteins that can be delivered to recipient cells and change their phenotype. EVs can be released from nerve endings and have been found to carry a-syn inside their cargo, but whether such EVs can originate from the gut is unknown. The overarching goal of this project is to elucidate a novel gut-to-brain transmission route of a-syn via EVs originating from the gut. The aims are 1) to isolate and characterise gut-specific EVs in serosal samples for subsequent identification in blood plasma and 2), to elucidate the potential of a-syn positive EVs to spread from the gut to the blood circulation.

Method: Serosal fluid from colonic biopsies mounted in Ussing chambers were collected from both patients with PD (n=17) and matched controls (n=13). EVs were isolated from 12 pooled serosal samples of each participant using ultra centrifugation. Flow cytometry was used to confirm the presence of isolated EVs, via detection of EV markers CD63, CD81 and CD9. Protein extracted from isolated EVs were sent to Linköping University Core Facility for proteomic analysis. EVs were also investigated for their a-syn content using ELISA kits against total a-syn and aggregated a-syn.

Result: Flow cytometry showed positive signals for the EV markers CD63, CD81, CD9, as well as the epithelial marker EPCAM. The marker Cadherin-17 stood out as the most gut-specific marker in the preliminary proteomics analysis. Several unique protein signatures were also discovered that could separate PD patients from non-PD controls. Both total – and aggregated a-syn forms were detectable but only in a few samples, with no statistical difference between PD and controls.

Conclusion: Despite small tissue samples we were able to detect positive signals for the EV markers CD63, CD81 and CD9 in the serosal fluids, providing evidence for the presence of EVs in the colonic serosal fluid samples. This proof-of-concept demonstrates that it is possible to detect a-syn in colonic serosal samples, possibly as a cargo of EVs, showing potential for coming experiments to detect them systemically.

Fitness versus Football: The practice and experience of performance analysis technologies in Swedish Elite Football

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Background/Objective: Digital technologies for tracking and analysing athletes' performance and well-being have become an integral part of elite sport. Although these tools contribute to performance enhancement, there are reasons to be cautious. The excessive quantification of athletes has been shown to lead to feelings of constant surveillance, distort lived experiences, and create a digital divide among coaching staff and athletes. However, research on this topic has been conducted predominantly in the Anglosphere and has focused mainly on men's sports; therefore, conclusions should be generalised to other sporting contexts with caution. To develop contextually grounded understandings and provide context-specific directions for productive implementation, more research is needed in other contexts. Therefore, the purpose of this paper is to examine the practices and experiences of performance analysis technology among coaching staff and players in Swedish elite football. Based on the results, recommendations for productive ways of implementing technology will be presented.

Method: To generate data, semi-structured interviews were conducted with coaching staff as well as three to four players from each of two clubs in Swedish men's elite football and two clubs in Swedish women's elite football. To analyse the data, the lens of digital transformation was employed. Digital transformation refers to the process by which an organisation fundamentally changes how it operates, creates value, and interacts with stakeholders through the use of digital technologies.

Result: Preliminary results indicate that although all stakeholders acknowledge the value of technological data, both coaching staff and players feel that it can sometimes be excessive. They experience that physiological data is valued too highly at the expense of aspects related to football performance and, consequently, that the physiological and medical team sometimes has too much influence. In particular, they highlight a lack of opportunities to better relate physical performance data to actual football performance, which they attribute to a lack of competence, time, and resources. This differs from more resource-rich contexts, where clubs may have several dedicated analysts supporting the coaching staff in this work. In general, these findings reflect previous research pointing to the risk of sports clubs becoming too data-driven rather than data-informed, thereby neglecting other important aspects.

Conclusion: While performance analysis technologies are perceived as valuable, there is a risk of prioritising fitness over football performance to too great an extent. To address this, Swedish club management needs to facilitate competence development as well as the infrastructure and routines required for communication and collaboration among coaching staff and players.

Health-care professionals' experiences of atrial fibrillation screening in Swedish health care: a mixed-methods study

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Background/Objective: Screening for atrial fibrillation (AF) is both controversial and a topic of growing research interest. However, the perspectives of health-care professionals involved in systematic population (PS) and opportunistic (OS) AF screening have not yet been adequately explored. The aim was to explore health-care professionals' experiences of PS and OS, and to identify their feasibility in clinical practice.

Method: Health-care professionals representing the PS and OS groups were invited to semi-structured group interviews. Transcripts were analysed using qualitative content analysis and a succeeding survey was constructed and distributed to health-care professionals involved in the STROKESTOP III project.

Result: Qualitative content analysis revealed a complex relationship between health-care professionals' desire to contribute to preventive screening efforts and their experience of feeling limited by organizational factors and available resources, such as time, administrative systems, and health economic evaluations. AF screening was perceived meaningful, but results highlighted the importance of peer support and collaboration making the screening process feasible in routine practice. The OS group further highlighted the perceived value of direct patient contact to immediately address potential concerns and questions when required.
Nineteen health care professionals responded to the survey (response rate 40%). Based on current organization and resource availability, most respondents (58%) consider PS to be the most feasible method to use in clinical practice. However, OS was perceived as the most feasible method to reach the largest number of participants, regardless of available resources (74%). Most respondents confirm the lack of available resources as a barrier for clinical implementation (63%), while expressing a desire to engage in screening, provided sufficient resources (84%).

Conclusion: Health-care professionals are willing to engage in AF screening, but clinical implementation depends on availability of resources and peer collaboration, highlighting the need for targeted organisational strategies to facilitate the screening process.

In-silico exploration of T-cell repertoires in melanoma, focusing on diversity, risk association, and target recognition

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Background/Objective: Melanoma has one of the highest mutation burdens among cancers, leading to diverse neoepitopes that influence antitumor immunity. This antigen diversity drives selective growth of tumor-reactive T cells, resulting in a TCR repertoire characterized by strong connectivity and clonotype convergence around shared antigens. We employed transcriptomic profiling and high-resolution TCR sequencing with MiXCR to accurately reconstruct TCRα, TCRβ, TCRγ, and TCRδ clonotypes, utilizing immunogenomic databases like IMGT for V(D)J gene annotation and assessment of neoepitope-specific TCR signatures. Our integrated approach allowed us to quantify clonal expansion and evaluate repertoire diversity across melanoma samples. Our findings show that neoantigens impact T-cell response intensity and TCR repertoire structure, revealing interconnected networks of expanded clonotypes. This emphasizes the link between mutational load, neoepitope presentation, and T-cell repertoire, providing insights for biomarker development and next-generation immunotherapy design.

This study aims to identify TCR-α, β, γ, and δ lineages related to outcomes in melanoma patients through literature and database mining, followed by T cell repertoire (TCRp) prediction using single-cell and bulk RNA sequencing. We will model and dock the most frequent TCR clonotypes to assess their interaction with tumor antigens. Ultimately, these TCR repertoires will help predict therapeutic responses and evaluate tumor prognosis.

Method: This study conducts a systematic search to identify melanoma-associated T-cell receptor (TCR) datasets and develops a computational workflow for extracting V (D)J regions, assembling complementary-determining region 3 (CDR3), and reconstructing protein sequences from RNA sequencing (RNA-seq) data. It reconstructs dominant TCR clonotypes and models their interactions with peptides. Molecular docking and validation methods assess the stability and specificity of these interactions. Additionally, AI tools are employed to identify potential TCR binding ligands and characterize antigen recognition patterns in melanoma.

Result: We have identified three of the significant CDR3 V(D)J regions that are eligible to analyze their binding affinities and specificities with melanoma-associated antigens.

Conclusion: This study identifies key melanoma-associated CDR3 sequences and evaluates their antigen-binding potential through structural modeling and AI tools, laying the groundwork for future validation and therapeutic exploration.

International Perspectives on Governing Action Sports: Trade-Offs from Community Roots to Olympic Recognition

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Background/Objective: Action sports are marked by thrill, risk taking, adventure and an alternative lifestyle that exists on the fringe of the traditional professional sporting world. While the sports of surfing, climbing, and skateboarding have large grassroots participation, the recent addition and inclusion to the Olympic games presents a whole new set of challenges to these typically self-organized sports. The inclusion of action sports into the Olympics has disrupted the self-organized and alternative nature of the sports to conform to the traditional governance of models of more well-established sports that have clear and well-resourced Olympics pathways (e.g., swimming, athletics) (Batuev & Robinson, 2022; Coates et al., 2010; Strittmatter et al., 2018; Wheaton & Thorpe, 2021). Thus, a complete understanding of how a mix of stakeholders from commercial activity providers (i.e., gyms, equipment), and governing bodies to the participants themselves across the action sports community support the sport is needed. This study aims at answering the following research questions:
RQ1: How do stakeholders perceive the key issues and challenges in the governance of action sports as they transition from community-based cultures to institutionalized sport systems, including Olympic structures?
RQ2: How do action sport organizations advocate for legitimacy within mainstream sport systems, and what governance trade-offs emerge from this process, particularly regarding organizational structures, practices, and cultural identity?

Method: This study employs a qualitative research design combining semi-structured interviews and document. Interviews are conducted with representatives from action sport organizations, and relevant stakeholders in Sweden, Norway and Australia. Document analysis includes strategic plans, policy documents, funding applications, political hearings and other public communications.

Result: Preliminary findings suggest that the framing of advocacy for action sports often emphasizes their "different" and "other" nature, which presents challenges for funding providers who struggle to understand and support these sports. Governmental funders attempt to influence democratic structures within action sport clubs, sometimes at the expense of the democratic principles they advocate for. While action sport organizations prioritize the voices of athletes—particularly in the design of facilities - this approach often clashes with institutionalized sport systems.

Conclusion: This research illuminates the tensions and opportunities faced by unconventional sport communities navigating established systems. Disagreements with stakeholders hinder grassroots sport development and elite sport pathways. The study contributes to the sport governance literature on systems and organizational level.

Life without companion service applied for - experiences from adults with Usher syndrome

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Background/Objective: This qualitative interview study objective was to describe experiences of adults with Usher syndrome (USH) related to the application process of companion service according to The Swedish Act (1993:387) concerning support and service for persons with certain functional impairments (LSS), the rejection of it, and their lives thereafter. The project that started in 2023 was approved by the Ethics Review Authority and conducted through an interdisciplinary collaboration between researchers and a counsellor with experience from clinical practice, now working for a knowledge center in the field of deafblindness and with lived experiences as next of kin to persons with deafblindness.

Method: The study had a qualitative descriptive design. Data collection was divided into two rounds of individual semi-structured interviews conducted digitally or in a face-to-face setting. The first round was conducted within a master thesis in psychology. The second round contained member validation follow-up interviews of the preliminary data from the first round. Five adults with USH of mixed ages participated in the first round and four of them in the second round. Data was analyzed in accordance with interpretative phenomenological analysis, IPA.

Result: The analyses yielded six sub-themes: Lacking freedom to decide for myself, Fighting for my rights, Being in an unequal position in relation to others, Being worried, Being socially isolated, and Psychological and physical health at risk, with a main theme: Lack of empowerment over my life.

Conclusion: The findings indicate that the rejection of companion service negatively affected the participants' psychological basic needs. Hence, their well-being were at risk. This underlines the importance of social support, such as companion service for the well-being of those persons with deafblindness who view themselves as in need of such service.

Longevity, mortality and aging on Ikaria: A decade analysis of death records and a retrospective health records study of a cohort.

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Background/Objective: The Greek Island of Ikaria is known for its high prevalence of nonagenarians and centenarians. This study analysed all-cause mortality among the Ikarian population over a ten-year period, as well as disease prevalence and percentage of medication-free participants of a longevity cohort of Ikarians aged 80-100+ years

Method: A retrospective study was conducted analysing data from 796 validated death certificates from the municipalities of Agios Kirykos, Evdilos, and Rahes between 2008-2018. Additionally, an extensive health record data from 126 inhabitants aged 80–100+ years was analysed for prevalence of diagnosis and medication use.

Result: Mean life expectancy on Ikaria was 88.6 for females and 85.0 for males. Predominant causes of death were cardiovascular diseases (84.5%) and cancer (19.5%), with accidents (n=14) and suicide (n = 2) contributing by roughly 2.0%. Retrospective health records show that among individuals aged 91–100+, cardiovascular disease was most common (35%), while cancer was least frequent (4%). In the 80–90-year age group, type II diabetes was most prevalent (19%), and neurodegenerative mental disorders least common (3%). Notably, no participant was diagnosed with depression or psychosis in the 80-100+ cohort, roughly 10% had no chronic diagnosis and 7% were totally medication-free.

Conclusion: It is known that mental disorders such as psychosis and depression substantially lower life expectancy. The Ikarian population that exhibited exceptional longevity had a remarkably low prevalence of psychiatric disorders. Compared with the older Swedish population, a notable difference in the prevalence of depression was observed. To elucidate the mechanisms underlying factors that promote healthy aging in this population, further interdisciplinary studies integrating molecular-genetic, lifestyle, and sociocultural factors are warranted.

Nutritional neuroimaging – the exemplary case of probiotics for gut-brain axis research

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Background/Objective: Modulating the gut-brain axis via probiotic supplementation has emerged as a strategy to promote mental well-being across the entire lifespan.

Method: We have conducted a randomised, double-blinded, placebo-controlled crossover study assessing four-weeks probiotic intake in 22 healthy young to middle-aged adults; and a randomised, double-blinded, placebo-controlled parallel study comparing six-weeks probiotic intake in two different formulations in 90 healthy, community-dwelling elderly. One third of the latter study population was followed up four to six weeks after they stopped the intake of the probiotic supplementation.
In all studies, participants (female to male ratio circa 2:1) were intensively examined at baseline, rated their mental health including perceived stress, anxiety and depression symptoms, sleep quality – using validated psychological rating scales, and underwent structural and functional magnetic resonance imaging (fMRI), the latter for assessment of resting state functional connectivity. In some of the studies, participants underwent cognitive testing with or without task-related fMRI, as well as donated blood, faecal and/or saliva samples for assessment of biomarkers related to various gut-brain signalling routes and of importance for cognitive functioning and mental well-being.

Result: The results across our studies show distinct effects of probiotics on brain morphometry and functional connectivity during rest as well as while subjected to cognitively demanding negative emotional or stress stimuli. Generally, there were only few indications of probiotic effects on psychological symptom scores and cognitive performance, which often derived from longitudinal changes within groups. Analyses of various blood markers are indicative of a possible involvement of circulating serotonin or brain-derived neurotrophic factor in signal transduction, and alterations in the immunological gut-brain communication pathway.

Conclusion: fMRI is a sensitive method to detect subtle effects as well as post-intervention cessation effects of mild and short-term nutritional interventions to a greater extent than alternative and classical assessments, especially in a healthy population, and possibly before effects may be noticed subjectively. Analyses of relevant blood markers and immune cell populations can give insights into potential gut-brain signalling routes, hence modes-of-action. Additionally to analysing the various outcomes individually, we are currently performing analyses focusing on the correlation of various outcomes. In the long-term, we aim to enable a priori identification of so-called responders and non-responders to interventions.

Prediction of toxicant mechanisms based on public cell painting data and alternative embeddings of functional information

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Background/Objective: High-content imaging assays such as Cell Painting provide a promising alternative to traditional toxicology approaches by capturing rich morphological changes across thousands of cellular features. This enables compound effects to be compared at the phenotypic level and may support the identification of shared biological mechanisms. In this study, we examined whether phenotypic similarity among annotated compounds reflects common modes of action - using a collection of alternative approaches, both for compressing cell painting feature information to a low number of dimensions and for representing annotation of function for toxicants.

Method: Morphological profiles from 305 annotated compounds were analyzed using a combination of unsupervised and supervised strategies to evaluate similarity patterns and classification performance. We applied alternative approaches to represent Cell Painting data in lower-dimensional spaces, enabling comparison of how well different compact feature representations preserve biologically meaningful relationships. In parallel, biological function was annotated using multiple complementary approaches, allowing compounds to be grouped by shared targets, pathways, and network-based functional similarity.

Result: Compounds affecting cellular structure most strongly showed the clearest and most consistent phenotypic grouping, indicating that pronounced morphological effects are more readily captured by Cell Painting profiles. In contrast, compounds associated with more heterogeneous or subtle biological responses showed weaker clustering and lower separability. Lower-dimensional representations differed in performance, with some more effectively grouping compounds with overlapping modes of action.

Conclusion: Our findings suggest that morphology-based profiling can support mode-of-action prediction, particularly for compounds that induce strong and distinctive phenotypic changes. However, its broader applicability is constrained by subtle effects, annotation quality, limited sample sizes, and the complexity of high-dimensional data. Morphological profiling could be strengthened through improved functional annotation, integration with other data types, and analysis across multiple biological contexts.

Providing services in crisis - Experiences of professionals in deafblindness rehabilitation during the Covid 19 pandemic

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Background/Objective: The COVID-19 pandemic, with its prescribed physical distancing, affected everyone in society and posed particular challenges for people with disabilities who required physical proximity, including those with deafblindness. Experiences from healthcare workers and professionals in residential homes for the elderly have shown that providing services during the pandemic was a great challenge. However, experiences of professionals providing rehabilitation to people with sensory impairments such as deafblindness have not been explored. Hence, the objective of this study was to explore the experiences of professionals in specialized rehabilitation providing services to people with deafblindness during the Covid-19 pandemic.

Method: The study has a qualitative explorative design. Twenty-two professionals specializing in deafblindness rehabilitation from seven regions in Sweden participated in six semi-structured focus group interviews. Data were analyzed using inductive content analysis.

Result: Preliminary findings reveal a burdensome time for professionals, with worry of risking patients' and own health. They felt alone and abandoned by managers and organisations, and troubled as they sometimes could not provide services. However, when professionals had access to team support it eased their burden. Nonetheless, professionals took on the challenge with the patients' best in focus. They showed flexibility to handle prescribed restrictions and were inventive in meeting needs.

Conclusion: During the time of the pandemic, the professionals were "bending but not breaking". The study reveals unique experiences of professionals in deafblindness rehabilitation providing services in a specific time of crisis but also highlights more general insights of what it means to work in a specialized rehabilitation unit for people with deafblindness. In the event of a future crisis accessible services must be at hand for this group, in-person or digitally. The Professionals call for action plans and access to supervision, to be able to meet future crisis.

Quality of life and economic burden in Swedish adults with atopic dermatitis: a cross-sectional survey of patient-reported outcomes.

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Background/Objective: Atopic dermatitis (AD) is a chronic skin disease associated with impaired health-related quality of life (HRQoL). Evidence from Sweden on out-of-pocket expenses and productivity losses remains limited, particularly from a patient-reported perspective.
Aim of the study was to assess the burden of AD among Swedish adults in relation to HRQoL, work productivity, activity impairment, willingness to pay for symptom relief, and economic outcomes, considering disease severity and comorbid conditions.

Method: A cross-sectional survey was conducted in 2024-2025 among adult members of the Swedish Asthma and Allergy Patient Association. Validated instruments included the Dermatology Life Quality Index (DLQI), EQ-5D-5L, Patient Benefit Index (PBI), and the Work Productivity and Activity Impairment (WPAI) questionnaire. Descriptive and regression analyses were performed.

Result: Respondents (mean age 43 years; 89.8% female) reported moderate HRQoL impairment (mean DLQI 10.1). HRQoL worsened with increasing disease severity and was lower among individuals with allergic or non-atopic comorbidities, but did not differ by asthma status. Mean annual out-of-pocket costs were €900 (95% CI: 401.1-1758.4) and mean annual productivity losses were €1,972 (95% CI: 1198.7-2828.0). Higher itch intensity and activity impairment were associated with poorer HRQoL and higher costs.

Conclusion: Atopic dermatitis is associated with substantial impairment in HRQoL, work functioning, and economic burden among Swedish adults. These findings highlight the need for comprehensive management strategies that address both clinical symptoms and the broader functional and economic consequences of the disease.

Rectal diameter, functional constipation and assisted infant toilet training at 9 months of age: a randomized intervention study

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Background/Objective: Transabdominal ultrasound measuring the transverse rectal diameter is clinically used to diagnose and evaluate treatment in functional constipation. Age dependent normal values for infants are limited. We aimed to provide normal values for the rectal diameter at 9 months of age and examine possible association with functional constipation or assisted infant toilet training.

Method: The transverse rectal diameter was measured investigator blinded at 9 months of age in infants participating in the ongoing Swedish randomized intervention study BABITT. The intervention group was asked to introduce assistant infant toilet training at 0-2 months. Functional constipation was diagnosed according to the Rome IV criteria by parents answering validated web questionnaires.

Result: Of the 271 infants included in the BABITT study, 243 infants completed transabdominal ultrasound measurement. The median transverse rectal diameter was 1,73 cm (range 0,83-3,42) and did not differ between the intervention and control group. Upper 95% limit for normal transverse rectal diameter was 2,67 cm (mean +2SD). The prevalence of parent reported functional constipation was 14,9% (36/243). The rectal diameter did not significantly differ between infants with or without functional constipation. Furthermore, the use of laxatives, defecation frequency and flatulence did not differ significantly between groups.

Conclusion: The upper 95% limit for transverse rectal diameter was 2,67 cm and this value is suggested as cut-off for normality at 9 months of age. Transverse rectal diameter was not associated with functional constipation at this age, nor with the intervention of assisted infant toilet training.

Reference values of the cross-sectional area in the median and ulnar nerve in a healthy Swedish population

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Background/Objective: The ultrasound examination can provide important information about the structure and appearance of the nerves in assessment of nerve entrapment, inflammatory, and degenerative nerve diseases. Reference values have been published internationally, and factors such as age, ethnicity, gender, and body size are important for the cross-sectional area of the nerves. For that reason, it is important to collect local reference values for healthy individuals.

Method: Healthy individuals aged 18-80 years without known neurological disease or other nerve damage, for example nerve entrapment in the carpal tunnel or in the elbow, were recruited for the study. The median and ulnar nerves were examined with ultrasound and with motor and sensory electroneurography. Exclusion criteria were known neurological disease/nerve damage, previous surgery at wrist level, or electrophysiological signs of nerve entrapment, polyneuropathy or other nerve damage. Ultrasound examinations were performed on Philips Epic 7G (Philips Healthcare, Andover, MA, USA). A linear probe with frequency 4–18 MHz was used to visualize the median nerve and ulnar nerve in transverse sections. Cross-sectional areas were measured at standardized levels in the transverse section within the epineurium. Electrophysiological examinations on the median and ulnar nerve were carried out at Keypoint (Medtronic, Skovlunde, Denmark) according to international guidelines. Body composition (height, weight, percentage of body fat, wrist circumference) was measured with a wall-mounted measuring stick, body impedance scale (Tanita Europe B.V Tanita BC-418 MA, Amsterdam, The Netherlands) and measuring tape.

Result: So far 140 individuals (93 women and 47 men) were included in the study and data were analyzed from the first 74 individuals (mean age 40 years) The cross-sectional area of the median nerve at wrist, forearm, antecubital fossa, and upper arm presented as mean ± standard deviation in mm2 were 9,3±2,8, 7,1±1,8, 8,0±2,2 and 8,4±1,8 respectively. The cross-sectional area of the ulnar nerve at wrist, forearm, elbow, and upper arm presented as mean ± standard deviation in mm2 were 5,3±1,4, 6,0±1,5, 6,7±2,0 and 6,5±1,9 respectively. Cross sectional area differed significantly between women and men at all measured locations. Moreover, at all locations, cross-sectional area was positively correlated with both wrist circumference and body mass index (BMI).

Conclusion: The study will contribute to local reference values of the cross-sectional area in peripheral nerves in the upper extremities in a Swedish population and highlights the importance of taking gender and body composition into account.

Regulatory T cells in primary tumors and lymph nodes in men with prostate cancer

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Background/Objective: Prostate cancer is one of the most common malignancies among men in Western countries. While many patients with localized disease can be cured, a subset progresses to metastatic and life-threatening cancer. Current risk stratification relies mainly on clinical parameters such as tumor stage, Gleason grade, and prostate-specific antigen (PSA) levels, which have limited prognostic accuracy. There is therefore a need for novel biomarkers to better identify patients at risk of aggressive disease. Growing evidence suggests that the tumor microenvironment, particularly regulatory T cells (Tregs) expressing FOXP3, plays a key role in tumor progression and immune evasion. Although Tregs are more abundant in prostate cancer tissue and have been associated with poor prognosis, their prognostic and biological significance, especially in relation to lymph node metastasis, remains incompletely understood.

Method: We evaluated the presence and distribution of CD4⁺FOXP3⁺ Tregs in primary prostate tumors and corresponding pelvic lymph nodes from 136 men who underwent radical prostatectomy with pelvic lymph node dissection. Treg infiltration was quantified using immunohistochemical double staining in tissue microarrays. Comparisons were made between patients with and without lymph node metastases, as well as between primary tumors and lymph nodes.

Result: Treg infiltration was significantly higher in lymph nodes than in primary tumors. Patients with lymph node metastases exhibited a significantly higher number of Tregs in metastatic lymph nodes compared with patients without lymph node metastases. No statistically significant differences in Treg frequency were observed in primary tumors in relation to lymph node status or other clinicopathological variables, although a trend toward higher Treg levels in more aggressive disease was noted.

Conclusion: Regulatory T cells are markedly enriched in lymph node metastases in prostate cancer and may play an important role in the immunobiology and metastatic progression of the disease. Characterization of Tregs within lymph nodes may provide valuable insight into tumor immune dynamics and represent a potential prognostic biomarker in prostate cancer.

Safety and acute effects of Hot water immersion in rehabilitation after Myocardial Infarction (HOT-MI) –a randomized controlled study

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Background/Objective: Several studies have investigated thermotherapy, including saunas and warm water baths, as a potential strategy to reduce cardiovascular risk in both healthy individuals and patients with cardiovascular disease. However, a randomized controlled study on thermotherapy has not previously been conducted in patients with recent myocardial infarction (MI). Given the well-documented benefits of exercise training in cardiac rehabilitation after MI and emerging evidence that thermotherapy may enhance cardiovascular function and reduce inflammation, this study aimed to assess the feasibility and safety of hot water immersion (HWI) as a complementary post-MI rehabilitation method. **Purpose:** Our objective was to assess the safety and acute physiological effects of HWI as a complementary method in cardiac rehabilitation for post-MI patients. Future analyses will examine its impact on inflammatory and metabolic status, cardiovascular function, and psychological well-being.

Method: This prospective, randomized, controlled study (NCT05725655) included 30 MI patients (STEMI or NSTEMI) enrolled in center-based cardiac rehabilitation at Örebro University Hospital, Sweden. After providing informed consent, participants were randomized 1:1 to an 8-week intervention with pre- and post-testing. Throughout the program, they engaged in supervised progressive aerobic and strength training (60 minutes) two times per week, followed by either 20 minutes of HWI or passive rest (control group). Here, we report safety data on vital parameters.

Result: HWI resulted in significant changes in heart rate (+4.9 9.8 beats/min; $p < 0.001$), oxygen saturation (-2.5 2.3 SpO2%; $p < 0.001$), body temperature (+1.0 0.4 ° C; $p < 0.001$), and diastolic blood pressure (-7.9 8.7 mmHg; $p < 0.001$). Self-reported heat stress (+1.7 0.6; $p < 0.001$) and sweating (+1.2 0.6; $p < 0.001$) increased. No significant changes in systolic blood pressure were observed. No long-term physiological adaptations to repeated HWI were found.

Conclusion: HWI led to an acute rise in several vital parameters but was well tolerated, indicating its safety in post-MI patients. The long-term effects of HWI on inflammatory and metabolic status, as well as cardiovascular recovery, will be reported in future analyses. If shown to be effective, HWI could serve as a novel, simple, and safe complementary therapy in cardiac rehabilitation, particularly benefiting patients with limited exercise capacity.

Sex differences in long-term sick leave after Graves' disease: a population-based cohort study

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Background/Objective: Graves' disease (GD) commonly affects working-age adults and may impair long-term work ability. We aimed to investigate sex differences in the risk of long-term sick leave after GD diagnosis.

Method: This register-based cohort study included patients with newly diagnosed GD from seven Swedish cities during 2003–2005 and matched individuals from the general population without hyperthyroidism. The outcome was long-term sick leave, defined as >60 consecutive net days. Sex-stratified relative risks (RRs) with 95% confidence intervals (CI) were estimated for different follow-up periods after the index date. Models were adjusted for education level, marital status, comorbidity, sick leave during the year before diagnosis, number of children, and occupational skill level. Analyses were performed for long-term sick leave excluding and including ICD-10 code E05.

Result: GD was associated with an increased risk of long-term sick leave in both women and men, but men showed consistently higher relative risks throughout follow-up. During the first year after diagnosis, the adjusted RR was 4.16 (95% CI 3.37–5.13) in women and 11.66 (95% CI 5.47–24.84) in men. The excess risk remained significantly elevated at 2–5 years after diagnosis in both sexes, again with higher estimates in men than in women.

Conclusion: GD is associated with an increased risk of long-term sick leave, particularly during the first year after diagnosis. Although GD is more common in women, men demonstrated higher relative risks of long-term sick leave. These findings suggest that GD may have a greater impact on work capacity in men and highlight the importance of considering sex differences in the management and follow-up of patients with GD.

Synchronous brain activity in newborn infants and their mothers during parent-led multimodal pain alleviation with skin-to-skin contact, breastfeeding and lullaby singing

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Background/Objective: Protecting infants' vulnerable brain during repeated painful procedures like blood-sampling and immunizations in early life is a top priority in neonatal health care. Use of parent-delivered pain management may safeguard the infant brain but at the brain level, it is still unclear what drives the analgesic effect of parent-led interventions such as skin-to-skin contact, breastfeeding, and the parent's live singing. The objective of this study is to advance our understanding of the synchronous neural mechanisms behind parent-led pain management in newborn pain care.

Method: Twenty mother-infant dyads will be studied during a planned blood sampling venepuncture, with skin-to-skin contact, breastfeeding and mother's live singing. The potential interbrain synchronous cerebral activation in cortical regions of interest will be registered using functional Near-Infrared Spectroscopy (fNIRS) hyperscanning. Secondly, registration of skin conductance, heart rate variability and the mother's gaze will be registered. Social and music interactions will be studied with microanalysis.

Result: Participant recruitment is ongoing.

Conclusion: Despite a growing body of evidence supporting parent-led pain management, health care professionals still don't prioritize parent involvement in infants' pain care.
The results from this fNIRS hyperscanning project will hopefully advance both theoretical understanding and clinical practice in neonatal pain management and improve the parents' possibilities to protect their infant's brain from pain during the many painful procedures early in a child's life.

The agreement between parent- and child-reported measures of somatic distress, gastrointestinal symptoms, mental health and self-rated health, in girls 9-13 years old with functional abdominal pain

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Background/Objective: To explore the agreement between parent and child-reported measures of somatic distress, gastrointestinal symptoms, mental health, and self-rated health, in girls 9-13 years old with functional abdominal pain.

Method: Secondary analysis of data from a prospective randomized controlled trial called the Just in TIME study (1, 2) on girls aged 9–13 years with Functional Abdominal Pain Disorders (FAPDs). We analyzed data from instruments that bothgirls and their legal guardiansanswered separately, at studystart: Children's Somatization Inventory - gastrointestinaldistress (CSSI-GI) and somatic distress (CSSI-nonGI), Self-rated Health (SRH), and Mental Health Symptoms (MHS).

Result: Data from 121 girls (mean age 10.6 years) were analyzed, including 74 with FAPD and 47 with Irritable Bowel Syndrome. For CSSI-GI the girls reported a mean score of6.98 (SD 4.39) and the guardians 7.27 (4.31) with an intraclass correlation (ICC) of0.84 ($p<0.001$). Corresponding numbers for CSSI-nonGI were 8.75 (6.51) and 6.79 (5.05), ICC 0.75 ($p<0.001$). The weightedCohen's kappa was 0.32 ($p<0.001$) for SRH and for the MHS items the kappa variedfrom 0.20 to 0.52, all significant.

Conclusion: The findings reveal good agreement for gastrointestinal and general somatic symptoms, but lower agreement when reporting mental and general health. Understanding parent-child agreement in self-reported health measures enhances insight into how symptoms are perceived across informants and contexts. It also informs when and for whom a child's self-report may be considered sufficient in clinical or research settings.

The first systematic review of granulosa cell tumors in pediatric females

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Background/Objective: Granulosa cell tumors (GCTs) are rare ovarian malignancies. The objective was to conduct a systematic review describing the clinical presentation and prognostic factors in a large pediatric population.

Method: The databases MEDLINE, Embase, Web of Science, and CINAHL were searched, and Swedish physicians were contacted to identify new cases. Studies reporting new data on nonpregnant females <19 years of age with GCTs, published in any language from 1970–2021, were included. Information on age, symptoms, comorbidities, tumor type, size, mitotic activity, stage, treatment, and outcomes was collected.

Result: The search yielded 1,894 studies, of which 352 met the eligibility criteria, encompassing 632 cases. Nineteen new cases were identified, resulting in 651 cases. Most patients presented within the first year of life and had juvenile GCTs. Presenting symptoms differed significantly in frequency by developmental groups. Precocious puberty occurred in 83% of patients aged <10 years, whereas abdominal symptoms predominated in older patients. Females aged ≥10 years had larger tumors of more advanced stages. Significant comorbidities occurred in 39 patients and included, among other conditions, tuberous sclerosis, other tumors, Ollier's disease and Maffucci, Beckwith–Wiedemann, Potter, Proteus, and McCune–Albright syndromes. Fifty-four patients relapsed, and 57 died. In multivariate analysis, independent and significant risk factors for a poor outcome were higher stage disease and higher mitotic activity.

Conclusion: Girls aged ≥10 years with GCTs often lack endocrine symptoms, likely delaying diagnosis and resulting in more advanced disease and poorer outcomes. Higher disease stages and higher mitotic activity are independent and significant risk factors for a poor outcome. The diverse comorbidity associated with JGCTs points at a shared pathogenesis probably involving aberrant AKT1/mTOR signaling.

The role of cardiac fibroblasts in maintaining structural integrity of multicellular cardiac spheroids

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Background/Objective: Cardiovascular diseases are the leading global cause of death, necessitating advanced in-vitro 3D models that better reflect multicellular architecture of human myocardium than traditional 2D cultures. This study aimed to generate multicellular cardiac spheroids by incorporating human iPSC-derived cardiomyocytes (iCMs), human coronary artery endothelial cells (EC) and human cardiac fibroblasts (CF) to characterize their structural and functional responses to stimulations.

Method: Cardiac spheroids were generated in four combinations (iCM+EC, iCM+CF, EC+CF and iCM+EC+CF) using non adherent 384-well plate. Morphology was assessed via Fiji ImageJ at 24 and 48h. Following LPS stimulation (5µg/ml) for 24 h, contractility was quantified using CytoMotion high speed imaging system. Additionally, confocal microscopy is being employed to investigate the role of HCF driven collagen production and its role in structural remodeling.

Result: Morphological analysis showed that iCM+EC spheroids were the largest and least circular, undergoing significant compaction by 48 hours. Fibroblast containing spheroids exhibited fibroblast driven remodeling with increased perimeter and reduced circularity without the area collapse. LPS treatment significantly affected contractile parameters across all groups: iCM+CF spheroids displayed prolonged relaxation time and increased departure velocity; iCM+EC+CF spheroids showed reduced departure velocity and prolonged time to 50% relaxation; and iCM+EC spheroids exhibited increased peak height and return velocity.

Conclusion: These findings highlight the critical role of fibroblasts in regulating myocardial structural stability and mechanical response.