

# **Health Sciences Research Day 2018**

## **Programme and Abstracts**



## Programme: Health Sciences Research Day 23 April 2018

8.30-9.00 Arrival, coffee and bread

### Workshops including oral presentations

09.00 – 10.40 Presentation and discussion of research projects

10.40 – 11.10 Networking

11.10 – 12.00 Presentation and discussion of research projects

12.00 – 13.00 Lunch and networking

**Research Support:** Meet the experts from the GCP Unit at Odense University Hospital, SDU Research & Innovation Organization (SDU RIO), Odense Patient Data Explorative Network (OPEN), the regional committees on health ethics for Southern Denmark, Southern Denmark Research Support and the SDU Research Support, Funding, Financial Services in the reception area.

### Theme of the afternoon: Personal medicine

The programme will be in Danish

13.00 – 15.00

*Welcome*

Director Kurt Espersen, the Region of Southern Denmark and Dean Ole Skøtt, Faculty of Health Sciences, SDU

*The history of Personal Medicine*

Dean Ole Skøtt, Faculty of Health Sciences, SDU

*Presentation of the National Strategy for Personal Medicine (2017 - 2020) and “the National Genome Centre”*

Director Gert Sørensen, Nationalt Genom Center

*PREmedico – a centre for personal medicine in the Region of Southern Denmark*

Professor Bjarne Winther Kristensen, Head of PREmedico



# Morning program

## 09.00-12.00

## Session overview

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# Abstracts

# Room T8 - BRIDGE Session – 09.00-12.00

## Cerebral Metabolism after Transient Ischemia - Monitoring and Treating Mitochondrial Dysfunction

<b>Authors</b>	A Forsse ( <a href="mailto:jon.axel.forsse@rsyd.dk">jon.axel.forsse@rsyd.dk</a> ), T H Nielsen, K Nygaard, CH Nordström, J B Gramsbergen & F R Poulsen, Department of Neurosurgery OUH / Department of Clinical Research SDU
<b>Speaker</b>	Axel Forsse
<b>Background and Aim</b>	Mitochondrial dysfunction (MD) ensues after transient cerebral ischemia, is probably amenable to treatment, however, insufficiently characterized. In a combination of translational experimental and clinical studies we attempt to describe 1) the biochemical pattern of MD through cerebral and jugular bulb microdialysis 2) the impact of two different neuroprotection candidates on these parameters and 3) the prevalence of MD in neurovascular intensive care patients.
<b>Design and Methods</b>	The experimental studies are conducted in the Endothelin-1 model of transient focal cerebral ischemia with regular as well as labelled cerebral microdialysis and randomized blinded treatment using Cyclosporin A (CsA) and Ethyl pyruvate (ET). The clinical study is a prospective observational cohort of acute phase subarachnoid haemorrhage patients with multimodal monitoring including cerebral and the novel technique jugular bulb microdialysis at the neurointensive care unit of OUH.
<b>Primary variables</b>	Redox metabolites and infarct size in treatment and control groups are studied in the experimental models. In the clinical study metabolite patterns in jugular bulb microdialysis and conventional cerebral microdialysis are investigated as well as brain oxygen concentrations, intracranial pressure and neurological outcome.
<b>Preliminary results</b>	Using conventional microdialysis in our experimental studies we can confirm the biochemical pattern of MD in the post-ischemic rat brain, and the changes are ameliorated by CsA treatment. In labelled microdialysis, mitochondrial inhibition can be detected through temporal variations in Krebs cycle intermediates. In our clinical study preliminary results support the hypothesis that continuous microdialysis of cerebral venous drainage reflects global cerebral metabolism.
<b>Conclusions</b>	CsA ameliorates pathological changes in cerebral metabolism after transient ischemia and labelled microdialysis is a viable method to measure Krebs cycle intermediates in mitochondrial dysfunction. The potential neuroprotective effect of ethyl pyruvate remains to be shown. Jugular bulb microdialysis mirrors the metabolic state of the brain and the current study will reveal the clinical implications of this.

## Incidence, prevalence and characteristics of drug resistant Idiopathic Generalized Epilepsy in adults

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<b>Speaker</b>	Joanna Gesche
<b>Background and Aim</b>	<p>The ILAE defines drug resistance as lack of seizure freedom after the trial of two adequately chosen drugs in therapeutic dosages. Idiopathic Generalized Epilepsy (IGE) according to prior publications has a remission rate of 85% on drug treatment, and the clinical long-term outcome is still debated. Several predictors have been suggested as to determine treatment outcome in IGE patients.</p> <p>Our aim was to find out the incidence and prevalence of drug resistance in IGE, including Juvenile Absence Epilepsy (JAE), Juvenile Myoclonic Epilepsy (JME) and Epilepsy with Generalized Tonic Clonic Seizures only (EGTCS) as defined by the ILAE and by studying a large Danish cohort of IGE patients identify characteristics that can be used to identify drug resistance as early as possible in the clinical course.</p>
<b>Design and Methods</b>	We identified patients treated for IGE at the Epilepsy Clinic at the University Hospital in Odense and The Epilepsy Hospital in Dianalund, Denmark, and evaluated their patient files. We obtained baseline data, paraclinical information on radiologic imaging and electroencephalography, comorbidities and data on their seizure types, prior and current antiepileptic treatment and treatment outcome.
<b>Primary variables</b>	age, psychiatric comorbidity, drug and alcohol abuse, focality on EEG, valproic acid resistance.
<b>Preliminary results</b>	<p>Our final study population consisted of 345 patients with IGE. 14.5% of the study population fulfilled ILAE's criteria on drug resistance, and 21.2% had at some time point during their treatment course fulfilled those criteria. 9.3% were considered pseudo refractory.</p> <p>There were significant differences in employment status and age between the groups. EEG in treatment refractory patients has significantly more focality and treatment refractory patients are significantly more prone to valproic acid resistance and have a significantly higher frequency of psychiatric diagnoses and current or prior drug or alcohol abuse.</p>
<b>Conclusions</b>	Valproic acid resistance, psychiatric comorbidity and drug or alcohol abuse are good markers to identify difficult to treat IGE patients.

## Precision medicine in severe epilepsies caused by mutations in voltage-gated sodium channels genes

<b>Authors</b>	Katrine M Johannesen ( <a href="mailto:kamaa@filadelfia.dk">kamaa@filadelfia.dk</a> ) <sup>1,2</sup> ; Elena Gardella <sup>1,2</sup> ; Guido Rubboli <sup>1,3</sup> ; Rikke S Møller <sup>1,2</sup> .  1) The Danish Epilepsy Centre, Dianalund, Denmark 2) Institute for Regional Health Services, University of Southern Denmark, Odense, Denmark 3) University of Copenhagen, Copenhagen, Denmark
<b>Speaker</b>	Katrine M Johannesen
<b>Background and Aim</b>	<p>Voltage-gated sodium channels are widespread in the human CNS, and accurate functioning of these channels are crucial for maintaining the delicate electrochemical balance of the brain. Developmental and epileptic encephalopathies are severe forms of epilepsy with difficult to treat seizures and often associated with severe intellectual disability</p> <p>Mutations in several genes encoding voltage-gated sodium channels have been discovered as causes of developmental and epileptic encephalopathy within the last few years. These genes include <i>SCN1A</i>, <i>SCN2A</i> and <i>SCN8A</i>. Due to extensive investigations in these genes, we are now at a point where precision medicine in patients with mutations in these genes, is becoming a realistic option.</p> <p>Sodium channel blockers are a group of antiepileptic drugs that inhibits the voltage-gated sodium channels, and thereby minimize the activity of these channels.</p> <p><i>SCN1A</i> encoding the Nav1.1 voltage-gated sodium channel leads to Dravet Syndrome, a devastating childhood developmental and epileptic encephalopathy. Through functional analysis it has been proven that mutations in <i>SCN1A</i> mainly leads to loss-of-function of the ion-channel. Thus, in Dravet Syndrome medical treatment should not include sodium channel blockers, as these could potentially worsen the seizure activity. Opposite <i>SCN1A</i> we find gain-of-function mutations in <i>SCN8A</i> encoding Nav1.6, respectively, in patients with severe developmental and epileptic epilepsy. In our studies, we found that in children with these severe epilepsies, as expected, patients show diminished seizure frequency or even seizure freedom, with the use of sodium channel blockers.</p> <p>We aimed to investigate the treatment response to sodium channel blockers in patients with pathogenic mutations in <i>SCN2A</i>.</p>
<b>Design and Methods</b>	Patients were recruited through an international collaboration with epilepsy genetics centers worldwide. Data on clinical picture, treatment response and genetics were obtained. All patients signed informed consent. Furthermore, four mutations were selected for functional studies.
<b>Primary variables</b>	All patients were evaluated for their treatment response, and treatment regime were divided into sodium channel blockers and non-sodium channel blockers. Response were graded as worsening/no response, partial response and seizure freedom. In the functional studies, we evaluated whether the mutations caused changes that were gain-of-function or loss-of-function.
<b>Preliminary results</b>	We collected a cohort of 60 <i>SCN2A</i> positive patients in which data was available on treatment response. Clinically, two distinct groups of patients emerged; those with onset of epilepsy before the age of three months, and those

	<p>with onset after three months. In the group with onset before three months, we found a favorable response to sodium channel blockers, with several patients showing a partial response or even achieving seizure freedom, especially with oxcarbazepine or phenytoin. On the other hand, the group with onset after three months showed no response, or even experienced a worsening in seizures with sodium channel blockers. To support this, the functional studies showed that the mutations from the group with early seizure onset were gain-of-function, whereas the mutations from the group with later seizure onset were loss-of-function.</p>
<b>Conclusion</b>	<p>In patients with SCN2A mutations and seizure onset before the age of three months sodium channel blockers should be considered as a first-line treatment option. The above shows us, that even though precision medicine in epilepsy treatment seems like a phantom of the future, it might not be as far away as we think.</p>

## Conditional ablation of myeloid TNF improves functional outcome and decreases lesion size after spinal cord injury in mice

<b>Authors</b>	<p>Minna Christiansen Lund (<a href="mailto:mclund@health.sdu.dk">mclund@health.sdu.dk</a>)<sup>1</sup>, Ditte Gry Ellman<sup>1</sup>, Emilie B. Lester<sup>1</sup>, Hans G. Novrup<sup>1</sup>, Sergei A. Nedospasov<sup>2</sup> and Kate Lykke Lambertsen<sup>1</sup></p> <p>1) Neurobiology Research, Institute of Molecular Medicine, University of Southern Denmark, Odense, Denmark 2) Engelhardt Institute of Molecular Biology, Russian Academy of Sciences and Lomonosov Moscow State University, Russia.</p>
<b>Speaker</b>	Minna Christiansen Lund
<b>Background and Aim</b>	<p>Spinal cord injury (SCI) initiates many detrimental cellular and molecular events, which includes both primary and secondary injury cascades. One major component of the secondary injury is the inflammatory response, however its role following SCI has shown to be both harmful and beneficial. During the inflammatory response resident microglia, blood-borne monocytes and macrophages will be activated and infiltrate the tissue and start to express cytokines etc. One of such cytokines is tumor necrosis factor (TNF). TNF derived from myeloid cells (macrophages and neutrophils) has shown to play a more detrimental role in neuroinflammation and demyelination, while microglial-derived TNF might be more neuroprotective.</p> <p>Thus, the aim of this project was to investigate the effect of conditional ablation of TNF in mesodermal-derived cells following a SCI.</p>
<b>Design and Methods</b>	<p>We induced a moderate SCI in the genetically modified mouse model LysMCreTNF<sup>fl/fl</sup> with the infinite horizon spinal cord injury device, and estimated injury volume with different stainings and evaluated the mice functional recovery with Basso Mouse Scale (BMS). Furthermore, protein levels were investigated with western blotting and multiplex analysis.</p>
<b>Preliminary results</b>	<p>By volume estimation of the injury and BMS scoring of hind limb performance in the open field, we found that lack of myeloid TNF decreases the lesion size and improves the functional recovery after SCI. Multiplex analysis revealed decreased TNFR2 levels in LysMCreTNF<sup>fl/fl</sup> mice compared to control under naïve conditions. Also, the level of TNF was decreased in LysMCreTNF<sup>fl/fl</sup> compared to control mice 3 days after SCI, and altered phosphorylated Akt and STAT5a and 5b levels in LysMCreTNF<sup>fl/fl</sup> mice 6 hours after SCI.</p>
<b>Conclusion</b>	<p>In conclusion, these findings demonstrate that lack of myeloid TNF decreases injury volume and improves functional recovery, possibly through altered phosphorylated Akt and STAT5a and 5b signaling.</p>

## Open-label phase 1 clinical trial testing Personalized and Targeteted Intervention with skull remodelling surgery to MAXimize Levels of TTFields intensity - OptimalTTF

<b>Authors</b>	<p>Korshøj, AR (<a href="mailto:anders.rosendal.korshoj@rsyd.dk">anders.rosendal.korshoj@rsyd.dk</a>)<sup>1,2</sup>, Frantz Rom Poulsen<sup>2</sup>, Hansen FL<sup>1</sup>, Lukacova S<sup>3</sup>, Cortnum SOS<sup>1</sup>, Lassen-Ramshad Y<sup>3</sup>, Guldborg TL<sup>3</sup>, Rahbek C<sup>4</sup>, Thielscher A<sup>5</sup>, Mikic N<sup>1</sup>, Sorensen JCH<sup>1</sup>, von Oettingen GB<sup>1</sup></p> <p>1) Aarhus University Hospital, Department of Neurosurgery          2) Odense University Hospital, Department of Neurosurgery          3) Aarhus University Hospital, Department of Oncology          4) Aarhus University Hospital, Department of Neuroradiology          5) Danish Research Center for Magnetic Resonance</p>
<b>Speaker</b>	Anders Rosendal Korshøj
<b>Abstract</b>	<p>We present an ongoing open label phase 1 investigator-sponsored trial (NCT02893137) testing safety/efficacy of a novel therapeutic concept for recurrent glioblastoma (GBM). The intervention combines best choice chemotherapy with tumor treating fields (TTFields) and personalized targeted skull remodeling surgery. The objective of skull remodeling surgery is to create paths, which facilitate electric current flow through into the region of pathology. This may involve formation of strategically placed minor craniectomies or burr holes and thinning of the skull. Finite element (FE) calculations indicate that skull remodeling surgery provides a marked and focal enhancement (~100%) of TTFields intensity without significantly compromising patient safety. Patient accrual began Dec 2016. As of April 2018 thirteen patients out of fifteen have been enrolled. Major eligibility criteria include age &gt; 18 years, first recurrence supratentorial GBM, Karnofsky performance score (KPS) &gt; 60, focal tumor &lt; 2 cm to cortical surface, lack of uncontrollable epilepsy, and lack of significant co-morbidity. Upon inclusion, personalized FE-calculations are performed to validate TTFields enhancement &gt; 25% due by skull remodeling surgery. The primary endpoint is toxicity assessed by CTCAEv4.0. Secondary endpoints include overall survival, progression free survival (PFS), PFS at six months (PFS6), objective response rate (RANO), quality of life (EORTC QLQ-C30 and BN20), KPS, and steroid dose. Follow-up is 18 months and includes regular toxicity assessment (6 week intervals) as well as quality of life and response assessments (3 month intervals). Patients are censored at the end of scheduled follow-up, occurrence of serious or unacceptable adverse events, withdrawal of consent, or loss to follow-up. Interim analysis showed promising efficacy of the intervention and no suspected unexpected serious adverse reactions. Median PFS was 5.4 months and 50% PFS6 which is more than a two-fold increase compared to historical controls. Only two patients have died during the initial 18 months of the trial. The tested concept holds promising potential for improving TTFields outcome by focally and individually enhancing the field intensity in the tumor. The trial will hopefully lay the foundation for future efficacy investigation.</p>

## Fluorescein in glioma surgery

<b>Author(s)</b>	Jesper Peter Bömers, Frantz Rom Poulsen, Christan Bonde Pedersen. Mail: jesper.peter.bomers@rsyd.dk
<b>Speaker(s)</b>	Jesper Peter Bömers
<b>Background and Aim</b>	<p>Glioblastoma multiforme (GBM) continues to be the cancer resulting in most years of life lost. Current treatment is the largest possible extent of resection (EOR) followed by concomitant chemotherapy and radiation. A recent meta-analysis has concluded a significant reduction in the relative risk of death when undergoing gross total resection (GTR).</p> <p>Currently, 5-ALA, a fluorophore, is used during fluorescence surgery. Since 1996 high-dose SF (20mg/kg) has been used during white light surgery to visually inspect fluorescence and improve EOR. With the introduction of the YELLOW 560 filter it is possible to use low dose SF (2-5mg/kg). SF accumulates in the extracellular matrix due to breakdown of the blood-brain barrier (BBB) and therefore comparable to contrast-enhanced (CE) tissue on T1 MRI.</p> <p>SF has not been used in neurosurgery in Denmark before. This descriptive study aimed to increase EOR in GBM, secondary outcome is the feasibility of the method.</p>
<b>Design and Methods</b>	<p>Prospective, non-randomized study. Patients suspected of GBM were included. Neuronavigation was used in all patient. After anaesthesia, 200mg SF was administered intravenously and the surgery was performed alternating between YELLOW 560 and white light. Postoperatively MRI was performed within 72 hours.</p> <p>Neuro radiologists compared pre- and postoperative pictures. Total resection (TR) was defined as no CE-tissue on the postoperative MRI, near total resection (NTR) defined as non-measurable visible tumor and lastly measurable resection, sub-total resection (STR).</p> <p>Three neurosurgeons graded SFs ability to locate and remove tumor from 1 (being not helpful) to 4 (being very helpful).</p> <p>Biopsies were taken in fluorescent, non-fluorescent and marginal zone tissue to compare tumor cell aggregation.</p>
<b>Preliminary results</b>	<p>19 patients with GBM were included. 5/19 (26.3%) with TR, 8/19 (42%) with NTR and 6/19 (31.6%) with STR. Pooling TR and NTR (as GTR) together results in a total resection rate of 68.4%. Nationwide GTR resection rate was 38%, it is important to note this includes biopsies.</p> <p>Biopsies taken show a correlation between fluorescent tissue and tumor cell aggregation,</p> <p>In regards to the efficiency of tumor localization 12 was scored. For location 10/12 scored 4 and 2 scored 3. For removal 9/12 scored 4 and 3 scored 3. Mean is 3.8 and 3.75.</p> <p>No serious adverse events were registered in patients.</p>
<b>Conclusions</b>	<p>This study indicates using SF for GBM resection improved the EOR and without serious adverse events. Likewise, surgeons now favour this method. A necessary prospective, randomized trial is underway to further document the method.</p>

## Mitochondrial diagnostics and neuroprotection in transient cerebral ischemia: 13c-Succinate microdialysis

<b>Author(s)</b>	<i>KH Nygaard, J Havelund, TH Nielsen, C-H Nordström, NK Færgeman, FR Poulsen, JB Gramsbergen, A Forsse, Department of Neurosurgery OUH / Department of Clinical Research SDU. <a href="mailto:Knygaard@health.sdu.dk">Knygaard@health.sdu.dk</a></i>
<b>Speaker(s)</b>	Kevin Heebøll Nygaard
<b>Background and Aim</b>	Using conventional, enzymatic microdialysis mitochondrial dysfunction (MD) has been described after transient cerebral ischemia. MD is probably amenable to treatment, however, insufficiently characterized. The aim of this study is to show, that microdialysis with labelled succinate yields a detailed measure of intermediate metabolites from the cerebral mitochondria. Furthermore, we wish to demonstrate that we can affect this metabolism, e.g. by means of perfusion with malonate (complex II inhibition) or induced focal transient ischemia and analyse impact of treatment with the potential neuroprotectants Cyclosporin A (CsA) and Ethyl pyruvate (EP).
<b>Design and Methods</b>	We have used the Endothelin-1 rat model of transient, focal cerebral ischemia with <sup>13</sup> C- labelled cerebral microdialysis and randomized, blinded treatment using CsA (n = 4) and EP (n = 12) (control n = 11). We also administered a mitochondrial inhibitor, malonate (n = 8), to monitor the changes in the labelling ratio when the Krebs cycle activity is affected.
<b>Primary variables</b>	Redox metabolites and labelling ratios are analysed using LC-MS. Additionally, histological infarct size in treatment and control groups are studied.
<b>Preliminary results</b>	In labelled microdialysis, mitochondrial inhibition can be detected through temporal variations in Krebs cycle intermediates. It is also possible to detect a labelling ratio, which corresponds to mitochondrial function.
<b>Conclusions</b>	Labelled microdialysis is a viable method to measure Krebs cycle intermediates in mitochondrial dysfunction. The potential neuroprotective effects of the tested neuroprotectants is yet to be fully analysed.

# Room T7- PREmedico – 09.00-10.40

## MicroRNA expression profiles predict recurrence-free survival in systemically untreated breast cancer

<b>Author(s)</b>	Ines Block <sup>1</sup> , Mark Burton <sup>1,2</sup> , Kristina P. Sørensen <sup>1</sup> , Martin J. Larsen <sup>1,2</sup> , Martin Bak <sup>3</sup> , Søren Cold <sup>4</sup> , Mads Thomassen <sup>1,2</sup> , Qihua Tan <sup>2,5</sup> , Torben A. Kruse <sup>1,2</sup> <sup>1</sup> Department of Clinical Genetics, Odense University Hospital, Denmark <sup>2</sup> Human Genetics, Department of Clinical Research, University of Southern Denmark, Denmark <sup>3</sup> Department of Pathology, Odense University Hospital, Denmark <sup>4</sup> Department of Oncology, Odense University Hospital, Denmark <sup>5</sup> Epidemiology, Department of Public Health, University of Southern Denmark, Denmark
<b>Speaker(s)</b>	Ines Block
<b>Background and Aim</b>	Breast cancer is a common and potentially lethal disease. Not the primary tumor is life threatening but the spreading of cancer cells to more vital organs like lung, liver and brain. As present prognostic markers are not optimal, more than 90% of all patients are classified as having a high risk for the formation of lethal metastasis and consequently receive endocrine treatments or chemotherapy although approximately 40% of these patients may have been cured by surgery and radiotherapy alone. Accordingly, we aimed at developing a better prognostic signature for recurrence prediction which may reduce overtreatment in breast cancer in the future.
<b>Methods</b>	After collecting breast tumor tissues from 160 systematically untreated breast cancer patients, we compared the microRNA expression in 80 patients who developed metastasis with profiles of 80 patients who remained recurrence-free over an average period of 20 years. For validation, we analyzed the prognostic value of microRNA profiles of two previously-published breast cancer studies.
<b>Preliminary results</b>	Using seven classification methods and voting we were able to distinguish metastatic patients from non-metastatic patients with a balanced accuracy of up to 88% (sensitivity: 88%, specificity: 89%).
<b>Conclusions</b>	Our study suggest that microRNA profiles allow to better identify breast cancer patients that could avoid unnecessary systemic adjuvant therapy than current state-of-the-art techniques. However, further studies are required to validate these results.

## Clonal Evolution in Oral Cavity Cancer: Exome and Deep Sequencing

<b>Authors</b>	<p>Siavosh Tabatabaeifar<sup>1,2,4</sup>, Mads Thomassen<sup>2,4</sup>, Martin J. Larsen<sup>2,4</sup>, Stine R. Larsen<sup>3,4</sup>, Torben A. Kruse<sup>2,4*</sup>, Jens A. Sørensen<sup>1,4*</sup>.</p> <p>Departments of</p> <ol style="list-style-type: none"> <li>1) Plastic Surgery,</li> <li>2) Clinical Genetics and</li> <li>3) Pathology, Odense University Hospital, Odense, Denmark</li> <li>4) University of Southern Denmark, Institute of Clinical Research, Odense, Denmark.</li> </ol> <p>*Authors contributed equally to the study.</p>
<b>Speaker</b>	Siavosh Tabatabaeifar
<b>Background and Aim</b>	<p>Oral cavity cancer, which consists predominantly of squamous cell carcinomas (OSCC), is primarily caused by alcohol consumption and tobacco use. Recent DNA sequencing studies suggests OSCC are very heterogeneous between patients; however clonal evolution and intra-tumor heterogeneity remains unexplored.</p>
<b>Design and Methods</b>	<p>We applied whole-exome sequencing combined with targeted deep targeted sequencing on biopsies from 13 stage IV OSCC patients. From each patient, a series of biopsies were sampled from 3 distinct sites in primary tumor and at least 1 lymph node metastasis. A whole blood sample was taken as the matched reference. In 7 patients, a plasma sample for use in circulating tumor DNA detection was taken.</p>
<b>Preliminary results</b>	<p>Our study is ongoing with data analyzed for 5 patients; the remaining 8 are expected to be finalized in May. Our preliminary results demonstrate that OSCCs show a high degree of inter-patient heterogeneity but a low degree of intra-patient/tumor heterogeneity. However, some OSCC cancers contain complex subclonal architectures comprising distinct subclones only found in distinct regions of the tumors. The metastatic potential of the tumor is acquired early in tumor evolution.</p>
<b>Conclusions</b>	<p>Deep sequencing of multiple biopsies from OSCC and metastasis enables detection of intra-tumor heterogeneity and clonal evolution. The metastatic potential of OSCC is acquired early in the tumor evolution, and our preliminary results indicate that the tumor may not need to acquire additional alterations for it to be able to metastasize and adapt.</p>

## Molecular signature of brain lesion evolution and fate in progressive MS

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<b>Speaker</b>	Maria Louise Elkjær
<b>Background and Aim</b>	<p>In about 50% of patients with multiple sclerosis (MS), a progressive phase evolves (SPMS), and treatments become ineffective. Development of new therapies is challenging, since key aspects of the pathogenesis are unresolved: the evolution of active lesion, and its fate into repairing, inactive or chronic active lesion is not well understood. We hypothesized that the different lesion types in the brain of SPMS patients can be characterized by specific transcriptome signatures. These could unmask mechanisms that drive the evolution and fate of lesions, and lead to discovery of biomarkers and potential drug targets that can halt progression.</p>
<b>Design and Methods</b>	<p>With immunohistochemistry, we classified 98 brain areas covering lesion evolution (NAWM and active lesions), lesion fate (inactive, chronic active, repairing) and control WM from 10 MS and 5 non-neurological diseased brains. We created the transcriptome profile of each lesion type by next generation RNA sequencing. We produced clusters and networks of significant genes using KeyPathwayMiner and TiCoNE to find genes important for the evolution and fate of the lesions. We extracted molecules that could influence either the maintenance or halt of active inflammation.</p>
<b>Preliminary results</b>	<p>Out of 18000 detected genes, over 4000 were differentially expressed between MS and controls (FDR&lt;0.05). During the evolution of active lesion from NAWM, over 3000 genes changed significantly (FDR&lt;0.05). For fate of active lesions, we discovered a radical change in the transcriptome when active lesions were compared to chronic active lesion, and less prominent changes compared to inactive and repairing lesions. Next, we retrieved the major hubs in networks, when an active lesion developed into a chronic active, inactive or repairing lesion. Lastly, we extracted genes uniquely expressed in the different lesion types, and compared them with our CSF proteome database of MS patients in the early and progressive disease stages.</p>
<b>Conclusions</b>	<p>Our data support lesion type specific transcriptome signatures. We used de novo network analysis to identify gene clusters and hubs that are important for lesion evolution, and for its fate. Our data implies that the NAWM in the MS brain is much more similar to the WM from control subjects than to lesions within the same brain, and that development of a chronic active lesion is very uniquely regulated on gene expression level. Future functional studies on recognized key molecules of evolution and fate are needed to confirm their role, and that may lead to potential targets to halt progression. Lastly, the protein products of lesion specific genes that were also found in the CSF proteome of MS should be validated in cohorts for potential biomarkers of progression.</p>

### Plasma DNA in precision medicine – monitoring treatment effect.

<b>Authors</b>	Rikke Fredslund Andersen <sup>1</sup> , Caroline Brenner Thomsen <sup>2</sup> , Torben Frøstrup Hansen <sup>2</sup> , Jan Lindebjerg <sup>3</sup> , Lars Henrik Jensen <sup>2</sup> , Anders Jakobsen <sup>2</sup> .  1) Biochemistry and Immunology 2) Oncology 3) Pathology Departments. Vejle Hospital.
<b>Speaker</b>	Rikke Fredslund Andersen
<b>Background</b>	Indicators of treatment effect are needed to facilitate precision medicine in oncology. Analyses of circulating DNA in plasma is a promising way of monitoring solid tumors over time. Genetic aberrations found in the tumor DNA can also be found in the circulating DNA and quantified with highly sensitive techniques. Association between effect of treatment and consecutive changes of circulating tumor DNA (ctDNA) was explored during first line chemotherapy in RAS/RAF mutated metastatic colorectal cancer (mCRC) patients.
<b>Methods</b>	The study included 138 mCRC patients receiving standard first line treatment. Primary tumors were analyzed for 27 RAS/RAF mutations and if a mutation was found, the same mutation was quantified in plasma using droplet digital PCR. The fractional abundance of ctDNA was assessed in plasma before treatment start and at every treatment cycle until radiologically defined progressive disease (PD).
<b>Results</b>	At baseline ctDNA was detected in 94% of the patients with RAS/RAF mutated tumors. The baseline fractional abundance was significantly related to progression free survival. A low level of ctDNA after the first cycle of chemotherapy was associated with a low risk of progression. On the other hand, a significant increase of ctDNA at any time during the treatment course was associated with a high risk of progression on continuous treatment. The first increase in ctDNA level occurred at a median of 51 days before radiologically confirmed progression.
<b>Conclusion</b>	The results indicate that analyses of ctDNA may be clinically valuable for monitoring treatment effect in mCRC. A rapid decrease in ctDNA was associated with a prolonged progression free interval, whereas a significant increase gave notice of early progression with a relevant lead time.

## Impact of red and processed meat and fibre intake on treatment outcomes among patients with chronic inflammatory diseases

<b>Authors</b>	<p>Signe Bek Sørensen<sup>1,2</sup>, Vibeke Andersen<sup>1,2</sup></p> <p>1) Focused research unit for Molecular Diagnostic and Clinical Research (MOK), Hospital of Southern Jutland, Aabenraa and Institute of Regional Health Research, University of Southern Denmark, Odense, Denmark</p> <p>2) Institute of Molecular Medicine, University of Southern Denmark, JB Winsløw Vej 25, 5000 Odense, Denmark</p>
<b>Speaker</b>	Signe Bek Sørensen
<b>Background</b>	<p>Chronic inflammatory diseases (CID) are frequently treated with biologic medications, specifically TNF inhibitors [TNFi]. These medications inhibit the pro-inflammatory molecule tumour necrosis factor (TNF)-<math>\alpha</math>, which has been strongly implicated in the aetiology of these diseases. However, up to one-third of the patients do not respond to treatment with biologics. Lifestyle factors are assumed to affect treatment outcomes. Little is known about the effects of dietary lifestyle as a prognostic factor that may enable personalised medicine. This study aims to identify dietary lifestyle factors that support optimal treatment outcomes.</p>
<b>Design and Methods</b>	<p>This prospective cohort study will enroll 320 CID patients who are prescribed a biological treatment between June 2017 and March 2019. These patients are diagnosed with inflammatory bowel disease (Crohn's disease and ulcerative colitis), rheumatic disorders (rheumatoid arthritis, axial spondyloarthritis, psoriatic arthritis), and inflammatory skin diseases (psoriasis, hidradenitis suppurativa). At baseline (pre-treatment), patient characteristics will be assessed using patient-reported outcome measures, clinical assessments of disease activity, quality of life, and lifestyle, in addition to registry data on comorbidity and concomitant medication(s). By current Danish standards, follow-up will be conducted 14-16 weeks after treatment initiation. For each disease, evaluation of successful treatment response will be based on established primary and secondary endpoints, including disease-specific core outcome sets. The major outcome of the analyses will be to detect variability in treatment effectiveness between patients with different dietary characteristics.</p>
<b>Preliminary results</b>	<p>Inclusion of patients is ongoing at nine sites located in, Region of Southern Denmark, Central Denmark Region and Capital Region of Denmark.</p>

# Room T7- PREmedico Session – 11.10-12.00

## Expression and prognostic value of EGR1 and EGR3 in gliomas

<b>Authors</b>	<p>Arnon Møldrup Knudsen (<a href="mailto:Arnon.knudsen@rsyd.dk">Arnon.knudsen@rsyd.dk</a>)<sup>1,2</sup>, Ida Eilertsen<sup>1</sup>, Susanne Kielland<sup>1</sup>, Mikkel Warming Pedersen<sup>1</sup>, Mia Dahl Sørensen<sup>1,2</sup>, Rikke Hedegaard Dahlrot<sup>3</sup>, Henning Bünsow Boldt<sup>2</sup>, Caspar Schau Mellegaard<sup>1</sup>, Sune Munthe<sup>4</sup>, Frantz Rom Poulsen<sup>1,4</sup>, Bjarne Winther Kristensen<sup>1,2</sup>.</p> <p>1) Department of Clinical Research, University of Southern Denmark, Odense, Denmark.          2) Department of Pathology, Odense University Hospital, Odense, Denmark.          3) Department of Oncology, Odense University Hospital, Odense, Denmark.          4) Department of Neurosurgery, Odense University Hospital, Odense, Denmark.</p>
<b>Speaker</b>	Arnon Møldrup Knudsen
<b>Background and Aim</b>	<p>Gliomas are the most frequent primary brain tumors. For the most malignant glioma – the glioblastoma - the median survival is only 15 months. Few prognostic biomarkers are useful in daily practice, and new markers are urgently needed. EGR1 and EGR3 are transcription factors involved in cell differentiation, mitogenesis and migration. This study investigated the expression and prognostic value of EGR1 and EGR3 in gliomas.</p>
<b>Design and Methods</b>	<p>Tissue from 214 glioma patients was stained with anti-EGR1 and -EGR3 antibodies, and assessed by digital quantification and a semi-quantitative scoring system.</p>
<b>Primary variables</b>	<p>Kaplan-Meier estimates and Log-rank tests were used for comparison of overall patient survival. Cox-regression was performed to identify independent prognostic variables.</p>
<b>Preliminary results</b>	<p>EGR1 expression ranged from 1-83% positive cells while EGR3 expression was found in 5-95% of cells. High EGR1 levels were associated with improved survival in glioblastomas both in univariate (P=0.02) and multivariate (P=0.01) analysis. In glioblastomas, the EGR1 high/EGR3 low group showed improved survival when compared to the EGR1 low/EGR3 high group in univariate (P=0.01) and multivariate (P=0.03) analysis. Similar results were found in MGMT-methylated chemo-sensitive glioblastomas.</p>
<b>Conclusion</b>	<p>High levels of EGR1 were associated with improved survival in glioblastomas, as was the combination of EGR1 high/EGR3 low. Validation in an additional patient cohort is necessary.</p>

## Differential diagnostic impact of DNA methylation profiling on brain tumor classification

<b>Authors</b>	<p>K. Petersen, J. (<a href="mailto:Jeanette.Krogh.Petersen@rsyd.dk">Jeanette.Krogh.Petersen@rsyd.dk</a>)<sup>1,2</sup>, Boldt, H.<sup>1,2</sup>, Wirenfeldt, M.<sup>1,2</sup>, Daa Schrøder, H.<sup>1,2</sup>, H. Dalhrot, R.<sup>3</sup>, Hansen, S.<sup>3</sup>, R. Poulsen, F.<sup>4</sup>, Schulz, M.<sup>4</sup>, Capper, D.<sup>5</sup> von Deimling, A.<sup>6,7</sup>, W. Kristensen, B.<sup>1,2</sup></p> <p>1) Department of Pathology, Odense University Hospital, Odense, Denmark.  2) Department of Clinical Research, University of Southern Denmark, Odense, Denmark.  3) Department of Oncology, Odense University Hospital, Odense Denmark.  4) Department of Neurosurgery, Odense University Hospital, Odense Denmark.  5) Department of Neuropathology, Charité - Universitätsmedizin Berlin, Germany  6) Department of Neuropathology, Institute of Pathology, Ruprecht-Karls-University, Heidelberg, Germany.  7) Clinical Cooperation Unit Neuropathology, German Cancer Research Center (DKFZ) and German Cancer Consortium (DKTK), Heidelberg, Germany.</p>
<b>Speaker</b>	Jeanette Krogh Petersen
<b>Background and Aim</b>	Genome-wide DNA methylation profiling is a new promising approach for improvement of brain tumor classification. The diagnostic potential of this approach has recently been explored by the German Cancer Research Center. We report the diagnostic impact of this DNA methylation-based classifier tool tested in a clinic-pathological setting.
<b>Design and Methods</b>	We prospectively collected tissue from 136 brain tumor cases. DNA methylation profiling was performed using the EPIC BeadChip (850K) generating IDAT files ready for data analysis. Data were uploaded to a DNA methylation-based classifier tool and matched to a brain tumor reference cohort with more than 2800 CNS tumors covering more than 80 tumor methylation classes. A report was generated including a classifier score and a DNA copy-number variation (CNV) profile.
<b>Preliminary results</b>	In total 90 tumors (66%) appeared to significantly match a methylation class. The initial histopathological diagnoses were changed in 24 out of 90 cases representing a reclassification rate of 27%. This was based on significant methylation profiling scores representing match to specific DNA methylation classes as well as CNV changes, immunohistochemical findings and next-generation sequencing results. A change in WHO tumor grade among the reclassified tumors, was observed in 58 % of the tumors, with downgrading of 16 % and upgrading of 42%.
<b>Conclusions</b>	DNA methylation profiling initiated re-evaluation and incorporation of additional tools in the differential diagnostic work up. This resulted in integrated and improved precise diagnostics.

## Expression and prognostic value of the immune checkpoint molecule galectin-9 in glioblastomas

<b>Authors</b>	<p>Sisse Josephine Andersen (<a href="mailto:sisse.josephine.andersen@rsyd.dk">sisse.josephine.andersen@rsyd.dk</a>)<sup>1,2</sup>, Arnon Møldrup Knudsen (<a href="mailto:arnon.knudsen@rsyd.dk">arnon.knudsen@rsyd.dk</a>)<sup>1,2</sup>, Rikke Hedegaard Dahlrot (<a href="mailto:rikke.dahlrot@rsyd.dk">rikke.dahlrot@rsyd.dk</a>)<sup>3</sup>, Mia Dahl Sørensen (<a href="mailto:mia.soerensen@rsyd.dk">mia.soerensen@rsyd.dk</a>)<sup>1,2</sup>, Bjarne Winther Kristensen (<a href="mailto:bwk@rsyd.dk">bwk@rsyd.dk</a>)<sup>1,2</sup>.</p> <p>1) Department of Clinical Research, University of Southern Denmark, Odense, Denmark.                  2) Department of Pathology, Odense University Hospital, Odense, Denmark.                  3) Department of Oncology, Odense University Hospital, Odense, Denmark.</p>
<b>Speaker</b>	Sisse Josephine Andersen
<b>Introduction</b>	<p>Glioblastomas are highly malignant primary brain tumors classified as grade IV according to the 2016 World Health Organization classification. The prognosis is poor with a mean survival time of 15 months. It has been suggested that the immune checkpoint molecule galectin-9 is a potential therapeutic target. Galectin-9 is known to play role in cancer cell aggregation, induced T-cell apoptosis, and tumor progression. The aim of this study was to investigate the expression and potential prognostic value of galectin-9 in glioblastomas.</p>
<b>Methods</b>	<p>Tissue from 167 glioblastoma patients from the Region of Southern Denmark glioma cohort was included in this study. The tissue sections were immunohistochemically stained with anti-galectin 9 antibody. Image analysis and quantification of the stainings were performed using the Visiopharm software. Survival analyses was conducted with Kaplan-Meier estimates and Log-rank tests.</p>
<b>Results</b>	<p>The immunohistochemical stainings showed that the galectin-9 protein was highly expressed in cells with macrophage and microglial morphology in most glioblastomas. The expression did not correlate with survival.</p>
<b>Conclusion</b>	<p>Galectin-9 protein is widely expressed in glioblastoma. Targeting of galectin-9 may therefore be relevant in most glioblastoma patients. Potential correlation with PDL-1 expression will be investigated.</p> <p>This project is funded by Familien Erichsens Mindefond</p>
<b>Keywords</b>	galectin-9, glioblastoma, anti-cancer therapy

## Genomic Analyses of Breast Cancer Progression Reveal Distinct Routes of Metastasis Emergence

<b>Author</b>	Mads Thomassen ( <a href="mailto:Mads.Thomassen@rsyd.dk">Mads.Thomassen@rsyd.dk</a> )
<b>Speaker</b>	Mads Thomassen
<b>Abstract</b>	<p>A main controversy in cancer research is whether metastatic abilities are present in the most advanced clone of the primary tumor or result from independently acquired aberrations in early disseminated cancer cells as suggested by the linear and the parallel progression models, respectively. The genetic concordance between different steps of malignant progression is mostly unexplored as very few studies have included cancer samples separated by both space and time. We applied whole exome sequencing and targeted deep sequencing to 26 successive samples from six patients with metastatic estrogen receptor (ER)-positive breast cancer. Our data provide support for both linear and parallel progression towards metastasis. We report for the first time evidence of metastasis-to-metastasis seeding in breast cancer. Our results point to three distinct routes of metastasis emergence. This may have profound clinical implications and provides substantial novel molecular insights into the timing and mutational evolution of breast cancer metastasis.</p>

# Auditorium - Session 1 – 09.00-09.45

## Community Reinforcement and Family Training Concerned Significant others of Treatment-refusing (CRAFT)

<b>Authors</b>	Rikke Hellum, PhD Student, ( <a href="mailto:rhellum@health.sdu.dk">rhellum@health.sdu.dk</a> ) <sup>1,2</sup> ; Professor Kjeld Andersen, PhD <sup>1,2</sup> ; Assoc. Prof. Anette Søggaard Nielsen, PhD <sup>1,2</sup> ; Ass. Prof. Randi Bilberg, PhD <sup>1,2</sup> .  1) Unit of Clinical Alcohol Research, Clinical Institute, SDU, 2) Department of psychiatry, OUH.
<b>Speaker</b>	Rikke Hellum
<b>Background and Aim</b>	The Danish National Clinical Guideline for treatment of alcohol dependence recommends that alcohol treatment centers offer interventions aimed at concerned significant others (CSOs), providing them with the support and empowerment that will enable them to motivate the problem drinker to enter treatment. In the US, the Community Reinforcement and Family Therapy (CRAFT) intervention has been shown to offer effective support to CSOs in 7 out of 10 times. The aim of this study is to investigate which format of CRAFT is optimal to empower individuals close to an addicted person to create changes in their family environment: changes that increase the likelihood of the addicted person seeking treatment and changes that increase life quality of the CSOs.
<b>Design and Methods</b>	This is a clinical cluster randomized trial where the CSOs receive either CRAFT in a group format, in an individual format, or a control condition, consisting of self-help material only. The study is carried out in 17 Danish public alcohol treatment centers by therapists who are trained in CRAFT. Based on a power calculation we expect to include 405 patients in the study.
<b>Primary variables</b>	The primary outcome is frequency of individuals with alcohol use disorder entering treatment following the intervention targeted at the CSOs within three months from its initiation. Data will be collected from all CSOs at baseline, three, and six months after baseline.
<b>Preliminary results</b>	At the moment 35 CSOs are included in the study.
<b>Discussion</b>	We expect to show which of the three interventions (individual, group or self-help) is the most effective in the case of getting the drinking person into treatment. We also expect to show an increased life of quality for the CSO when they have accomplished the six CRAFT modules.

## Perioperative cardiovascular complications following urogynecological operations

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<b>Speaker</b>	Michael Due Larsen
<b>Background and Aim</b>	<p>The risk of perioperative cardiovascular complications following urinary incontinence (UI) and pelvic organ prolapse (POP) operations must be taken into consideration when planning urogynaecological operations. The literature on the cardiovascular risk following UI and POP operations shows diverging results.</p> <p>To facilitate the clinicians' decision making on complications following urogynaecological procedures, we aimed to estimate the mortality and the risk of cardiovascular complications following UI and POP operations.</p>
<b>Design and Methods</b>	<p>This nationwide register-based study includes 13,992 UI and 35,765 POP operations during a period of ten years from 1 July 2007 through 30 June 2017 in 44,580 patients, collected from the Danish National Patient Registry and supplemented with clinical data from the Danish Urogynaecological Database. Women undergoing UI and POP operations will in general be in a condition where an operation is not contraindicated for any reason and therefore these women will be in a better health condition than the control group in the general population when matching a control group by age and comorbidity. We therefore used a study design similar to the case crossover design to analyse for a temporary increased risk of cardiovascular events 30 days following operation. We used a 31-180 days observation period as baseline, assuming the risk of cardiovascular events to uniformly distribute a following operation. The increased risk was estimated as an incidence rate ratio for women with and without cardiovascular comorbidity and adjustments were made for the relevant confounders' age, BMI, smoking, use of alcohol, parity, ASA-score and the extent of procedure.</p>
<b>Preliminary results</b>	<p>The 30-days morbidity was low with eleven registered deaths out of a total of 49,757 UI and POP operations. Overall, we found 84 cardiovascular events in the period 0-30 days after operation and 326 in the 31-180 day period. 0.59% of the women with a cardiovascular risk had cardiovascular complications following an operation, corresponding to the incidence rate ratios at 3.64 (95% CI: 2.67-4.97) compared with the baseline risk for this group.</p>
<b>Conclusions</b>	<p>The risk of cardiovascular complications in urogynaecological operations is generally low, despite the fact that we found a lower rate of cardiovascular complications than in other register studies. A more conservative approach in treating UI and POP in Denmark and a higher part of vaginal procedures could be an explanation for a lower complication rate compared to other reported complication rates.</p>

## Elective abortions in women with ulcerative colitis and Crohn's disease - a nationwide cohort study

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<b>Speaker</b>	Bente Mertz Nørgård
<b>Background and Aim</b>	It is speculated whether women with inflammatory bowel disease (IBD) have an increased tendency to choose an elective abortion due to fear that their fetus is harm by use of medications and/or disease flares during periods of gestation. Therefore, we examine the risk of elective abortions in women with ulcerative colitis (UC) and Crohn's disease (CD), compared to women without IBD.
<b>Design and Methods</b>	A nationwide cohort study based on Danish health registries. Included were all pregnancies in the period of 1 January 1996 through December 31, 2015. The exposed groups constituted pregnancies of women with UC or CD, and the unexposed cohort constituted all pregnancies of women without IBD. We used logistic regression models and calculated the odds ratio (OR) for an elective abortion in women with IBD, controlled for confounders.
<b>Primary variables</b>	Our outcome was elective abortion on maternal request up until the end of the 12 <sup>th</sup> completed week of gestation.
<b>Preliminary results</b>	The prevalence of elective abortions in women with UC and CD was 12.4% and 14.9%, respectively; and in women without IBD 16.9%. For all calendar years, the yearly proportions of women with IBD choosing an elective abortion were less than the proportions of elective abortions in women without IBD. In women with UC, the adjusted OR was 0.80 (95% CI: 0.74–0.86), and in women the CD the adjusted OR was 0.96 (95% CI: 0.89–1.04).
<b>Conclusions</b>	Our results suggest that pregnant women with UC and CD are not more likely to choose an elective abortion compared to pregnant women without IBD. This reassuring result may reflect that women with IBD are well- informed regarding the safety of IBD medications during pregnancy.

## Prostate cancer: Can bone biomarkers be used for diagnostics and monitoring?

<b>Authors</b>	<p>Palle Osthert<sup>1</sup>; Lone Volmer<sup>2</sup>; Jonna Skov Madsen<sup>3</sup>; Bettina Nørby<sup>1</sup>; Inge Mejlholm<sup>2</sup>; Mads Poulsen<sup>4</sup>; Lars Lund<sup>4</sup>; Jean-Marie Delaissé<sup>5</sup>; Kent Sjøe<sup>5</sup>.</p> <p>1) Dept of Urology SLB  2) Dept of Oncology SLB  3) Dept of Immunology &amp; Biochemistry SLB  4) Dept of Urology OUH  5) Clinical Cell Biology SLB</p>
<b>Speaker</b>	Kent Sjøe
<b>Background</b>	<p>Prostate cancer (PC) was the most common cancer (4,519 new cases) and the second most common cause of cancer-related deaths amongst men in Denmark (1,254 deaths) in 2016. Around 15% of patients (pts) have metastatic disease at the initial diagnosis and more than 80% will during their remaining lifetime develop bone metastases, reducing quality of life and survival. Cancer cells in the marrow trigger elevated bone resorption and an overproduction of weak bone, which makes cancer cells resistant and grow causing severe bone disease. We believe a future use of bone biomarkers (PINP: formation; CTX-I: break-down) may improve the diagnostic precision.</p>
<b>Hypotheses/aims</b>	<p>1) Absolute levels of PINP and CTX-I can (together with PSA, biopsy and scintigraphy/PET) identify pts with bone metastases.  2) <math>\Delta</math>PINP and <math>\Delta</math>CTX-I enable an earlier and more precise detection of resistance to castration.  3) <math>\Delta</math>PINP and <math>\Delta</math>CTX-I predict responders/non-responders.</p>
<b>Design and Methods</b>	<p><i>Group1</i>: 100 newly diagnosed PC pts (without identified bone metastases) will have PINP and CTX-I measured prior to any treatment. Six months later their clinical status will be determined.  <i>Group2</i>: <math>\approx</math>200 PC pts under suspicion of having bone metastasis will have blood samples taken to determine PINP and CTX-I levels before scanning.  <i>Group2a</i>: <math>\approx</math>150 will have a negative answer from their bone scan. No further blood samples will be taken. Six months later their clinical status will be determined.  <i>Group2b</i>: 50 pts will have bone metastases and will in the following 3 years have blood samples taken every 3 months for measuring PINP and CTX-I. Subsequently, data and diagnostic conclusions will be collected. Recruiting to Group2 will stop when 50 pts have been enrolled in Group2b.  <i>Group3</i>: 50 PC pts with castration-resistant bone metastases will have PINP and CTX-I analyzed every month for 2 years. Subsequently, these data will be compared with diagnostic conclusions during this period.</p>
<b>Primary variables</b>	Absolute and $\Delta$ PINP and $\Delta$ CTX-I levels, occurrence or progression of bone metastases and death.
<b>Preliminary results</b>	Enrollment started ultimo September 2017 - status: 42.
<b>Conclusions</b>	We wish to identify thresholds for absolute and $\Delta$ PINP and $\Delta$ CTX-I levels that may predict new diagnostic conclusions earlier than today, thereby enabling individualized treatment strategies improving quality of life.

## Mobile intervention to increase cervical screening attendance among Tanzanian women

<b>Authors</b>	<p>Ditte Søndergaard Linde, (<a href="mailto:dsondergaard@health.sdu.dk">dsondergaard@health.sdu.dk</a>)<sup>1,2</sup>; Marianne Skovsager Andersen, (<a href="mailto:Marianne.Andersen1@rsyd.dk">Marianne.Andersen1@rsyd.dk</a>)<sup>3</sup>; Julius Douglas Mwaiselage, (<a href="mailto:jmwaiselage@yahoo.com">jmwaiselage@yahoo.com</a>)<sup>4</sup>; Rachel Manongi, (<a href="mailto:naeraheli@gmail.com">naeraheli@gmail.com</a>)<sup>5</sup>; Susanne Krüger Kjaer, (<a href="mailto:susanne@cancer.dk">susanne@cancer.dk</a>)<sup>6,7</sup>; Vibeke Rasch, (<a href="mailto:vrasch@health.sdu.dk">vrasch@health.sdu.dk</a>)<sup>1,2</sup>.</p> <p>1) Department of Obstetrics and Gynaecology, Odense University Hospital, Odense, Denmark          2) Institute of Clinical Research, University of Southern Denmark, Odense, Denmark          3) Department of Medical Endocrinology, Odense University Hospital, Odense, Denmark          4) Department for Cancer Prevention Services, Ocean Road Cancer Institute, Dar es Salaam, Tanzania          5) Institute of Public Health Kilimanjaro Christian Medical University College, Moshi, Tanzania          6) Department of Gynaecology, Rigshospitalet University Hospital, Copenhagen, Denmark          7) Department of Virus, Lifestyle and Genes, Danish Cancer Society Research Center, Copenhagen, Denmark</p>
<b>Speaker</b>	Ditte Søndergaard Linde
<b>Background and Aim</b>	<p>Cervical cancer is a major health concern in Tanzania, caused by poor attendance for cervical cancer screening and follow-up of women at risk. Mobile telephone health interventions are proven effective tools to improve health behaviour in African countries. So far, no knowledge exists on how such interventions may perform in relation to cervical cancer screening in low-income settings. This study aims to assess the degree to which a Short Message Service (SMS) intervention can increase attendance at appointments among women who have tested positive for high-risk (HR) Human Papillomavirus (HPV) during cervical cancer screening.</p>
<b>Design and Methods</b>	<p><i>Connected2Care</i> is a non-blinded, multicentre, parallel-group, randomised controlled trial. Tanzanian women testing positive to HR HPV at inclusion are randomly assigned in an allocation ratio of 1:1 to the SMS intervention or the control group (standard care). In a period of 10 months, the intervention group will receive 15 one-directional health educative text messages and SMS reminders for their appointment. The total sample size is 700 with 350 women in each study arm. Primary outcome is attendance rate for follow-up. Barriers against implementing the intervention will be assessed in a mixed-methods sub-population study.</p>
<b>Discussion</b>	<p>This study may provide information on the potential effects and barriers in implementing an SMS intervention targeting a group of women who are followed up after testing positive for HR HPV and are, therefore, at increased risk of developing cervical cancer. This can guide decision-makers on the effective use of mobile technology in a low-income setting. Trial status: Ongoing.</p>

# Auditorium - Session 2 – 09.55-10.40

## Costs and consequences of introducing robotic surgery for women with gynecological cancer.

<b>Authors</b>	<p>Korsholm, M., PhD stud., M.Sc.PH, (<a href="mailto:malene.korsholm@rsyd.dk">malene.korsholm@rsyd.dk</a>)<sup>1</sup>; Gyrd-Hansen, D., Prof., M.Sc. Econ, <a href="mailto:dgh@sdu.dk">dgh@sdu.dk</a><sup>2</sup>; Mogensen, O., Prof., MD, (<a href="mailto:omogensen@sdu.dk">omogensen@sdu.dk</a>)<sup>3</sup>; Wu, C., Assoc. Prof., MD, (<a href="mailto:chunsen.wu@rsyd.dk">chunsen.wu@rsyd.dk</a>)<sup>1</sup>; Sopina, L., PhD stud., M.Sc.PH, (<a href="mailto:lsopina@sdu.dk">lsopina@sdu.dk</a>)<sup>2</sup>; Jensen, PT., Prof., MD, (<a href="mailto:pernille.tine.jensen@rsyd.dk">pernille.tine.jensen@rsyd.dk</a>)<sup>1</sup>.</p> <p>1) Dep. of Gyn. and Obs., OUH, Clinical Institute, SDU Odense.          2) COHERE - Center for Health Economic Research, Dep. of Public Health, SDU Odense.          3) Dep. of Pelvic Cancer, Karolinska University Hospital and Karolinska Institute, Stockholm, Sweden. Clinical Institute, SDU Odense.</p>
<b>Speaker</b>	Malene Korsholm
<b>Background and Aim</b>	<p>The demand for more advanced medical technologies is growing. Robotic Minimally Invasive Surgery (RMIS) is the latest technology and assumed to be more expensive in the short-run compared to Laparoscopic Minimally Invasive Surgery (LMIS) and Open Abdominal Hysterectomy (OAH). RMIS has been rapidly adopted in the treatment of gynecological cancer, and is increasingly used for advanced surgical procedures. The aim is to evaluate the costs and consequences of RMIS compared to LMIS and OAH in women with endometrial cancer.</p>
<b>Design and Methods</b>	<p>A register-based study comprising 5,700 women from the Danish Gynecological Cancer Database. Data are linked in Statistics Denmark with comprehensive information on visits in all hospitals, activities in primary healthcare, prescription medication and social data such as education, labor market affiliation, income, and unemployment benefit reimbursement.</p> <p>The study consists of:</p> <ol style="list-style-type: none"> <li>1. A systematic review evaluating costing methodology for robotic surgery in gynecology.</li> <li>2. Evaluation of the societal costs of RMIS in the Region of Southern Denmark.</li> <li>3. Assessment of changes in long-term costs and consequences of RMIS. Nationwide register data will be used for the analysis.</li> </ol>
<b>Preliminary results</b>	<p>The systematic review found that inadequate reporting of the study perspective, short-term horizon, and use of charge data decreased the methodological quality.</p> <p>Further results will be provided; comparing the costs and consequences before and after the introduction of RMIS with LMIS and OAH.</p>
<b>Conclusions</b>	<p>In Denmark there is a unique possibility to follow high quality health care data over time. This project provides comprehensive analysis using the societal perspective with a long follow-up.</p>

## The Self-Match Study

<b>Authors</b>	<p>Morten Ellegaard Hell, (<a href="mailto:mbell@health.sdu.dk">mbell@health.sdu.dk</a>)<sup>1,2,3</sup>; William R. Miller, (<a href="mailto:wrmiller@unm.edu">wrmiller@unm.edu</a>)<sup>4</sup>; Bent Nielsen, (<a href="mailto:bnielsen@health.sdu.dk">bnielsen@health.sdu.dk</a>)<sup>1,2,3</sup>; Anette Søggaard Nielsen, (<a href="mailto:ansnielsen@health.sdu.dk">ansnielsen@health.sdu.dk</a>)<sup>1,2,3</sup>.</p> <p>1) Institute of Clinical Research, Unit of Clinical Alcohol Research (UCAR), University of Southern Denmark, Odense, Denmark.  2) OPEN, Odense Patient data Explorative Network, Odense University Hospital, Odense, Denmark.  3) Psychiatric Research Unit, Region of Southern Denmark.  4) Department of Psychology, University of New Mexico, Albuquerque, USA.</p>
<b>Speaker</b>	Morten Ellegaard Hell
<b>Background and Aim</b>	<p>Research on matching patients to treatment has shown that matching grounded in expert views is little better than allocating patients by chance. Furthermore, there is growing emphasis on involving patients in their own treatment as a key to health behavior change. Research has been limited on the benefit of having patients choose their treatment from among options, in contrast to being assigned to a treatment by experts. Consequently, we designed a rigorous test of patient self-matching to determine whether it does improve retention, adherence and outcome in alcoholism treatment.</p>
<b>Design and Methods</b>	<p>The present study is conducted as a randomized controlled trial running from June 2017 to June 2019. 400 consecutive patients aged 18 or more will be enrolled and randomized to either self-matching or expert-matching to one of five different treatment approaches. Inclusion criteria: all patients entering the alcohol outpatient clinic in Odense are offered to participate in the study. Exclusion criteria: cognitive dysfunction measured by mini mental state examination, and non-Danish or non-English speaking individuals. The following instruments will be administered at intake to provide standardized measures of alcohol problems: Addiction Severity Index, Time Line Follow Back, WHO quality of life questionnaire, NEO Five-Factor inventory-3 and Personal Happiness Form.</p>
<b>Primary variables</b>	<p>For each outcome measure, two analyses will be conducted. Intention-to-treat analyses (ITT) will be carried out with all patients, irrespective of whether they completed the interventions or were re-interviewed. Regarding incomplete data, multiple imputations will be used together with ITT. Completer analyses will also be carried out with patients who complete their respective interventions.</p>
<b>Primary outcome</b>	<p>Decrease in number of monthly excessive drinking days 6 months after initiation of treatment.</p>
<b>Secondary outcomes</b>	<p>(1) Compliance. (2) Quality of life. The influence of personality traits on outcome will also be examined in both groups.</p>
<b>Discussion</b>	<p>The debate on matching patients to treatment has been going on for decades. This study will cast light on this by focusing on patients' choice and thereby clarifying if patients' perceived autonomy yields better outcome.</p>

## The effect of transfer between hospitals on Quality of Life on lung cancer patients 90 days after surgery

<b>Authors</b>	Maria Iachina; Majken Munk Brønserud; Erik Jakobsen
<b>Speaker</b>	Maria Iachina
<b>Background</b>	The Danish Lung Cancer Registry (DLCR) has since 2003 reported all cases of lung cancer in Denmark. In 2013 - 2015 information about patients' symptoms and health related quality of life (QLQ-C30) have also been included in the registry. In Denmark, patients with lung cancer are often transferred between hospitals with diagnostic facilities to hospitals with treatment facilities during the care pathway. We wanted to investigate whether this organizational set-up influenced patients' well-being. The objective of this study was to uncover the impact of transfer between hospitals on quality of life self-reported 90 days after resection in lung cancer patients.
<b>Methods</b>	The study includes all resected Danish lung cancer patients from 1 October 2013 until 30 September 2015. Effect of transfer between hospitals was estimated using the uni- and multivariate ordinal regression analysis. Missing data in QLQ-C30 was treated by Multiple Imputation.
<b>Preliminary results</b>	A total of 1646 patients were included for further analyzes. Univariate complete case analysis showed that transfer patients had a lower quality of life (with coefficient -2.9 and 95%CI (-5.83; 0.02)) and the complete case multivariate analysis adjusted for age, sex, socio-economic group, living alone status education level showed that transfer patients had a lower quality of life (with coefficient -3.4 and 95%CI (-7.08; 0.29)). After handling the missing data using Multiple Imputation, univariate analysis showed that transfer patients had a statistically significant lower quality of life (with coefficient -2.8 and 95%CI (-5.38; -0.22)) and multivariate analysis showed also that transfer patients had a statistically significant lower quality of life (with coefficient -3.1 and 95%CI (-6.13; -0.16)).
<b>Conclusions</b>	We found that for resected non small-cell lung cancer patients' transfer between hospitals during the care pathway has an influence on quality of life 90 days after surgery. The difference between no-transfer and transfer patients persists after adjusting for known predictors.

## Elderly Wellbeing and Alcohol - A Tricky Cocktail

<b>Authors</b>	Klausen, S. H., Engelsen, S., Christiansen, R. & Emiliussen, J. (MSc Psychology, PhD)
<b>Speaker</b>	Jakob Emiliussen
<b>Background</b>	<p>Older adults' use of alcohol in nursing homes is a rising challenge, expected to increase in the coming 10-15 years. Alcohol and alcohol use encompass functions and consequences that go beyond mere health concerns and stretch into social, personal and institutionalized life. However, a continuing increase in the focus on life quality makes it difficult to be only critical of alcohol use in nursing homes.</p> <p>The "A tricky cocktail" study encompasses four projects meant to illuminate quality of life in nursing homes among residents, professionals and relatives. The study is an interdisciplinary, humanistic study involving philosophers and a psychologist developing both theory and methodology based on empirical data. The overarching aim of the study is to develop a product for nursing home practitioners to assist in balancing health and care-concerns with the residents' quality of life.</p>
<b>Methods</b>	<p>The study is made in close collaboration with the Vejle municipality in Denmark. The five sites that have agreed to participate in data collection are all placed in Vejle.</p> <p>The study consists of four phases: 1) exploration, 2) interpretation in collaboration with practitioners, 3) developing practice-oriented product, 4) implementation.</p> <p>The first phase has two steps. Step one runs from March to May 2018, and step two is scheduled for the autumn of 2018. Phase one consists of 25 days of participant observations on the five sites. These observations will serve as a starting point for developing an interview guide for phase two, in which 20 participants will be interviewed for 45-60 minutes. Phase two, three and four will be executed during 2019 and 2020. Data will be analyzed in different ways in the four projects, including: phenomenological analysis, linguistic analysis and value-based analysis.</p>
<b>Project status</b>	<p>The collaboration between Vejle municipality and the research group was initiated at the end of 2016. The project funding application was sent in the middle of 2017. The project received full unconditional funding from the VELUX-foundation in November 2017. The official start date was February 1<sup>st</sup>, 2018. Data collection starts in April 2018. Phase two to four will be executed in 2019 and 2020. A more in-depth description of the four phases of the study will be presented.</p>

**DIATAST-The Diabetes Patient Takes Responsibility clinical trial: Baseline data**

<b>Authors</b>	<p>Nina Drøjdahl Ryg, MSc, PhD, (<a href="mailto:nina.droejdahl.ryg@rsyd.dk">nina.droejdahl.ryg@rsyd.dk</a>)<sup>1,2</sup>; Jeppe Gram, (<a href="mailto:jeppe.gram@rsyd.dk">jeppe.gram@rsyd.dk</a>)<sup>3</sup>; Claus Bogh Juhl, (<a href="mailto:claus.bogh.juhl@rsyd.dk">claus.bogh.juhl@rsyd.dk</a>)<sup>1,2</sup>.</p> <p>1) Medicinsk afd., Endokrinologisk afsnit, Sydvestjysk Sygehus.  2) Institut for Regional Sundhedsforskning-Center Sydvestjylland.  3) Endokrinologisk Afd., OUH</p>
<b>Speaker</b>	Nina Drøjdahl Ryg,
<b>Background and Aim</b>	<p>Life-long control of Type 1 diabetes (T1DM) with pre-planned visits in outpatient clinics has been a standard for decades. However, research data on patient preferences and organizational changes are sparse.</p> <p>The aim of the study is to test a new model, where patients are offered a higher degree of self-planning.</p> <p>Baseline data on patient preferences and satisfaction are presented.</p>
<b>Design and Methods</b>	<p>T1DM patients, aged 18-80 years and internet-users, were included. In addition, eligible patients who rejected inclusion were encouraged to answer a baseline questionnaire.</p> <p>Included patients were randomized to 1) pre-scheduled visit procedure, or 2) open unrestricted access to visits.</p>
<b>Primary variables</b>	Primary outcome is patient reported satisfaction estimated from a validated questionnaire. Preliminary data are reported, as the clinical trial is ongoing.
<b>Preliminary results</b>	<p>598 of 852 T1DM patients fulfilled the inclusion criteria (70.2%). 357 patients accepted inclusion in the intervention trial. 241 eligible patients rejected inclusion, of which 96 completed the questionnaire.</p> <p>Included patients had lower mean age (47.9 years) and median diabetes duration (21 years) compared to eligible non-included patients.</p> <p>Data indicated high overall satisfaction with use of the outpatient clinic for both included (95%) and eligible non-included patients (97%).</p> <p>Most included (58%) and eligible non-included patients (89%) reported that it was important to receive unsolicited appointments from the outpatient clinic. Concurrently, 30% of the included patients had experienced unnecessary visits. This was only the case for 16% of the eligible non-included patients.</p>
<b>Conclusions</b>	Data indicates overall satisfaction with the outpatient clinic, and preference for pre-planned visits despite the experience of redundant visits.

# Auditorium - Session 3 – 11.10-12.00

## Lifestyle factors in somatic patients with and without potential alcohol problems

<b>Authors</b>	A. Schwarz ( <a href="mailto:asschwarz@health.sdu.dk">asschwarz@health.sdu.dk</a> ) <sup>1</sup> , B. Nielsen ( <a href="mailto:bnielsen@health.sdu.dk">bnielsen@health.sdu.dk</a> ) <sup>1</sup> , A.S. Nielsen ( <a href="mailto:ansnielsen@health.sdu.dk">ansnielsen@health.sdu.dk</a> ) <sup>1</sup>  1) Enheden for Klinisk Alkoholforskning, SDU
<b>Speaker</b>	Anne-Sophie Schwarz
<b>Background and Aim</b>	In the present study, we investigated the overall lifestyle of patients with hazardous alcohol use and alcohol dependence, who are admitted to hospital, and we wished to investigate unhealthy lifestyle factors and their clustering in in-patients.
<b>Design and Methods</b>	Patients admitted to the gastrointestinal, neurological or orthopaedic departments at Odense University Hospital or to the emergency department at Aabenraa Hospital in the inclusion period, October 2013 to June 2016, completed a lifestyle questionnaire in which they were asked questions about their diet, alcohol consumption, exercise and smoking habits. Patients were divided into three groups depending on their score from the alcohol use disorder identification test which was embedded in the lifestyle questionnaire and odds ratios were calculated using logistic regression.
<b>Primary variables</b>	AUDIT scores and lifestyle factors.
<b>Preliminary results</b>	Patients with alcohol dependence had statistically significantly higher odds of being smokers, having unhealthy diet and being physically inactive compared with patients without alcohol problems. Amongst patients with hazardous alcohol drinking we found an increased occurrence of smokers and we found an inverse association between hazardous alcohol drinking and being physically inactive. A rather large amount of the patients had attempted to change their unhealthy lifestyle.
<b>Conclusion</b>	We found that alcohol problems are related to a clustering of other lifestyle factors and that a large portion of the patients admitted to certain departments show signs of various kinds of alcohol problems, therefore, specific hospitals departments would seem like an opportune setting for preventive alcohol interventions.

## Disease control in pediatric and adolescent patients with inflammatory bowel disease: aspects of anti-TNF- $\alpha$ and physical activity

<b>Authors</b>	<p>Lund K<sup>1</sup>, Nielsen RG<sup>2</sup>, Larsen MD<sup>1</sup>, Kjeldsen J<sup>3</sup>, Knudsen T<sup>4</sup>, Nørgård BM<sup>1,5</sup>  Speaker: Ken Lund, PhD student, ken.lund@rsyd.dk</p> <ol style="list-style-type: none"> <li>1) Center for Clinical Epidemiology, OUH, and Research Unit of Clinical Epidemiology, Institute of Clinical Research, University of Southern Denmark</li> <li>2) Hans Christian Andersen Children's Hospital, OUH, and Research Unit of Pediatric, Institute of Clinical Research, University of Southern Denmark</li> <li>3) Department of Gastroenterology S, OUH, and Research Unit of Medical Gastroenterology, Institute of Clinical Research, University of Southern Denmark</li> <li>4) Department of Medicine, Esbjerg Hospital, Institute of Clinical Research, University of Southern Denmark</li> <li>5) Brigham and Women's Hospital, Boston, Massachusetts and Harvard Medical School, Boston</li> </ol>
<b>Speaker</b>	Ken Lund
<b>Background and Aim</b>	Physical activity is recognized to be anti-inflammatory and might have a positive influence on disease activity and improved psychosocial factors. Our studies will show whether physical activity should be considered as a compound part in the treatment regimens. In the past 10 years, anti-TNF- $\alpha$ therapy has been the first-line treatment in specific situations, but the long-term efficacy is not well elucidated and is still debated.
<b>Design and Methods</b>	This PhD-study includes a prospective cohort of pediatric and adolescent patients with IBD recruited from four specialized units in the Region of Southern Denmark, and includes an objectively measured (accelerometer) level of physical activity. Based on nationwide register data, we will also investigate the long-term efficacy of anti-TNF- $\alpha$ therapy according to steroid consumption and surgical procedures.
<b>Primary variables</b>	Physical activity level fecal calprotectin, clinical disease scores, coping/compliance, and health related quality of life after 6 months. Anti-TNF- $\alpha$ , surgery, steroids.
<b>Conclusion</b>	The PhD-study is planned to have a clinical impact by bringing novel knowledge on the potential of physical activity. The PhD-study will also provide important news on the anticipated long-term prognosis and efficacy after anti-TNF- $\alpha$ therapy.

## Obstetric perineal tears –risk factors, wound infection and dehiscence: a prospective cohort study.

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<b>Speaker</b>	Ditte Gommesen
<b>Background and Aim</b>	<p>Perineal repair after spontaneous obstetric lacerations or episiotomies is a common surgical procedure. More than 80% of primiparous women sustain injury to the labia, vagina or perineum during vaginal childbirth and may experience infection or lack of wound healing. The prevalence of perineal wound infection and dehiscence is still to be established. The aim was to examine prevalence and risk factors for perineal wound infection and dehiscence among women sustaining a perineal tear during vaginal birth.</p>
<b>Design and Methods</b>	<p>A prospective cohort study conducted among 200 primiparous women with 2<sup>nd</sup> degree perineal tears/mediolateral episiotomies and 200 primiparous women with 3<sup>rd</sup> and 4<sup>th</sup> degree perineal tears. The women delivered from July 2015 until January 2018. Questionnaire interviews and clinical examinations were performed 11-21 days postpartum. Main outcome measurements were wound infection defined as either purulent drainage or wound abscess and wound dehiscence defined as a wound gap <math>\geq 3</math> mm.</p>
<b>Results</b>	<p>The risk of infection and dehiscence were 6% and 13%, respectively. Women with an episiotomy had more than two times increased risk of wound infection (OR 2.31 95% CI: (0.70-6.49)) and dehiscence (OR 2.13 (95% CI: 0.94-4.54)). Treatment with antibiotics during delivery and in the study period didn't seem to influence the risk infection (OR 0.64 (95% CI: 0.18-1.85)) but women treated with antibiotics had lower risk of dehiscence (OR 0.45 (95% CI: 0.19-0.97)). Related to perineal injury, 3<sup>rd</sup> and 4<sup>th</sup> degree lacerations seemed to be protective against wound infection (OR 0.33 (95% CI: 0.11-0.91)) while no difference was seen according to dehiscence (OR 0.73 (95% CI: 0.38-1.37)).</p>
<b>Conclusions</b>	<p>The overall risk of wound infection was low (6%), while 13% experienced dehiscence <math>\geq 3</math>mm. Treatment with antibiotics didn't seem to protect against infection but against dehiscence. Though not statistically significant, episiotomies seemed to increase the risk of infection as well as dehiscence and should be thoroughly considered before performed.</p>

## Do biomarker levels and their changes in adult haematological malignancy patients mainly reflect infectious episodes and what is their prognostic utility?

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<b>Speaker</b>	Kim Gradel
<b>Background and Aim</b>	Patients with haematological malignancies (HM) are more susceptible to infections. We wish to assess whether levels and changes of neutrophils, C-reactive protein (CRP), and serum albumin (SA) can predict the severity of infections and refine the prediction of mortality.
<b>Design and Methods</b>	All patients with HM, diagnosed, treated and followed at OUH, 2000-2017, were included. Disease specific factors as well as biochemical results, bacteraemic/fungaemic episodes, comorbidity, and vital status are being comprised in a database. Studies will focus on trajectories of biochemical values in relation to bacteraemic/fungaemic episodes, HM exacerbation, and mortality.
<b>Primary variables</b>	Date of HM diagnosis, height, weight, weight loss, HM treatment (chemotherapy, immunotherapy, radiation therapy), treatment response, WHO performance status, prognostic indices, comorbidity, levels of neutrophils/CRP/SA, age, gender, bacteraemic/fungaemic episodes, type of microorganism, vital status.
<b>Preliminary results</b>	Compilation of the study database is in progress. A total of 6984 HM patients have been identified including ~275,000 neutrophil, ~405,000 CRP, and ~308,000 SA results.
<b>Conclusions</b>	Construction of the database is proceeding as planned. It will be used for several projects as outlined aiming at improving clinical care in patients with HM.

## Prevalence and risk factors for non-attendance among patients in hospital outpatient treatment for chronic diseases: A register-based cohort study.

<b>Authors</b>	<p>Donna Lykke Wolff (<a href="mailto:Donna.wolff@rsyd.dk">Donna.wolff@rsyd.dk</a>)<sup>1,2</sup>, Frans Boch Waldorff<sup>3</sup>, Christian Von Plessen<sup>1,2</sup>, Christian Backer Mogensen<sup>2,4</sup>, Thomas Lund Sørensen<sup>6</sup>, Kim Christian Houliind<sup>2,7</sup>, Søren Bie Bogh<sup>1</sup>, Katrine Hass Rubin<sup>8</sup></p> <p>1) Centre for Quality, Region of Southern, Middelfart, Denmark.          2) Institute of Regional Health Research, University of Southern, Odense, Denmark.          3) Research Unit and General Practice, Odense, Denmark.          4) Hospital of Southern Denmark, Aabenraa, Denmark.          5) The Danish Patient Safety Authority, Kolding, Denmark.          6) Department of Vascular Surgery, Kolding hospital, Part of Hospital Lillebaelt, Kolding, Denmark.          7) OPEN - Odense Patient Data Explorative Network, Department of Clinical Research, University of Southern Denmark and Odense University Hospital, Odense, Denmark</p>
<b>Speaker</b>	Donna Lykke Wolff
<b>Background and Aim</b>	Failure to keep medical appointments results in inefficiencies, high costs and potentially poor outcome for the patient. The aim of this study is to describe non-attendance rate and investigate risk factors for non-attendances among patients in hospital outpatient treatment for chronic diseases.
<b>Design and Methods</b>	We conducted a historic register-based cohort study based on data from Hospital Lillebaelt, Denmark. Patients 18+ years of age who were registered in an ongoing outpatient treatment course for chronic disease (seven selected diseases) on July 1 <sup>st</sup> , 2013 were included. A total of 5895 patients were included and information about their appointments extracted in the period July 1 <sup>st</sup> , 2013 to June 30 <sup>st</sup> , 2015.
<b>Primary variables</b>	The outcome measure was missed appointments (non-attendances). The association between non-attendances and covariates (age groups, gender, marital status, education level, occupational status, duration of outpatient treatment, number of annual appointments, weekday and type of chronic diseases) was investigated using multivariate logistic regression models including mixed effect.
<b>Preliminary results</b>	5 % of all appointments ended with non-attendance. (4,393 of 82,989 appointments). The strongest significant risk factors for non-attendance were younger age, COPD or several hospital outpatient treated diseases, unemployment or affiliation to labour market (vs. retired), appointments on Tuesdays, male gender, unmarried status and low educational level.
<b>Conclusions</b>	One out of 20 appointments were not attended. We found several risk factors for non-attendances. To reduce non-attendance initiatives could target these risk groups for non-attending.

# Room S1 - Session 1 – 09.00-09.45

## Impact of uterine fibroids on fertility

<b>Authors</b>	Kamilla Karlsen <sup>1</sup> , Ole Mogensen, Peter Humaidan, Ulrik Kesmodel, Pernille Ravn  1) Department of Gynecology and Obstetrics OUH, phd student SDU
<b>Speaker</b>	Kamilla Karlsen
<b>Background and Aim</b>	Uterine fibroids are the most common benign tumors in the uterus. They occur in up to 10 % of women aged 20-30 and about 40 % of women aged 40-50 years. Fibroids are believed to reduce fertility and removal is often recommended to improve fertility. However, there is no clear evidence for this recommendation. Treatments have been shown effective on symptoms such as bleeding and pain, but it is unclear whether they improve fertility. The purpose of this study is to investigate fertility among premenopausal women with uterine fibroids. In addition, we will investigate whether surgical removal of uterine fibroids improves fertility.
<b>Design and Method</b>	Historical cohort study based on data from The Danish National Birth Cohort and the Danish National Patient Registry. The Danish National Birth Cohort is a large cohort of 101,042 pregnancies obtained between 1996 and 2002. The Danish National Patient Registry contains diagnoses and treatment provided in The Danish Health Care system. We are preparing a comparison of 3 groups of women; A. Women without uterine fibroids. B. Women with uterine fibroids prior to pregnancy and no surgical treatment. C. Women who have had surgical treatment of uterine fibroids prior to pregnancy. The primary outcome is time to pregnancy.
<b>Preliminary results</b>	We expect the results to be ready in May.
<b>Conclusion</b>	The results of this large register based study can contribute to more accurate recommendations for treatment of uterine fibroids in relation to fertility.

## Mechanical Property Change of Red Blood Cell Membrane with Photosensitizer Cis-Porphyrin

<b>Authors</b>	<p>Koji Kinoshita (<a href="mailto:koji@health.sdu.dk">koji@health.sdu.dk</a>)<sup>1</sup>, Gustavo Campos<sup>2</sup>, Tayana Tsubone<sup>2</sup>, Vita Solovyeva<sup>3</sup>, Jonathan Brewer<sup>3</sup>, and Rosangela Itri<sup>2</sup></p> <p>1) Department of Molecular Medicine, University of Southern Denmark, Odense, Denmark  2) Instituto de Fisica da Universidade de São Paulo, São Paulo, Brazil  3) DaMBIC and MEMPHYS-Center for Biomembrane Physics, Department of Biochemistry and Molecular Biology, University of Southern Denmark, Odense, Denmark</p>
<b>Speaker</b>	Koji Kinoshita
<b>Background and Aim</b>	<p>Photodynamic therapy (PDT) with photosensitizer molecules, such as porphyrin, has been developed well to treat a cancer and skin disease by destroying tumor or damaged tissues. However, in molecules level, the mechanism of cell mechanical property change with the photodamaging is still not well understood. Here, we aim to 1) Characterize RBC membrane elasticity with photodamaging of therapeutic photosensitizer-mediated oxidant, cis-porphyrin; and 2) Investigate the signal transduction and cytoskeletal network reformation of it.</p>
<b>Design and Methods</b>	<p>Homemade micropipette manipulation setup was used to measure the shear modulus of RBC membrane with and without cationic cis-porphyrin, CisDiMPYP. To find cytoskeletal network formation of RBC membrane, we applied the techniques of Stimulated Emission Depletion (STED) microscopy at DaMBIC facility at SDU.</p>
<b>Variables and results</b>	<p>We found that the shear modulus of the RBC membrane was increased with increasing of the degree of photodamaging: from <math>6.4 \pm 0.4 \times 10^{-6}</math> N/m (none porphyrin damaging) to <math>10.4 \pm 0.4 \times 10^{-6}</math> N/m (5 nM porphyrin with 600s irradiation damaging); and also, the photodamaging for the RBC elasticity was irreversible after removing of the photosensitizer by washing. Continuation of photodamaging also caused RBC lysis. STED microscopy showed two peaks, 169 and 224 nm, of RBC contour length distributions between band 4.1R proteins at RBC cytoskeleton.</p>
<b>Conclusions</b>	<p>CisDiMPYP porphyrin could make photodamaging for the RBC mechanical property permanently. However, the affect for the RBC membrane elasticity was not in linear trend against irradiation time. Especially, it had non-reaction (or recovered) period for the irradiation. Therefore, we assume that there is some resistances for damaging with mechanosensing reaction.</p>

## At the Forefront of Older Peoples' Care

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<b>Speakers</b>	Eva Hoffmann, Maiken Persson, Mette Elkjær & Lilian Boye.
<b>Background and Aim</b>	<p>The population of elderly <math>\geq 65</math> in Denmark is increasing. Elderly often have multiple comorbidities, functional limitations and cognitive impairment, increased consumption of healthcare services, hospitalization and readmission. When the elderly are acutely admitted they are extraordinary challenged and are at risk of deterioration of health and quality of life.</p> <p>At the Forefront of Older Peoples' Care, is a research cooperation between the emergency and psychiatric departments in Southern Jutland, the general practitioners (GP) and the municipalities of Haderslev, Toender, Soenderborg, Aabenraa, University College South and several research institutes at the University of Southern Denmark.</p> <p>The project focuses on the acutely admitted citizens' <math>\geq 65</math> and wishes to make the elderly and their relatives' as wells as the healthcare professionals key players in the development of high quality Health Care in Denmark. The citizen must experience a dignified, effective and good preventive effort and cross-sectorial treatment in close cooperation with their GP, municipality and the hospital. The overall aim of this project is to provide nuanced knowledge about coherence in treatment and transitions among elderly <math>\geq 65</math> experiencing an acute hospitalization.</p>
<b>Design and Methods</b>	<p>The study consists of five PhD studies focusing on the perspectives of the healthcare professionals, the citizens' /patients', the relatives, the citizens' quality of life in connection with home care and on citizens with dementia.</p> <p>The PhD projects use interviews, observations and surveys as research methods and they are all contributing to the overall aim.</p>

	Participants will be recruited from the municipalities of Haderslev, Toender, Soenderborg, Aabenraa in relation to an acute admission at the Hospital of Southern Jutland.
<b>Preliminary result</b>	First preliminary results will be available in 2018. The overall results of the PhDs will form a basis for new initiatives and recommendations on how to strengthen the citizen's quality of life, intersectoral cooperation as well as increase the coherence of treatment and transitional care for the acutely admitted older people.

## Filaggrin expression and immune-pathomechanisms in eczema and asthma

<b>Author</b>	Millie Nguyen Basu ( <a href="mailto:millie.basu@rsyd.dk">millie.basu@rsyd.dk</a> ) <sup>1</sup> 1) HCA Research Unit, Odense University Hospital
<b>Speaker</b>	Millie Nguyen Basu
<b>Background and Aim</b>	Eczema/atopic dermatitis (AD) has increased 4-6 fold since the 1960s. Evidence points to causation involving a complex interplay between gene and environment, skin barrier and immune dysfunction. Filaggrin (FLG) gene plays an important role in the pathogenesis of AD. Its product and degradation products contribute to maintain skin barrier function and hydration. Recent findings have demonstrated that filaggrin expression is significantly down-regulated in AD patients in both FLG mutation and wild-type populations. The mutation has also been correlated with an increased risk for asthma in the context of AD. Pathomechanistic factors for this link possibly involve T-helper 2 (Th2) cytokines, which are strongly associated with allergic disease. CCL18 is a chemokine associated with an AD phenotype and is a chemoattractant of Th2 cells. Our study investigates the environmental factors that play a role in up- or down-regulation of filaggrin expression, and its association with immune regulatory factors. We also investigate a possible pathway involving CCL18 that may play a role in the causal link between AD and asthma.
<b>Design and Methods</b>	Our project is a case-control cohort study recruiting participants with AD, asthma and healthy controls from the Odense Child Cohort. There is an experimental sub-study, using cell culture to simulate possible mechanistic pathways linking AD and asthma.
<b>Primary variables</b>	Filaggrin biomarker levels.
<b>Preliminary results/ conclusions</b>	Pending.

## DNA methylation linked to all-cause mortality in older people: An epigenome-wide association study

<b>Authors</b>	<p>Jesper Lund, Ph.d.-studerende, MSc (<a href="mailto:jlund@health.sdu.dk">jlund@health.sdu.dk</a>)<sup>1</sup>, Jan Baumbach<sup>2,3</sup>, Shuxia Li<sup>4</sup>, Anne Marie Svane<sup>1</sup>, Jacob Hjelmberg<sup>1</sup>, Lene Christiansen<sup>1</sup>, Kaare Christensen<sup>1,4</sup>, Paul Redmond<sup>5</sup>, Riccardo E. Marioni<sup>6,7</sup>, Ian J. Deary<sup>5,7</sup>, Qihua Tan<sup>1,4,*</sup></p> <ol style="list-style-type: none"> <li>1) Epidemiology and Biostatistics, Department of Public Health, University of Southern Denmark, Odense, Denmark</li> <li>2) Experimental Bioinformatics, TUM School of Life Sciences Weihenstephan, Technical University of Munich, Munich, Germany</li> <li>3) Department of Mathematics and Computer Science, University of Southern Denmark, Odense, Denmark</li> <li>4) Unit of Human Genetics, Department of Clinical Research, University of Southern Denmark, Odense, Denmark</li> <li>5) Department of Psychology, University of Edinburgh, Edinburgh, Scotland, United Kingdom</li> <li>6) Center for Genomic and Experimental Medicine, University of Edinburgh, Edinburgh, Scotland, United Kingdom</li> <li>7) Center for Cognitive Aging and Cognitive Epidemiology, University of Edinburgh, Edinburgh, Scotland, United Kingdom</li> </ol>
<b>Speaker</b>	<p>Jesper Lund</p>
<b>Background and Aim</b>	<p>The risk of death can be affected by demographic, epidemiological and clinical factors. At the molecular level, epigenetic mechanisms have been shown to be influential. Therefore, we seek to investigate the evidence of DNA methylation effects with respect to mortality, using DNA methylations levels extracted from whole blood samples.</p>
<b>Design and Methods</b>	<p>Using genome-wide DNA methylation data from large-scale cohort studies of older Scottish individuals, we performed an epigenome-wide association study to identify DNA methylation sites related to all-cause mortality and verified these using independent data on Danish twins. For this, we fit the Cox proportional hazard model to find likely influential causes of increased and decrease in mortality within the segment of older individuals.</p>
<b>Primary variables</b>	<p>Whole blood DNA methylation from Illumina 450K Methylation chips, gene-set enrichment, de-novo pathway enrichment, large-scale cohorts.</p>
<b>Preliminary results</b>	<p>By fitting the Cox proportional hazard models, we identified 2,552 CpG sites (linked to 2,036 genes) with a genome-wide significance of FDR &lt; 0.05. Among them, 1,403 positively and 1,149 negatively correlated with mortality. A total of 57 CpGs and 330 genes were replicated in Danish twin cohorts. In addition, we performed gene set enrichment analyses for genes linked to significant CpGs and found 41 and 49 over-represented gene-sets for CpGs showing positive and negative correlation with mortality respectively, verified in Danish twins. In addition, we performed gene set enrichment analyses for genes linked to significant CpGs and found 41 and 49 over-represented gene-sets for CpGs showing positive and negative correlation with mortality respectively, verified in Danish twins. As well as, we performed de-novo pathway enrichment analysis based on the verified genes</p>
<b>Conclusions</b>	<p>We have performed an epigenetic association study on all-cause mortality based on whole blood samples of LBC cohorts, have confirmed our findings in a similar study on elderly Danish twins and sought further support from a study on age-related DNA methylation patterns. Likewise, gene-sets enriched</p>

	<p>by significant CpGs displayed high overlap with that from the replication cohort and from previously published studies. Finally, our de-novo pathway analysis revealed gene networks implicated in cancer, anatomical and neurological diseases. Our results provide further evidence of the association between epigenetic factors and the risk of death in the older populations.</p>
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# Room S1 - Session 2 – 09.55-10.40

## Danish Translation and Cultural Adaption of the 9-Item Shared Decision Making Questionnaire (SDM-Q-9) patient version.

<b>Authors</b>	<p>Mette Hulbæk<sup>1</sup>, Marianne J Jørgensen<sup>2</sup>, Jette Primdahl<sup>3</sup> Jesper Bo Nielsen<sup>4</sup>, Regner Birkelund<sup>5</sup></p> <ol style="list-style-type: none"> <li>1) Gynecological department, Hospital of Southern Jutland, Aabenraa, Denmark, <a href="mailto:mette.hulbaek@rsyd.dk">mette.hulbaek@rsyd.dk</a></li> <li>2) Department of Clinical Medicine, Aarhus University, Denmark</li> <li>3) King Christian X's Hospital for Rheumatic Diseases, Graasten, Southern Hospital of Jutland, University of Southern Denmark</li> <li>4) Research Unit for General Practice, Department of Public Health, University of Southern Denmark</li> <li>5) Lillebaelt Hospital, Vejle &amp; Institute of Regional Health Research, University of Southern Denmark</li> </ol>
<b>Speaker</b>	Mette Hulbæk
<b>Background and Aim</b>	<p>Measure instruments that measure the extent to which patients are involved in the process of decision-making are developed and validated and being used worldwide. So far, no validated self-report instrument for the shared decision making (SDM) process is available in Denmark.</p> <p>The aim was to translate and cultural adapt a Danish translation of the SDM-Q-9 patient version to the context of Danish women with pelvic organ prolapse and patients with cruciate ligament injuries in the Outpatient Gynecology Clinic and the Department of Sports Traumatology.</p>
<b>Design and Methods</b>	<p>In accordance with and acceptance of the German authors the original SDM-Q-9, patient version was translated from German and cultural adapted into a Danish context following WHO's four phased recommended process; (1) Forward translation (2) Expert panel discussion – Back translation (3) Pre-testing and cognitive interviewing and (4) Final version and documentation.</p>
<b>Preliminary results</b>	<p>A forward and backward translation were completed by four different translators and followed by an adjustment made by the expert panel. The expert panel included the three of the four translators, experts in health, instrument development and translation and an expert in the field of gynecology. Minor changes to the first Danish draft was made based on results from a cognitive pretest among six women with pelvic organ prolapse and five patients with knee injuries recruited from the outpatient clinics. The final Danish version was approved by the German author.</p>
<b>Conclusions</b>	A Danish translated version of SDM-Q-9 patient version, is now available.

## Anti-TNF therapy alters neurogenesis and affects learning and memory

<b>Authors</b>	Minna Yli-Karjanmaa*, Kathrine Solevad Larsen*, Stephanie Lindeman Carlsen, David E. Szymkowski, Jane Stubbe, Lars Henrik Frich, Roberta Brambilla, Kate Lykke Lambertsen  *Shared first authors
<b>Speaker</b>	Minna Yli-Karjanmaa
<b>Background</b>	Non-selective inhibition of TNF can cause suppression of the immune system and due to this inhibitors are used for long-term treatment of peripheral autoimmune diseases such as rheumatoid arthritis and Crohn's disease. Inhibition of TNF is known to cause demyelination but otherwise little is known about the effects of long-term treatment in central nervous system (CNS) when CNS itself is not affected by an autoimmune disease or an insult. Since TNF signaling is associated with synaptic function and plasticity and there is evidence that it is involved in learning and memory, it is possible that long-term treatment with TNF inhibitors could alter hippocampal functions in otherwise healthy brain.
<b>Aim</b>	To test the effect of a long-term inhibition of TNF in learning and memory and cell proliferation in hippocampus.
<b>Methods</b>	Adult male mice (C57BL6/J) were divided in three groups; treated with non-selective TNF inhibitor etanercept, selective soluble TNF (solTNF) inhibitor XPro1595 or saline. Drugs were administered 10 mg/kg subcutaneously every third day for two months. Spatial learning and memory were tested on Barnes maze after the treatment period. Proliferation marker BrdU was administered i.p. in the beginning of the treatment period and EdU before the Barnes maze test. The number of BrdU <sup>+</sup> and EdU <sup>+</sup> cells were counted in hippocampal dentate gyrus.
<b>Results</b>	We found that non-selective inhibition of TNF with etanercept impairs learning and memory while animals treated with solTNF inhibitor XPro1595 express normal behaviour. Also number of BrdU <sup>+</sup> cells was decreased after treatment with etanercept suggesting non-selective inhibition of TNF to alter neurogenesis in hippocampus. No differences in the number of EdU <sup>+</sup> positive cells were seen between the treatment groups.
<b>Conclusion</b>	Non-selective inhibition of TNF can impair learning and memory and decrease neurogenesis, while inhibiting only solTNF does not cause a decline in cognitive functions.

## Atrial fibrillation and infection among acute patients in the Emergency Department: a multicentre cohort study of prevalence and prognosis

<b>Authors</b>	<p>Hansen TG<sup>1</sup>, Brandes A<sup>2</sup>, Brabrand M,<sup>1,3</sup> Ekelund U<sup>3</sup>, Lundager J<sup>4</sup>, Jensen H<sup>1</sup>, Pottegård A<sup>5</sup>, Lassen AT<sup>1</sup></p> <p>1) Department of Emergency Medicine, Odense University Hospital, Denmark, Odense, Denmark  2) Department of Cardiology, Odense University Hospital, Odense, Denmark  3) Department of Emergency Medicine, Hospital of South West Jutland, Esbjerg, Denmark  4) Department of Clinical Sciences, Emergency Medicine, Lund University, Lund, Sweden  5) Emergency Medicine, Helsingborgs Lasarett, Sweden  6) Department of Clinical Pharmacology, University of Southern Denmark, Denmark</p>
<b>Speaker</b>	Tobias Graversgård Hansen
<b>Introduction</b>	<p>Patients with infection presenting with atrial fibrillation (AF) are frequent in emergency departments (ED). This combination is probably related to a poor prognosis compared to lone AF or infection, but existing data are scarce.</p> <p>Aim: to describe the prevalence and prognosis for AF and, infection individually and concomitantly in an ED setting.</p>
<b>Methods</b>	<p>Cohort study in adult (<math>\geq 18</math> years) ED patients with ECG performed on presentation at Odense University Hospital and Hospital of South West Jutland, Denmark, from March 13 2013 to April 30 2014. AF was identified by electronic ECG records, and infection was identified based on discharge diagnoses. The absolute 30-day mortality and stroke rate were calculated for all patients, for those with AF, infection and those with both.</p>
<b>Results</b>	<p>Among 39393 contacts to the ED, 27879 patients (median age 66, 50 % women) had an ECG recorded and were included in the study. 2341 (8.4%) had AF, 5672 (20.3%) had an infection and 670 (2.4%) had both infection and AF, of which 230 (34.3%) had no previous AF diagnosis or AF identified by ECG in the past 10 years (new-onset AF).</p> <p>In these groups, 30-day mortality was 11.3% in patients with infection, 10.4% in patients with AF and 22.6% in patients with new-onset AF and infection. One-year stroke rate in patients with AF was 56.6 /1000 person-years (95% CI, 46.5 to 68.9), 23.2 /1000 person-years (95% CI, 19.1 to 28.1) in patients with infection and 62.5 /1000 person-years (95% CI, 32.5 to 120.2) in patients with new-onset AF and infection. Among patients with new-onset AF and infection, 20.9% had registered further AF episodes within one year after discharge and 30.2% in patients with new-onset AF without infection.</p>
<b>Conclusion</b>	<p>Compared to ED patients with lone AF or infection, patients with concomitant new-onset AF and infection show an increased 30-day mortality, one-year stroke rate, and increased risk of further AF episodes.</p>

## Impact of red and processed meat and fibre intake on risk of chronic inflammatory diseases: a prospective cohort study on prognostic factors using the Danish "Diet, Health and Cancer" cohort (PROCID-DHC)

<b>Authors</b>	<p>Nathalie Fogh Rasmussen<sup>1</sup>, Katrine Hass Rubin<sup>2</sup>, Anne Tjønneland<sup>3</sup>, Vibeke Andersen<sup>4, 5,6</sup></p> <p>1) Department of Health, Aarhus University, Aarhus, Denmark, <a href="mailto:201205491@post.au.dk">201205491@post.au.dk</a>          2) OPEN, University of Southern Denmark, Odense, Denmark, <a href="mailto:Katrine.rubin@rsyd.dk">Katrine.rubin@rsyd.dk</a>          3) Danish Cancer Society, <a href="mailto:anet@cancer.dk">anet@cancer.dk</a>          4) Focused research unit for Molecular Diagnostic and Clinical Research, IRS-Center Sonderjylland, Hospital of Southern Jutland, Aabenraa, Denmark, <a href="mailto:vandersen@health.sdu.dk">vandersen@health.sdu.dk</a>          5) Institute of Regional Health Research, University of Southern Denmark, Odense, Denmark          6) Institute of Molecular Medicine, University of Southern Denmark, Odense, Denmark</p>
<b>Speaker</b>	Nathalie Fogh Rasmussen
<b>Background and Aim</b>	Chronic inflammatory diseases (CIDs), including Crohn's disease, ulcerative colitis, psoriasis/psoriatic arthritis, rheumatoid arthritis/ankylosing arthritis, and multiple sclerosis, have some shared genetic and environmental predisposing factors. The primary objective of this observational study is to investigate the impact of low fibre/high red and processed meat intake on risk of CID, with the ultimate aim of supporting future diet recommendations for effective personalized prevention.
<b>Design and Methods</b>	This study use data from the 57.053 participants in the prospective Danish "Diet, Health and Cancer" (DHC) cohort study, together with registry data, with follow up from 1993 to April 2018.
<b>Primary variables</b>	The outcome CID is defined as a first diagnosis of a CID during the follow-up. The outcome of the analyses is to detect variability in disease risk of any CID and disease risk of each CID diagnosis between persons with different dietary and other lifestyle habits.

# Room S1 - Session 3 – 11.10-12.00

## Psychiatric comorbidity in Back Pain Disorders

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<b>Speaker</b>	Pernille Møller Ljungdalh
<b>Background and Aim</b>	This aim of this PhD thesis is to estimate the risk of psychiatric comorbidity in patients with inflammatory back diseases, degenerative back disease and unspecific back pain. 2) Investigate if psychiatric comorbidity prior to or after back pain diagnosis affects the type of treatment given. 3) Examine if the presence of psychiatric comorbidity affects the levels of pharmacological treatment given.
<b>Design and Methods</b>	The association between back pain disorders and psychiatric comorbidity will be investigated using population-based registry data. The population will be defined using The National Danish Patient Registry. The following registries will be also utilized: A subdivision of the DNPR, the National Patient Registry – Psychiatry (NPD-Psych), The Danish National Prescription Database and The Danish National Health Service Register.
<b>Primary variables</b>	Age, sex, living situation, children in the household, socio-economic income, level of education, job type, somatic comorbidity (CCI), Pharmacological treatment in daily defined dosage (DDD), surgery (time of), use of physiotherapist, psychologist, chiropractor or occupational therapist (covered via tax-funded health insurance).
<b>Preliminary results</b>	Our pilot study suggests that there is a difference in the occurrence of psychiatric comorbidity, where unspecific BPD has higher risk of developing psychiatric comorbidity compared to specific BPD. The PhD project is planned to start in September 2018.
<b>Conclusions</b>	This PhD study is expected to contribute with new knowledge on the association between different types of back pain disorders and psychiatric comorbidity. The results will be used to increase clinical awareness of vulnerable patients in the intersection between rheumatology and psychiatry.

## Intimate hygiene with soap and water or disposable wet wipes ?: Effectiveness on microbial skin flora

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<b>Speaker</b>	Pia Lysdal Veje
<b>Background</b>	Intimate hygiene is important for hospitalized patients' opportunity to stay clean and fresh, and it is regarded as a necessary intervention to maintain patients' quality of life, social acceptance and wellbeing. Furthermore, the purpose of intimate hygiene is to remove dirt, odor and microorganisms, and it may potentially reduce the risk for urinary tract infection (UTI) and Catheter associated Urinary Tract Infections (CAUTI). Traditionally, soap and water (SAW) have been used for intimate hygiene, but recently, disposable wet wipes (DWW) have been introduced as an alternative. So far, only few studies have compared the effectiveness of washing methods to reduce microbial skin flora.
<b>Aim</b>	To compare the reduction in microbial skin flora and microorganisms related to UTI and CAUTI after washing with SAW and DWW.
<b>Design and Methods</b>	A prospective cross-over block-randomized trial including 72 inpatients from three Danish Hospital units. Skin swaps from patients' groin and perineum were obtained before and after washing with SAW and DWW. Characterization of bacterial diversity and microbiological analysis was performed by the use of 5% blood agar, Chromager Orientation Medium and Matrix Assisted Laser Desorption Ionization (MALDI-TOF). Descriptive and multilevel statistical analyses will be performed using STATA version 15.
<b>Primary variable</b>	Predefined skin microorganisms and potentially pathogen microorganisms related to UTI and CAUTI. In addition, potential modifier variables such as sex, diagnosis, antibiotics, length of admission, diaper, and use of urinary catheter were registered.
<b>Preliminary results and conclusion</b>	Design, challenges in obtaining the data, descriptive analysis and preliminary results will be presented.

## Virtual Reality Based Exercise to Recruit Mirror Neurons in the brain: Implications for motor rehabilitation in neurological patients

<b>Authors</b>	Kenny Brinckmann ( <a href="mailto:kebri13@student.sdu.dk">kebri13@student.sdu.dk</a> ), Rasmus R. M. Jørgensen, Christina S. V. Silverwing, Jacob Nielsen, Per Aagaard
<b>Speaker</b>	Kenny Brinckmann
<b>Background</b>	<p>Stroke is one of the most common causes of neurological deficit and can cause major damage in different areas of the brain. A frequent consequential result from stroke is hemiparesis. In Denmark approx. 12.000 people suffer from stroke each year. Rehabilitation of hemiparesis after stroke is a major challenge, especially for restoring arm motor function.</p> <p>It is well-known that the brain demonstrates significant adaptive plasticity throughout the life span. It may be speculated whether it is possible to utilize this neurological plasticity to facilitate post-stroke rehabilitation of the paretic arm. Activation of cerebral mirror neurons (MNs) might stimulate processes and mechanisms related to brain plasticity. MNs are known to be activated during movement, but also during observation of movements performed by others. It is possible that the use of virtual reality (VR) to simulate movements in the paretic limb can activate cerebral MNs in post-stroke patients. Thus, use of VR based rehabilitation exercise in neurological patients might be a feasible way to activate MNs and facilitate cerebral recovery processes.</p>
<b>Aim</b>	To develop VR exercise applications for rehabilitation of neurological patients with full or partial arm paresis.
<b>Methods</b>	A systematic literature review was performed to retrieve 24 original study publications and 6 reviews within the specific topic of cerebral MNs in relation to rehabilitation of neurological patients. Furthermore, a VR based unilateral arm exercise model was developed. The application is in current development through an iterative process, which is scheduled to involve testing in healthy subjects and subsequently in post-stroke patients.
<b>Conclusion</b>	Previous reports show positive results from implementing VR into the field of neurological rehabilitation. However, more knowledge is needed to elucidate how VR can be used effectively to gain functional recovery in hemiparesis patients.

## Arterial Blood Gas Analysis: as Safe as we Think? A multicentre retrospective cohort study

<b>Author</b>	Sacha Rowling, ( <a href="mailto:sacha.charlotte.rowling@rsyd.dk">sacha.charlotte.rowling@rsyd.dk</a> ) <sup>1</sup> 1) Odense University Hospital, University of Southern Denmark
<b>Speaker</b>	Sacha Rowling
<b>Background and Aim</b>	Arterial blood sampling is one of the most common invasive tests used in medical research on a daily basis, yet, up to now, no big studies have been done on the major complications. The aim of this study is to describe these by answering the question: “What is the seven-day incidence of serious complications (i.e. those requiring surgery or an intervention) after sampling for arterial blood gas analysis?”
<b>Design and Methods</b>	Data was analysed from the Danish National Patient Registry on arterial blood gases taken from patients who were $\geq 18$ years old between 1 January 1993 and 25 February 2013, in three hospitals in the region of Southern Denmark. Patients were excluded if the sample was possibly drawn from an indwelling arterial catheter. Using ICD-10 coded interventions – medical classifications listed by the World Health Organisation – two clinical physicians compiled a list with all interventions that could possibly have been performed as a consequence of a possible sampling complication. This list was used for analysis, giving the punctures’ maximum possible complication rate, defined as the “worst-case scenario”.
<b>Primary variables</b>	Arterial punctures, complications followed by surgery or an intervention.
<b>Preliminary results</b>	We analysed 410.103 arterial punctures in 107.450 patients with a median age of 70 years (IQR 59 – 78 years) at the time of the puncture. 50.4% of the patients were male (n=203.121). We found that 1.217 (0.30%, CI 0.28 – 0.31) punctures led to a serious complication.
<b>Conclusions</b>	Even though our analysis will give an overestimation of the complication rate, arterial blood-gas sampling is a low risk test. Nevertheless the possible major complications should be kept in mind.

## Detecting the Association Between DNA Methylation and Body Mass Index Using Co-Twin Design and Reduced Representation Bisulfite Sequencing Technology

<b>Authors</b>	<p>Weilong Li (<a href="mailto:wli@health.sdu.dk">wli@health.sdu.dk</a>)<sup>1</sup>, Jan Baumbach<sup>2,3</sup>, Lene Christiansen<sup>1</sup>, Qihua Tan<sup>1,4</sup></p> <p>1) Unit of Epidemiology and Biostatistics, Department of Public Health, University of Southern Denmark, Denmark          2) Department of Mathematics and Computer Science, University of Southern Denmark, Denmark          3) Chair of Experimental Bioinformatics, TUM School of Life Sciences, Technical University of Munich, Munich, Germany          4) Unit of Human Genetics, Department of Clinical Research, University of Southern Denmark, Denmark</p>
<b>Speaker</b>	Weilong Li
<b>Background</b>	<p>Body mass index (BMI) serves as an important measurement of obesity and adiposity which are highly correlated with cardiometabolic disease. Many genetic variants have been identified in genetic association studies, but only small proportion of BMI variation was explained. Meanwhile little is known due to epigenetic changes and few studies that focus on BMI with bisulfited sequencing technology. Being genetic identical, monozygotic twins that discordant for BMI are the perfect subjects for exploring the association between DNA methylation profile and BMI. We seek to detangle the environmental influence on BMI, using discordant twin design for controlling the genetic effect.</p>
<b>Material and Methods</b>	<p>Thirty Monozygotic twin pairs are included for this study with 11% minimum and 38% maximum BMI difference. There are 15 male pairs and 15 female pairs with age ranging from 39 to 72 years old. Methylation data from whole blood sample is collected using reduced representation bisulfite sequencing (RRBS). RRBS is a cost-effective approach for genome-wide methylation pattern profiling and RRBS data require many processing procedures to obtain methylation data for whole CpG sites. Reads were mapped to the reference genome using Bowtie and the methylation data was extracted using Bismark and smoothed using BeSeq. We did single CpG analysis using co-twin design that regress intra-pair methylation difference on BMI difference, and results were exported for gene enrichment analysis using GREAT software.</p>
<b>Result</b>	<p>Several metabolic related pathways were identified that associated with the BMI changes. We believe our results would be valuable for prediction and prevention of adiposity and further improve the life quality of the public.</p>

# Room S2 - Session 1 – 09.00-09.45

## Improved mechanical muscle function following combined blood-flow restricted training and heavy-load resistance training

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<b>Speaker</b>	Sofie K. Hansen
<b>Background</b>	It is well-documented that resistance training with heavy external loading (HRT) can induce increased skeletal muscle strength and power. However, HRT also results in high levels of force stress on tendons, joints and bones, typically contraindicating this type of training in rehabilitation. While low exercise loads during resistance training appear less stressful to joints and ligaments, mechanical muscle function remains largely unaffected with this training regime. However, by restricting blood-flow during low-load resistance training (BFR-RT) marked gains in mechanical muscle function and muscle size have been demonstrated. <u>Aim:</u> To investigate if heavy-load resistance training (HRT) could be partly substituted (50%) by low-load blood-flow restricted resistance training (BFR-RT) to evoke comparable training effects compared to HRT alone.
<b>Design and Methods</b>	Eighteen recreationally active young males and females ( $23 \pm 1.2$ yrs) were randomized into two groups completing 6 weeks of HRT (CR, n= 9) or combined HRT and BFR-RT (50/50%) (OCR, n= 9), with CR and OCR matched for total training time. Maximal isometric knee extensor strength (MVC), rapid force capacity assessed by rate of force development (RFD) and power/RFD during counter movement jumping (CMJ) were examined before and after the intervention period.
<b>Results</b>	Similar gains in MVC were observed after 6 weeks of OCR and CR training (OCR: + 12% p < 0.001, CR: + 7% p = 0.01), whereas increases in RFD (0-100 ms, + 11.9%, p = 0.037) were observed only following OCR. Tendencies for improved CMJ power (CR: + 2.3% p = 0.059) and RFD (OCR: + 49.3% p = 0.067) were also noted.
<b>Conclusion</b>	Replacing parts of HRT with BFR-RT led to more pronounced gains in mechanical muscle function compared to HRT alone. Thus, conventional HRT appears to be partly replaceable by BFR-RT without compromising the training-induced strength/power response. In fact, a more consistent training response was observed with the combined training. Consequently, the use of low training loads with BFR-RT may be attractive in the clinical setting when intending to avoid excessive loading on tendons and joints.

## “I felt understood and listened to” – A Survey in a Hospital based Migrant Health Clinic

<b>Authors</b>	<p>Leila Saud Abdulkadir (<a href="mailto:leilasabdulkadir@gmail.com">leilasabdulkadir@gmail.com</a>)<sup>1</sup>, Morten Sodemann<sup>2</sup>, Charlotte Sølvér Reihling<sup>2</sup> &amp; Dorthe Nielsen<sup>1,2,3</sup></p> <p>1) Migrant Health Clinic, Odense University Hospital                  2) Centre for Global Health, Southern University of Denmark                  3) University College Lillebælt,</p>
<b>Speaker</b>	Leila Saud Abdulkadir
<b>Background and Aim</b>	<p>A large proportion of patients with ethnic minority background have poor access to health information, prevention and treatment compared to ethnic Danish patients.</p> <p>Every year around 250.000 Danish patients are invited to participate in a national survey (Landsdækkende Undersøgelse af Patientoplevelser LUP), to give their feedback on either an admission or an outpatient visit they have had within the healthcare system. The survey is in Danish, which excludes many patients with minority background. The aim of the present study was to investigate patient experience of their encounter with a Migrant Health Clinic compared to the health professionals in the clinic. The clinic welcomes a distinct group of chronic patients with severe complex symptoms, uncharacteristic pain conditions, post-traumatic stress, complicated by language problems, social isolation and low health literacy.</p>
<b>Design and Methods</b>	<p>Data was collected between December 2017 and February 2018, collected by pre-validated questionnaire containing closed and open-ended questions. Data were entered in SurveyXact. Data were collected by three research assistants not known to patients. All assistants had different minority background (two spoke Arabic). Patients and health professionals were asked to participate in the study after each consultation. A professional interpreter was used when needed.</p>
<b>Preliminary results</b>	<p>In total 65 questionnaires were completed by both the patient and health professional. Data collection was challenged mainly because the data collectors didn't reach the patient before the patient had left the department, or the patient declined to participate, or didn't show up in the clinic. Most patients 63 (97%) expressed they could talk about their problems. A total of 54 (83%) patients used an interpreter, only two patients had problems understanding the interpreter and 59 (91%) patients expressed they were well-informed about the course of treatment. Results were in agreement with health professionals' feedback.</p>
<b>Conclusions</b>	<p>The level of satisfaction was surprisingly high with course of treatment among patients and staff in the Migrant Health Clinic. Involving patient with language barriers in surveys is possible, but it requires special setups such as an interpreter, a very short and simple questionnaire.</p>

## Danish translation and linguistic validation of the BODY-Q Chest Module

<b>Authors</b>	<p>Mike Mikkelsen Lorenzen (<a href="mailto:mike.mikkelsen.lorenzen@rsyd.dk">mike.mikkelsen.lorenzen@rsyd.dk</a>)<sup>1,*</sup>, Lotte Poulsen<sup>1</sup>, Jørn Bo Thomsen<sup>1</sup>, Diana Lydia Dyrberg<sup>1</sup>, Anne Klassen<sup>2</sup>, Jens Ahm Sørensen<sup>1</sup></p> <p>1) Department of Plastic Surgery, Odense University Hospital, Odense, Denmark          2) Department of Pediatrics, McMaster University, Hamilton, Canada</p>
<b>Speaker</b>	Mike Mikkelsen Lorenzen
<b>Background and Aim</b>	The aim of this study was to translate and linguistically validate the patient-reported outcome (PRO) instrument BODY-Q Chest Module, designed to measure outcomes following chest contouring surgery.
<b>Design and Methods</b>	The BODY-Q Chest Module includes 2 scales that measure appearance of chest and nipples. The translation and validation were performed according to the guidelines from the World Health Organization (WHO) and the International Society for Pharmacoeconomics and Outcomes Research (ISPOR). This approach involved 2 independent forward translations, a backwards translation, an expert panel meeting and cognitive debriefing interviews with patients. Each step was undertaken with the aim of achieving a conceptual and culturally equal instrument.
<b>Results</b>	This process led to a linguistically validated and conceptually equivalent Danish version of the BODY-Q Chest Module. The forward translation resulted in several discrepant translations of items that were harmonized to form the backward translation. This translation included 3 items with conceptual differences that required further revision. The revised version presented at the expert panel meeting had 6 items that needed to be revised due to conceptual discrepancies. The cognitive debriefing interviews led to revision of 1 item.
<b>Conclusions</b>	The practices from the WHO and ISPOR guidelines were essential to developing a translation that preserved the meaning of the content of the BODY-Q Chest Module from the original development study. The translation and linguistic validation methods used in our study could be used for further translations and validation of PRO instruments. These new scales have since been field-tested as part of an international psychometric study.

## Falling in old age – a qualitative study

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<b>Speaker</b>	Ann Sophia Bertelsen
<b>Background and Aim</b>	Older persons falling are a frequent and serious problem in public health. Every year the Danish hospitals treat approximately 40,000 patients above the age of 65 years for injuries related to falling making falls the cause for 75% of the contact to emergency departments among older persons. Falling is associated with increased morbidity and mortality as well as loss of skills and increased need for assistance. Accordingly, falls among older persons are the cause of immense cost both for the individual and for society. Furthermore, having fallen once increases the risk of falling again. Research in this field is therefore of utmost importance both for the patient and the healthcare system in order to insure further health care improvements. One important way of doing that is to assess the patient perspective. Therefore, the aim of the study was to explore the perspectives of older persons experiencing a recent fall and how the fall had affected their everyday life.
<b>Design and Methods</b>	A phenomenological and hermeneutical approach was used together with a qualitative explorative design. To identify the variations of the older persons' perspective, thoughts, and experiences, semi-structured interviews were used to gather data. The data was analyzed by systematic text condensation by Kirsti Malterud (2012). All data were managed in NVIVO.
<b>Preliminary results</b>	A total of nine (five women, four men) patients attending the Falls Clinic at OUH, were interviewed in the period of September-December 2017. Median age of the participants was 78 years old [IQR 76-84]. The analysis provided four themes: <i>“The importance of getting professional help”</i> , <i>“To maintain meaningfulness in everyday life”</i> , <i>“Help supplies”</i> , and <i>“The silent patient”</i> . The analysis emphasized that wishes and needs varied depending on what the older person found most meaningful in life. This highlights the importance that professionals should pay attention and be able to understand the priorities in life of the individual patient. Some participants expressed specific requests for help supplies, which tended to be more frequent among women. We also identified a group of participants who rejected or did not express any specific needs or wishes related to their fall. This could represent a social and cultural norm, where need for help are considered a threat to the personal identity and autonomy. However, it could also emphasize a group of patients who are simply not aware of the possibilities of personal help, help-supplies, or treatment.
<b>Conclusions</b>	The analyses showed that it is of great importance for the older persons to get help and care from health professionals following a fall. Furthermore, data provided a deeper understanding of their needs and wishes after a fall. This knowledge seems crucial to ensure further improvement of the quality of care, prevention, and treatment of older patients with falls.

## Weighted gene co-expression network analysis of microarray experiment in response to electroacupuncture

<b>Authors</b>	Afsaneh Mohammadnejad <sup>1</sup> , Hongmei Duan <sup>2</sup> , Shuxia Li <sup>3</sup> , Qihua Tan <sup>1,3</sup>  1) Unit of Epidemiology and Biostatistics, Department of Public Health, University of Southern Denmark, Denmark 2) Institute for Clinical Medicine, Copenhagen University, Denmark. 3) Unit of Human Genetics, Department of Clinical Research, University of Southern Denmark, Denmark
<b>Speaker</b>	Afsaneh Mohammadnejad
<b>Background</b>	Electroacupuncture (EA) has been extensively considered as a tool for treating and relieving various pains. However, understanding the molecular mechanisms underlying its effect is of high importance. In this study, we performed a weighted gene co-expression network analysis (WGCNA) on data collected from a microarray experiment to investigate the relationship underlying EA within three factors, time, frequency and tissue regions (periaqueductal gray (PAG) and spinal dorsal horn (DH)) as well as biological implication of gene expression changes.
<b>Methods</b>	Microarray gene expression data on rats in PAG-DH regions induced by EA with 2 HZ and 100 HZ at 1 h and 24 h were taken from the Gene Expression Omnibus (GEO) database. The WGCNA was used to identify distinct network modules related to EA effects. To find the function of genes and pathways DAVID software was applied.
<b>Results</b>	We identified one network module (705 genes) which is significantly correlated with time, another module (395 genes) positively correlated with frequency and a third module (1091 genes) negatively correlated with tissue regions. Furthermore, meaningful biological pathways such as cAMP signaling, citrate cycle (TCA cycle), nicotine addiction and additional gene ontology results were identified in relation to EA.
<b>Conclusion</b>	We identified important genes within specific modules and pathways which might be activated in response to EA stimulation.

# Room S2 - Session 2 – 09.55-10.40

## Translation and cultural adaption of the Communication Assessment Tool (CAT), developing a Danish and Norwegian version.

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<b>Speaker</b>	Else Dalsgaard Iversen
<b>Background</b>	The Communication Assessment Tool (CAT), a 14 items survey measuring patients' perspective on communication skills, developed and validated in the USA, was translated, validated and psychometrically tested for use in Denmark and Norway.
<b>Methods</b>	The survey was translated according to international guidelines. Data collection took place in a Danish outpatient clinic and in several Norwegian GP offices. Randomly selected patients participated in interviews for content and face validation and the CAT were filled out on iPads or paper immediately after consultations for psychometric properties.
<b>Results</b>	The CAT was successfully translated. For validation, 10 Danish patients were interviewed and had no comments for the items but asked for 'non-applicable' as an option on the 5-point response scale. In all, 440 patients completed the CAT on iPads or paper and confirmatory factor analysis gave a one-factor solution. Cronbach' alfa was as high as in other similar studies. Item 2 'Treated me with respect' received the highest score.
<b>Conclusion</b>	The translated and validated CAT can be used to measure patients' perspectives on clinicians' communication skills in both Denmark and Norway and despite minor differences in wording, the CATs are very similar and in both countries the answering option 'non-applicable' was added to the original 5-point scale during validation.

## Do red meat and dietary fibre intake affect treatment outcomes of biologic drugs among patients with Inflammatory Bowel Diseases.

<b>Authors</b>	<p>Mohamad Jawhara<sup>1,2</sup>, Signe Bek Sørensen<sup>1,2</sup>, Vibeke Andersen<sup>1,2,3</sup></p> <p>1) Focused Research Unit for Molecular Diagnostic and Clinical Research (MOK), Hospital of Southern Jutland, Aabenraa  2) Institute of Regional Health Research, University of Southern Denmark, Odense, Denmark  3) OPEN, University of Southern Denmark, 5000 Odense, Denmark</p>
<b>Speaker</b>	Mohamad Jawhara
<b>Background</b>	Inflammatory bowel diseases (IBD), including Crohn's Disease (CD) and ulcerative colitis (UC), are part of a broad group of disorders of the immune system that results in chronic inflammatory diseases. These diseases are frequently treated with TNF-inhibitors. However up to one-third of patients do not respond to the treatment, and we suggest that lifestyle factors including diet may affect treatment outcomes.
<b>Aim</b>	This study aims to explore whether red meat and dietary fiber intake have a prognostic factor on treatment outcomes, which may enable precision medicine in IBD.
<b>Methods</b>	<p>In this prospective cohort study we are recruiting 100 Danish patients with IBD who are prescribed a biologic drug. Before treatment, patient characteristics will be assessed using patient-reported outcome measures (PROMs), clinical assessments of disease activity, quality of life and lifestyle, in addition to registry data on comorbidity and concomitant medication(s). Following current Danish standards, follow-up will be conducted 14–16 weeks after treatment initiation.</p> <p>The primary evaluation of successful treatment response will be based on 1) Crohn's disease: clinical remission, defined as Harvey-Bradshaw Index (HBI) of 4 or less; 2) Ulcerative colitis: clinical remission, defined as Mayo Clinic Score of 2 or less (with no individual subscore of &gt;1). Moreover, The Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) program 's score will be used as a secondary outcome in the evaluation of successful treatment response of UC and CD patients.</p> <p>Exposure variables will be categorised in the following form: 1) The upper tertile of the sample based on the ratio of dietary fiber to meat intake is correlated to better treatment outcomes. 2) The lower tertile of the sample concerning intake of red and processed meat and the upper tertile of the sample concerning intake of dietary fibres are independently associated with better treatment outcomes; Potential interaction between them may further improve treatment outcomes.</p>
<b>Conclusions</b>	The main outcome of the analyses will be to detect variability in treatment effectiveness between patients based on the ratio of dietary fibers to red and processed meat intake.
<b>Acknowledgment</b>	<p>This project is part of a project that has received funding from the European Union's Horizon 2020 Research and Innovation Programme under grant agreement No 733100".</p> <p>Funding has furthermore been received from Odense Patient data Explorative Network, "Knud og Edith Eriksen's Mindefond", Region of Southern Denmark, and The University of Southern Denmark.</p>

**An open multicenter study to investigate efficacy and tolerability of olanzapine in patients with advanced cancer suffering from nausea not induced by chemotherapy or irradiation.**

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<b>Speaker</b>	Signe Harder
<b>Introduction</b>	The anti-psychotic drug olanzapine is of interest because it is effective against chemotherapy-induced nausea and targets multiple receptors known to be involved in the emetic reflex arch. The drug has a half-life of 30 hours, which allows for a single daily administration.
<b>Objectives</b>	To investigate the anti-emetic effect and tolerability of olanzapine in patients with advanced cancer not receiving chemotherapy or irradiation.
<b>Methods</b>	Patients with advanced cancer (no curable treatment options) with at least 'moderate' nausea and/or one emetic episode within 24 hours were included if they had not received chemotherapy or irradiation within the previous 14 days and had no reversible causes of nausea/vomiting. The patients were administered 10 mg olanzapine daily for five days (first dose subcutaneously and the following four orally). Nausea, vomiting and adverse effects were assessed for seven days.
<b>Results</b>	Twenty-five patients have been included. Twenty-two patients experienced some degree of improvement. Mean combined N/V score (0-100) at baseline was 68. After 24 hours and seven days it was 20 and 21, respectively. We recorded no extrapyramidal symptoms, hypotension or seizures. Fatigue, dizziness and sedation were numerically (but not statistically significant) worse 24 hours after the first dose. No adverse events seemed to be present at seven days.
<b>Conclusions</b>	Olanzapine appears effective and tolerable as an anti-emetic in patients with advanced cancer. Recruitment continues and updated results will be presented. Future research should examine a lower dose (5 or 2.5 mg), preferably in a randomized controlled trial.

## Genomic instability and mutational profiling of advanced rectal cancer according to response to neoadjuvancy.

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<b>Speaker</b>	Silvia Regina Rogatto
<b>Background and Aim</b>	Genomic instability (GI) is a feature of several human cancers, which is associated with deregulation of a complex network of DNA damage response involving cell-cycle checkpoints and DNA repair pathways. Pre-operative chemoradiotherapy (5-FU) followed by mesorectal surgery is the standard treatment for patients with locally advanced rectal cancer (ReCa). The treatment response varies from complete (~30%) to partial or incomplete response. Currently, no biomarker is available to predict the treatment response.
<b>Design and Methods</b>	Thirty-three ReCa samples (biopsies collected previous to the treatment) were evaluated by SNP array (CytoScan HD, Affymetrix) to identify the GI index and the Homologous Recombination Deficiency (HRD) scores (LST: large-scale transitions, tAI: telomeric allele imbalance, HRD-LOH: loss of heterozygosity). Targeted-NGS (105 cancer-related genes panel; 13 genes involved in the HR and 5 in the mismatch repair pathways) was performed in 31 cases.
<b>Primary variables</b>	GII, HRD scores (LST, tAI, HRD-LOH) and mutational status.
<b>Preliminary results</b>	Overall, a high burden of genomic alterations was observed in ReCa samples. Patients with complete pathological response (pCR) presented higher GI index (0.475) compared to those with partial or incomplete response (0.294). In agreement, the GI index showed significant difference comparing responders and non-responders according to Tumor Regression Grade (TRG: 0+1 <i>versus</i> 2+3) ( $p = 0.043$ ). We found 161 mutations in 51 genes including <i>TP53</i> (84%), <i>APC</i> (81%) and <i>KRAS</i> (45%). Three tumors presented mutations in <i>MLH3</i> or <i>MSH6</i> . Seven of 31 cases presented mutations in HR pathway; three of them showed high tAI scores. In addition, <i>PTEN</i> loss (5 cases), <i>PIK3CA</i> mutations (5 cases), and <i>BRAF</i> mutation (1 case) have been reported as promising predictors for treatment response in colorectal cancer.
<b>Conclusions</b>	Higher genomic instability (GI index) was associated with better response to treatment in ReCa. Deregulation of the HR pathway may be therapeutically exploited in ReCa; since HRD tumors have been associated with better platinum response rates.

## Meal-induced thrombin generation in obese women and men before and after gastric bypass - a model of intentional weight loss

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<b>Speaker</b>	Line Espenhain Andersen
<b>Background and Purpose</b>	Recently, studies have indicated that intentional weight loss is associated with unknown harmful effects leading to increased mortality. The link between intentional weight loss and thrombotic risk is poorly investigated. One candidate mechanism is postprandial coagulation activation following high-fat meals. The purpose of this study is to investigate postprandial coagulation activation in relation to intentional weight loss.
<b>Design</b>	Randomized cross-over study (2 days)
<b>Methods</b>	Thirty obese patients admitted to gastric bypass are included in the study, which is carried out before weight loss, after >8 % lifestyle-induced weight loss, and 3-4 months after gastric bypass. All participants consume a high-fat meal and a low-fat meal randomly served on 2 days (2-7 days apart) in each of the three periods. The meal effects are investigated by measuring relevant biomarkers in blood and faeces.
<b>Main variables</b>	Markers of coagulation activation, thrombin generation, tissue factor, inflammation, leptin, and endotoxin in plasma, and the gut microbiota profile in faeces.
<b>Result and Conclusion</b>	The clinical trial was initiated in October 2017, and the first results will be analysed in 2018 and published in 2019 and 2020. If high-fat meals increase the thrombotic risk in obese patients during intentional weight loss, existing dietary recommendations and disease prevention strategies must be modified.

# Room S2 - Session 3 – 11.10-12.00

## Challenges to a coherent course of treatment across sectors for patients with LBP

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<b>Speakers</b>	Lisbeth Petersen
<b>Background</b>	At some point in their life, 80% of the population will experience low back pain (LBP). This requires both social and personal resources. During the course of treatment, a large group of patients with LBP are in contact with many different health care professionals across sectors, and patients often end up circling the health care system with repeated assessments at primary or secondary health care facilities.
<b>Aim</b>	To understand the challenges to a coherent course of treatment across sectors for patients with LBP.
<b>Design</b>	Semi structured qualitative interview study.
<b>Methods</b>	Interviews with patients with LBP, health care professionals and social workers working with LBP patients. Nvivo is used to structure data. Systematic text condensation is used to analyze data.
<b>Primary variables</b>	Barriers to a coherent course of treatment across sectors.
<b>Preliminary results</b>	By looking at the empirical data through Aaron Antonovsky's Sense of Coherence concept, we find that a coherent course of treatment across sectors for LBP patients is challenged by different needs of patients and professionals in different sectors. Patients' abilities to comprehend, manage and find meaning in the course of treatment are vital in order to gain a sense of coherence. These abilities seem to be counteracted by health care professionals' different narratives, approach to LBP, final goal for patients, as well as a lack of consensus of expectations.
<b>Conclusion</b>	This analysis will be used in the process of developing methods and tools that can support LBP patients' sense of coherence. It is part of a larger project aiming to strengthen a coherent course of treatment across sectors for back pain patients.

**The association between prenatal alcohol exposure and Attention-Deficit-Hyperactivity-Disorder (ADHD) and Autism-Spectrum-Disorder (ASD): a prospective cohort study.**

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<b>Speaker</b>	Louise K. K. Weile
<b>Background and Aim</b>	Alcohol is a solvent passing the placental barrier. Hence, prenatal alcohol exposure is a risk factor for neurological damage in the fetus. We will examine the association between prenatal alcohol exposure and Attention-Deficit-Hyperactivity-Disorder (ADHD) or Autism-Spectrum- Disorder (ASD) among children.
<b>Design and Methods</b>	We included 42,055 live-born, singletons from Aarhus Birth Cohort born 2000-2012. Prenatal alcohol exposure was reported by mothers in a questionnaire completed in early pregnancy. Time to diagnosis of ADHD among children was obtained from Danish health registries in February 2018.
<b>Primary variables</b>	Exposure was defined as average alcohol intake per week and binge-drinking-episodes, whilst outcome was defined as time to a clinical diagnosis of ADHD or ASD.
<b>Results</b>	We found that 32.1% of the children were exposed to a weekly intake of alcohol during pregnancy; 25.6% being exposed to <1 unit/week, 3.3 to 1 unit/week, 2.8% to 2-3 units/week and 0.4% to $\geq$ 4 units/week. In all, were exposed to binge-drinking-episodes 35.4%; 20.6% to 1 episode, 8.9% to 2 episodes and 5.7% to $\geq$ 3 episodes. The incidence of ADHD/ASD was 2.25%.
<b>Conclusions</b>	Although average intake of alcohol has decreased, many children are still exposed to alcohol especially binge-drinking during pregnancy. Understanding how these exposures affect the long-term outcomes in the children is pertinent.

## Pseudoexons: underestimated intronic elements in treatment and disease

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<b>Speaker</b>	Maja Dembic
<b>Background and Aim</b>	Pseudoexons are intronic sequences that “resemble” real exons. When activated they are included wrongly in the mRNA, disrupting correct gene expression and causing disease. The number and level of activation of pseudoexons is not known. Our aim is to establish a map of the pseudoexons in the human genome and to study the mechanisms of their activation.
<b>Design and Methods</b>	We have developed a software for the analysis of RNA sequencing data to identify pseudoexons and used “minigenes” and splice-shifting oligonucleotides (SSOs) to study their splicing mechanism, and the effects of single nucleotide polymorphisms (SNPs) on their inclusion.
<b>Preliminary results</b>	We have so far identified 46,520 novel pseudoexons from public RNA sequencing data, making up an average of 2-3 pseudoexons per gene. We selected 13 pseudoexons and confirmed their activation in different cell lines. In minigenes, many uncharacterized SNPs were demonstrated to activate pseudoexons; SSOs were found to efficiently block the inclusion of a PCCA pseudoexon, with concomitant increase in the protein activity. This provided proof-of-concept that regulation of pseudoexons may be a powerful tool in regulating gene expression.
<b>Conclusions</b>	Pseudoexons are vulnerable parts of the introns, and their activation is a heavily underestimated disease mechanism. Many uncharacterized intronic SNPs may cause disease by a pseudoexon-activating mechanism. Global identification and characterization of pseudoexons will allow for better clinical diagnostics of genetic diseases, and may be used in personalized medicine for development of future therapies.

## Patient-reported quality of life in lung cancer:

### - The use of patient reported outcomes (PROs) as performance indicators

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<b>Speaker</b>	Majken M. Brønserud
<b>Background and Aim</b>	<p>For many years, treatment of lung cancer in Denmark has been audited on an annual basis using national performance indicators via the Danish Lung Cancer Registry (DLCR). However, data in DLCR give no information from the patients' perspective on the life lived with lung cancer. A well accepted way to gain information about patients' symptoms and quality of life is through the collection of patient reported outcomes (PROs). In this study, we wished to examine the feasibility of a nationwide collection of these PROs in a lung cancer population. Through analyses of the PROs collected, together with data from DLCR, we wished to develop a model, which could convert PROs into measures of quality in the treatment of lung cancer.</p>
<b>Design and Methods</b>	<p>All patients diagnosed with lung cancer in Denmark are registered in DLCR. The 7,295 patients registered in DLCR from 1 October 2013 until 30 September 2015 who had received treatment, were eligible for inclusion. They were asked to complete the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 and QLQ-LC13 questionnaires at least four times within the first year after diagnosis (before treatment, and then 3, 6 and 12 months later).</p>
<b>Preliminary results and conclusion</b>	<p>At least one questionnaire was completed by 4,229 patients (58%), and 3,066 patients did not respond to any of the questionnaires. Responders and non-responders differed significantly on almost all variables; the responders were generally in a much better health state. The subgroup of patients treated with surgery had remarkably better response rates than the group with oncological treatment, and response rates were lowest in the group receiving palliative treatment. We found that collection of PROs was possible in a national setting, and that import to a clinical database was feasible. The next step in our study is to finish analyses of the PROs collected. Because of the heterogeneity of the patients and their prognoses, analyses will be done in subgroups according to patients' treatments for lung cancer. From the analyses of the patients treated with surgery, we wish to develop a model, which can convert PROs into measures of quality in the surgical treatment of lung cancer.</p>

## Muscle strain in multiple sclerosis patients measured by ultrasound speckle tracking technique

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<b>Speaker</b>	Maria Thorning
<b>Background</b>	<p>The majority of multiple sclerosis (MS) patients experience difficulties in walking and in need of a walker or wheelchair. Medical treatment of walking difficulties is possible with fampridine. The treatment is offered on the basis of an improved walking distance measured using simple walking tests. However, patients with limited and/or no gait function could still benefit from fampridine treatment. Ultrasound speckle tracking (UST) is a non-invasive technique, with the potential to directly analyse muscle strain in the musculature. UST is designed for dynamic cardiac muscular examination, but can be used in modified version for skeletal muscle examination. The technique has already been tested in a minor pilot study with MS patients.</p>
<b>Purpose</b>	<p>To validate UST for use in MS patients, but also to establish a validated basis for assessing the treatment effect of fampridine in patients with MS, thus expanding the clinical guidelines for which MS patients may have effect of fampridine treatment.</p>
<b>Design and Methods</b>	<p>The present study is a prospective cohort study. MS patients are recruited from the sclerosis clinics at OUH and Southern Jutland, and are selected on the basis of current criteria for fampridine treatment. Patients' regular walking tests are expanded to also include UST and collection of blood and urine samples during the first visit, after 14 days and after 1 year. Patients who fail to achieve the effect of fampridine persist in the trial as untreated controls.</p>
<b>Primary variables</b>	<p>Muscle strain, gait function, biomarkers (neurofilament, cytokines, chemokines, etc.)</p>
<b>Expected clinical impact:</b>	<p>Validation of UST to clinical assessment of MS patients could assist in determining which MS patients may benefit from fampridine treatment, at what point of the disease course fampridine treatment may be effective, monitor treatment response and/or disease progression independent of fampridine treatment. Furthermore, new opportunities for diagnostic and prognostic biomarkers could open from the analysis of blood and urine samples hence, serve as potential targets for future treatments.</p>

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