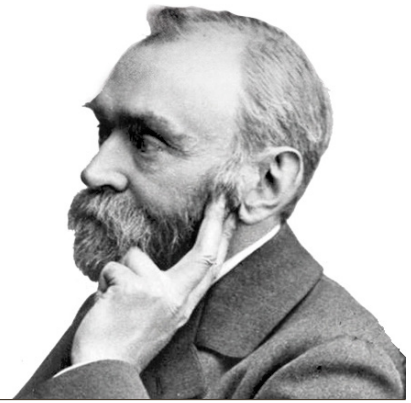


Örebro University's **NOBEL DAY FESTIVITIES**



BOOK OF ABSTRACTS

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Preface

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

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

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

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

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Detecting Copy Number Variants from Next Generation Sequencing data: development and benchmarking CNVExpo

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Background/Objective: Next Generation Sequencing (NGS) is a powerful sequencing technology that is causing a paradigm shift in diagnostics (1). NGS allow massive parallel sequencing of many samples at the same time. Since the launch in 2004, the cost-per-genome has been reduced 50000-folds, and capacity increased 100-1000 times, and NGS is now central in clinical diagnostics and research (2).

NGS primarily detects single nucleotide variants in human disease. However, another important class of mutations are copy number variants (CNV), ranging from 50 bp to megabases (3). Several CNV callers exist that can detect CNVs from NGS data, however, many have a high false positive rate. Also, targeted gene panels often used in clinical laboratories have additional challenges when it comes to CNV detection. (4) For this reason we developed CNVExpo. It compares the read depth per nucleotide against a reference cohort. In this work, we benchmarked CNVExpo against selected competitors.

Method: CNVExpo, panelcn.MOPS and cnvkit were run on 99 targeted gene panel NGS datasets, searching for CNVs in *LDLR*, *PCSK9*, *APOE*, *APOB*, *LIPA*, *LDLRAP1*, *ABCG5/8* and *SLCO1B1*. Multiplex ligation-dependent probe amplification (MLPA) were used as golden standard for *LDLR*. Agreement and non-agreement were analysed between the three CNV callers.

Result: CNVExpo had a diagnostic sensitivity and specificity of 100 % for *LDLR* (compared to MLPA). Benchmarked against cnvkit and panelcn.MOPS, CNVExpo resulted in higher sensitivity and specificity in the detection of CNVs in all analyzed genes with above all fewer false positive calls. Furthermore, CNVExpo provides single-base resolution and identifies deletions and insertions from single nucleotide to whole gene.

Conclusion: CNVExpo is a new CNV caller suitable for targeted NGS data. It is user friendly, does not require command line skills, and is freely available at <https://github.com/xxx>

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The feasibility of regular physical exercise as treatment for core symptoms of Attention Deficit Hyperactivity Disorder.

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Background/Objective: Regular physical exercise is known to improve depression and anxiety, and some evidence indicates that physical exercise can reduce symptoms of attention deficit hyperactivity disorder (ADHD) in children and adolescents with ADHD. Evidence for the effectiveness of regular physical exercise as a treatment is lacking for adults with ADHD.

The aim of this study was to test the feasibility and acceptability of a structured moderate-intensity 12-week physical exercise intervention for adults with ADHD in front of implementing a larger randomized controlled study (RCT) with the purpose of testing the potential benefits of such an intervention. A secondary objective was to detect any trends in the chosen outcome measures.

Method: Fourteen adults with ADHD were recruited and randomized to a physical exercise intervention or a control group. The intervention group received structured physical exercise for 150 minutes per week for 12 weeks, with the support of a physiotherapist. The control group received treatment as usual (TAU). TAU was in most cases medication or no treatment at all. The participants were assessed at baseline and 12 weeks after inclusion using clinical and physical evaluations, self-rating questionnaires, semi-structured interview, and functional magnetic resonance imaging (fMRI).

Result: Eighty percent of the participants conducted the intervention according to protocol. Twenty percent of the participants dropped out before receiving any intervention. We observed consistent trends indicating that the intervention is beneficial, including symptoms of ADHD, quality of life, quality of sleep and body awareness. Overall, participants were satisfied and reported no major difficulties in following the intervention protocol. Some participants expressed difficulties in managing time to get room for exercise in their daily life which created stress.

Conclusion: Twelve weeks of physical exercise with the support of a physiotherapist is potentially feasible for adults with ADHD. Larger studies are needed in order to draw any conclusions about effect. Trying to reduce drop-out and improve adherence, we will add a third randomized arm to the planned RCT. One 3rd of the participants will receive physical exercise together with cognitive intervention, administered by an occupational therapist.

The ambulance nurse's experience of collaboration with the rescue service in traffic accidents

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Background/Objective: A traffic accident can involve a complex situation and the demand is great on both the ambulance service and the rescue service. An optimal collaboration in the event of a traffic accident is necessary to maintain patient safety and a high quality of care. However, little is known about what factors that influences such collaboration.

The aim of this study was to describe the ambulance nurse's experience of collaboration with the emergency services in the emergency care of critically injured patients in traffic accidents.

Method: A qualitative interview study with inductive approach, using content analysis, was used.

Result: A main theme "Collaboration for the best interests of the patient", three themes "Situation-related factors", "Personal factors" and "Communication" and eight sub themes were identified.

Conclusion: The collaboration between the ambulance nurses and the rescue service in traffic accidents with critically injured patients was affected by both situational and person-related factors, as well as by communication.

Collaboration can be developed by structured exercises and feedback and in that way provide both individual and organizational benefits to increase security and understanding of each other's professions. Collaboration is essential for patient safety and high quality of care in traffic accidents.

Measures patients living in the community can take for the prevention and treatment of skin tears: A comprehensive review of the literature

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Background/Objective: Skin tears are acute injuries caused by the separation of the skin layers due to shear forces, friction or blunt trauma and are quite common. A crucial role in reducing the occurrence of skin tears and their severity lies in the promotion of skin health and the prevention of skin lesions, especially in individuals with sensitive skin.

Aim: To find measures for the prevention and treatment of skin tears that patients can take in the community.

Method: Four electronic databases were searched: PubMed, Embase, CINAHL (EBSCO interface) and Web of Science. The search string combined index terms and words related to skin tears, prevention and management. Studies reporting on the prevention and management of skin tears in adults were included. Articles published before 2011 were excluded. The quality of articles was assessed using the Critical Appraisal Skills Programme (2019) for systematic reviews, the SIGN methodology checklist for randomised controlled trials and the AGREE II tool for consensus documents and best practice standards. Eight studies were included.

Result: Articles reviewed provided numerous prevention and treatment measures: emollient therapy, bathing regimen, protective clothing, nutrition and hydration, polypharmacy, mobility and education.

Conclusion: We found a limited body of knowledge, with studies contributing to best practices, prevention and management strategies and the prevalence of skin tears in older, community-dwelling adults. Elderly people living at home, especially those at high risk for skin tears, should be encouraged to participate in the prevention and treatment of skin tears.

Surgical Management of Acute Appendicitis During the European COVID-19 Second Wave: Safe and Effective.

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Background/Objective: The COVID-19 (SARS-CoV-2) pandemic drove acute care surgeons to pivot from long established practice patterns. Early safety concerns regarding increased postoperative complication risk in those with active COVID infection promoted antibiotic-driven non-operative therapy for select conditions ahead of an evidence-base. Our study assesses whether active or recent SARS-CoV-2 positivity increases hospital length of stay (LOS) or postoperative complications following appendectomy.

Method: Data was derived from the prospective, multi-institutional observational SnapAppy cohort study. This preplanned data analysis assessed consecutive patients aged ≥ 15 years who underwent appendectomy for appendicitis (November 2020 - May 2021). Patients were categorized based on SARS-CoV-2 seropositivity: no infection, active infection, and prior infection. Appendectomy method, LOS, and complications were abstracted. The association between SARS-CoV-2 seropositivity and complications was determined using Poisson regression, while the association with LOS was calculated using a quantile regression model.

Result: Appendectomy for acute appendicitis was performed in 4047 patients during the 2nd and 3rd European COVID waves. The majority were SARS-CoV-2 uninfected (3861, 95.4%), while 70 (1.7%) were acutely SARS-CoV-2 positive, and 116 (2.8%) reported prior SARS-CoV-2 infection. After confounder adjustment, there was no statistically significant association between SARS-CoV-2 seropositivity and LOS, any complication, or severe complications.

Conclusion: During sequential SARS-CoV-2 infection waves, neither active nor prior SARS-CoV-2 infection was associated with prolonged hospital LOS or postoperative complication. Despite early concerns regarding postoperative safety and outcome during active SARS-CoV-2 infection, no such association was noted for those with appendicitis who underwent operative management.

Patient perspective in clinical research of ANCA-associated vasculitis- An integrative review

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Background/Objective: Alongside with the more physical pathophysiological symptoms, patients with ANCA associated vasculitis (AAV) suffer from a substantial disease burden. Including the patient perspective of the disease and its impact are important parts of patient care and outcome assessment (1).

This review aims to analyse how AAV patients' perspective has been captured in clinical research.

Method: Since the aim was to include publications of diverse methodologies and origins, the methodology for an integrative review (2) was chosen. A comprehensive search was performed May 2021 in several databases (PubMed, Cinahl, Web of Science and Psych Info). Key terms: patient reported outcome measures, health related quality of life, assessments, patient outcome, patient outcome assessment, patient preference, experience, perspective, perception, patient view, ANCA associated vasculitis, small vessel vasculitis.

A total of 1731 studies were identified through databases. After abstract and full text screening, 122 publications were included in the review. Inclusion criteria were adult patients, and publications where the patient perspective was expressed by a patient.

Result: Of the 122 included publications, 64 were original studies, 23 conference abstracts and 17 reviews. 18 publications were classified as "other", and were published between 1998 and 2021. All publications were described and categorised, and in addition, the 64 original articles were thoroughly analysed. Patient perspective was captured with a wide diversity of PROMs (Patient Reported Outcome Measures), with interviews and study specific questionnaires. 43 different PROMs were used in the publications, the most common were SF-36 (health-related quality of life), n 31, followed by HADS (anxiety and depression), n 10, MFI-20 (fatigue), n 6 and SNOT-22 or SNOT-25 (rhinosinusitis-specific health status and health-related quality of life), n 5. The variety of PROMs and questionnaires covered a wide diversity of domains. Impact on health-related quality of life, impact of AAV, impact on daily life and physical and emotional impact were the most often occurring. Less occurring were educational needs, employment, relationships, lifestyle habits and pain.

Conclusion: This review presents an overview of how the patients perspective has been captured in clinical research. The results display the areas where patient perspective is most commonly addressed and in what areas patient perspective is missing.

Utilization of audiological rehabilitation interventions for adult hearing aid users: interventions and contextual factors that matters

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Background/Objective: Previous research on audiological rehabilitation aimed for adults with severe-to-profound hearing loss have so far primarily been based on quantitative data, particularly on cochlear implants. (e.g. Birman & Sanli, 2020). The majority of patients in Sweden with severe-to-profound hearing loss use hearing aids instead of cochlear implants (Hjaldaahl et al, 2017). It is therefore important that studies also focus on other audiological rehabilitation interventions than cochlear implants. The aim was twofold: 1) from a bio-psycho-social perspective investigate audiological rehabilitation interventions that adult hearing aid users with severe-to-profound hearing loss have taken part in, 2) and to explore contextual factors that affect the individual utilization of the audiological rehabilitation interventions.

Method: The study has an explorative inductive design with qualitative individual interviews. Participants who fulfilled the inclusion criteria were recruited from two Swedish regions. A total of 21 individuals were interviewed (17 men and 4 women, aged 33-88 years). The verbatim-transcribed interviews were analyzed with conventional content analysis according to Hsieh and Shannon (2005).

Result: Four themes emerged from the data: *managing hearing loss, own perception of hearing loss, life events* and *environmental aspects*. The first theme is about aspects that the participants expressed as important to handle their hearing loss in everyday life, such as hearing aids and assistive technical devices. *Own perception of hearing loss* addresses how personal characteristics influence everyday life. *Life events* capture other aspects in life that were expressed as affecting living with hearing loss. The fourth theme summarizes aspects in the environment that the participants experienced as hindering or facilitating for coping with hearing loss.

Conclusion: The results of the study indicate that hearing aids were considered indispensable, but not enough for beneficial functioning in everyday life. Environmental and individual factors are important in order to utilize the audiological rehabilitation interventions in everyday life.

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Total Knee Arthroplasty and Bariatric Surgery: Change in BMI and Risk of Revision Depending on Sequence of Surgery

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Background/Objective: Patients with obesity have higher risk of complications after total knee arthroplasty (TKA). We investigated the weight change at one and two years after Bariatric Surgery (BS) in patients that had both TKA and BS and the risk of revision after TKA depending on if BS was performed before or after the TKA.

Method: Patients having BS within two years before or after TKA were identified from the Scandinavian Obesity Surgery Register (SOReg) and the Swedish Knee Arthroplasty Register (SKAR) between 2007 and 2019 and 2009 and 2020 respectively. The cohort was divided into two groups; patients with TKA before BS (TKA-BS) and patients with BS before TKA (BS-TKA). Multilinear regression analysis and Cox proportional hazards model were used to analyze weight change after BS and the risk of revision after TKA respectively.

Result: Of the 584 patients included in the study, 119 patients had TKA before BS and 465 had BS before TKA. We found no association between the sequence of surgery and total weight loss at one and two years after BS (risk ratio -0.1 (95% confidence interval (CI) -1.7 to 1.5) and -1.2 (CI -5.2 to 2.9 respectively), and the risk of revision after TKA (hazard ratio 1.54 (CI 0.5-4.5).

Conclusion: The sequence of surgery in patients undergoing both BS and TKA seems not to have any association with the weight loss after BS or the risk of revision after TKA.

Long-term reoperation rate following primary ventral hernia repair: a register-based study

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Background/Objective: The aim of this study was to analyse the risk for reoperation following primary ventral hernia repair.

Method: The study was based on umbilical hernia and epigastric hernia repairs registered in the population-based Swedish National Patient Register (NPR) 2010-2019. Reoperation was defined as repeat repair after primary repair.

Result: Altogether 29,360 umbilical hernia repairs and 6514 epigastric hernia repairs were identified. There were 624 reoperations registered following primary umbilical repair and 137 following primary epigastric repairs. In multivariable Cox proportional hazard analysis, the hazard ratio (HR) for reoperation was 0.292 (95% confidence interval (CI) 0.109-0.782) after open onlay mesh repair, 0.484 (CI 0.366-0.641) after open interstitial mesh repair, 0.382 (CI 0.238-0.613) after open sublay mesh repair, 0.453 (CI 0.169-1.212) after open intraperitoneal onlay mesh repair, 1.004 (CI 0.688-1.464) after laparoscopic repair, and 0.940 (CI 0.502-1.759) after other techniques, when compared to open suture repair as reference method. Following umbilical hernia repair, the risk for reoperation was also significantly higher for patients aged <50 years (HR 1.669, CI 1.389-2.005), for women (HR 1.401, CI 1.186-1.655), and for patients with liver cirrhosis (HR 2.544, CI 1.049-6.170). For patients undergoing epigastric hernia repair, the only significant risk factor for reoperation was age <50 years (HR 2.046, CI 1.337-3.130).

Conclusion: All types of open mesh repair were associated with lower reoperation rates than open suture repair and laparoscopic repair. Female sex, young age and liver cirrhosis were risk factors for reoperation due to hernia recurrence, regardless of method.

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Genetic variants of *Neisseria meningitidis* and outcome of infection in mice

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Background/Objective: *Neisseria meningitidis*, a human restrictive bacterium, is frequently carried asymptotically in nasopharynx, but can also provoke invasive meningococcal disease [1,2]. Bacterial genetic factors, associated with carriage or with invasive disease, are not fully understood. In a genome-wide association study, the gene *porB* class 2 was significantly associated with invasive isolates of *N. meningitidis* [3]. The aim of this study was to examine the virulence of meningococcal isolates of carriage and invasive type in transgenic mice. Additionally, to construct PorB-meningococcal isolates and to compare the virulence of the mutants to their parental isolates in the same mouse model.

Method: Transgenic BALB/c mice, expressing human transferrin, were infected intraperitoneally with meningococcal isolates of carriage or invasive type. After 3 and 24 hours of infection, clinical scores (fur quality, general force, and temperature) and blood bacteria loads were used to evaluate bacterial virulence, in addition to measuring the blood levels of inflammatory cytokines. Similar methods for evaluating virulence were used to compare PorB-mutants to their wildtype parent isolates, after the creation of isogenic mutants with inactivated *porB*, and infection with these in transgenic mice.

Result: Invasive isolates provoked significantly more severe infections in mice compared to carriage isolates. However, no such a difference was observed for the PorB- mutant when compared to its parent isolate.

Conclusion: This study confirms that invasive isolates of *N. meningitidis* have a greater ability to cause a more severe outcome of infection than carriage isolates in transgenic mice. The impact of the gene *porB* cannot be verified and must be further validated.

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Patients' experiences regarding severe leg wound infection associated with coronary artery bypass grafting: a qualitative study

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Background/Objective: The aim of this study was to describe patients' experiences associated with acquiring a severe infection in the harvesting site after CABG.

Method: A qualitative study with descriptive design was conducted at the department of vascular and cardiothoracic surgery in a Swedish university hospital. Patients diagnosed with a severe surgical site infection in the harvesting site following CABG were included. The interviews were analysed with inductive qualitative content analysis.

Result: A total of 16 patients (13 men and three women) aged 49–85 years participated in the study. The main category, *varying impact on body and mind*, was the core of the patients' experiences of severe wound infection in the harvesting site after CABG. Two generic categories were identified: *physical impact* and *thoughts about the complication*. The participants gave varying descriptions of how the symptoms appeared in the harvested leg: more clearly or more discreet, as soon as a couple of days up to a couple of months after the surgery, and ranging from mild to severe. The experience of pain in the wound varied greatly between the participants, from no pain at all in several of the patients to severe pain in others. Some participants experienced pain continuously while others had intermittent pain. Different participants reacted differently to the message of the complication. Several of them said it led to increased fear and anxiety, with thoughts and reflections regarding why the infection had occurred or whether there would be even more difficult complications in their recovery, while others were affected only slightly or not at all. Everyday life was affected to varying degrees due to the complication in the harvesting site.

Conclusion: The findings indicate that a severe infection in the harvesting site after CABG was experienced as an important issue with varying impact on pain, anxiety, and limitations in daily life. Most of them were satisfied with the outcome after the wound had healed.

Patients should be advised to seek care at an early stage if symptoms of infection occur. Improved individual pain management is needed for those with severe pain, and varied experiences imply a need for person-centred care.

Faster typing of Methicillin-resistant *Staphylococcus aureus* with Nanopore sequencing: a comparison

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Background/Objective: Long read sequencing with Oxford Nanopore Technology (ONT) is fast and less expensive compared to short read sequencing. The technology has been associated with higher error rates and concerns regarding stretches of the same nucleotide (1). However, the development of ONT sequencing is advancing rapidly and the error rate has been improving over time (2). The aim was to compare long read ONT sequencing with short-read sequence data from methicillin-resistant *Staphylococcus aureus* (MRSA) to shorten the sequencing time in routine diagnostics.

Method: Subcultured MRSA isolates (n=18) were pre-lysed prior to DNA extraction. ONT DNA libraries were then prepared for six MRSA samples per run using the Rapid Barcoding Sequencing kit according to the ONT protocol, except for the use of below the recommended DNA input. DNA libraries were sequenced on the GridION X5 Mk1 for 24 hrs. Basescalling was done using MinKNOW v5.1.0 and Guppy v6.1.5. Demultiplexing of barcodes and quality control of the reads were accomplished in real-time using EPI2ME platform. Assembly and polish of the draft genomes were performed with command line tools. The processed data files were analysed for core genome MLST (cgMLST) analysis of 1,861 core genes followed by a minimum spanning tree (MST) analysis. The previously obtained short-read sequencing data for these samples was used for comparison.

Result: All the sequenced isolates achieved high quality scores containing 1-2 contigs. ONT sequencing gave the same result in the cgMLST analysis, *spa*, and toxins (PVL, TSST-1, ETA/B) when compared to the results obtained with Illumina. The MST displayed core allele differences between Illumina and ONT in 14 isolates with one difference seen in 9 isolates, 2 in 3 and 3 differences in 2 isolates, however the differences did not result in any shift in complex type. In four of the isolates, the MST results for ONT and Illumina were identical.

Conclusion: According to our results, ONT meet the requirements for typing of MRSA in routine laboratories and shorten the analysis time from 5 to 3 days (sample to final results). ONT sequencing shows the capability for rapid sample-to-genotype of MRSA to facilitate surveillance and reveal outbreak situations.

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Sexually transmitted infections and syndromic management of vaginal discharge in women in Mozambique

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Background/Objective: Sexually transmitted infections (STIs) remain a public health problem worldwide. Sub-Saharan Africa is the most affected sub-region, with about 40% of the global burden of STIs. In Mozambique, STIs diagnosis and treatment rely on syndromic management. Data are need for evaluation of the effectiveness of the syndromic management of STIs. This study aimed to assess the diagnostic accuracy of vaginal discharge syndrome in the diagnosis and treatment of STIs

Method: A cross-sectional study was carried out in Maputo, Mozambique, from February 2018 to January 2019, in which 924 women of reproductive age were enrolled. Ethical approval was obtained from the National Bioethics Committee of Mozambique. DNA was extracted using the Qiagen Kit (Qiagen, GmbH, Germany) from cervical swabs and a multiplex real-time PCR was performed for diagnosis of chlamydia, gonorrhea, trichomonas and mycoplasma using the AmpliSens kit (InterLab service Ltd, Moscow Russia). Data were analyzed in STATA/IC 12.1 (StataCorp LP, USA) using descriptive statistics, chi-square tests and logistic regression.

Result: Most participants were under 24 years old, (38.9%) asymptomatic (56.2%), single (50.8%), with secondary school level of education (50.8%) and started their sexual activity between 12-17 years of age (62%).

The overall prevalence of STIs was 8% (n=79). More than half (58.1%) of participants had genital herpes; 15.5% with chlamydial infections and 12.6% with trichomonas. HIV prevalence was 22%. Gonorrhea and chlamydia were more prevalent in women under 24 years of age (5% and 17.3% respectively) living in rural areas (4.4% and 16.4%), Trichomonas was prevalent in women over 35 years of age (13.8%), married/cohabiting (13.5%). The proportion of specific infections was almost evenly distributed in both groups of symptomatic and asymptomatic women.

Chlamydia infection was significantly associated ($p < 0.005$) with age at first sexual intercourse (high positivity rate if first sexual intercourse before age 24) and the number of sexual partners in the last 3 months (lower positivity rate if 2 or more partners compared with only 1 partner). The syndromic approach had sensitivity ranging from 73% to 84%, specificity of 25% and low PPV ranging (from 4 to 15%) for the management of STIs.

Conclusion: Conclusion:

The prevalence of gonorrhea and chlamydia was high in women under 24 years of age. The vaginal syndrome was not specific to STIs and showed low accuracy in the management of STIs. An accurate and confirmatory point-of-care diagnostic approach is necessary for successful STI prevention and eradication.

Mode of anesthesia is not associated with outcomes following emergency hip fracture surgery: a population-level cohort study

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Background/Objective: Hip fractures often occur in frail patients with several comorbidities. In those undergoing emergency surgery, determining the optimal anesthesia modality may be challenging, with equipoise concerning outcomes following either spinal or general anesthesia. In this study, we investigated the association between mode of anesthesia and postoperative morbidity and mortality with subgroup analyses.

Method: This is a retrospective study using all consecutive adult patients who underwent emergency hip fracture surgery in Örebro County, Sweden, between 2013 and 2017. Patients were extracted from the Swedish National Hip Fracture Registry, and their electronic medical records were reviewed. The association between the type of anesthesia and 30-day and 90-day postoperative mortality, as well as in-hospital severe complications (Clavien-Dindo classification $\geq 3a$), was analyzed using Poisson regression models with robust SEs, while the association with 1-year mortality was analyzed using Cox proportional hazards models. All analyses were adjusted for potential confounders.

Result: A total of 2437 hip fracture cases were included in the study, of whom 60% received spinal anesthesia. There was no statistically significant difference in the risk of 30-day postoperative mortality [adjusted incident rate ratio (IRR) (95% CI): 0.99 (0.72 to 1.36), $p=0.952$], 90-day postoperative mortality [adjusted IRR (95% CI): 0.88 (0.70 to 1.11), $p=0.281$], 1-year postoperative mortality [adjusted HR (95% CI): 0.98 (0.83 to 1.15), $p=0.773$], or in-hospital severe complications [adjusted IRR (95% CI): 1.24 (0.85 to 1.82), $p=0.273$], when comparing general and spinal anesthesia.

Conclusion: Mode of anesthesia during emergency hip fracture surgery was not associated with an increased risk of postoperative mortality or in-hospital severe complications in the study population or any of the investigated subgroups.

Existential Loneliness and Life Suffering in Being a Suicide Survivor: A Reflective Lifeworld Research Study

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Background/Objective: Every year, more than 700 000 people die due to suicide. For each suicide an average of about 15 extended family members are estimated to be affected and become a suicide survivor. A family who has been affected by suicide has a higher risk of being affected by suicide again. Suicide survivors are not only faced with the typical reactions following a death, but they also have unique experiences. The suicide survivors' grief differed significantly concerning levels of rejection, shame, stigma, blaming, and concealing the cause of death when compared with all other survivor groups. Previous research do not fully address the essence of what it means to lose someone by suicide by openly and curiously engaging with the suicide survivors' own stories. Therefore, the aim of the study was to describe the loss of a family member by suicide, based on the lived experience of suicide survivors.

Method: A phenomenological study with a Reflective Lifeworld Research approach was conducted, consisting of sixteen interviews with eight suicide survivors.

Result: The essence of losing a family member by suicide encompasses experiences of involuntary and existential loneliness, life suffering, and additional burdens in a life that is radically transformed, comprising prolonged and energy-intensive attempts to understand. Life for family members encompass a constant fear of being judged and also an ambiguous silence that, seemingly paradoxically, that can lead to involuntary loneliness and be a source of support and fellowship. Support mechanisms inside the family fall apart, and it becomes obvious that the survivors' experiences affect others. The loss also implies an active endeavor to maintain the memory of the deceased.

Conclusion: Based on the phenomenon of losing a family member by suicide and the present results, the question of "losing" should be understood in relation to "being" a suicide survivor, that is to say, human existence in all its dimensions. For professionals it is important to early accept the survivors as suffering human beings – from the point of the notification of death – and consider them as patients in need of compassionate care. Such support might reduce life suffering, counteract stigma and involuntary loneliness, and be suicide preventive.

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Ultrasound accurately assesses depth of invasion in T1-T2 oral tongue cancer

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Background/Objective: Depth of invasion (DOI) is important for the T-classification of squamous cell carcinoma of the oral tongue (SCCOT) and incorporated in the TNM 8 classification of oral cavity cancer. To determine DOI clinical palpation is performed, but the preferred radiological modality remains controversial. The aim of this study was to investigate the assessment of DOI using ultrasound (US-DOI).

Method: The DOI was assessed in 40 patients with T1–T3 SCCOT by ultrasound, palpation, computed tomography and magnetic resonance imaging (MRI). Histopathological DOI (H-DOI) was gold standard. Bland-Altman analysis was used to compare mean difference and 95% limits of agreement (LOA).

Result: DOI could not be assessed by US in 3% and by MRI in 21% of the cases respectively. The mean difference of US-DOI was -0.5mm (95% LOA -4.9 to 4.0) compared to H-DOI and the mean difference for MRI was 3.9mm (95% LOA -2.3 to 10.2). In the subgroup analysis of cT1-T2 the US-DOI mean difference was 0.1mm and the 95% LOA limits -2.5 to 2.7.

Conclusion: Ultrasound seems to be the most accurate method to assess DOI in T1–T2 SCCOT. MRI overestimates DOI and cannot assess a substantial proportion of the tumors.

Conflict of Interest Statement: All authors declare that they have no conflicts of interest.

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Liquid biopsies used for early detection of recurrent disease in HPV positive oropharyngeal cancer and cancer of unknown primary

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Background/Objective: Human papilloma virus (HPV) is a known causative agent for oropharyngeal squamous cell carcinoma (OPSCC) and cancer of unknown primary (CUP). The incidence of HPV+OPSCC/CUP has increased in the last decades. Even though the prognosis is good, 10-25 % relapse. A biomarker for treatment evaluation and early detection of recurrent disease is of great clinical interest.

Cell-free tumor HPVDNA (ctHPVDNA) are small DNA fragments that are secreted into the circulation from HPV-driven tumor cells. ctHPVDNA can be detected in plasma using digital droplet PCR (ddPCR).

Our aim was to investigate if circulating tumor HPVDNA (ctHPVDNA) can be used for post-treatment surveillance in patients with HPV+OPSCC and CUP.

Method: This is an ongoing prospective longitudinal multicenter study with patients diagnosed with HPV+OPSCC and HPV+CUP. qPCR was used for HPV genotyping. Blood samples were collected at diagnose (baseline), post-treatment (radiotherapy +/- chemotherapy or TORS) and follow-up. ctHPVDNA was extracted from plasma and analyzed with HPV genotype specific assays for ddPCR. Increasing levels of ctHPVDNA in two consecutive samples were considered a molecular recurrence (1).

Result: 48 (89%) out of 54 patients had detectable ctHPVDNA at baseline. Of these 48 patients, 32 had a rapid decline to undetectable levels post-treatment, while 12 had a prolonged post-treatment decline. 4 patients had persistent ctHPVDNA post-treatment, 2 out of 4 have so far been diagnosed with residual disease.

6 patients (11%) had no detectable ctHPVDNA at baseline, post-treatment nor follow-up.

Three patients have a documented molecular recurrence during follow-up, All of them have confirmed clinical recurrences, 100% PPV. Median lead time between molecular- and clinical recurrence were 132 days (range, 98 - 301 days).

Conclusion: ctHPVDNA is a promising biomarker for detection of minimal residual disease, and for recurrence detection, possibly enabling earlier salvage treatment.

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Potential biomarker for CS treatment response in ADHD patients

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Background/Objective: Approximately 20-30% of patients with Attention-deficit/hyperactivity disorder (ADHD) are non-responders to the currently most common treatment for ADHD, central stimulant (CS) medication. Multiple studies have tried to find behavioural, genetic, neuroimaging and biochemical biomarkers that can be used to evaluate treatment efficacy, but currently there are no clinically applicable biomarkers available to identify non-responding patients. For the paper presented here, we studied if incentive salience and hedonic experience rated after the administration of single dose CS medication could predict whether ADHD patients were responders or non-responders to CS medication.

Method: To evaluate incentive salience and hedonic experience, we used a bipolar visual analogue ‘wanting’ and ‘liking’ scale in 25 healthy controls (HC) and 29 ADHD patients. HC were administered 30 mg methylphenidate (MPH) and ADHD patients received either MPH or lisdexamphetamine (LDX), in individually determined dosage for optimal effect. To evaluate response, ASRS V1.1. and CGI-I were used. In order to correlate wanting and liking to changes in functional connectivity, resting state fMRI (rs fMRI) was performed.

Result: About 20% of those with ADHD were non-responders to CS treatment (5 of 29). When evaluated using the ‘liking’ ‘wanting’ visual analogue scales, responders had significantly higher incentive salience and hedonic experience scores compared to non-responders. Analysis of rsfMRI showed that scores for ‘wanting’ were significantly associated with functional connectivity in ventral striatum including nucleus accumbens.

Conclusion: Incentive salience and hedonic experience evaluated immediately after single dose CS medication can distinguish between responders and non-responders to CS treatment, which can be further supported by corresponding neuroimaging biomarkers in the brain reward system.

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Attitudes and knowledge about HPV vaccination of school children and their parents following use of targeted information

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Background/Objective: This study aimed to investigate children's' and parents' attitudes and knowledge about HPV (human papilloma virus) following introduction of gender neutral HPV vaccination in the national immunization program (NIP) in Sweden. An evaluation of a tailored information package for parents and children launched by the Public Health Agency (PHAS) alongside the introduction of gender neutral HPV vaccination was also performed.

Method: In total, 276 parents and 206 children from 22 School Health Services responded to a web-based survey, spring 2021 to January 2022.

Result: Overall, parents (78%) perceived HPV vaccination to be of importance for their child's health. About half of the participating children and two thirds of the parents had used the tailored information package for the HPV vaccination. The fact sheet was mostly used by parents (55%) and children (20%) and also perceived as easy to understand (99% and 68% respectively). For both children and parents the school nurse (70% respectively) was the primary source for information. The teacher (59%) was also a common source of information of HPV vaccination for the children.

Conclusion: The school health nurse is essential for informing about HPV vaccination for both children and parents. There is a need to strengthen the knowledge regarding HPV vaccination among teachers as they also are a key source of information for the majority of the children. Additional interventions are needed to support parents in making informed decisions for HPV vaccinations.

Experience of living with crooked and blurred vision caused by epiretinal membrane

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Background/Objective:

Purpose To describe people's experience of living with crooked and/or blurred vision caused by epiretinal membrane (ERM)

Background/Objective The study population was patients diagnosed with the eye disease ERM. This visual disturbance is characterized by a crooked vision (metamorphopsia), i.e., straight objects are perceived as wavy/crooked. There is also reduced visual acuity. The disease is most common in the elderly and is often remedied by surgery.

Method: Using a qualitative content analysis, information from 16 semi-structured interviews has been analysed through an inductive approach. Through repeated readings of the text, the material became familiar and thus obtained a sense of wholeness. The text was divided into meaning units to be followed by codes and then subcategories and categories. A process that oscillates back and forth to finally discern a theme.

Result: The theme 'To see life through other eyes' illustrated the patients experience of living with ERM. Four categories were identified; physical expressions, emotional reactions, limitations in daily life and strategies to compensate for impaired vision. Physical symptoms such as headaches, dry eyes and/or nausea occurred. Visual problems were also common like blurred vision, affected detail vision and crooked vision. Restrictions in everyday life in the form of reduced activities such as sports or driving were also found. Even one's self-image seemed to be affected due to the loss of identity. Strategies to compensate for lack of vision were shown by taking support from their surroundings, changing settings on for example a mobile phone and in some cases stopping the activity altogether.

Conclusion: By acquiring this knowledge, the understanding of their life situation and how vision effects them in everyday life increases. Based on this, be able to offer person-centred care, as well as enable priorities in terms of measures.

Long term outcome after toxic nodular goitre

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Background/Objective: The purpose of treating toxic nodular goitre (TNG) is to reverse hyperthyroidism, prevent recurrent disease, relieve symptoms and preserve thyroid function. Treatment efficacies and long-term outcomes of antithyroid drugs (ATD), radioactive iodine (RAI) or surgery vary in the literature. Symptoms often persist for a long time following euthyroidism, and previous studies have demonstrated long-term cognitive and quality of life (QoL) impairments. We report the outcome of treatment, rate of cure (euthyroidism and hypothyroidism), and QoL in an unselected TNG cohort.

Method: TNG patients (n=638) de novo diagnosed between 2003–2005 were invited to engage in a 6–10-year follow-up study. 237 patients responded to questionnaires about therapies, demographics, comorbidities, and quality of life (ThyPRO). Patients received ATD, RAI, or surgery according clinical guidelines.

Result: The fraction of patients cured with one RAI treatment was 89%, and 93% in patients treated with surgery. The rate of levothyroxine supplementation for RAI and surgery, at the end of the study period, was 58% respectively 64%. Approximately 5% of the patients needed three or more RAI treatments to be cured. The patients had worse thyroid-related QoL scores, in a broad spectrum, than the general population.

Conclusion: One advantage of treating TNG with RAI over surgery might be lost due to the seemingly similar incidence of hypothyroidism. The need for up to five treatments is rarely described and indicates that the treatment of TNG can be more complex than expected. This circumstance and the long-term QoL impairments are reminders of the chronic nature of hyperthyroidism from TNG.

Partial REBOA in hemorrhagic shock – Carbon dioxide versus blood pressure titrated occlusion

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Background/Objective: The definition of partial resuscitative endovascular balloon occlusion of the aorta (pREBOA) is not yet determined and clinical markers of the degree of occlusion, metabolic effects and end-organ injury that are clinically monitored in real time are lacking. The aim of the study was to test the hypothesis that end-tidal carbon dioxide (ETCO₂) targeted pREBOA causes less metabolic disturbance compared to proximal systolic blood pressure (SBP) targeted pREBOA in a porcine model of hemorrhagic shock.

Method: Twenty anesthetized pigs (26-35 kg) were randomized to 45 minutes of either ETCO₂ targeted pREBOA (pREBOAETCO₂, ETCO₂ 90-110% of values before start of occlusion, n=10) or proximal SBP targeted pREBOA (pREBOASBP, SBP 80-100 mmHg, n=10), during controlled grade IV hemorrhagic shock. Autotransfusion and reperfusion over three hours followed. Hemodynamic and respiratory parameters, blood samples and jejunal specimens were analyzed.

Result: ETCO₂ was significantly higher in the pREBOAETCO₂ group during the occlusion compared to the pREBOASBP group, whereas SBP, femoral arterial mean pressure and abdominal aortic blood flow were similar. During reperfusion, arterial and mesenteric lactate, plasma creatinine and plasma troponin concentrations were higher in the pREBOASBP group.

Conclusion: In a porcine model of hemorrhagic shock, ETCO₂ targeted pREBOA caused less metabolic disturbance and end-organ damage compared to proximal SBP targeted pREBOA, with no disadvantageous hemodynamic impact. End-tidal CO₂ should be investigated in clinical studies as a complementary clinical tool for mitigating ischemic-reperfusion injury when using pREBOA.

Uncommon metastases- a retrospective cohort study in patients with small intestine and pancreatic neuroendocrine tumours

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Background/Objective: Neuroendocrine tumours (NET) are rare tumours often developed in the gastropancreatic system. When patients with NET are diagnosed and followed up, they often undergo a disease specific radiology examination with a tracer ligand binding to tumour cells called ⁶⁸Galium/DOTATOC/PET/CT.

Metastatic disease is often seen in patients when diagnosed and mostly located in surrounding lymph nodes, in the liver and peritoneal space. Small population based studies have shown metastases to other locations, such as bone, heart, breast, orbita and from small intestinal NET to the pancreas in a small number of patients. Large studies in prevalence of metastases in the disease have not been done.

Method: Between the years of 2010 and 2022, 2092 patients underwent ⁶⁸Galium/DOTATOC/PET/CT at Uppsala Akademiska Hospital and USÖ. The latest radiology examination was studied. Patients were divided into groups of negative examinations, NET other than pancreatic or small intestinal NET, pancreatic NET and small intestinal NET.

Result:

- In 2092 patients, 421 patients underwent radiology due to pancreatic NET
- In 2092 patients, 755 patients underwent radiology due to small intestinal NET
- 10 % of the patients with pancreatic NET presented bone metastases (42/421)
- 23 % of patients with small intestinal NET presented bone metastases (175/755)
- In patients with small intestinal NET spreading to heart, breast, orbita, lung and pleura was seen in about 2 %

Conclusion: Uncommon metastases in pancreatic and small intestinal NET are more common than previously described. Especially in small intestinal NET, 23 % of the patients presented skeleton metastases. In future studies, we aim to study whether uncommon metastases can be used as a prognostic factor.

References:

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Molecular Epidemiology of Neonatal-Associated *Staphylococcus haemolyticus* Reveals Endemic Outbreak

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Background/Objective: *Staphylococcus haemolyticus* is a major cause of late-onset sepsis in neonates, and endemic clones are often multidrug-resistant. The bacteria can also act as a genetic reservoir for more pathogenic bacteria. Molecular epidemiology is important in understanding bacterial pathogenicity and preventing infection. The aim of this study was to describe the molecular epidemiology of *S. haemolyticus* isolated from neonatal blood cultures at a Swedish neonatal intensive care unit (NICU) over four decades, including antibiotic resistance genes (ARGs), virulence factors, and comparison to international isolates.

Method: The *S. haemolyticus* isolates were whole-genome sequenced, and single nucleotide polymorphisms in the core genome were used to map the relatedness. The occurrence of previously described ARGs and virulence genes were investigated. Disc diffusion and gradient tests were used to determine phenotypic resistance.

Result: The results revealed a clonal outbreak of *S. haemolyticus* at this NICU during the 1990s. Multidrug-resistance was present in 28 (82%) of all isolates and concomitant resistance to aminoglycoside and methicillin occurred in 27 (79%). No isolates were vancomycin resistant. Genes encoding ARGs and virulence factors occurred frequently. The isolates in the outbreak were more homogenous in their genotypic and phenotypic patterns. Genotypic and phenotypic resistance combinations were consistent.

Conclusion: Pathogenic traits previously described in *S. haemolyticus* occurred frequently in the present isolates, perhaps due to the hospital selection pressure resulting in epidemiological success. The clonal outbreak revealed by this study emphasizes the importance of adhering to hygiene procedures in order to prevent future endemic outbreaks.

Global microRNA and protein expression in human term placenta

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Background/Objective: Description of the global expression of microRNAs (miRNAs) and proteins in healthy human term placentas may increase our knowledge of molecular biological pathways that are important for normal fetal growth and development in term pregnancy. The aim of this study was to explore the global expression of miRNAs and proteins, and to point out functions of importance in healthy term placentas.

Method: Placental samples (n = 19) were identified in Örebro biobank. All samples were from uncomplicated term pregnancies with vaginal births and healthy, normal weight newborns. Next-generation sequencing and nano-scale liquid chromatographic tandem mass spectrometry were used to analyse miRNA and protein expression, respectively.

Result: A total of 895 mature miRNAs and 6,523 proteins were detected in the placentas, of which 123 miRNAs and 346 proteins were highly abundant. The miRNAs were in high degree mapped to chromosomes 19, 14 and X. Analysis of the highly abundant miRNAs and proteins showed several significantly predicted functions in common, including immune and inflammatory response, lipid metabolism and development of the nervous system.

Conclusion: The predicted function inflammatory response may reflect normal vaginal delivery, while lipid metabolism and neurodevelopment may be important processes for the term fetus. The data presented in this study, with complete miRNA and protein findings, will enhance the knowledge base for future research in the field of placental function and pathology.