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ABSTRACT BOOK

Danish Comprehensive Cancer Center

DANSKE MULTIDISCIPLINÆRE CANCER GRUPPER DMCG.dk

Indhold

Personalised medicine, biomarkers and diagnostics: Poster #1-30

Personalised medicine, biomarkers and diagnostics

#1 Er vi klar til translationel forskning baseret på data fra Dansk Gynækologisk Cancer Database og materialer og data fra Dansk CancerBiobank?

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Abstract
Introduktion
Der er ingen kendskab til i hvilket omfang der eksisterer korresponderende kliniske data og data om biologiske materialer fra patienter med gynækologisk kræftsygdom. Personlig medicin forudsætter viden fra biomarkørundersøgelser, således kræves både kliniske data samt mulighed for biologiske materialer med tilhørende præ-analytiske data. Formålet er at undersøge dækningsgraden af biologisk materiale i Regionernes Bio- og GenomBank (RBGB) for patienter med primær ovariecancer (tubae, peritoneal og ovarie) registreret i Dansk Gynækologisk Cancer Database (DGCD) i perioden 2015 - 2018.

Materialer og metoder
Opgørelse er baseret på udtræk fra DGCD og RBGB. Deskriptiv statistik er anvendt (SAS v 9.4).

Resultater
I alt er 2.182 kvinder registreret i DGCD med en primær ovariecancer diagnose i perioden. Ved samkøring ses, at der i RBGB findes biologisk materiale fra hhv. 322 (70%, 2018), 399 (70%, 2017), 403 (70%, 2016) og 323 (56%, 2015) patienter. For i alt 1.069 patienter findes blod (49%) og for 821 patienter findes væv (38%). Der findes korresponderende blod og væv på i alt 443 patienter (20%). Resultaterne repræsenterer en national en dækningsgrad på biologisk materiale på 66%. Yderligere resultater fra kobling af kliniske data til detaljerede biobanksdata vil blive præsenteret.

Konklusioner
Biologiske materialer i RBGB kan både anvendes til patientens nuværende og fremtidige behandling samt til kommende forskning, som kan danne grundlag for ny individualiseret behandling. Opgørelsen viser, at fremtidens projekter kan bruge disse to kilder til translationel forskning. Der bør forsat være fokus på at sikre både kliniske men også biologiske data/materiale for at sikre fremtidige mulige molekylære undersøgelser baseret på nationale udtræk. Med strategien for personlig medicin er det vigtigt at sikre optimalt biologisk materiale som kan danne basis for både patientens personlige behandling og forskning til at generere viden og bidrage til personlig medicin.

Personalised medicine, biomarkers and diagnostics

#2 Can HPV be measured in the blood of cervical cancer patients?

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Abstract
Introduction
HPV is the main cause of cervical cancer, and even though current techniques can detect the virus in tissue samples from patients with HPV related cervical cancer, no stable method has yet been developed to detect the virus by other means. This study hypothesises that HPV DNA may be released into the bloodstream from tumour cells, and that these fragments of HPV DNA can be measured in blood samples from patients.

Materials and methods
Blood samples from patients diagnosed with cervical cancer at Aarhus and Odense University Hospital (June 2018 to December 2020) are collected. A baseline sample is collected before treatment, and follow-up samples are collected during and after treatment for up to two years.

Results
The study is ongoing, and currently we have results on blood samples from the first ten cervical cancer patients; four with localised cervical cancer (stage lB), who have undergone surgery, and six with disseminated cervical cancer (> stage lB), who have received radio- and chemotherapy. Analyses have shown that HPV DNA can be qualitatively and quantitatively measured in blood samples from patients with disseminated disease, and analyses on follow-up blood samples have shown that HPV DNA quantity decreases during treatment. For patients with localised cancer, HPV DNA has not been detectable.

Conclusions
DdPCR can detect HPV DNA in blood samples from patients with disseminated cervical cancer, and preliminary results suggest that an HPV DNA measurement before treatment correlates to disease stage. For patients who develop a disease recurrence, we expect to see an increase in HPV DNA prior to this, and by analysing follow-up blood samples, we may have found a method to predict a recurrence, enabling us to start treatment early. Since HPV also causes other cancer types, we expect the method to be applicable in these cancers too.

Personalised medicine, biomarkers and diagnostics

#3 HOXA9 methylation in circulating tumor DNA as a prognostic biomarker in patients with platinum-resistant recurrent ovarian cancer

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Abstract
Introduction
Up to 80% of the patients with ovarian cancer (OC) will despite primary response to treatment experience recurrence of disease. Recurrent OC remains a challenge with few or no treatment options.
Aberrant DNA methylation is observed in early cancer development and can be detected in plasma as circulating tumor DNA (ctDNA). Methylation of the HOXA9 gene has been found in plasma of the majority of patients with OC, it is however, not found in blood from healthy individuals. The aim of this study was to evaluate if HOXA9 methylated ctDNA could predict outcome and identify patients who can benefit from palliative chemotherapy.

Materials and methods
Plasma from 27 patients with platinum-resistant OC was analyzed by digital PCR with a HOXA9 methylation-specific assay at baseline and before cycle two. The fractional abundance of HOXA9 methylated ctDNA was calculated and the patients with values increasing above the 95% confidence interval of baseline values was compared with patients having stable or decreasing values. The primary endpoint was progression free survival (PFS).

Results
At baseline 22 patients (81.5%) had measurable HOXA9 methylation in plasma. Patients (N=4) with a significant increase in HOXA9 methylated ctDNA after the first cycle had a median PFS of 1.4 months compared to 5.4 months in patients (N=23) with stable or decreasing HOXA9 (p=0.0019). Nine patients were negative for HOXA9 methylated ctDNA before cycle two. The median PFS in this group was 9 months compared to 2.6 months for patients (N=18) with measurable HOXA9 at second cycle (p=0.001).

Conclusions
The study demonstrated that an increase in HOXA9 methylated ctDNA could be used as an early marker to predict poor outcome in platinum-resistant OC and allow for early discontinuation of an ineffective treatment. Furthermore, absence of HOXA9 methylated ctDNA was prognostic favorable indicating the potential to identify patients who can benefit from palliative chemotherapy.

Personalised medicine, biomarkers and diagnostics

#4 Blood natural killer cells as a new, independent prognostic factor in recurrent ovarian cancer

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Abstract
Introduction
Recurrent ovarian cancer (OC) is challenged by poor prognosis. Natural killer (NK) cells are a subset of lymphocytes with antitumor capabilities yet the clinical significance of this cell type remains unclear. The study aimed to investigate the prognostic value of blood NK cells in recurrent ovarian cancer.

Materials and methods
Patients receiving chemotherapy for recurrent OC were included (N=72). Blood samples were drawn before treatment cycles. NK cells were quantified by flow cytometry and NK cell activity was measured by the NK Vue® assay using interferon gamma production as read out. Overall survival (OS) was the primary endpoint.

Results
Patients with low vs high NK cell count at baseline (cut off 184 cells 109/l based on reference values from Bisset et al, Eur J Haematol. 2004;72(3):203-212) had a median OS of 8.0 months vs 13.2 months (p=0.0451). A similar prognostic impact was found before 2nd treatment cycle where patients with low vs high NK cell count had a median OS of 6.1 months vs 17.3 months (p<0.0001). Similar results were obtained using median values as cut offs. No significant correlation was found regarding NK cell activity and OS. In multivariate Cox regression analysis NK cell count at both baseline and 2nd treatment cycle remained independent markers of favorable prognosis with adjusted hazard ratios (HR) of 0.38 (p=0.008) and 0.19 (p<0.0001), respectively.

Conclusions
High level of NK cells is associated with favorable OS, and may be a new favorable factor in recurrent OC. This could influence future chemotherapy strategy and support research regarding NK cell based treatment.

Personalised medicine, biomarkers and diagnostics

#5 Plasma miRNA as potential biomarkers for ovarian cancer in women with a pelvic mass

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Abstract
Introduction
Ovarian cancer (OC) is diagnosed at late stage in 65% of all cases, impacting on a poor overall survival for the patient. Predictable diagnostic markers for differentiating between benign and malignant pelvic masses are still a clinical challenge with unmet needs. Here, we chose a non-invasive screening approach by profiling plasma miRNA in individuals with a pelvic mass.

Materials and methods
This study was carried out in plasma samples from a total of 190 women with a benign (n= 95) or malignant (n= 95) pelvic mass. Quantitative RT-PCR analysis was performed in a panel of 48 OC-associated miRNA's. Further validation was implemented on an independent cohort (benign= 95 and malignant= 95).

Results
We found 6 miRNA's (miR-200c-3p, miR-221-3p, miR-195-5p, miR-21-5p, miR-451a, and miR-484) associated with late stage OC (AUC> 0.60). Among those, miR-200c-3p and miR-221-3p showed the best predictive accuracy (AUC= 0.78 and 0.65, respectively), validated by multiple statistical analyses. None of the miRNA's individually performed better than CA-125 measurements alone (AUC= 0.92). However, a combination of all 6 miRNA's and CA-125 showed an improved prediction of malignant cases (AUC= 0.96). Furthermore, such findings were confirmed on our second independent cohort, where combined miRNA/CA-125 showed a similar diagnostic efficiency.

Conclusions
In conclusion, our results showed consistent plasma miRNA profiles with the potential to identify risk markers between benign pelvic mass and late stage OC. The combination of miRNAs with CA-125 levels outweighed the performance of CA-125 alone, indicating that such combination may improve early detection of OC. Hereof, we next seek to validate these findings in individuals with early stage OC.

Personalised medicine, biomarkers and diagnostics

#6 Predicting chemosensitivity in ovarian cancer patients using the IndiTreat test

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Abstract
Introduction
Treatment of ovarian cancer is surgery combined with platinum/taxol-based chemotherapy. 20% of the patients are resistant to and have no effect of the chemotherapy. One approach, which may increase treatment efficacy, is to test chemosensitivity of cancer cells obtained from the patient's tumor. 3D cultures represent a promising method for modelling patient tumors in vitro1,2. The aim of this study was to create 3D micro-tumors of ovarian cancer cells and to examine their growth and chemosensitivity.

Materials and methods
Tissue was collected from 27 ovarian cancer patients. Cancer cells were released by collagenase and transferred to a StemPro® growth medium and incubated for 3-71. 3D micro-tumors were added to an IndiTreat screening array containing concentration gradients of carboplatin, topotecan, treosulfan, docetaxel and cisplatin. The arrays were screened on day 0, 4, 7 and 10. Dose response curves and ED50 values were plotted to evaluate drug sensitivity.

Results
3D cultures were established with a success rate of 85%: 14 ovarian biopsies and 13 omental biopsies. Chemosensitivity testing for carboplatin, topotecan, treosulfan, docetaxel and cisplatin was performed on 5 patients. Significant difference between chemosensitivity was observed. Highest sensitivity towards carboplatin was seen in patient (Reg81). Two patients (Req79 and Req80) showed relative high sensitivity to topotecan and treosulfan, while patient (Reg78) showed relative low sensitivity. Growth rate varied, and the highest growth rate was seen in patient (Req81).

Conclusion
3D cultures of ovarian cancer cells represent a promising in vitro model for predicting chemosensitivity and thus personalizing therapy. We can establish 3D cultures from ovaries and omentum with high success rate, and chemosensitivity and growth differ between patients. A future study will evaluate if 3D functional chemosensitivity screening can predict outcome of chemotherapy in ovarian cancer patients.

Personalised medicine, biomarkers and diagnostics

#7 Gene co-expression network analysis of precursor lesions in familial pancreatic cancer

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Abstract
Introduction
High grade Pancreatic Intraepithelial Neoplasia (PanIN) are aggressive pre-malignant lesions, associated with risk of progression to pancreatic ductal adenocarcinoma (PDAC). A depiction of dysregulated gene activity in high grade PanIN lesions in patients with Familial Pancreatic Cancer (FPC) can characterize the molecular events during the progression of familial PanIN lesions to PDAC.

Materials and methods
We performed weighted gene co-expression network analysis (WGCNA) to identify genes associated with FPC related PanIN lesions using microarray gene expression profiles from 13 pancreatectomy specimens with PanIN lesions (stage 2-3) from FPC patients, 6 pancreatectomy specimens with PDAC from sporadic pancreatic cancer (SPC) patients, and 4 specimens of normal donor pancreatic tissue.

Results
WGCNA detected co-expressed genes as modules/clusters and summarized each module by a representative gene: the module eigengene. Correlation analysis identified 2 up-regulated modules or co-expressed gene clusters ($p<1e-05$) and 2 down-regulated modules ($p<1e-05$) in FPC compared to SPC. The upregulated gene modules include 5 significant genes ($p<1e-06$) consisting of FMO4, FMO2, CORO1B, TPP1, CIB4. The down-regulated gene modules include 170 significant genes ($p<1e-06$), among them 13 highly significant genes ($p<1e-10$) consisting of: COL10A1, SAMD9, PLPP4, COMP, POSTN, IGHV4-31, THBS2, MMP9, FNDC1, HOPX, TMEM200A, INHBA, SULF1. The down-regulated modules are significantly enriched for Gene Ontology (GO) terms functionally related to: extracellular structure organization, cell-substrate junction, focal adhesion, extracellular vesicle, etc.

Conclusions
The differential molecular pathology of FPC and SPC involves multiple co-expressed gene clusters significantly enriched for GO terms including functions in extracellular activities and focal adhesion. These findings provide reference for genomic characterization of the progression of PanIN lesions to PDAC in FPC.

Personalised medicine, biomarkers and diagnostics

#8 Peptide Receptor Radionuclide Therapy in Gastroenteropancreatic NEN G3: a multicenter cohort study

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Abstract
Introduction
Peptide receptor radionuclide therapy (PRRT) is an established treatment of metastatic neuroendocrine tumors grade 1-2 (G1-G2). However, its possible benefit in high-grade gastroenteropancreatic (GEP) neuroendocrine neoplasms (NEN G3) is unknown. We therefore aimed to assess the benefits and side effects of PRRT in patients with

GEP NEN G3.

Materials and methods
We performed a retrospective cohort study at 12 centers to assess efficacy and toxicity of PRRT in patients with GEP NEN G3. Outcomes were response rate, disease control rate, progression-free survival (PFS), overall survival (OS) and toxicity.

Results
We included 149 patients (primary tumor: pancreatic n=89, gastrointestinal n=34, unknown n=26). PRRT was 1st-line (n=30), 2nd-line (n=62) or later line treatment (n=57). Of 114 patients evaluable, 1% had complete response, 41% partial response, 38% stable disease and 20% progressive disease. Of 104 patients with documented progressive disease before PRRT, disease control rate was 69%. The total cohort had median PFS of 14 months and OS 29 months. Ki-67 21-54% (n=125) vs. Ki-67≥55% (n=23): PFS 16 vs. 6 months ($p<0.001$) and OS 31 vs. 9 months ($p<0.001$). Well (n=60) vs. poorly-differentiated NEN (n=62): PFS 19 vs. 8 months ($p<0.001$) and OS 44 vs.19 months ($p<0.001$). Grade 3-4 hematological or renal toxicity occurred in 17% of patients.

Conclusions
This large multicenter cohort of patients with GEP NEN G3 treated with PRRT demonstrates promising response rates, disease control rates, PFS and OS as well as toxicity in patients with mainly progressive disease. Based on these results, PRRT may be considered for patients with GEP NEN G3.

Danish Neuroendocrine Tumor Society, DANETS Supported by DCCC -Danish Comprehensive Cancer Center.

Personalised medicine, biomarkers and diagnostics

#9 Immunohistochemical profiles in benign vs. malignant resected insulinomas

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Abstract
Introduction
Ninety percent of insulinomas are benign. There are no immunohistochemical criteria that can distinguish a benign from a malignant insulinoma.

Aim
We aimed to evaluate the immunohistochemical profiles of benign and malignant insulinomas.

Materials and methods
The cohort (n=80, age 52 ± 16 years) was recruited (1989-2014) from 2 ENET Centers of Excellence. All patients with a resected insulinoma were included. Immunohistochemistry evaluation was performed by central reading (BF). Results were divided in 3 groups: Negative (<5% of cells with positive staining), intermediate (5-50%) and positive (>50%).

Results
Seven patients had a malignant insulinoma. Six had metastatic disease at time of diagnosis, whereas 1 developed metastases during follow-up. Five were stage IV and 2 were stage IIB. Malignant tumors were larger than benign 35 (10-80) vs. 14 (7-35) mm (p=0.04), with increased Ki-67 proliferation index (median (range)) 6% (3-100) vs. 3% (1-15) (p=0.08). Eighty-six percent of benign tumors stained for insulin vs. 43% of malignant tumors (p=0.015). The corresponding numbers for pro-insulin and UMB1 were 98% vs. 40% (p<0.001) and 42% vs. 80% (p=0.24). Three of 7 malignant tumors were negative for both insulin and proinsulin vs. none in the benign group (p<0.001). Positive staining for glucagon was observed in 40% of malignant tumors vs. none of the benign tumors (p<0.001). All tumors stained positive for synaptofysin and chromogranin A. Amyloid, somatostatin, pancreatic peptide and CD117 were negative in the vast majority of tumors with no differences between benign and malignant types.

Conclusions
Nine percent of the insulinomas were malignant. Malignant insulinomas were larger than benign tumors, with reduced staining for insulin and pro-insulin and increased staining for glucagon. Lack of staining for pro-insulin/insulin and positive staining for glucagon might be a sign of poor differentiation and thereby associated with malignant behavior.

Personalised medicine, biomarkers and diagnostics

#10 Assessment of TP53 Status using Next Generation Sequencing and Immunohistochemistry in G3 Neuroendocrine and Mixed Neuroendocrine-Nonneuroendocrine Neoplasms

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Abstract
Introduction
Neuroendocrine G3 neoplasms and Mixed Neuroendocrine-Nonneuroendocrine neoplasms (MiNEN) with Ki67>20% referred to the Neuroendocrine Tumor Centre at Rigshospitalet since Oct. 2015 was analysed using Next Generation Sequencing (NGS). In the cohort, that comprise 294 patients, the concordance between TP53 mutational status obtained using NGS and conventional p53 immunohistochemistry was assessed.

Materials and methods
TP53 mutation status was assessed on FFPE material using AmpliSeq Cancer Hotspot Panel v2 (ThermoFischer) and conventional immunohistochemistry (anti-p53; DO-7, Roche). TP53 mutation data and p53 immunostains were available for 233 neuroendocrine G3 and MiNEN samples. In this study normal p53 was defined as positivity in <20% of tumor nuclei and abnormal p53 was defined as both overexpressed (>20%) or completely absent.

Results
Concordance analysis revealed an overall agreement of (197/233) 85% between TP53 mutational status assessed using NGS and p53 status using immunostaining. For the 36 discordant samples; 24 showed strong immunostaining (>40%) but no mutation, 6 showed absent immunostaining but no mutation, 3 showed immunostaining (around 30%) but no mutation and finally 3 showed normal staining but harbored a TP53 mutation.

Conclusions
This study underlines the need to assess the mutational status of an important biomarker as p53 using different technologies given that they separately harbor different pitfalls. The importance of correct p53 status assessment has recently been emphasized by the involvement of p53 mutational status in the subdivision of neuroendocrine G3 neoplasms into well and poorly differentiated groups, which is crucial for the treatment of these tumors.

Personalised medicine, biomarkers and diagnostics

#11 Incidence and Clinicopathological Features of Colorectal Neuroendocrine Carcinomas and Mixed Neuroendocrine-Nonneuroendocrine neoplasms

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Abstract
Introduction
Colorectal neuroendocrine carcinomas (NEC) are rare, but aggressive tumors with a reported incidence of 0.1-3.9% of all colorectal malignancies. Morphologically most have features of a neuroendocrine tumor. However, some resemble an adenocarcinoma and are primarily diagnosed as such.

Aim
To find the incidence and study clinicopathological features of colorectal NEC and Mixed Neuroendocrine-Nonneuroendocrine Neoplasms (MiNEN).

Materials and methods
Between April 2015 and September 2016, all the resected colorectal carcinomas were stained for synaptophysin, chromogranin and Ki67. Next generation sequencing, detecting the most common mutations in NEC was performed on all NEC and MiNEN cases. Their pathology and clinical features were reviewed.

Results
398 cases were included, of which 11 cases of NEC (2.8%) and 3 cases (0.7%) of MiNEN were found. Average age was 75 years (range 54-88 years) including 10 males (71.4%) and 4 females (28.6%). The most common location of the tumor was right sided colon (n=9) followed by rectosigmoid (n=5). Immunohistochemically all tumors showed positive reaction for synaptophysin, while most of the tumors were negative for chromogranin (71%). Ki67% range was 70-100%. Most tumors had advanced clinical stage at the time of presentation with UICC stage 3 (n=8) and stage 4(n=1). Mutations were seen in most cases including KRAS mutation (5 of 11 cases) and BRAF V600E mutation (2 of 11 cases).

Conclusions
Although colorectal NECs are rare, it is important to detect neuroendocrine features in an otherwise suspected adenocarcinoma. The threshold for performing immunostaining for neuroendocrine markers should be low. These tumors are often disseminated at the time of diagnosis and have a dismal prognosis, but may be amenable for targeted treatment. Keywords: colorectal, neuroendocrine carcinoma, minen, pathology.

Personalised medicine, biomarkers and diagnostics

#12 microRNAs in Neuroendocrine Neoplasms

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Abstract
Introduction
Neuroendocrine Neoplasms (NENs) are slow growing tumors originating from the neuroendocrine cells in the gastro-intestinal tract and pancreas. MicroRNAs (miRNA) are small non-coding RNAs that modulate posttranscriptional gene expression involved in central roles in cancer and can be used as biomarkers. We wanted to investigate miRNA expression in NENs and in plasma.

Materials and methods
miRNA expression in 6 NEN primary tumors, 6 NEN metastases and 4 normal intestinal tissues was characterized by miRNA arrays and validated by ISH and qPCR. miRNA induced mRNA expression by transfecting cell lines with target miRNAs was characterized by mRNA expression arrays and validated by IHC. miRNA/mRNA interactions were validated by western blot and luciferase assay. Growth assays was performed by transfecting miRNAs or siRNAs in the NCI-H727 and CNDT2.5 carcinoid cell lines. miRNA expression in plasma from 10 normal and 10 patients with Neuroendocrine colon carcinomas was identified by NGS and analyzed for enrichment in specific GO terms.

Results
miR-129-5p and the let-7 family were down-regulated in NENs and inhibited growth of the carcinoid cell lines. EGR1 and G3BP1 were identified as miR-129-5p targets and found robustly expressed in NETs by IHC. Knockdown of EGR1 and G3BP1 mimicked the growth inhibition induced by miR-129-5p. let-7 inhibition increased expression of HMGA2, BACH1

and MMP1 all involved in metastases. PCA and heat-map analysis of differentially expressed plasma miRNAs discriminated between the groups. GO term analysis revealed differentially expressed miRNAs involved in angiogenesis, cell growth and receptor and chemokine signaling.

Conclusions
miR-129-5p and the let-7 family are down-regulated in NENs and their targets contribute to the growth and metastatic potential of NENs. miRNA plasma expression profiles discriminate between controls and colon NECs and circulating miRNAs are involved in hallmarks of cancer.

Personalised medicine, biomarkers and diagnostics

#13 Prospective study of chromogranin A as a predictor of progression in patients with pancreatic, small intestinal and unknown primary neuroendocrine tumors.

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Abstract
Introduction
Retrospective studies are conflicting but most report that an increase in plasma chromogranin A (CgA) predicts tumor progression in neuroendocrine tumor (NET) patients. Prospectively we investigated if changes in plasma CgA was associated with tumor burden changes in NET patients with disseminated disease.

Materials and methods
We included 239 patients from five NET centers between 2010-2013. CgA needed to be measured within six weeks of a CT or an MRI in a patient undergoing at least two scan examinations performed with 1-24 months. In a post-hoc analysis, CgA measured 3-6 month prior to the CT/MRI was analyzed. Changes in tumor size were evaluated by RECIST1.1. A 25% change in CgA was chosen to discriminate between increased, decreased or unchanged levels.

Results
In 671 events (2 CT/MRI scans and 2 corresponding CgA measurements) we found a weak positive correlation between the RECIST 1.1 responses and change in plasma CgA levels from baseline (Spearman's rank correlation coefficient: 0.15; $p<0.05$). Of 304 events in the post-hoc analysis, 58 showed progression, 228 stable disease, and 18 regression and the median change in CgA was +19%(IQR:57-(-20)), -12%(+23-(-38)) and -73%(-55-(-83)), respectively. The correlation coefficients for all sites were 0.17($p=0.003$); and 0.16($p=0.07$), 0.18($p=0.04$); and 0.20($p=0.21$) for small intestinal NETs (n=137 events), pancreatic NETs (n=123) and unknown primary (n=40), respectively. In the 58 events showing tumor progression, sensitivity and specificity of an increased CgA concentration were 36% and 82%, respectively with positive and negative predictive values of 32% and 85%, respectively.

Conclusions
In this prospective study of GEP-NET patients we observed only a weak association between change in plasma CgA and change in tumor burden. CgA as a single biomarker was inadequate to predict tumor progression.

Personalised medicine, biomarkers and diagnostics

#14 FDG-PET for risk-stratification of patients with neuroendocrine neoplasms: a prospective cohort study

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Abstract
Introduction
Accurate grading of patients with neuroendocrine neoplasms (NENs) is essential for risk stratification and optimal choice of therapy. Currently, grading is based on histologically assessed degree of tumor proliferation according to the WHO classification. The aim of the present study was to assess the long-term prognostic value of FDG-PET imaging for risk stratification of NENs and compare it with grading (WHO 2010 classification).

Materials and methods
We conducted a prospective, single-center cohort study evaluating the prognostic value of FDG-PET imaging and compared it to histological grading. Patients (n = 166) of all grades and with histologically confirmed NENs of gastro-entero-pancreatic origin were enrolled. The primary end point was overall survival (OS). Progression-free survival (PFS) was a secondary end point.

Results
Analysis of the whole cohort revealed that a positive FDG-PET was associated with a poorer OS than a negative FDG-PET (Hazard Ratio (HR): 3.8; 95% Confidence interval (CI): 2.4 – 5.9; $p < 0.001$). In WHO grade 1 and 2 patients (n = 140) a positive FDG-PET was the only identifier of high-risk for death (HR: 3.6; 95% CI, 2.2 – 5.9; $p < 0.001$). In multivariate analysis, entering FDG-PET and WHO grading, only FDG-PET had independent prognostic value.

Conclusions
FDG-PET is useful for risk stratification of all NEN grades and is superior to histological grading (WHO 2010 classification). FDG-PET could differentiate WHO grade 1 and 2 tumors into low and high-risk groups. In the selection of therapy and for risk stratification of NEN patients FDG-PET status should be considered.

Personalised medicine, biomarkers and diagnostics

#15 FLT-PET and FDG-PET/CT for the detection of relapse following definitive radiotherapy in lung cancer. Preliminary results

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Abstract
Introduction
Diagnosing relapsed lung cancer after radiotherapy is challenging. CT and 18F-fluorodeoxyglucose (FDG)-PET/CT have a low specificity in this setting, and invasive procedures might be unfeasible due to poor lung function, small tumor size or difficult location.
18F-fluorothymidine (FLT)-PET is considered more cancer specific compared to FDG-PET. Therefore, we investigated if FLT-PET could improve diagnosis of relapse in patients treated with radiotherapy.

Materials and methods
Lung cancer patients suspected for relapse after radiotherapy were included in this prospective clinical study.
FDG-PET/CT and FLT-PET/low-dose-CT were conducted within one month.
PET scans were evaluated visually, blinded for previous PET-scans. Lung lesions were evaluated as malignant, benign or inconclusive. FDG- and FLT-PET from the same patient were evaluated at least three months apart.
Sensitivity and specificity were analysed for FDG-PET/CT and FLT-PET. The reference standard was based on histology if available otherwise on independent review of subsequent imaging, conference decisions, and clinical course within 6 months after FLT-PET.

Results
We present the results from the first 28 patients treated with definitive radiotherapy (45-66 Gy/30-33 fractions) for non-small cell lung cancer or small cell lung cancer. Twenty-seven patients received concurrent chemotherapy.
FLT-PET/CT was performed 34-581 days after radiotherapy (median 250 days). FDG- and FLT-PET/CT were conducted 1-22 days apart (median 7 days).
During follow up 16 patients had relapse.
The sensitivity of FDG-PET was 88 % (95 % CI: 62-98 %), and the specificity was 50 % (21-79 %).
The sensitivity of FLT-PET was 56 % (30-80 %), and the specificity was 100 % (74-100 %).

Conclusions
With a specificity of 100 %, FLT-PET is promising for non-invasive diagnosis of relapse after radiotherapy with the potential to obviate invasive procedures in some patients. The sensitivity of FLT-PET was low; therefore FLT-PET cannot stand alone.

Personalised medicine, biomarkers and diagnostics

#16 Neurofilament light chain as biomarker for brain metastasis in lung cancer patients

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Abstract
Introduction
Brain metastases are feared complications in cancer patients. Neurosurgical resection and stereotactic radiosurgery are preferred treatment modalities, but only available if there are limited metastatic lesions. Neurofilament light chain (NfL) is a neuron-specific protein released following neuronal damage. As brain metastases in lung cancer patients show an infiltrative growth pattern into the adjacent brain parenchyma, neuronal damage is expected with a release of NfL. Here, we explored if the serum NfL level can be used as a diagnostic or predictive biomarker of brain metastases in lung cancer patients.

Materials and methods
Serum was collected from 64 lung cancer patients: 39 with brain metastases and 25 without brain metastases. NfL was quantified in serum by use of the NF-light® assay on the ultra-sensitive Simoa™ HD-1 platform. Median NfL levels were compared by the Mann-Whitney rank sum. The diagnostic value of NfL was estimated by area under the curve (AUC).

Results
In 39 lung cancer patients with brain metastases, a median NfL level of 35 pg/L was significantly higher than the NfL level of 16 pg/L observed in patients without brain metastases ($p<0.0001$). Furthermore, the diagnostic value of NfL demonstrated an AUC of 0.77 (0.66 – 0.89), which is considered a fair separation. In 13 patients, NfL was measured in samples collected months prior to diagnose of the brain metastases. In 12 out of these 13 patients, the NfL level was increased at time of the brain metastasis diagnosis compared to time of lung cancer diagnosis.

Conclusions
In this study, NfL is a fair separator of patients with brain metastasis compared with patients without. Furthermore, elevated levels of NfL can be measured months prior to the clinical diagnosis of brain metastasis and levels of NfL are increasing during the development of the brain metastasis. This implies that NfL could be a predictive marker of brain metastasis.

Personalised medicine, biomarkers and diagnostics

#17 Day-to-day and semidiurnal biological variation of total cell-free DNA in healthy subjects and lung cancer patients

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Abstract
Introduction
Cell-free DNA (cfDNA) has been extensively studied as a potential biomarker in cancer patients. Especially, longitudinal monitoring of cfDNA levels, either by monitoring of the total cfDNA level or the circulating tumour DNA as a fraction of the total cfDNA level, has attracted much attention. Yet, in order to make clinical decisions based on cfDNA measurements, it is essential to understand the magnitude of inherent biological variation of cfDNA so as to not confuse them with changes that actually represent a clinically relevant status. Here, we evaluated the magnitude of biological variation of cfDNA in healthy subjects and lung cancer patients.

Materials and methods
Plasma samples were collected from 33 healthy subjects and 10 lung cancer patients for 3 days in a row as well as during 1 day. CfDNA was extracted from plasma and quantified using digital droplet PCR targeting the reference gene EIF2C1. The within-subject variation (CVI) and between-subject variation (CVG) were estimated using linear mixed effects models.

Results
The mean value of cfDNA was 1500 copies/ml plasma and significantly lower than the mean level in the lung cancer patients (7472 copies/mL, p=0.026). CVI (24%) was lower than CVG (30%). A change in two serial measurements had to exceed 70% to be classified as significant. There was no difference in cfDNA levels from day-to-day ($p > 0.61$), however there was a significant decrease in cfDNA levels during the day in healthy subjects ($p<0.01$).

Conclusions
The biological variation was considerable on both the within-subject and between-subject levels. The mean level of cfDNA declined significantly during the day suggesting that the exact time of blood draw affects the cfDNA level. Further, the variation will significantly affect tumour allele frequencies and extreme caution must therefore be taken when interpreting these in longitudinal monitoring. The data offer a substantial contribution to the interpretation of the clinical significance of cfDNA.

Personalised medicine, biomarkers and diagnostics

#18 Implementering af analyser til detektion af mutationer i cellefrit DNA fra patientplasma i et klinisk biokemisk rutinelaboratorium

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Abstract
Introduktion
Cellefrit DNA (cfDNA) findes i blodbanen som følge af apoptose, nekrose og sekretion fra kroppens celler. Ved cancer kan kræftforårsagende og andre klinisk relevante mutationer påvises i cfDNA fra tumorceller. Et behandlingsregimes virkning kan afhænge af disse mutationer. Yderligere kan målinger over tid informere om tumorens udvikling, f.eks. om den vokser i størrelse og om et skift af behandlingsregime er nødvendigt. cfDNA oprenses fra blodprøver og analysen er derfor ikke-invasiv. En kvantitativ analyseplatform med lav detektionsgrænse er ønskværdig for at mutationer kan identificeres, selvom kun minimale mængder af tumor-cfDNA er til stede i patientens blod. Desuden skal metoden være tilstrækkelig robust til, at den kan anvendes rutinemæssigt. Droplet digital PCR (ddPCR) opfylder disse krav. Ved at adskille DNA-molekylerne inden opformeringen af DNA'et opnås en yderst lav detektionsgrænse for kvantiteringen.

Materialer og metoder
cfDNA oprenset fra plasma fra raske individer og kræftpatienter samt DNA oprenset fra cellelinjer blev analyseret med ddPCR for mutationerne BRAF V600E, EGFR T790M samt KRAS G12A, G12C, G12D, G12R, G12S, G12V og G13D. Resultater: Ti analyser blev valideret inkl. ni singleplex analyser og en KRAS multiplex analyse. Analyserne blev grupperet ind i tre forskellige rekvisitioner i laboratorieinformationssystemet og omfatter analyse af hhv. BRAF, EGFR og KRAS. KRAS-rekvisitionen indeholdt en multiplex screeningsanalyse, som ved positivt svar førte til singleplex analyser af de enkelte KRAS-mutationer.

Konklusioner
Implementeringen muliggjorde den kliniske anvendelse af måling af kræftforårsagende mutationer i BRAF, EGFR og KRAS i cfDNA. Analysernes resultater anvendes i forbindelse med diagnostik, overvågning af kræftpatienter under behandling og til overvågning for recidiv efter behandling. Desuden har metoden store potentialer inden for udforskning af kræftforløb; fra før symptomer til efter progression af tumor.

Personalised medicine, biomarkers and diagnostics

#19 Analysis of Plasma Cell-Free DNA by Ultradeep Sequencing in Patients With Stages I to III Colorectal Cancer

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Abstract
Introduction
Novel sensitive methods for detection and monitoring of residual disease can improve post-operative risk stratification with significant impact on patient selection for adjuvant chemotherapy (ACT), ACT duration, intensity of radiological surveillance, and ultimately outcome for patients with colorectal cancer (CRC). We investigated the prognostic and predictive impact of longitudinal ultra-deep sequencing of cell-free DNA in CRC patients.

Materials and methods
In this prospective, multicenter cohort study, ctDNA was quantified in the preoperative and postoperative settings of stages I to III CRC by personalized multiplex, PCR-based, next generation sequencing. The study enrolled 130 patients at the surgical departments of Aarhus University Hospital, Randers Hospital, and Herning Hospital. Plasma samples (n = 829) were collected before surgery, postoperatively at day 30, and every third month for up to 3 years.

Results
Pre-operatively, ctDNA was detectable in 89% of patients. Following definitive treatment, longitudinal ctDNA analysis identified 88% of the relapses. At the clinical decision points such as post-operative day 30 for ACT and post-ACT for additional therapy, ctDNA-positive patients were 7 and 18 times more likely to relapse than ctDNA-negative patients (day 30: HR=7.2, 95% CI 2.7-19,0 P<.001; post-ACT: HR=17.5, 95% CI 5.4-56.5, P<.001). In fact, 100% of the patients who were ctDNA-positive after ACT experienced relapse (n=7). Monitoring demonstrated that 30% of ctDNA-positive patients were cleared by ACT. During surveillance after definitive therapy, ctDNA-positive patients were over 40 times more likely to recur than negative patients (HR, 43.5.0; 95% CI, 9.8-193.5; P<.001). In all multivariate analyses, ctDNA status remained an independent predictor of relapse.

Conclusions
Circulating tumor DNA analysis can potentially change the postoperative management of CRC by enabling risk stratification, ACT monitoring, and early relapse detection.

Personalised medicine, biomarkers and diagnostics

#20 The effect of surgical trauma on postoperative circulating free DNA levels in patients with colorectal cancer – implications for studies of circulating tumor DNA

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Abstract
Introduction
Trauma caused by surgery is associated with an increase in cell-free DNA (cfDNA) levels, which complicates efforts to identify circulating tumor DNA (ctDNA), an emerging tool for residual disease detection. We wish to explore the nature of surgically induced cfDNA shedding to optimize blood sampling for ctDNA detection.

Materials and methods
Using digital droplet PCR, we quantified cfDNA levels in plasma samples drawn before and up to six weeks after surgery in 220 patients undergoing colorectal cancer surgery. The fold change of postoperative cfDNA concentrations compared to preoperative was monitored. For a subset of patients cfDNA fragments were profiled and quantified and compared directly in each postoperative sample.

Results
Total cfDNA levels were elevated 1.7-3.9-fold up to four weeks after surgery. The elevation was significantly higher for patients undergoing laparotomy compared to laparoscopy (P=0.001). When dissecting whether the elevation was due to short (nucleosomal size, as normal cfDNA) or long (>1Kb) cfDNA fragments, a significant increase was seen in the level of short cfDNA fragments (8.1-fold, P=0.01) but not long fragments (1.3-fold, P=0.31).

Conclusions
Due to the surgically induced trauma, postoperative cfDNA levels were elevated for up to four weeks. The size profile of trauma-induced cfDNA was similar to that of normal cfDNA. The effects of surgery on cfDNA levels thus cannot be removed by size selection methods. To minimize the effect of trauma-induced cfDNA on ctDNA detection, the timing of blood sampling should be considered carefully.

Personalised medicine, biomarkers and diagnostics

#21 MethCORR: DNA Methylation-based Characterization, Classification and Prognostication of Colorectal Cancer using Archival Formalin-fixed, Paraffin-embedded Tissue

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Abstract
Transcriptional subclassification has potential to resolve the extensive inter-tumor heterogeneity of colorectal cancer (CRC) and improve patient management. Yet, robust transcriptional profiling cannot be performed using formalin-fixed, paraffin-embedded (FFPE) samples, which complicates clinical testing. Here we present MethCORR, an approach that allows uniform molecular characterization and classification of fresh-frozen and FFPE samples. MethCORR identifies genome-wide correlations between RNA expression and DNA methylation in fresh-frozen samples. This information is used to infer RNA expression in FFPE samples from their DNA methylation profiles. MethCORR was applied to methylation profiles from 877 fresh-frozen and FFPE samples and comparative analysis identified the same two major CRC subtypes in four independent cohorts. Furthermore, subtype-specific prognostic biomarkers that better predicted relapse-free survival (HR=2.66, 95% CI [1.70-4.17], p<0.001) than TNM staging and MSI status was identified and validated using DNA methylation-specific PCR assays. The MethCORR approach is general, and may be similarly successful for other cancer types.

Personalised medicine, biomarkers and diagnostics

#22 Artificial intelligence-based assessment of prostate cancer using PET/CT

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Abstract
Introduction
Advanced cancer imaging relies on predominantly visual assessment. The use of artificial intelligence (AI) is expected to change this radically, but AI-based methodologies need validation before clinical implementation. The aim of this study was to compare a fully automated AI-based method to manual measurements for measurement of prostatic PET measures and to study its correlation with post-operative data in patients undergoing radical prostatectomy (RP).

Materials and methods
A convolutional neural network (CNN) was trained for automated measurements in 18F-choline (FCH) PET/CT scans obtained prior to RP in 45 patients with newly diagnosed PCa. Automated values were obtained for prostate volume, maximal standardized uptake value within the prostate (SUVmax), mean standardized uptake value of voxels considered abnormal (SUVmean) and volume of abnormal voxels (Volabn). The product SUVmean x Volabn was calculated to reflect total lesion uptake (TLU). Corresponding manual measurements were performed. CNN-estimated data were compared with the weighted surgically removed tissue specimens and manually derived data and related to clinical parameters.

Results
The mean (range) weight of the prostate specimens was 44 g (20-109), while CNN-estimated volume was 62 ml (31-108) with a mean difference of 13.5 g or ml (95% CI: 9.78 – 17.32). The two measures were significantly correlated ($r=0.77$, $p<0.001$). Mean differences (95% CI) between CNN-based and manually derived PET measures of SUVmax, SUVmean, Volabn (ml) and TLU were 0.37 (-0.01 - 0.75), -0.08 (-0.30 – 0.14), 1.40 (-2.26 – 5.06) and 9.61 (-3.95 – 23.17), respectively. PET findings Volabn, and TLU correlated with PSA ($p<0.05$), but not with Gleason score or stage.

Conclusions
Automated CNN-segmentation provided in seconds volume and simple PET measures similar to manually derived ones. For more accurate and precise measurements, studies applying more highly trained networks are warranted.

Personalised medicine, biomarkers and diagnostics

#23 BoneProst: Prostate cancer and bone biomarkers

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Abstract
Introduction
Prostate cancer (PC) is the most common cancer amongst men in Denmark (4,519 new cases in 2016) and the second most common cause of cancer-related deaths (1,254 deaths in 2016). PC pts frequently develop bone metastases, reducing quality of life and survival. Cancer cells in the marrow trigger elevated bone resorption and an overproduction of weak bone, making cancer cells resistant and causing severe bone disease. Question: Can bone biomarkers (CTX: break-down; PINP: formation) be used for diagnosis and monitoring?

Materials and methods
Group1: 100 newly diagnosed PC pts (without bone metastases) - only base line. Group2a: ~25 PC pts suspected to have bone metastases but with a negative scintigraphy/NaF-PET - only base line. Group2b: 50 pts with newly confirmed bone metastases - follow for 3 years. Group3: 50 PC pts with newly identified castration-resistant PC - follow for 2 years. Primary variables: absolute and delta-values for CTX and PINP, occurrence or progression of bone metastases, and death.

Results
Start of recruitment: September 2017 - status: 157 pts. Preliminary results: Group2b (12 pts): 3 months after castration median CTX levels are significantly elevated by 56% (p=0.0005) while PINP is unchanged (p=0.470). This results in a net bone loss based on CTX/PINP ratio (p=0.014). Group3 (35 pts): 43% of pts have CTX values at baseline that are above the 2x standard deviation cut-off based on Group1 (98 pts). Group3 (28 pts): 28% and 14% respond poorly to zoledronic acid treatment after 1 and 3 months, respectively. Group3 (21 pts): 6-8 months after treatment start 55% show signs of disease progression based on CTX development.

Conclusions
CTX and PINP seem to be promising biomarkers that could be a future powerful supplement for diagnosis and monitoring of PC pts. Our trial is still ongoing and the last patient is expected to leave the trial in 4 years.

Personalised medicine, biomarkers and diagnostics

#24 BoneBio: The variable sensitivity of breast cancer patients to zoledronic acid

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Abstract
Introduction
Breast cancer (BC) is the most prevalent cancer among women in Denmark. BC cells frequently metastasize to bone tissue, where they initiate a “vicious cycle” involving the bone resorbing osteoclasts. This results in local bone loss, increased fracture risk, resistance of cancer cells, a reduced quality of life, and survival.

Questions
Can bone biomarkers (CTX: degradation, PINP: formation) be used for diagnosis and monitoring? Can it detect those patients that are least sensitive to zoledronic acid?

Materials and methods
50 BC patients with newly diagnosed bone metastases (80 years or younger).
Primary variables: absolute and delta-values of CTX and PINP, progression of bone disease, and death.

Preliminary results
Start of recruitment: May 2016 - status: 49/50 pts.

After 3 months of treatment with zoledronic acid the median CTX levels are decreased by 69% from baseline ($p<0.0001$) while median PINP levels are decreased by 62% ($p=0.0008$). But the percent change from baseline after 3 months of treatment varies from +170% to -90% for CTX and from +300% to -92% for PINP, indicating large variations in sensitivity to zoledronic acid among patients. In addition, our results indicate that the 9 patients that have died so far were all amongst the less sensitive. Finally, patients with clinical signs of progression in bone disease show elevated marker levels several months in advance.

Conclusions
Bone biomarkers CTX and PINP seem promising as a complementary tool for diagnosis and monitoring of BC patients with bone metastases. The trial is still ongoing and the last patient is expected to leave the trial in 1 to 3 years. We hope to determine thresholds for PINP and CTX that can be used to detect relapse in bone disease earlier than today. A future routine use of these markers may lead to new individualized treatment strategies improving quality of life and possibly survival.

Personalised medicine, biomarkers and diagnostics

#25 Tolerance-inducing mechanisms modulated by cancer cells – a study on immune regulation in breast cancer

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Abstract
Introduction
Cancer cells exploit multiple mechanisms in order to avoid immune recognition including recruitment of specific regulatory immune cells and expression of immunosuppressive molecules. Within recent years immunotherapy has become an important treatment strategy and shows great potential. However, the success has been limited in cases of breast cancer. The focus of the current project is the importance of the tumor microenvironment in breast cancer, specifically the local immune response with emphasis on genetic and molecular changes of specific immune cell populations in relation to clinical parameters in individual patients with different disease manifestations and progression.

Materials and methods
A retrospective study based upon formalin and paraffin embedded biopsies from patients with breast cancer with at least 5 years follow up. The composition of immune cells present in the tumor stroma is analyzed by immunohistochemistry.
A prospective study based on fresh tumor biopsies and blood samples collected from patients prior to surgery independent on breast cancer subtype, and control samples from healthy donors. Immunohistochemical staining is used to identify subgroups of breast cancer by estrogen and progesterone receptors and HER2 expression. Flow cytometry and magnetic bead-based cell separation techniques are used to characterize and isolate CD56+ Natural Killer cells and CD4+CD25+ regulatory T cells. A comparative analysis of global gene expression changes in the stroma-associated immune cells and cancer cells is performed by transcriptome analysis using Next Generation Sequencing.

Expected result/perspectives
The results are expected to expand our knowledge on how the immune system can be manipulated and exploited for cancer immunotherapy treatment, especially by identification of biomarkers in breast cancer irrespective of the molecular subtype that may predict, whether a patient will benefit or not from specific immunotherapies.

Personalised medicine, biomarkers and diagnostics

#26 Evaluation of PD-L1 expression in BRCA-germline mutated breast cancer

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Abstract
Introduction
Approximately 3-5% of breast cancer patients are BRCA1 or BRCA2 germline mutation carriers. Programmed death ligand-1 (PD-L1) is a transmembrane protein with immune regulatory function, expressed in tumor cells and immune cells. The purpose of this study was to investigate the expression of PD-L1 in BRCA1/2 germline mutated breast cancers and the association of PD-L1 with Estrogen receptor status (ER) and Tumor infiltrating lymphocytes (sTILs).

Materials and methods
Formalin-fixed paraffin-embedded tumor tissue from 411 breast cancer patients with germline BRCA1/BRCA2 mutation were included in this study. Immunohistochemical staining for PD-L1 with VENTANA PD-L1 (SP263) Assay was successfully performed on Tissue Micro Array and full sections from 373 patients. ER positivity was defined as ≥ 1% ER positive nuclear staining. PD-L1 expression was defined as ≥ 1% positive membraneous staining in the tumor cells. sTILs were assessed according to the International Immuno-Oncology Biomarkers Working Group's guidelines.

Results
Fifty-three percent of the tumors were ER positive and PD-L1 positivity was identified in 132 (35%) of the tumors. PD-L1 was significantly associated with BRCA1 ($p<0.0001$), ER negative status ($p<0.0001$), medullary differentiated histology ($p<0.0001$) and sTILs ($p<0.0001$).

Conclusions
In this study we demonstrated a high PD-L1 expression in tumor cells from BRCA germline mutated breast cancers. This is in contrast to previous studies on sporadic breast cancer with the PD-L1 (SP142) Assay. Our results might have an impact on treatment options for BRCA germline mutated breast cancer patients. Further investigation of the correlation between PD-L1 status, subtypes of CD4/CD8 positive sTILs and association with prognosis is in progress.

Personalised medicine, biomarkers and diagnostics

#27 A pilot study of the safety, tolerability, feasibility and efficacy of anti-PD-1 or anti-PD-L1 in combination with a personalized neo-antigen vaccine in advanced solid tumors (NeoPepVac).

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Abstract
Introduction
The human immune system can recognize the products of somatic genetic alterations in tumors, or neo-antigens, which are not expressed on normal cells. These neoantigens are an attractive immune target because their selective expression on tumors can minimize immune tolerance as well as the risk of side effects such as autoimmune reaction. Novel technical advances in next-generation sequencing allow fast and systematic prediction of cancer neoantigens for each individual patient. In this study, the proprietary platform PIONEER will be used for fast and accurate identification of a neo-antigen vaccine tailored to each individual patient. The vaccine, based on 5-15 peptides derived from a patient's tumor individual neo-antigens, will be formulated with a novel adjuvant to strengthen CD8+ T cell immunity to cancer. Immune checkpoint inhibitors targeting PD-1 or PD-L1 will be administered both before, during and after vaccination to unleash the activity of vaccine-induced immune responses.

Materials and methods
The study is designed as an open phase I trial. We will include 25 Patients with either unresectable or metastatic melanoma, non-small cell lung cancer (NSCLC) or bladder (urothelial) cancer who meet the criteria for treatment with anti-PD-1 or anti-PD-L1. The Neo-Pep-vaccine is given every second week, for a total of 6 vaccines. First three will be administered intraperitoneal, and the last three will be administered intramuscular.

Results
One Patient has been included. A biopsy from a metastasis in the leg has been collected, and a vaccine with 9 peptides has been produced. The patient has received 3 vaccinations intraperitoneal without any side effects.

Conclusions
We are hoping to find the vaccine tolerable and safe. Also, we want to see if it is feasible to manufacture a personalized neo-antigen vaccine within 6 weeks of enrolment with the PIONEER pipeline, and to evaluate the immune response before, during and after treatment.

Personalised medicine, biomarkers and diagnostics

#28 The importance of exercise-dependent regulation of immune-function for cancer related disease control

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Abstract
Introduction
The beneficial role of physical activity in disease prevention and promotion of physical health dates back more than 60 years (1). In cancer, the aim has mainly been to improve physical functioning, quality of life and cancer-related fatigue (2-5). While exercise can influence the anti-cancer treatment in diverse ways, regulation of the host immune system seems to play a pivotal role, but underlying mechanisms are still lacking.

Materials and methods
In a setting of newly diagnosed, early stage prostate cancer patients undergoing surgery, we investigate the influence of one acute bout of exercise on immune cell function and regulation (NCT03675529). To this end, 30 eligible patients will be randomized to perform one session of high intensity interval bike training. Immune cell populations are evaluated by flow cytometry to monitor distribution, cytotoxicity and function and utilized to measure the killing capacity against in vitro cancer cell lines throughout the exercise. In addition, serum samples are used to conduct in vitro cancer cell incubation studies to identify the anti-tumoral effects of exercise serum and responsible factors.

Results
To date, 10 patients have successfully completed the protocol. Exercise has a profound effect on NK cell (2-4 fold increase) and NK like T cell (1.5-2 fold increase) mobilization. Other results are currently not accessible due to sample blinding.

Conclusions
Acute exercise elicits immune cell mobilization to the circulation, resulting in increased immune surveillance and clearance of tumor cells. After cessation, the immune cells egress to the periphery and support anti-cancer processes. This acquired knowledge of one acute bout of exercise (NCT03675529) can be transformed to long-term training adaptions (NCT02954783) for cancer patients, unravelling the molecular mechanisms linking exercise training to the observed benefits in clinical trials.

Personalised medicine, biomarkers and diagnostics

#29 Real-world Experience with First-Line Immunotherapy in Advanced Non-Small Cell Lung Cancer Patients

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Abstract
Introduction
Lung cancer is the leading cause of cancer-related death in Denmark. In clinical trials, immunotherapy has shown better responses, survival, durable benefit and less severe toxicity compared to chemotherapy in patients with advanced non-small cell lung cancer (NSCLC). However, experience with first line Pembrolizumab in the real-world setting is missing. Elderly patients and patients in ECOG performance status (PS) 2 account for a great amount of patients in this field but they are poorly represented in clinical trials.

Materials and methods
A retrospective cohort study is performed including around 175 patients with advanced NSCLC treated at the departments of oncology at Aalborg and Aarhus University Hospitals from March 2017 to October 2018. Baseline and demographic data are collected. Primary endpoints are progression free survival and overall survival. Subgroup analysis is performed on elderly patients (>70-75 years) and patients in PS 2.

Results/conclusions
We expect that outcomes in the first-line real-world setting are comparable to outcomes in the clinical trials. Outcome may be worse in elderly patients and patients in PS 2.

Personalised medicine, biomarkers and diagnostics

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

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Abstract
Introduction
Glioblastomas are highly malignant with a median survival time below15 months. Immunotherapy has shown promising results in different types of cancer, and novel therapies targeting PD-1/PD-L1 signalling have been approved for treatment of patients with melanoma and lung cancer. Galectin-9, a checkpoint molecule, may be a potential therapeutic target. Galectin-9 and its receptor, TIM-3, are involved in cancer cell aggregation, induced T-cell apoptosis, and tumor progression. Previous studies indicate that galectin-9 may be expressed in high-grade gliomas. The aim of this study was to investigate the expression and prognostic value of galectin-9 in glioblastomas.

Materials and methods
Glioblastomas are highly malignant with a median survival time below15 months. Immunotherapy has shown promising results in different types of cancer, and novel therapies targeting PD-1/PD-L1 signalling have been approved for treatment of patients with melanoma and lung cancer. Galectin-9, a checkpoint molecule, may be a potential therapeutic target. Galectin-9 and its receptor, TIM-3, are involved in cancer cell aggregation, induced T-cell apoptosis, and tumor progression. Previous studies indicate that galectin-9 may be expressed in high-grade gliomas. The aim of this study was to investigate the expression and prognostic value of galectin-9 in glioblastomas.

Results
Galectin-9 was highly expressed in most glioblastomas, especially in cells with microglial and macrophage morphology, but some glioblastomas had a very limited expression. The mean positive area fraction was 0.06 (range 0.01-0.32). When dichotomized at the median no difference in the median overall survival was observed. Galectin-9 was not associated with overall survival (HR= 0.97, p=0.8) in multivariate analysis including age, performance status, post-surgical treatment and MGMT-status.

Conclusions
The galectin-9 protein was expressed in most glioblastomas. Targeting of galectin-9 may therefore be of potential value in most glioblastoma patients in order to obtain immune-mediated anticancer effects. Galectin-9 expression was not associated with patient survival. Potential co-localization of galectin-9 and its receptor TIM-3 will be investigated in our future work, as will the correlation with PD-L1 expression, to discover potential strategies for combination treatment.

Clinical trials:
Poster #31-45

Clinical trials

#31 DBCG RT Natural trial: Partial versus no breast radiation therapy for women ≥ 60 years operated with breast conservation for a relatively low risk early breast cancer, a clinically controlled randomized trial

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Abstract
Introduction
Since April 2016 partial breast irradiation (PBI) has been DBCG (Danish Breast Cancer Group) standard for selected low risk breast cancer patients operated with breast conservation. This is based on results from the UK IMPORT LOW trial and from the DBCG PBI trial. The 5-year risk of local recurrence after PBI is around 0.5% compared with a 2% risk of contralateral new breast cancer. Data from randomized trials on gain from radiation therapy (RT) indicates a risk reduction of local recurrence from RT by 2/3. Thus, omission of PBI may increase the 5-year risk of local recurrence to 1.5-2%, i.e. to the level of contralateral new primary. In the DBCG RT Natural trial the DBCG RT Committee tests if omission of PBI in selected patients is possible without causing unacceptable more local recurrences.

Materials and methods
Patients ≥60 years operated with breast conservation for a low risk breast cancer (non-lobular, pT1, pN0, ER+, grade 1-2, HER2-, margin ≥2mm) are randomized ± PBI, where PBI is based on 3DCRT 40 Gy/15 fr. Strata are institution and endocrine therapy. The study will randomize 1:1, and 926 patients will be accrued. Primary endpoint is 5-year invasive local recurrence. Secondary endpoints are local morbidity, fear of cancer recurrence and pattern of recurrences. NCT 03646955.

Results
Accrual was initiated Oct 2018, and as of April 2019, 35 patients were included, 21 randomized and 14 opted for no PBI. The trial will be active in RT departments in Denmark (n=7), Norway (n=6), Sweden (n=2), Germany (n=1) and Chile (n=1).

Conclusions
The DBCG RT Committee constantly aims to optimize the indication for adjuvant breast radiation therapy to ensure a balance between gain and harm. The DBCG RT Natural trial is part of that strategy.

Clinical trials

#32 The DBCG RT Skagen Trial 1: Hypo- vs normofractionated loco-regional radiation of early stage breast cancer in a randomized trial

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Abstract
Introduction
Based on poor results using hypofractionated adjuvant radiotherapy (RT) of early breast cancer (BC) 50 Gy/25 fr. has been Danish Breast Cancer Group (DBCG) standard for loco-regional therapy since 1982. Results from the DBCG HYPO trial stimulated a renewed interest in hypofractionation, and the non-inferiority DBCG SKAGEN TRIAL 1 was initiated. The hypothesis is that 40 Gy/15 fr does not result in more arm lymph oedema than 50 Gy/25 fr 3 years post RT. If the patient needs a breast boost, this is provided as simultaneous integrated boost (SIB).

Materials and methods
Since 2015, patients ≥18 years operated for BC with an indication for loco-regional RT are randomized 1:1 to 50 Gy vs. 40Gy. Strata are institution and systemic therapy. The primary endpoint is ipsilateral arm lymph oedema 3 years post RT. Oedema is present if the circumference of the ipsilateral arm is 10% higher compared with the other arm. Secondary endpoints are other normal tissue responses, patient reported outcomes and recurrences. The RT planning is based on the ESTRO consensus for target volume delineation, and fields and dose distribution follow the DBCG guidelines. Accrual remains open until 3 years morbidity information has been collected in 1012 patients.

ClinicalTrial NCT02384733.

Results
The trial is open for accrual in 16 sites in 7 countries, and as of April 2019, 1833 patients are accrued. Quality assurance of the RT planning is published and demonstrate high compliance with DBCG guidelines. The trial has stimulated a similar trial in France (HYPO-G-01).

Conclusions
With the current accrual rate it is estimated that the DBCG SKAGEN TRIAL 1 will close with 2700 patients in 2020/2021, thus providing statistical power for analyses of the importance of fractionation in subgroups treated with different systemic therapies. The DBCG RT Committee will decide what is the future standard fractionation for loco-regional radiation therapy when the trial closes.

Clinical trials

#33 DBCG The NAME trial: A direct comparison of Oral Navelbine given either classic or Metronomic in metastatic HER2 neg breast cancer

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Abstract
Introduction
Navebine is an antineplastic agent that has shown afficacy in the treatment of a variety of solid tumors, including breast cancer. The drug can be given intriavenously, but also as oral tablet treatment. Preclinical studies, as well as clinical observations, suggest that the administration of small, frequent doses of chemotherapy (metronomic dosing) has an effect, not only on cancer cells, but also on endothelialcells in the tumor vasculature. By giving smaller, but more frekvent doses of the drug, higher dose intensity, without corresponding side effects, is optained. Whether treatment under the metronomic principle is superior to conventional treatment has not yet been validated in the clinic, so this study is hoped to clarify this.

Materials and methods
This is an investigator-initated, prospective randomized fase II, non-blinded multinational, multicentre study running in Denmark and Norway. 200 women diagnosed with HER2 neg metastatic breast cancer will be enroled.

Patients are randomized to either:
Arm A Clasical treatment: Navelbine Oral: Navelbine Oralâ: 60 mg/m² day 1, day 8 (and day 15), every three weeks for the first cycle. Hereafter 80 mg/m² day 1 and day 8, every three weeks for de following cycles. Or
Arm B Metronomic treatment: Navelbine Oralâ: with 3 week cycles of daily doses of 30 mg. (Patients with body surface ≤ 1,54 m² or 65 Years or more start on 20 mg daily)

Treatment is first to fourth line (chemotherapy). The primary Objectives is to evaluate the Disease Control Rate (CR + PR + SD, SD > 3 months) in the two arms. Secondary Objectives are to compare the duration of Disease Control, TTP, RR, DR and OS and side effects for the two regimens. Also Evaluation of the Global Health Status/QoL, is made. A translational study with biomarkers is performed. The patients will be treated until progression or to high toxicity, or until the patient wishes discontinuation.
EUDRACT no: 2016-002165-63. Health Board no: 2017040059.

Clinical trials

#34 DAHANCA 30: Et randomiseret non-inferiority studie af hypoxi-profilvejledt nimorazolbehandling i forbindelse med primær strålebehandling af planocellulære hoved-halskarcinomer

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på vegne af DAHANCA

Abstract
Introduktion
Tumorhypoxi er årsag til stråleresistens og dårligere outcome ved behandling af kræftknuder i hoved-halsregionen (HNSCC) med stråleterapi. Nimorazol er en peroral hypoxisk radiosensitizer, som, givet konkommitant med stråleterapi, er vist at reducere stråleresistensen og dermed forbedre stråleeffekten i iltfattige kræftknuder. Stoffet gives i dag til næsten alle strålebehandlede patienter med HNSCC, velvidende at det formentlig kun er virksomt hos gruppen med de mest ilt-fattige svulster. Denne gruppe patienter har man hidtil ikke været i stand til at identificere. Med en gen-profil tyder det på, at man nu kan udpege såvel de iltfattige svulster, der har gavn af nimorazol (respondere), som de iltrige svulster, hvor nimorazol ikke har væsentlig betydning (non-respondere). Ved at undlade brug af nimorazol hos non-respondere kan disse patienter spares for bivirkninger til stoffet. Formålet med undersøgelsen er, at eftervise, hvorvidt hypoxi gen-profilen kan udpege patienter som skønnes ikke at have gavn af nimorazol.

Materialer og metoder
Patienter med HNSCC, hvor der er indikation for nimorazol under primær strålebehandling kan inkluderes. Studiet er et randomiseret non-inferiority studie med planlagt 1262 inkluderede og randomiserede patienter. Hos inkluderede patienter foretages hypoxisk profil på deres diagnostiske biopsi. Hvis denne tyder på en iltrig kræftknude, randomiseres til stråleterapi/kemostråleterapi +/- nimorazol. Hvis hypoxi-profilen tyder på en iltfattig kræftknude får patienten standard stråleterapi/kemostråleterapi (incl. nimorazol).

Resultater
Ultimo marts 2019 er der 389 inkluderede patienter, hvoraf 269 er randomiserede.

Konklusioner
Foreløbige sikkerhedsanalyser giver ikke anledning til at terminere studiet og der er ikke set uventet toksicitet hos patienterne i studiet.

Clinical trials

#35 DAHANCA 33: A phase II, multi-center study of dose escalated radiotherapy guided by functional imaging for patients with hypoxic head and neck squamous cell carcinoma

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Abstract
Introduction
Hypoxic cancer cells within a tumor have been shown to be resistant to radiation. This could lead to an increased risk of treatment failure in tumors treated with primary radiotherapy (RT). Hypoxic tumor areas can be visualized with PET-imaging and hypoxia-sensitive tracers, e.g. 18F-flouroazomycin arabinoside (FAZA). The resistant tumors can be targeted by increasing the radiation dose to tumor volume.

The main purpose of the study is to demonstrate improved curability of dose escalated radiotherapy in locally advanced HNSCC patients identified by hypoxic FAZA-PET scans.

Materials and methods
The study is an open, prospective, experimental single-arm, phase II multi-center study with a planned inclusion of approximately 60 patients with stage III-IV squamous cell carcinoma of the larynx, pharynx or oral cavity. Inclusion only of p16-negative tumors, if originating from oropharynx. Patients must be eligible to undergo treatment with hyperfractionated, accelerated radiotherapy (HART; 76Gy in 56 fractions, 2 fractions daily), concomitant hypoxic cell sensitizer nimorazole with or without low-dose cisplatin. A FAZA PET/CT scan is carried out as part of radiotherapy planning. If hypoxia is visualized, the patient undergoes dose escalated, intensified radiotherapy with HART, nimorazole and weekly cisplatin. The dose is escalated to the entire target volume.
The primary endpoint of the study is loco-regional failure defined as persistent or recurrent disease in the tumor or regional lymph nodes. No salvage surgery (e.g. neck dissection) is allowed. Secondary outcome measures are: overall survival, disease-specific death, acute and late radiation related morbidity.

Preliminary results
As per May 1st 2019, a total of 29 patients are enrolled and a hypoxic sub-volume is identified within tumors of 75% of patients. The study continues to actively recruit patients.

Trial registration: Registered on ClinicalTrials.gov with Identifier NCT02976051.

Clinical trials

#36 DAHANCA 35: Et nationalt randomiseret forsøg med strålebehandling med enten fotoner eller protoner til patienter med hoved-halskræft

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Abstract
Introduction
Med åbningen af DCPT (Dansk Center for Partikelterapi), bliver der mulighed for at behandle patienter med protonbehandling i Danmark. Bivirkninger efter strålebehandling for svælg og strubekræft er hyppige og alvorlige, og håbet er at protonbehandling kan mindske disse på både kort og lang sigt. Ved udvælgelsen af patienter med stor risiko for bivirkninger kan bruges matematiske modeller, der beskriver sammenhængen mellem bivirkninger og stråledosis. Imidlertid er disse kun kendt fra røntgen- (foton-) strålebehandling, og det er usikkert hvorvidt de kan overføres til strålebehandling med protoner. Der er derfor planlagt en række kliniske studier i andre lande, men meget få af disse er randomiserede undersøgelser.

Materials and methods
Patienter med kræft i svælg og strube i Danmark, egnede til strålebehandling, får lavet en computerbaseret sammenligning mellem den konventionelle røntgen behandling og proton behandling. Ved forventet betydelig reduktion i risikoen for bivirkninger med protonterapi, tilbydes patienterne lodtrækning til enten proton behandling på DCPT eller fotonterapi lokalt. Patienterne får før og efter behandlingen undersøgt synkefunktion, spytsekretion og livskvalitetsmålinger (spørgeskemaer). Undersøgelsen vil indledes med en pilotfase i maj 2019 og det randomiserede studie fra efteråret 2019.

Results
Alle danske centre, der behandler patienter med hoved-halskræft, deltager. Retningslinjer for planlægning med protonterapi og udvælgelse af patienter der måske har gavn af protonterapi er udarbejdet således at de sammenlignende stråleplaner kan laves lokalt på alle centre og efterfølgende gennemgås på nationale telekonferencer.

Conclusions
Med undersøgelsen håber vi at kunne skaffe evidens for hvilke hoved-hals kræft patienter, der har gavn af proton strålebehandling. Ved at inkludere patienter, der teoretisk har gavn af protonterapi, vil vi også undersøge modellernes evne til at udvælge patienter.

Clinical trials

#37 DAHANCA 37: Gen-bestråling med proton-strålebehandling ved tilbagefald af hoved-halskræft

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Abstract
Introduktion
Hvis man én gang er strålebehandlet mod hoved-halsområdet er det problematisk at give en ny strålebehandling for et tilbagefald eller en ny primær, pga. risikoen for alvorlige, inklusiv livstruende, bivirkninger. Hvis genbestråling er patientens eneste mulighed for at blive rask, kan strålebehandling med protoner nedsætte den samlede stråledosis til patienten, og måske nedsætte risikoen for alvorlige bivirkninger.

Materialer og metoder
DAHANCA (den Danske Hoved-Halskræft Gruppe) har godkendt en fase II genbestrålingsprotokol med meget vide inklusionskriterier. Den oprindelige stråleplan skal være til rådighed således at man kan lave en samlet dosisplan for både den oprindelige og den aktuelle dosisplan. Patienterne skal ydermere have lavet en sammenlignende dosisplan (både en foton- og en protonstråleplan) og diskuteres på en national videokonference før henvisning. Egnede patienter vil blive tilbudt hyperfraktioneret accelereret strålebehandling med 60 Gray på 50 fraktioner, 10 om ugen. Alle egnede patienter vil blive tilbudt samtidig medicinsk behandling i henhold til nationale retningslinjer. Det primære endepunkt er alvorlige bivirkninger (CTC grad ≥ 3). Vigtige sekundære endepunkter bliver tumorkontrol, patient rapporterede symptomer og livskvalitet. Det er planlagt at inkludere 20 patienter.

Resultater
Protokollen bliver indsendt til Videnskabsetisk Komité 2. kvartal 2019 og første patient starter behandling 3. kvartal 2019

Konklusioner
Med de tilgængelige samlede dosisplaner og adgang til strålebehandling med protoner mener vi at kunne tilbyde patienten den mest skånsomme strålebehandling. Patienterne behandles i dag ikke ensartet og de nationale videokonferencer forventes i sig selv at fremme kvalitet og ensartethed af behandlingen uanset om den gives med fotoner eller protoner. Med studiet får vi ny viden om de forventede bivirkninger og den optimale udvælgelse af patienterne, også mhp. fremtidige protokoller med evt. dosiseskalation.

Clinical trials

#38 Interim report on safety and immunogenicity of IO103 (PD-L1) and IO120 (PD-L2) peptide vaccine in follicular lymphoma

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Abstract
Introduction
Follicular lymphoma (FL) is mostly an indolent but incurable disease and current treatments are associated with severe side effects such as neutropenia. Checkpoint molecules such as programmed death ligands 1 and 2 (PD-L1 and PD-L2) are expressed on lymphoma cells and lymphoma supporting cells and inhibit anti-tumor immune responses. PD-L1 and PD-L2 peptides have proven immunogenic with anti-tumor properties in vitro. In this study we investigate if PD-L1 and PD-L2 peptides are safe in a clinical setting and if the vaccine can raise vaccine specific immune responses.

Materials and methods
A first-in-human phase I study evaluating the safety of PD-L1 (IO103) and PD-L2 (IO120) peptides in eight FL patients. The vaccine is offered to patients with at least partial remission to standard chemotherapy. 15 vaccines will be administered over the course of one year. Adverse events are graded according to CTCAE 4.03 and dose limiting toxicities (DLT) was defined as three or more grade III+ adverse reactions. Immune responses are measured by delayed type hypersensitivity and elispot.

Results
As of May 2019, 8 out of 8 patients have been included. All patients have reached the interim time point of six vaccines with a mean of 9 (6-15). Two patients have been excluded due to progression during vaccination. No DLT has been observed. Three patients experienced neutropenia related to previous chemotherapy and progression. Only CTCAE grade 1 and 2 adverse events have been related to the vaccine with injection site reactions being the most common event. Diarrhea and fatigue grade 1 were reported as related to the vaccine. Vaccine specific Immune responses with varying intensity have been observed in all patients.

Conclusions
The vaccine seems feasible with only low-grade adverse events related to the vaccine and can induce vaccine specific immune responses.

Clinical trials

#39 Arginase-1 Peptide Vaccine in Patients with Metastatic Solid Tumors. A clinical trial in progress

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Abstract
Introduction
The enzyme arginase-1 (ARG1) plays a role in immune regulation through the degradation of the amino acid L-arginine. A depletion of L-arginine suppresses T cell function and ARG1-producing cells in the tumor microenvironment inhibit L-arginine-dependent T cell-mediated anti-tumor effects. ARG1-specific anti-regulatory T cells (anti-Tregs) have been identified in cancer patients and healthy donors. We hypothesize that the ARG1 peptide vaccine will activate and stimulate ARG1-specific anti-Tregs to proliferate and infiltrate the otherwise immunosuppressive tumor microenvironment.

Materials and methods
In this clinical phase I study we aim to treat 10 patients with progressive solid tumors following treatment with standard of care agents. The ARG1 vaccines will be administered subcutaneously every third week for 45 weeks. The primary endpoint is to evaluate safety and toxicity. Immune responses will be assessed using blood- and tumor tissue samples. Clinical responses are evaluated using RECIST 1.1.

Conclusions
The enzyme ARG1 inhibits T cell function by reducing the availability of the amino acid L-arginine to T cells. In this phase I study we are planning to vaccinate 10 patients with metastatic solid tumors with the peptide ARG1. The aim of the study is to assess the safety and immunomodulatory characteristics of an ARG1 peptide vaccine in patients with metastatic solid tumors.

Clinical trials

#40 Predicting the Aggressiveness of Prostate Cancer by Plasma and Urine Biomarkers Combined in an Algorithm for elderly Men

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Abstract
Introduction
Prostate biopsy is currently the standard of care for prostate cancer diagnosis, oftentimes reflexed after the detection of an elevated serum prostate-specific antigen, PSA. Unfortunately, prostate biopsy is not without potential complications, which include discomfort, pain, bleeding, and infections ranging from cystitis to septic sepsis and even death. Furthermore, some newly diagnosed prostate cancers are indolent and will never harm the patient, while others are aggressive with metastatic potential. A PSA level >=4.0 ng/ml is frequently used as a threshold warranting a biopsy evaluation, but only 20-30% of patients with PSA 4 - 10 ng/ml, have prostate cancer, resulting in a high number of patients undergoing unnecessary biopsies of the prostate.

Materials and methods
We plan to test a new method predicting aggressive prostate cancer (GS >=7) using biomarkers present in the blood and urine: Liquid Biopsy. The assay measures the expression levels of PDLIM5, HSPD1, IMPDH2, PCA3, TMPRSS2, ERG, UAP1, PTEN, AR, GAPDH and B2M RNA in urine and peripheral blood plasma and combined with age and clinical data in an algorithm, the risk of having an aggressive GS >=7 prostate cancer can be estimated. The study will include 700 patients.

The primary objectives of this study are to test the ability of the “liquid biopsy” to

1) Detect as many patients with aggressive prostate cancer as the standard method (PSA).
2) Reduce the number of prostate biopsy sets taken and thereby reduce the number of patients detected with indolent prostate cancer.

The secondary objectives are to evaluate

1) The Quality of life.
2) Progression and survival
3) Safety

Conclusions
We aim to compare “Liquid Biopsy”, against prostate biopsy in a national multicenter randomized manner. We anticipate a reduction in prostate biopsy by 30 % and reduced detection in indolent prostate cancer by 40-50 %.

The study will be conducted by the Danish Prostate Cancer Group (DaProCa).

Clinical trials

#41 Community-based football in men with prostate cancer: One-year follow-up on a pragmatic multicentre randomised controlled trial

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Abstract
Introduction
Physical exercise has been shown to be effective on exercise-related outcomes in men with prostate cancer. However, research into the clinical relevant effects of real-world interventions is warranted.

Materials and methods
In a pragmatic, multicentre, parallel randomised controlled trial 214 men with prostate cancer were randomly assigned to either football twice weekly at a local club (FG) (n=109) or usual care (UG) (n=105). In this one year follow-up we evaluated the effects of community-based football training on bone mass, body composition, quality of life and hospital admissions. Intention-to-treat (ITT) and per-protocol (PP) analyses were conducted.

Results
Total hip bone mineral density improved for FG 0.007 g/cm2 (95% CI 0.004 to 0.013). Among patients allocated to football, 59% joined their local club after the end of the primary study period. Of those, 78 % had attended ≥50% of football sessions at one-year follow-up and had better scores on the Mental Component Summary 2.9 (95% CI 0.0 to 5.7) points higher, as well as a lower fat mass 0.9 kg (95% CI -1.7 to -0.1). Hospital admissions were more frequent in the UG compared to FG (33 versus 22, respectively; the odds ratio based on PP analyses was 0.34 for FG compared to UG).

Conclusions
Participants allocated to football improved hip BMD and had less hospital admissions. Men who played football more than once a week for one year lost fat mass and reported improved mental health. Community-based football proved to be acceptable, even when club membership was not subsidised.

Trial registration: ClinicalTrials.gov: NCT02430792.

Clinical trials

#42 SUrveillance with PET/CT and ctDNA of lung cancer patients after completion of definitive therapy; a Randomized trial

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Abstract
Introduction
Even after treatment with curative intent lung cancer patients have a high risk of relapse and a dismal prognosis. Patients are currently followed with CT scans. However, after surgery and radiotherapy CT has limited accuracy, potentially delaying the diagnosis of relapse. The use of 18F-Fluordeoxyglucose positron emission tomography/CT (PET/CT) for follow-up has increased and improved understanding of the role of imaging in surveillance is needed. Relapse can also be reflected by shedding of tumour DNA (ctDNA) into the blood stream. Measuring ctDNA in blood samples therefore represents a promising minimally-invasive and repeatable strategy to assess tumour changes. This on-going clinical trial aims to improve early detection of lung cancer relapse and enable more patients to receive definitive treatment of their relapse, ultimately leading to improved survival.

Materials and methods
This national, randomized trial compares standard CT follow-up with CT +/- PET/CT for surveillance of patients with non-small cell lung cancer treated with curative intent. Primary endpoint is frequency of treatable relapse.

Secondary endpoints are survival, quality of life, number and type of invasive procedures, adverse events, type of treatment after relapse and use of healthcare resources.
Based on samples collected during this trial we will evaluate if monitoring patients with ctDNA enable us to track cancer evolution and detect early signs of relapse.

Results
Inclusion started end-2018 and 4/5 Danish regions are now including patients. The aim is to include 750 patients by 2021. To obtain baseline blood sample for ctDNA, patients are included prior to curative treatment.

Conclusions
SUPE_R will provide the scientific basis for implementing new ways for surveillance of patients with lung cancer. This is the first study considering bioinformatics and methodological aspects of liquid biopsies and relating them directly to imaging and clinical benefits for the patients.

Clinical trials

#43 Fra kontrol til individualiseret opfølgning for kvinder med gynækologisk kræft - et randomiseret, kontrolleret studie

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Abstract
Introduktion
Udgivelsen af Opfølgningsprogram for gynækologiske kræftformer (SST 2014) medførte et opgør med de traditionelle kontrolprogrammer. Frem for faste kontroller uden evidens for øget overlevelse, anbefales i stedet individuel opfølgning baseret på løbende behovsvurderinger, og med fokus på at understøtte patienternes egenomsorgsevne (EOE).
Dette projekt har til formål at udvikle og evaluere et sygeplejerskestyret, individualiseret og behovsbaseret opfølgningstilbud til kvinder med gynækologisk kræft, der har specifikt fokus på styrkelse af patienternes EOE. Hypotesen er, at det nye tilbud har positiv effekt på kvindernes EOE og dermed frygt for tilbagefald, livskvalitet, samt oplevelse af kontinuitet og patientinddragelse.

Materialer og metoder
Patienter med cervix- og endometriecancer, der opereres på gynækologisk afdeling, Odense Universitetshospital, og som ikke skal modtage onkologisk efterbehandling, tilbydes deltagelse.
I alt skal 220 patienter inkluderes.
Alle patienter undersøges af læge 4 måneder efter operationen. Deltagerne randomiseres derefter til enten opfølgning i læge- (kontrol) eller i sygeplejerskeregi (intervention) i op til 3 år.
Patienter i interventionsgruppen følges af en specialuddannet sygeplejerske, og besvarer før hver kontakt et kort elektronisk spørgeskema, hvor svarene farvekodes efter graden af det enkelte problem. I den efterfølgende samtale har sygeplejersken således visuelt overblik over problemområder og udviklingen i disse over tid. Ved hver kontakt understøttes patienternes EOE aktivt.
Patienter i kontrolgruppen tilbydes undersøgelse af læge og behovsorienteret opfølgning.
Alle patienter kan i 3 år efter operationen til enhver tid henvende sig ved symptomer.
Effekten af interventionen evalueres via spørgeskemaer til alle patienter hhv. 3 (baseline), 12, 24 og 36 måneder efter deres operation.

Konklusion
Studiet forventes at bidrage med vigtig viden, der kan danne baggrund for organiseringen af fremtidige opfølgningsprogrammer.

Clinical trials

#44 Geriatrisk vurdering og intervention hos ældre som skal opereres for tyktarmskræft – projekt GEPOC

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Abstract
Introduktion
Hyppigheden af tyktarmskræft stiger med alderen. En grundpille i behandlingen af tyktarmskræft er operation med fjernelse af kræftsvulsten. Operationen belaster den enkelte, såvel psykisk som fysisk, og medfører for skrøbelige ældre risiko for bl.a. tab af livskvalitet og funktionsniveau.
Formålet med studiet er at undersøge om en helhedsorienteret ældremedicinsk (geriatrisk) vurdering og intervention før og efter kirurgi for tyktarmskræft kan forhindre tab i livskvalitet og funktionsniveau.

Materialer og metoder
GEPOC (NCT03719573) er randomiseret studie med 100 ældre (≥70 år) skrøbelige patienter med nydiagnosticeret kræft i tyktarmen, hvor der planlægges primær operation. Patienter rekrutteres fra Gastroenheden, Herlev og Gentofte Hospital. Patienterne screenes med G8, et multi-domæne screeningsværktøj udviklet til at identificere skrøbelige patienter. Patienterne randomiseres til interventions- eller kontrolgruppe. Begge grupper følges afdelingens retningslinjer for fast-track kirurgi. Interventionsgruppen får desuden forud for operation en helhedsorienteret geriatrisk vurdering af komorbiditet, medicin, psyko-kognitiv funktion, ernæringsmæssig status og funktionsniveau. Der interveneres på de identificerede problemstillinger. Efter operation gås ekstra stuegang ved geriater. Der opstartes superviseret træningsprogram før operation, under indlæggelsen og i efterforløbet. Primære endepunkt er 30 sekunder rejse-sætte-sig test, som er udtryk for styrke og dynamisk balance. Sekundære endepunkter inkluderer andre funktionstest, livskvalitet, patientoplevet rekonvalescens, kropssammensætning målt ved DXA skanning, komplikationer til kirurgi, antal genindlæggelser, overlevelse samt biomarkører associeret til immunonkologi og muskelstamcellefunktion.

Resultater
Status 1.maj 2019: 14 patienter screenet og 8 patienter er skrøbelige. I alt er 6 patienter inkluderet.

Konklusion
Undersøgelsen er pågående. Endelige resultater forventes i juni 2021.

Clinical trials

#45 Research protocol: Randomized Controlled Trial comparing the efficacy of therapist guided internet-delivered cognitive therapy (TG-iConquerFear) with augmented treatment as usual in reducing fear of cancer recurrence in colorectal cancer survivors

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Abstract
Introduction
Cognitive therapy has been shown to reduce fear of cancer recurrence (FCR) in mainly breast cancer survivors. The accessibility of cognitive behavioural interventions could be further improved by Internet delivery. The aim of this study is to test the efficacy of a therapist guided internet-delivered intervention (TG-iConquerFear) vs. augmented treatment as usual (aTAU) in Danish colorectal cancer survivors.

Materials and methods
A population-based randomized controlled trial (RCT) comparing TG-iConquerFear with aTAU (1:1) in colorectal cancer survivors who suffer from clinically significant FCR (Fear of Cancer Recurrence Inventory Short Form (FCRI-SF) ≥ 22 and semi-structured interview). Evaluation will be conducted at ½, 3 and 6 months post-treatment and compared to baseline measurements. Long-term effects will be evaluated after one year. Primary outcome will be 3 months post-treatment FCR (FCRI-SF). Secondary outcomes are global overall health and global quality of life (Visual Analogue Scales 0-100), bodily distress symptoms (BDS checklist), health anxiety (Whiteley-8), anxiety (SCL4-anx), depression (SCL6-dep) and sickness absence and health expenditure (register data). Explanatory outcomes include: Uncertainty in illness (Mishels uncertainty of illness scale, short form, MUIS), metacognitions (MCQ-30 negative beliefs about worry subscale), and perceived risk of cancer recurrence (Visual analogue Scale 1-100).

Results
If successful, TG-iCF has proven effective in reducing psychological morbidity among colorectal cancer survivors and lowering the overall health care costs due to more appropriate use of health care services.

Conclusions
This study will add to the currently limited knowledge regarding the prevalence of FCR in CRC survivors and how it can be addressed at a broad scale level. Data from this project can be used directly as guidance in the daily clinic. At the current time no guidelines exist.

Clinical epidemiology and database research:
Poster #46-75

Clinical epidemiology and database research

46# Uhelbredelig kræft – tid fra diagnose til død af kræft – et nationalt kohortestudie, 2012-2014

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Abstract
Introduktion
I takt med den stigende overlevelse for forskellige kræftformer, så omtales uhelbredelig kræft i stigende omfang som; 'en kronisk sygdom', som patienter kan leve med i lang tid.
Formålet med dette studie var at undersøge, hvor lang tid patienter rent faktisk lever med kræft, inden de dør af kræft.

Materialer og metoder
Studiet er populations-baseret og anvender registerkobling mellem Cancerregisteret (CReg) og Dødsårsagsregisteret. Data for alle, som døde i Danmark i perioden 2012-2014 blev koblet med data fra CReg. Varigheden fra diagnose til død for patienter i CReg, som døde af kræft, præsenteres for forskellige kræftformer, inddelt i 3 kategorier i forhold til deres mediane overlevelse.

Resultater
I perioden 2012-2014 havde 46.269 personer kræft registreret som dødsårsag i Dødsårsagsregisteret, heraf var 43.281 (47% kvinder) også registreret i CReg. Den mediane overlevelse for de 43.281 patienter i kohorten var 345 dage (p25/75; 95/991 dage, gns; 890 dage); 32% overlevede 2 år og 14% overlevede 5 år. Kræftformer med en median overlevelse længere end 2 år udgjorde kun 17% af hele kohorten; det drejede sig om brystkræft (44%), prostatakræft (44%) og malignt melanom (12%). Alder ved død var mediant 73 år; 64% var mellem 65-85 år, 22% mellem 40-64 år, 13% ældre end 85 år og 1% var yngre end 40 år. Personer registreret i CReg, som døde af andre årsager end kræft (N=17.367), havde til sammenligning en median overlevelse fra kræftdiagnose til død på 2642 dage (7.2 år).

Konklusioner
Kendskab til sammenhængen mellem forskellige kræftformer, som ikke kan kureres, og forventet tid til død er vigtig viden i forhold til at planlægge og prioritere indsatser som fx rehabilitering og palliation. De enkelte patienter har desuden krav på realistiske fremtidsperspektiver i forhold til deres forventede sygdomsvarighed. Den gængse opfattelse af, at mange lever med uhelbredelig kræft i lang tid', modsiges af resultaterne i nærværende studie.

Clinical epidemiology and database research

#47 Chemotherapy to cancer patients near end-of-life: A single centre retrospective study using reversed time competing risks

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Abstract
Introduction
The benefit-risk balance of chemotherapy degrades as cancer patients get closer to end of life. It has been recommended to stop chemotherapy for patients with limited survival. Notably, no more than 10% of cancer patients should receive chemotherapy within 14 days of death. Therefore, we investigated the frequency of chemotherapy near end of life at the Department of Oncology, Aalborg University Hospital.

Materials and methods
The study was based on retrospective data from North Denmark Region's Patient Administrative System combined with the real-time registration chemotherapy database (MedOnc) used at the Department of Oncology, Aalborg University Hospital. We included all patients treated at the department who died between January 1, 2008 and December 31, 2017 (n=5486). Only antineoplastic agents (ATC L01) were considered.
As death was the inclusion criteria, the ratio of patients receiving chemotherapy within 14 days of death was evaluated through a reversed time cumulative incidence function, from death to last treatment, using diagnosis event as a competing risk.

Results
Overall, 10.4% of treated patients received chemotherapy in their last 14 days, but with large disparities between cancer types ranging from 3% for endometrial cancer to 15% for lung cancer.
Concerning drug types, protein kinase inhibitors (PKI) were the most noticeable, with 26% of patients on PKI still being treated 2 weeks before death. The ratio of patients receiving chemotherapy in their last 14 days decreased between 2008 and 2017.

Conclusions
The upwards trend of chemotherapy near end of life reported in previous publications could not be confirmed. Nevertheless, the goal should be to lower overtreatment as much as possible.
On the other hand, PKI are used until the very end, counteracting efforts made to reduce overtreatment. Predictive models to predict short term survival, especially in lung cancer patients, should be built to better handle PKI near end of life.

Clinical epidemiology and database research

#48 Validity of chemotherapy procedure codes in the Danish National Patient Registry

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Abstract
Introduction
Procedure codes in the Danish National Patient Registry are used for administrative purposes and constitute a potentially valuable resource for epidemiological research. The validity of chemotherapy procedure codes has, however, only been evaluated in one smaller study.

Materials and methods
We abstracted a random sample of 431 patients in the Region of Southern Denmark with a diagnose of colorectal cancer and a contact to an oncological department. We systematically examined these patients' medical records and chemotherapy recorded in the Danish National Patient Registry during 1st May 2016 – 1st May 2018. Using the medical record as the gold standard, we computed the positive predictive value (PPV) and sensitivity of chemotherapy procedure codes in the Danish National Patient Registry.

Results
We identified 2297 and 2335 in the registry and in the medical records, respectively. The overall PPV was 0.91 (95% CI, 0.90 – 0.92), and the overall sensitivity was 0.89 (95% CI, 0.88 – 0.91). Allowing a 5-day gap between registrations did not change these findings. Odense University Hospital had the highest overall values, where the PPV was 0.95 (95% CI, 0.94 – 0.96), and the sensitivity was 0.92 (95% CI, .0.90 – 0.93). Considering the most frequent single chemotherapy regimens, the PPV ranged from 0.74, (95% CI, 0.67 - 0.81) for 5-floururacil to 0.98 (95% CI, 0.95 – 1.00) for cetuximab, while the sensitivity ranged from 0.81 (95% CI, 0.75 - 0.87) for FOLFIRI-regimen (5 FU/folinic acid and irinotecan) to 0.97 (95% CI, 0.94 – 0.99) for bevacizumab.

Conclusions
The validity of chemotherapy procedure codes in the Danish National Patient Registry is generally high and these codes are thus usable for epidemiological research.

Clinical epidemiology and database research

#49 Total burden of disease in cancer patients at diagnosis – A Danish nationwide study of comorbidity and prescribed medication across major cancer sites

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Abstract
Introduction
In an aging cancer population comorbidity and polypharmacy exist and challenge oncologic treatment tolerability and toxicity due to possible disease and treatment interactions. In this nationwide study, we investigate for the first time both the prevalence of comorbidity and polypharmacy at time of cancer diagnosis across 20 cancers.

Materials and methods
We conducted a nationwide register-based cohort study including all Danish residents diagnosed with first primary cancer in the period January 1, 2005 to December 31, 2015. Comorbidity was defined as ≥ 1 of 20 comorbidities according to International Classification of Diseases - 10th Revision (131 specific diagnoses) registered in the Danish National Patient Registry less than five years prior to cancer diagnosis. Polypharmacy was defined as five or more medications egistered in the Danish National Prescription Registry and redeemed twice between 2-12 months prior to cancer diagnosis. We calculated proportions across gender (male, female), age group at cancer diagnosis (<55, 55-69, >70 years old) and with 95% confidence intervals.

Results
261,745 patients with first primary cancer were included, and 55% had at least one comorbidity while 27% had two or more comorbidities at diagnosis. Across cancer diagnoses, cardiovascular diseases, chronic obstructive pulmonary disease, diabetes, stroke, and depression/anxiety were most prevalent at time of cancer diagnosis. Polypharmacy was present in 32% of the cancer patients with antihypertensives, antithrombotic agents, antihyperlipidemic agents, analgesics and diuretics as the most prevalent prescribed and redeemed medications.

Conclusions
Every second cancer patient has comorbidity and every third has polypharmacy at diagnosis, highlighting the magnitude of possible clinical and structural challenges in the future management of a large proportion of cancer patients.

Clinical epidemiology and database research

#50 The Risk of being granted disability pension among incident cancer patients up to five years after diagnosis before and after a structural reform: A Danish population-based matched cohort-study

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Abstract
Introduction
To study the risk of being granted a disability pension in incident cancer patients up to five years after diagnosis, before and after the structural reform of the disability pension act in 2013.

Materials and methods
All 20-60 year old incident cancer-diagnosed individuals from 2000 to 2015 were identified in the Danish Cancer Registry. A control group, not previously diagnosed with cancer, was identified in Statistics Denmark matched on gender, age, highest completed education and household income. Differences in cumulative incidence rates (IR) (risk difference (RD)) of being granted a disability pension between cases and controls were analyzed before and after the disability pension act reform with 95% confidence intervals.

Results
In total 156,045 incident cases and 780,068 matched controls were included in the study. Before the reform; the adjusted RD of being granted a disability pension for cases was significantly higher than the controls at all time points. The RD increased the most during the first (3.8 95% CI (3.7–4.0)) and second follow-up year (9.0 95% CI (8.8–9.3)) and levelled off the remaining three years. After the reform; the adjusted RD were lower for all follow-up years than before the reform, ranging from 2.7 (95% CI 2.4–2.9) after one year, reaching a maximum after three years of 5.3 (95% CI 5.0–5.6) and steadily decreasing to 4.3 (95% CI 3.9–4.7) after five years.

Conclusions
The reform of the disability pension act reduced the risk for cancer-diagnosed individuals to be granted pensions. The impact on a personal level is unknown and should be further explored.

Clinical epidemiology and database research

#51 Er der social ulighed i helbredsrelateret livskvalitet blandt kræftoverlevere? Analyser af data fra Den Nationale Sundhedsprofil koblet med Cancerregisteret

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Abstract
Introduktion
Kræftoverlevere oplever gener og nedsat helbredsrelateret livskvalitet (HRQOL). Det gælder særligt personer med lav socioøkonomisk status. Der mangler populationsbaserede studier af HRQOL blandt kræftoverlevere. Formålet er at sammenligne social ulighed i HRQOL for kræftoverlevere og personer uden kræft på populationsbaserede data.

Materialer og metoder
HRQOL blev målt med SF-12 i Den Nationale Sundhedsprofil i 2013 blandt 162.283 respondenter på 16 år og opefter (svarprocent 54). 11.166 respondenter var registreret i Cancerregisteret (6 %).
Data var vægtede for at sikre, at de var repræsentative. Vi anvendte regressionsmodeller med fysisk og mental HRQOL som afhængige variable. Kronisk sygdom, multisygdom og sociodemografi blev anvendt som uafhængige variable og i justering af analyserne.

Resultater
Fysisk HRQOL for kræftoverlevere med lavt, middel og højt uddannelsesniveau var 44,5; 48,3 og 49,8, og 46,5; 51,0 og 52,8 for personer uden kræft. Tilsvarende var mental HRQOL 46,4; 48,9 og 49,8 for kræftoverlevere og 48,2; 50,0 og 50,3 for personer uden kræft.
Forskellen i fysisk HRQOL mellem kræftoverlevere og personer uden kræft var 2,1 (1,5;2,6) for lavt, 2,7 (2,3;3,0) for middel og 3,0 (2,6;3,4) for højt uddannelsesniveau. For mental HRQOL var forskellene 1,8 (1,2;2,4), 1,1 (0,7;1,4) og 0,5 (0,1;0,9). Alle forskelle var statistisk signifikante. Ved sammenligning af forskellene mellem kræftoverlevere og personer uden kræft var der kun statistisk signifikant forskel mellem mental HRQOL for lavt og højt uddannelsesniveau.

Konklusioner
Ja, der er social ulighed i HRQOL blandt kræftoverlevere, men forskellen mellem de tre uddannelsesniveauer er på samme niveau som blandt personer uden kræft. En kræftdiagnose reducerer HRQOL, men den øger ikke den sociale ulighed i HRQOL. Men selvom uligheden ikke øges, så betyder det, at en i forvejen lav HRQOL hos personer med lavt uddannelsesniveau reduceres yderligere efter en kræftdiagnose.

Clinical epidemiology and database research

#52 Socioeconomic inequality in head and neck squamous cell carcinoma survival – a population-based study from DAHANCA

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Abstract
Introduction
The socioeconomic inequality in survival after cancer in Denmark is increasing, particularly pronounced for Head and Neck Squamous Cell Carcinoma (HNSCC). We investigate where in the trajectory of HNSCC the socioeconomic inequality arises.

Materials and methods
Clinical information on all patients registered with larynx, pharynx, or oral cavity squamous cell carcinoma in the Danish nationwide and population-based clinical database DAHANCA (Danish Head and Neck Cancer Group) between 1992 and 2017 were linked to nationwide, administrative registries to obtain information on socioeconomic factors, comorbidity and vital status. By fitting cox proportional hazards and logistic regression models we estimated, separately for each HNSCC sub-site, the effect of socioeconomic position on HNSCC survival and: stage at diagnosis, HPV-status, comorbidity and tobacco-use. All models were adjusted for age, gender and period of diagnosis.

Results
For all HNSCC sub-sites the adjusted HRs were increased for patients, particularly men, with short education, low income, and those living alone or in rural areas. The ORs for: advanced stage at diagnosis, not having a HPV-positive oropharynx cancer, having more than one comorbid disease, or being a smoker at diagnosis were likewise significantly increased among patients with short education, low income, and those living alone or in rural areas.

Conclusions
This large, population-based study reveals significant socioeconomic differences in the most important determinants for HNSCC survival, possibly explaining a considerable part of the excess burden of HNSCC deaths among deprived patients. We have defined a high risk group being: men, above 60, living alone, who have a short education or low income, who could be the target for early interventions and improved surveillance.

Clinical epidemiology and database research

#53 Longer Distance to a Specialized Treatment Center Does Not Adversely Affect Access to Treatment or Outcome in Acute Myeloid Leukemia: A Danish National Population-Based Cohort Study

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Abstract
Introduction
Treatment of acute myeloid leukemia (AML) is centralized at Danish University Hospitals. Longer distances to such specialized treatment centers may affect patients' access to curative-intended treatment. Especially during outpatient treatment, distance may also affect survival.

Materials and methods
We conducted a national population-based cohort study including all AML patients diagnosed in Denmark between 2000-2014. We investigated effects of distance (<10 km (ref), 10-25, 25-50, 50-100, >100) to nearest specialized center on chance of intensive chemotherapy, a transplant, and complete remission (CR) using logistic regression analysis (odds ratios; ORs). For overall survival, we used Cox proportional hazards regression (hazard ratios; HRs) and adjusted (a) for relevant baseline characteristics.

Results
Of 2992 patients, 53% received intensive chemotherapy and 12% received low-dose chemotherapy in an outpatient setting. The median distances to specialized centers were 40 km (IQR 10-77) and 197 km (IQR 47-293) to a transplant center.
No impact of distance to specialized treatment centers was seen on chance of intensive chemotherapy (10-25 km aOR 1.1 (CI=0.7-1.7), 25-50 km 1.1 (CI=0.7-1.7), 50-100 km 1.3 (CI=0.9-1.9), and >100 km 1.4 (CI=0.9-2.2)).

Overall survival regardless of therapy (<10 km aOR 1.0 vs. >100 km aOR 1.0 (CI=0.9-1.2)), in intensive therapy patients, or in patients post-remission was not affected by distance to a specialized center.
Finally, distance to a transplant center did also not affect chance of HSCT or survival post-transplant.

Conclusions
In Denmark, longer distance to a specialized treatment center offering intensive chemotherapy or transplants, does not negatively affect access to curative-indented therapy, treatment-response, or survival in AML patients.

The findings support that the current centralization of AML treatment at specialized high-volume centers does not negatively affects outcomes in Danish patients.

Clinical epidemiology and database research

#54 Trends in mortality and organ support in Danish ICU admitted patients with acute myeloid leukemia over an 11-year period

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Abstract
Introduction
The mortality in acute myeloid leukemia (AML) has decreased over the last decades as results of improved supportive care, allowing more aggressive treatment and increased use of stem cell transplantation. We evaluated trends in mortality of ICU admitted AML patients and trends in use of organ support during ICU admission.

Materials and methods
The study included all adult Danish patients registered in the Danish Acute Leukemia Registry with AML diagnosed between 2005 and 2016 being treated with a curative intent. Information on ICU admission and treatments was obtained from Danish Intensive Care Database. For patients with multiple admission, the first ICU admission after diagnosis was chosen. The trends were described by predicted change (percent points) with 95% CI estimated using linear probability regression.

Results
The 1-year mortality in AML patients (N=1378) diagnosed 2005 - 2016, decreased from 36.0% to 28.8% (predicted yearly diff.: -1.0 (CI: -1.7 - (-0.25)). In the ICU admitted cohort (N=370), the 1-year mortality after ICU admission decreased from 80.0% to 65.6% (predicted yearly diff.: -1.4 (CI: -2.8 - (-0.07)).
Most use of organ support was decreasing. The use of mechanical ventilation (MV) dropped from 66.7% to 40.6% over the study period (predicted yearly diff.: -2.0 (CI: -3.5 - (-0.5)). The use of vasopressors appeared to slightly decrease (from 60.0% to 56.3%), however, the predicted decrease was not conclusive (predicted yearly difference: -1.2 (CI: -2.8 - 0.3)). The use of dialysis also appeared decreasing with a predicted yearly difference of -1.7 (CI: -3.0 - (-0.4). On contrary, use of non-invasive ventilation (NIV) increased from 20.0% to 50.0% (predicted yearly diff.: 2.6 CI: 1.1 - 4.0).

Conclusions
The 1-year mortality rate declined in AML patients overall and after ICU admission in ICU-admitted patients. The use of mechanical ventilation and dialysis decreased over the studied time period, while the use of NIV increased.

Clinical epidemiology and database research

#55 Risk of pneumonia and respiratory mortality in individuals with myeloproliferative neoplasm: a population-based cohort study

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Abstract
Introduction
Myeloproliferative neoplasms (MPN) have been associated with risk of several comorbidities. However, less is known about the respiratory comorbidities and mortality. We tested the hypothesis that individuals with MPN have increased risk of pneumonia and respiratory mortality.

Materials and methods
We included 108283 adults from the Copenhagen General Population Study and determined lung function, respiratory symptoms, and risk of pneumonia and death from respiratory causes from 2003–2018 using Fine-Gray competing-risks regression. MPN included essential thrombocythemia, polycythemia vera, myelofibrosis, and unclassifiable myeloproliferative neoplasm.

Results
In total, 351(0·3%) had MPN. Individuals with MPN had nominal lower lung function and more often experienced respiratory symptoms, including chronic mucus hypersecretion, dyspnea, and cough, compared to those without MPN. However, the significant difference in lung function disappeared after multivariable adjustment. During a maximum follow-up time of 14years (median 8·7years), we observed 5993 pneumonias and 10305 deaths, of which 2290 had respiratory disease as a main contributing cause. Compared to individuals without MPN, multivariable-adjusted subdistribution hazard ratios in individuals with MPN were 1·95(1·43-2·67) for pneumonia and 1·86(1·19-2·91) for respiratory mortality. This risk remained increased irrespective of smoking status and presence of airflow limitation and was largely driven by those with polycythaemia vera, myelofibrosis, and unclassifiable myeloproliferative neoplasm and not essential thrombocythemia. In those with MPN, the risk of pneumonia and respiratory mortality were similar to the risk of those without MPN having smoked approximately 80pack-years.

Conclusions
Individuals with MPN more often experienced respiratory symptoms and had increased risk of pneumonia and respiratory mortality compared to individuals without MPN in the general population.

Clinical epidemiology and database research

#56 Late Effects of Cancer and Cancer-Treatment in Danish Twins and Singletons

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Abstract
We study health late effects in Danish cancer patients surviving the first cancer diagnosis by one or more years. We will use a 5% random sample of the Danish population as a cohort on which survival, the extent of hospital contacts and redeemed medications, and cause of death will be compared between cancer patients and individuals without cancer diagnoses. Comparisons of disease pattern subsequent to cancer will be made between younger (<70 years) and older (70+ years) cancer survivors. Via a linkage with Danish twin data, intrapair twin comparisons will be explored, controlling for genetic factors and early life conditions.

Clinical epidemiology and database research

#57 Initiering af tvillingestudie om tatoveringsblæk og risiko for cancer

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Abstract
Introduktion
Antallet af danskere, der vælger at blive tatoveret er steget markant de seneste årtier - især blandt unge stiger trenden. Det vurderes at omkring 1/5 af den voksne befolkning er tatoveret. Det er endnu et åbent spørgsmål, hvorvidt tatoveringer er skadelige for kroppen. Vi ved, at visse indholdsstoffer i tatoveringsblæk kan være carcinogene, og at blækrester kan transporteres rundt i kroppen via blodbanerne og lymfesystemet. Derfor er det et vigtigt første skridt at afdække potentielt blækrelaterede cancertyper og underliggende determinanter for disse.

Materiale og metoder
Vi anvender eksisterende litteratur til at identificere cancere, der forventes at være blækrelaterede. I de indledende undersøgelser af disse cancere anvendes opdaterede data fra de nordiske tvillingeregistre samt cancerregistre til at udrede genetiske og miljømæssige faktorers indflydelse på cancerrisiko samt indbyrdes genetiske relationer mellem disse cancertyper.
Vi vil endvidere søge om adgang til Landsregistret for Patologi for at få informationer om, hvor i kroppen der er fundet blækrester. Hermed kan vi beskrive tætheden af forekomsterne og eventuelt komme med flere kvalificerede bud på potentielt blækrelaterede cancere.
Afslutningsvis ønsker vi at initiere matchede tvillingestudier af de udvalgte cancertyper for bedre at kunne svare på, hvorvidt tatoveringsblæk øger risikoen for cancer.

Resultater
Vi demonstrerer, at forekomsten af potentielt blækrelaterede cancere hos tvillinger er den samme som i baggrundsbefolkningen og vi præsenterer konkordanssandsynligheder samt relativ risiko indenfor par. Hermed kan vi belyse underliggende genetiske og miljømæssige faktorer for disse cancere samt deres tidslige variation med alder.

Konklusioner
Ved at identificere blækrelaterede cancertyper og udrede genetiske og miljømæssige faktorers indflydelse har vi gjort forarbejdet og kan begynde at undersøge, hvorvidt tatoveringsblæk kan knyttes til forekomsten af visse cancertyper.

Clinical epidemiology and database research

#58 Impact of sentinel lymph node metastasis size and localization on recurrence and death of melanoma - a nationwide study 2010-17 of 1322 patients

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Abstract
The incidence of melanoma continues to increase 4-5% yearly in Denmark, with more than 2700 new invasive cases last year.

Melanoma spreads most commonly to the regional lymph nodes, and dissemination carries a poor prognosis. The treatment of patients with microscopic spread to the sentinel lymph nodes (SN) has changed, so that complete lymphadenectomy, which has a high morbidity, is no longer performed routinely. Instead the patients are offered adjuvant systemic therapy and are monitored closely and only undergo major surgery in case of recurrence. It is therefore important to know the SN status to allocate the patients correctly for further treatment and follow-up.

This study aims to describe impact of SN metastasis size and -location and relation to primary tumor and patient characteristics on recurrence and death of the patients in the Danish Melanoma Database, with first invasive melanoma registered between 2010-2017. This has not previously been done as a Danish population-based study. By using multiple regression analysis and Kaplein-Meier curves, the study intents to investigate factors of prognostic importance for survival and death.

Preliminary results
6284 patients underwent SN biopsy and 21% (1322) of these had SN metastasis. In total 14,210 SNs were removed, 12.2% (1737) being positive. Mean age at diagnosis was 58 years, and 51% were females. Mean metastasis size was 0.24 mm and the most common locations were axillary (48%) and inguinal (32%). 15% (917 patients) had nodal recurrence of the disease, only 79% (723) of whom had a prior positive SN. 31% (282/917) of these had distant metastasis as well, only 67% (189) of whom had a positive SN biopsy prior.

Further calculations are in process, and the results are expected in august 2019 for Herlev patients, followed by the nationwide data. The results are expected to impact guideline development nationally and internationally for less invasive and more individualized treatment.

Clinical epidemiology and database research

#59 Characterization of hepatitis as an immune-related adverse event in real-world metastatic melanoma patients treated with immune checkpoint inhibitors

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Abstract
Introduction
The aim of this study was to examine the risk of developing immune-related hepatitis in metastatic melanoma patients treated with CPIs and describe medical management and response.

Materials and methods
A retrospective observational study was conducted on all patients with metastatic melanoma treated with pembrolizumab, ipilimumab, nivolumab or ipilimumab combined with nivolumab at Herlev Hospital between June 1, 2010 and February 1, 2019. The Danish Metastatic Melanoma Database was used to identify the patients. Hepatitis was identified by elevated ALT, AST and/or total bilirubin in accordance with the Common Terminology Criteria for Adverse Events (CTCAE) v5.0.

Results
The study included a total of 521 patients who received a total of 637 treatment regimens (53.4% pembrolizumab, 33.1% ipilimumab, 3.9% nivolumab and 9.6% ipilimumab plus nivolumab). Hepatitis of any- (CTCAE grade 1-4) and high-grade (CTCAE grade 3-4) was identified in 34.9% and 4.4% of patients. The highest incidence was observed with combination therapy (55.7% any- and 16.4% high-grade) and ipilimumab showed higher risk than pembrolizumab (36.5 vs. 30.9% any- and 4.7 vs. 2.4% high-grade). Time to onset of hepatitis from initiation of CPIs was longer in patients treated with pembrolizumab (median 12 weeks) compared to ipilimumab (median 7 weeks) and ipilimumab plus nivolumab (median 6 weeks). 72.1% of patients with grade ≥2 hepatitis received steroid treatment and 2 patients received additional second line immunosuppressants. Median time to resolution (grade 0/baseline value) on steroids was 48 days and 35.5% of patients experienced hepatitis relapse during treatment.

Conclusion
Compared to most previous studies we found higher incidences of hepatitis. The variety in incidence and timing among different CPI regimens corroborate those of previous studies. Second line immunosuppressants should perhaps be considered in more cases due to the high risk of hepatitis relapse during steroid treatment.

Clinical epidemiology and database research

#60 Statin use and breast cancer recurrence in postmenopausal patients treated with adjuvant aromatase inhibitors: a Danish population-based cohort study

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Abstract
Introduction
Observational studies suggest that statin use is associated with longer recurrence-free survival in breast cancer patients. Since 2007, aromatase inhibitors (AIs) have been guideline treatment for estrogen receptor (ER) positive postmenopausal breast cancer. AI therapy may be associated with increased cholesterol levels.

Materials and methods
We included a cohort of all postmenopausal patients diagnosed with stage I-III ER+ breast cancer during the years 2007-2016, treated with an AI in the adjuvant setting, and registered in the Danish Breast Cancer Group database and Danish Cancer Registry. We ascertained incident statin exposure (≥1 prescription post-diagnosis) from the Danish National Prescription Registry and modelled statins as a time-varying exposure lagged by 6 months. Follow-up began 7 months after diagnosis and continued to the first event of recurrence, death, emigration, 5 years, or 25th September 2018. We estimated incidence rates (IR) of recurrence at 5 years and used Cox regression models to compute crude and adjusted hazard ratios (HRs) with 95% confidence intervals (95% CI), comparing statin exposure with non-exposure.

Results
We enrolled 14,210 eligible patients. During the 5 years of follow-up, there were 37 recurrences in 3,430 person-years of follow-up for statin exposed, and 667 recurrences in 49,714 person-years in the unexposed group (IR per 1,000 person-years: 10.79 [95% CI :7.60-14.87] and 13.42 [95% CI :12.42-14.47], respectively). There was evidence of a reduced risk of recurrence associated with any statin exposure during the first 5 years of follow-up (adjusted HR: 0.72 [95% CI: 0.50-1.04]). Considering only lipophilic statins as exposure the results were similar (adjusted HR: 0.70 [95% CI: 0.48-1.02]).

Conclusions
Statin use was associated with a reduced risk of breast cancer recurrence among postmenopausal patients diagnosed with early stage breast cancer who received adjuvant aromatase inhibitor therapy.

Clinical epidemiology and database research

#61 National Database for Metastatic Breast Cancer

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Abstract
Introduction
DBCG was established in 1976 and have since maintained a clinical database for early breast cancer patients in Denmark. In 2017, DBCG created a database for patient with metastatic breast cancer, but no systematic reporting has been done.

Materials and methods
The present project will retrospectively collect clinical and pathological data from approximately 17.000 patients and prospectively data from all future metastatic breast cancer patients in the DBCG database with the aim to investigate the efficacy of new and already established therapies in a national representative population.

Results
The DBCG metastatic database has been in operation since 2017 and currently contains treatment information on approximately 1000 patients with mBC. It has been used for a recent request by the Danish Medicines Council on patients who received pertuzumab and thus proven to work both with data input and output. The retrospective part of the project has started in early 2019 and is expected to be finished by 2022.

Conclusions
To our knowledge, the DBCG metastatic breast cancer database will be the world's first national database on metastatic breast cancer. It will offer endless opportunities for future researchers in 'real-world' evidence in metastatic breast cancer.

Clinical epidemiology and database research

#62 Patienter med granulosacelletumor har øget risiko for bryst-og endometricancer

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Abstract
Introduktion
Granulosacelletumor (GCT) udgår fra granulosacellerne i æggestokkene og er en sjælden neoplasme. Tumoren udskiller ofte østrogener og diagnosticeres ofte på et tidligere stadium på grund af hormonrelaterede symptomer. På den baggrund er det relevant at undersøge om der findes en association til andre hormonrelaterede neoplasmer således at brystcancer og endometricancer kunne forekomme hyppigere ved GCT.

Materialer og metoder
Vi gennemførte et retrospektiv follow-up studie i perioden 1964-2008 i Danmark. Vi fandt 308 kvinder med GCT via landsregisteret for patologi. Lægejournaler og histologiske beskrivelser blev gennemgået.

Resultater
Vi fandt i studie perioden 308 kvinder med GCT, heraf havde 21 kvinder også brystcancer og 31 havde endometricancer. Baseret på beregninger af incidensrater på brystcancer og endometricancer ville vi have forventet 5,8 tilfælde af brystcancer og 0.49 tilfælde af endometricancer blandt de 308 GCT kvinder. Det vil sige at relativ risiko for brystcancer er 3,6 (95% CI: 2,2-5,5) og for endometricancer 63 (95% CI: 43-89) for kvinder med GCT.

Konklusioner
Opgørelsen viser en markant større sandsynlighed for at kvinder med GCT får brystcancer og endometricancer end baggrundsbefolkningen.

Clinical epidemiology and database research

#63 Hysterectomy-corrected mortality rates of corpus uteri cancer in Denmark, 2002-2015

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Abstract
Introduction
Corpus uteri cancer is the most common gynaecological malignancy in Denmark. Whereas the incidence of less aggressive histologic subtypes (i.e. endometrioid cancer) has been stable since 2000, the incidence of more aggressive subtypes (i.e. non-endometrioid cancer) has been reported to increase in Denmark. To assess whether this trend may be reflected in an increased mortality rate, we aimed to describe the hysterectomy-corrected mortality rate of corpus uteri cancer, overall and stratified by age and histologic subtype.

Materials and methods
Using data from national Danish registries, we calculated age-standardised uncorrected and hysterectomy-corrected mortality rates of corpus uteri cancer among women aged ≥35 years during 2002-2015. Hysterectomy-corrected mortality rates were calculated by subtracting post-hysterectomy person-years from the denominator, unless hysterectomy was performed due to corpus uteri cancer.

Results
Correction for hysterectomy resulted in a 25.5% higher mortality rate (12.3/100,000 person-years vs. 9.8/100,000 person-years). Hysterectomy-corrected mortality rates increased with age, reaching 43.2/100,000 person-years in women aged 70 years and older. The overall mortality declined during 2002-2009 after which rates reached a plateau at about 11.5/100,000 person-years. Of note, the hysterectomy-corrected mortality rate of endometrioid cancer declined during the study period, from 5.8/100,000 to 4.2/100,000 person-years, whereas the mortality of non-endometrioid cancer increased, from 1.4/100,000 to 3.7/100,000 person-years.

Conclusions
Among all women, the mortality rate declined over calendar time and increased with age. While the mortality of less aggressive histologic subtypes declined, although incidence rates were stable in this time period, the mortality of more aggressive histologic subtypes paralleled the incline in the incidence of these subtypes.

Clinical epidemiology and database research

#64 Gynecological cancers lead to long-term sickness absence and reduced working capacity years after diagnosis

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Abstract
Introduction
Knowledge on labour market prognosis following gynaecological cancers is lacking. Therefore, the aim of this nationwide, register-based study was to investigate overall timewise patterns in labour market participation, long-term sickness absence and risk for permanently reduced working capacity in this group of women.

Materials and methods
We followed 8451 women diagnosed with ovarian, endometrial and cervical cancer between 1998 and 2013 and 72,311 reference women in nationwide registers for up to 19 years. Timewise overviews of labour market position and annual proportions of long-term sickness absence were computed. Regression analyses were applied to compare the risk for permanent reduced working capacity among patients compared to reference women. Age, calendar period, amount of previous sickness absence, educational level, comorbidity and prior use of antidepressants were taken into account.

Results
Timewise patterns of labour market position differed across cancer diagnosis as well as stage of disease. Women with ovarian and cervical cancer had significantly higher proportions of long-term sickness absence than reference women up to five years after diagnosis. The risk of permanently reduced working capacity was increased for survivors of all three cancers. The highest relative risk was found in the period two to five years following diagnosis among women with advanced ovarian cancer (HR 19, 95 % CI 17.21-22.56). The increased risk persisted years after diagnosis in all groups, lasting up to 19 years in women with advanced cervical cancer.

Conclusions
Gynecological cancers lead to long-term sickness absence and reduced working capacity years after diagnosis. Women diagnosed with localized as well as advanced gynaecological cancer are more long-term sickness absent up to five years after diagnosis than women at the same age group, and are at prolonged risk for permanently reduced working capacity up to 19 years post diagnosis.

Clinical epidemiology and database research

#65 A validated algorithm to identify recurrence of ovarian cancer in Denmark: a register-based study

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Abstract
Introduction
Improved treatments are the main reason for an increasing survival among patients with ovarian cancer (OC). However, the recurrence rate remains high and for most patients the disease eventually becomes a continuum of symptom-free periods and recurrence episodes. Information about recurrences is not collected in the Danish cancer registry making recurrences difficult to ascertain. Oncologic data are registered in the Danish National Patient Registry (NPR). We aimed to investigate if it is possible to use oncologic data from NPR to assess oncologic treatments and recurrences in OC patients.

Materials and methods
Patients with OC FIGO stage I-IV diagnosed between 2010 and 2017, treated at Copenhagen University Hospitals, Rigshospitalet or Herlev, were included. Data concerning oncologic treatment were obtained from medical records. Data on recurrences and recurrence free intervals (RFI) from medical records were then compared with oncologic data from NPR to assess the correlation of the NPR estimated treatment free interval (TFI) in preliminary analyses.

Results
A total of 448 patients were randomized for review of medical records. Two hundred-and-ninety-eight patients were treated with primary debulking surgery. Of these, 235 (79%) received adjuvant chemotherapy and 106 (45%) patients had a recurrence. For patients with recurrence, we found a highly significant correlation (Rs=0.988, p=<0.001) between TFI from NPR data and RFI in data from medical records. The sensitivity for NPR data on TFI of 180 days, 1 year and 3 years was 90%, 100% and 100%, respectively. The specificity was 91%, 89% and 92%, respectively.

Conclusions
The preliminary results show high concordance between oncologic data from NPR and the validated oncologic data from medical records. If final analyses confirm this, import of oncologic data from NPR to the Danish Gynecological Cancer Database is planned, to enable quality assurance and use of data in future research settings.

Clinical epidemiology and database research

#66 Minimally invasive surgery in early stage cervical cancer, the Danish experience

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Abstract
Introduction
Since the introduction of robotic assisted laparoscopy has minimally invasive surgery (MIS) been the preferred surgical approach for early stage cervical cancer (ECC). Lately, a randomized trial comparing open access vs. MIS, questioned the oncological safety of MIS in ECC. The aim was to evaluate the safety of robotic MIS in the treatment of ECC in Denmark.

Materials and methods
Clinical and follow-up data on all consecutive patients with ECC stage IA2-IB1 who underwent radical hysterectomy in the period January 1st 2005 – June 30th 2017 were derived from the Danish Gynecologic Cancer Database (DGCD). Data was validated with other registers and patient files. Descriptive statistics with univariate and multivariate analyses were used.

Results
1125 ECC patients were included; 530 who underwent surgery before the introduction of robotic MIS (period 1) and 595 who underwent surgery after the introduction of robotic MIS (period 2). There were no significant differences in the rate of recurrence, recurrence location, or use of chemo-radiation between the two cohorts. Furthermore, no significant differences in the five-year cancer specific survival between cases diagnosed before and after the introduction of robotic MIS were found. Thus, five year cancer specific survivals of 94.1% and 95.9% (P = 0.10) were found in period 1 and period 2 respectively. Neither were any significant differences found between robotic MIS and open surgery (Robot vs. open HR 0.68, 95% CI 0.36 – 1.29, p = 0.24).

Conclusions
From our national cohort study, there is no indication that survival is compromised by introducing the robotic platform. The surgery for early cervical cancer will be followed closely in DGCD in the future.

Clinical epidemiology and database research

#67 Recurrence predictors in stage IA vulvar carcinoma

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Abstract
Introduction
To examine and describe risk factors of recurrence in women diagnosed with vulvar squamous cell carcinomas stage IA.

Materials and methods
Population-based prospectively collected data on 67 patients was retrieved through the Danish Gynaecological Cancer Database during the period 2011 to 2018. Chi-squared test and Fischer's Exact Test were used. P values were two tailed and considered statistically significant when p <= 0.05.

Results
In total we identified 667 women with vulvar cancer. Of these we included 67 women (10%) with stage IA vulvar squamous carcinoma. 12 (17.9%) of the included cases developed a recurrent cancer within the observation period. The recurrences were located in the vulva, inguens or in both in 7 (58.3%), 3 (25%) and 2 (16.7%) of the cases respectively. The risk of recurrence was significantly higher in primary tumors with an invasion depth of more than 0.5mm.

No other clinical and demographic factors showed a significant association with cancer recurrence.

Conclusions
Depth of invasion was of clinical relevance in the prediction of the recurrence.
Accordingly, these women may be offered regularly clinical re-examinations. Especially women with invasion depth of more than 0.5mm need follow-up.

Clinical epidemiology and database research

#68 Initial treatment and survival in a national unselected Danish cohort of 4163 patients with pancreatic cancer

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Abstract
Introduction
Nationwide register data on the efficacy of primary treatment on median overall survival (mOS) in an entirely unselected population of patients with pancreatic cancer (PC) have not been reported before. Thus, the aim of the study was to investigate the effect of initial treatment on mOS in all patients with PC in Denmark diagnosed in a recent five-year period.

Materials and methods
From 1 May 2011 to 30 April 2016, 4260 patients with PC were identified in the national Danish Pancreatic Cancer Database (DPCD). Ninety-seven patients were excluded, 56 due to preoperative chemotherapy followed by resection, 26 due to other malignancies, 13 due to incorrect registration of treatment and 2 were lost to follow up. In total 4163 patients were included. The mOS was estimated from the date of the initial treatment, either resection or chemotherapy. For the best supportive care (BSC) group the mOS was estimated from the date of diagnosis.

Results
Patients with initial resection accounted for 718 (17%) and showed a mOS of 22 months (95% CI; 20.0-24.2). Patients receiving initial chemotherapy, 1746 (42%) showed a mOS of 7 months (95% CI; 6.4-7.3). The preferred initial chemotherapy regimens were gemcitabine in 938 (54%) and FOLFIRINOX in 435 (25%) of the patients, and showed a mOS of 5 months (95% CI; 4.8-5.6) and 10 months (95% CI; 9.2-11.0) respectively. The BSC group accounted for 1699 (41%) and showed a mOS of only 2 months (95% CI; 1.5-1.7).

Conclusions
In the national Danish PC cohort of 4163 patients from 2011-2016, the patients initially treated with resection had the longest survival. Patients receiving palliative chemotherapy (gemcitabine or FOLFIRINOX) had slightly shorter mOS than found in randomized controlled trials, possibly reflecting patient characteristic of an unselected population. Improvement of the poor mOS in the large BSC group will need new early diagnostic options.

Clinical epidemiology and database research

#69 Survival from non-resected pancreas cancer (PC) is improved in specialized oncological units and associated with use of combination chemotherapy

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Abstract
Introduction
Data from the Danish Pancreas Cancer Database (DPCD) report showed significant differences in median overall survival (mOS) among PC patients treated at Danish oncological units. We studied factors potentially explaining the variation.

Materials and methods
We included 1,646 patients with histologically confirmed PC in DPCD, who had received chemotherapy as their first treatment between 2013 and 2018. We retrieved information on sex, age, stage and Charlson Comorbidity Index (CCI). Type of first-line chemotherapy was defined by the first three series. We divided the 7 oncological units treating PC into those with an in-house multidisciplinary HPB-team function, "specialized" units (N=4) and general units without such MDT function (N=3).

Results
A median of 47 new patients received chemotherapy per year per unit. Patients treated at specialized units had less comorbidity and more often metastatic disease. Monotherapy with gemcitabine was used less often in specialized units compared to general units (34% and 58%), whereas gemcitabine-combinations were used in 23% and 7%, and FOLFIRINOX in 27% and 15%, at specialized and general units, respectively.
The mOS differed significantly between patients treated at specialized (7.6 months; CI: 7.2-8.1 months) and general (6.2 months; CI: 5.6-7.3 months) units (P=0.0001). In a stratified analysis, the mOS was significantly different for patients with non-metastatic pancreas cancer (8.5 versus 6.6 months) (P=0.001), but not for metastatic cancer. The mortality was reduced in patients treated after 2017, but increased in patients with high CCI and in those treated with monotherapy. Hazard ratios for death according to unit type were attenuated after adjustment for type of chemotherapy.

Conclusions
We observed significant differences in survival of PC patients treated in Danish oncological units. Our study suggests that the use of multidrug chemotherapy may partly explain the variance.

Clinical epidemiology and database research

#70 Psychological late-effects in partners of pancreatic cancer patients - A nationwide register-based study with 17 years of follow-up

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Abstract
Introduction
Pancreatic cancer (PC) is a stressful condition for patients and their partners as the patients have a dismal prognosis. The primary aim of the study was to investigate the risk of depression, anxiety and insomnia in partners of PC patients.

Materials and methods
We used nationwide registries in a retrospective cohort study to examine the partners' use of psychotropic medication as a symptom proxy for depression, anxiety and insomnia. We followed 5,840 partners from 2000-2016 and compared them to an age-matched control cohort of 59,763 partners without a cancer diagnosis. The cumulated probability of psychotropic medication during the first two years of follow-up was estimated. Cox proportional hazard models were used to estimate hazard ratios (HRs) of the first prescription of psychotropic medication. We adjusted for socioeconomic positions.

Results
We found an increased cumulated probability risk of first-time medication against depression, anxiety and insomnia during two years in PC partners compared to controls. Use of antidepressants was increased up to 5 years after diagnosis (HR 1.24, 95% CI 1.05-1.46). The use of anxiolytics (HR 1.57, 95% CI 1.27;1.95) and hypnotics (HR 1.95, 95% CI 1.64; 2.32) was increased up to 2 years after diagnosis.

Conclusions
To our knowledge this is the first study to demonstrate the substantial psychological burden as a partner to a PC patient. Interventions to reduce psychological symptoms in partners warrant attention in clinical practice and future research.

Clinical epidemiology and database research

#71 Mixed Neuroendocrine-Non-Neuroendocrine Neoplasms (MiNEN) A retrospective analysis of 50 patients with gastroenteropancreatic tumors

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Abstract
Introduction
Gastroenteropancreatic Mixed Neuroendocrine-Non-Neuroendocrine Neoplasm (GEP-MiNEN) is a rare group of tumors consisting of more than 30% of each tumor component. Due to their rarity there are presently no international guidelines for diagnosis and treatment of these tumors. The aim of this retrospective analysis of GEP-MiNEN patients is to investigate clinical and pathological findings and to analyze treatment outcomes of patients with this rare disease entity.

Materials and methods
Fifty consecutive patients with GEP-MiNEN referred to our center in the period 2011-2017 were identified. Clinical data, overall survival and recurrence-free survival were analyzed according to Kaplan Meier's method. $P<0.05$ was considered significant.

Results
The median overall survival (OS) for all patients were 35 months. Recurrence-free survival were 23,5 months for the radically resected patients. Thirty-two patients were radically resected and median OS was 46 months in this group of patients compared to 10 months in the none-resected patients (P=0.002). A significant difference in median OS was observed between patients with localized disease/locally advanced disease and disseminated disease (P=0.002). Patients who presented with performance status (PS) 0 at diagnosis had a longer median OS than patients who presented with PS 1-2 at diagnosis (P=0.007). The predominant cell types in tumor and tumor location were not significant prognostic factors in this study (P=0.319 and P=0.349 respectively). Median follow-up time was 24,5 months.

Conclusions
Our results suggest that lower stage of disease at diagnosis, PS 0 at diagnosis and surgical intervention significantly improves median overall survival. Furthermore, esophageal tumor location compared to colonic tumor location shows a tendency to impaired prognosis of GEP-MiNEN.

Clinical epidemiology and database research

#72 Postopereative complications after elective colorectal cancer surgery – development and validation of a prediction model.

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Abstract
Introduction
Around 12% have serious complications within 30 days after elective colorectal cancer surgery. Complications lead to prolonged hospitalization, risk of delaying adjuvant chemotherapy and an increased risk of recurrence. If patients at high risk of complications can be identified before surgery, individualized treatment both before, during and after surgery can be implemented. The purpose of this study is to develop and validate a prediction model for postoperative complications following elective colorectal cancer surgery.

Materials and methods
Patients operated electively for stage I-III colorectal cancer from January 1st 2014 to December 31st 2017 and registered in the Danish Colorectal Cancer Group (DCCG.dk) database were included in the study. The model was developed in patients operated in the years 2014-2016 and validated in patients operated in 2017. The following variables were selected as possible variables for the model: gender, age, performance status, smoking, alcohol, BMI, UICC stage, surgical procedure planed, stoma, surgical approach, diagnosis detected by screening, preoperative chemo or radiation therapy. The outcome estimated with the model was complications classified by Clavien-Dindo ≥3b. The variables were selected by backwards selection and missing values were handled by multiple imputation. Discrimination will be evaluated with the area under an ROC curve, discrimination with a discrimination curve and accuracy with R2 test.

Results
A total of 7968 patients with a complication rate of 12% (Clavien-Dindo ≥3b) were included in the development of the prediction model. In the validation of the model, 1498 patients included a complication rate of 13%. Results for the model's performance are expected to be ready in June.

Conclusions
Not ready yet.

Clinical epidemiology and database research

#73 Postoperative mobilization - data driven quality improvements of fundamental cancer care

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Abstract
Introduction
Within the frame of fast track surgical programs, there is evidence that increased mobilization has a positive effect on post-operative recovery, and mobilization on postoperative day one to three is associated with a successful surgical outcome. Despite this, immobilization is still a widespread clinical challenge in postoperative cancer care. On this background, we aim to report how the establishment of a national, clinical nursing database for pre- and postoperative care in patients undergoing ovarian cancer surgery has impacted postoperative mobilization.

Material and methods
In this nationwide registry and quality improvement study, a multidisciplinary steering committee was responsible for the database in cooperation with a national registry support centre. During the treatment course, real time data entry was performed online by clinical nurses, since 2011 on 4400 women with ovarian cancer.
The quality indicator 'Mobilization' was defined as ≥ 3 hours out of bed on post-operative day one, in 60 %.

Results
Significant variations in duration and type of mobilization were observed, between cancer centres and between types of surgery. Totally 46.7% met the goal for mobilization on first post-operative day. Of the mobilized, 51.8% had been walking in the hallway on postoperative day one.

Conclusions
The database represents a bank of knowledge creating opportunities to optimize basic pre- and postoperative care. By comparing mobilization data with the oncological, surgical, and pathology data, it is possible to study mobilization in relation to cancer stage, co-morbidity, organization of care, and extent of surgery.
After major cancer surgery mobilization represents a basic yet complex intervention which is influenced by the way patients are prepared for their surgery and by the organization of care. However, type and length of sufficient postoperative mobilization needs further investigation.

Clinical epidemiology and database research

#74 The Effect of Different Comorbidities on Survival of Non-small Cells Lung Cancer Patients and Survival after Radiotherapy and Chemotherapy for Nonsurgically Treated Lung Cancer

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Abstract
Introduction
The Danish Lung Cancer Registry has accumulated data on all cases of lung cancer reported from all departments involved in the care of primary lung cancer in Denmark. This registry information is then supplemented with data on the patient's vital status retrieved from the Danish Civil Registration System, diagnoses and treatments from the Natioal Danish Patient register and pathology information related to the lung cancer from the Danish Pathology Register.

Materials and methods
The analysis is based on all patients with NSCLC registered in 2009–2011. 12,989 patients who were registered in 2009–2011. 2,611patients were excluded due to pathology which leads to a total sample size of 10,378 patients.

Results
For the general survival of non-small cells lung cancer patients the study showed that cardiovascular comorbidity is the primary driver of the prognostic value of the Charlson index. Diabetes, cerebrovascular disorders, and COPD also have a significant impact. Patients with multiple comorbidities had a significantly higher death rate compared with the patients without comorbidity.
For patients after Radiotherapy and Chemotherapy for Nonsurgically Treated Lung Cancer Treatment rates are highly dependent on age and to a lesser extent on comorbidity. Several factors significantly affect outcome of cancer treatment, such as stage, PS, age, sex, and comorbidity. Comorbidity appears to be weaker than PS. This has implications for the individual risk stratification of patients when selecting treatment.

Conclusions
The study shows the importance of cardiovascular disease in lung cancer. Diabetes, cerebrovascular disorders, and COPD also have a significant impact on survival of NSCLC patients. With focus on patients after Radiotherapy and Chemotherapy for Nonsurgically Treated Lung Cancer Comorbidity has a limited effect on it is rather the performance of the patient at diagnosis than the medical history that prognosticates survival in this patient group.

Clinical epidemiology and database research

#75 Risk of depression following prostate cancer workup - a nationwide registry-based study

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Abstract
Introduction
Little is known about the psychological impact of undergoing evaluation for prostate cancer (PCa). We investigated the risk of developing depression following PCa workup with benign and malignant findings, respectively, compared with cancer-free men.

Materials and methods
A nationwide cohort of men who underwent prostate needle biopsies in Denmark from 1997–2011 was identified through the Danish Prostate Cancer Registry. Primary outcome was depression defined as hospital contact for depression or use of an antidepressant prescription. For comparison, we selected a minimum of five age-matched cancer-free men per man who underwent PCa workup. We excluded men with cancer, major psychiatric disorder or use of antidepressants up to three years before study entry. Data on outcome and covariates (age, period, cohabitation status, income, and comorbidity) were retrieved from National Danish registries. We illustrated the risk of depression by cumulative incidence functions. Data were analyzed using Cox models adjusted for possible confounders.

Results
We identified 54,766 men who underwent workup, among these, 21,419 biopsy sets were benign and 33,347 men were diagnosed with PCa.
PCa patients had an increased cumulative incidence of depression throughout follow-up of up to 18 years. The adjusted hazard ratio of depression in men with PCa was increased throughout follow-up with the highest risk in the two years following diagnosis (HR 2.77, 95% CI 2.66–2.87). After biopsies, men with benign results had an increased risk of depression (HR 1.22, 95% CI 1.14–1.31) in the first two years compared with cancer-free men; hereafter, we found no difference.

Conclusions
We found an increased risk of depression in men following diagnostic workup for PCa compared with a matched background population. In men diagnosed with PCa, the risk remained increased throughout the study period. Future studies need to further analyze the impact of stage and treatment modalities.

Emerging treatments: Poster #76-103

Emerging treatments

#76 Treatment of locally advanced pancreatic cancer with irreversible electroporation - a Danish single center study of safety and feasibility

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Abstract
Introduction
Irreversible electroporation (IRE) is a novel non-thermal ablative technique applied in the treatment of unresectable locally advanced pancreatic cancer (LAPC). This paper reports on the initial experience with IRE of unresectable LAPC in our institution.

Materials and methods
From October 2013 to March 2018, patients with unresectable LAPC referred for IRE at the Department of Gastrointestinal Surgery, Aalborg University Hospital, were considered for inclusion in the study. Ninety-day morbidity, 30-day mortality, pain score, length of hospital stay (LOS) and overall survival (OS) was recorded.

Results
We included 33 patients receiving 40 IRE ablations in total. The median visual analogue scale (VAS)-score was four (range 0-10) two hours after IRE, and one (range 0-8) eight hours after IRE. The median LOS was one day (range 1-13 days). Post-procedural complications occurred in 21 of 40 ablations (53%), of which eight (20%) were major (Clavien-Dindo grade III or more). A proportion of the observed complications might be attributed to disease progression and not IRE per se. Although not statistically significant, we observed increased severity of complications in tumors above 3.5cm. The 30-day mortality was 5% (2/40). The median OS was 10.7 months (range 0.6-53.8 months) from the initial IRE procedure, and 18.5 months (range 4.9-65.8 months) from time of diagnosis.

Conclusion
In our institution, IRE seems as a feasible consolidative treatment of unresectable LAPC with an acceptable safety profile. The oncological outcome of IRE in patients with unresectable LAPC is to be further evaluated in a planned phase 2 clinical trial (CHEMOFIRE-2).

Emerging treaments

#77 Kan Pressurized IntraPeritoneal Aerosol Chemotherapy (PIPAC) behandlingen hindre tilbagefald af kræft fra mavesæk og tyktarm?

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Abstract
Introduktion
Patienter med kræftspredning til bughinden (peritoneale metastaser, PM) har kort restlevetid og nedsat livskvalitet på grund af svære symptomer herunder væskedannelse, tarmobstruktion og smerter. Patienter med fremskredne svulster i mavesæk og tyktarm har høj risiko for at udvikle PM trods initial fjernelse af kræften og almindelig kemoterapi. Ved Pressurized IntraPeritoneal Aerosol Chemotherapy (PIPAC) metoden sprøjtes kemo direkte ind i maven og disse studier skal afklare, om PIPAC kan nedsætte risikoen for udvikling af PM hos patienter med kræft i mavesæk eller tyktarm.

Materialer og metoder
PIPAC-OPC3 studiet (NCT03280511) skal inkludere 60 patienter, som er opereret for en fremskreden svulst i tyktarmen. Efter seks måneders kemoterapi modtager patienten to PIPAC behandlinger med oxaliplatin, som indgives under en almindelig kikkertoperation. Ved operationen tages vævsprøver og bughinden skylles med saltvand for at afsløre kræftceller. Patienten følges derefter med skanninger i tre år.
PIPAC-OPC4 studiet er et planlagt gennemførlighedsstudie af 20 patienter med kræft i mavesækken. I dette studie indgives kemoterapi ved PIPAC metoden i forbindelse med selve fjernelsen af mavesækken og bughinden skylles igen med saltvand for at afsløre kræftceller.

Resultater
PIPAC-OPC3 har inkluderet 12 patienter siden 12/2017. En patient havde PM ved første PIPAC og blev ekskluderet. På grund af kraftige smerter modtog kun seks patienter begge planlagte PIPAC behandlinger. Som følge deraf er dosis af oxaliplatin nu halveret. Fraset smerter har der ikke været betydende bivirkninger og ingen dødsfald. To patienter har gennemført første kontrolskanning, hvoraf den ene havde udviklet tilbagefald i den ene æggestok. PIPAC-OPC4 inkluderer endnu ikke patienter.

Konklusioner
Trods optimal behandling rammes mange patienter med mavesæk- og tyktarmskræft af tilbagefald på bughinden. Igangværende studier skal afklare, om PIPAC behandlingen kan nedsætte denne risiko.

Emerging treatments

#78 PIPAC (Pressurized IntraPeritoneal Aerosol Chemotherapy) in the treatment of peritoneal metastasis

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Abstract
Introduction
Peritoneal metastasis (PM) represents end stage disease in several types of cancer and systemic chemotherapy has limited effect on PM. PIPAC is a new technique where aerosolized chemotherapy is emitted inside the abdominal cavity during laparoscopy. PIPAC ensures a high concentration of chemotherapy in the PM without the side effects of systemic chemotherapy. Treatment response is monitored through repeated evaluation of biopsies (Peritoneal Regression Grading Score, PRGS) and peritoneal fluid collections.
The first Scandinavian PIPAC procedure was performed at Odense University Hospital in 2015.

Materials and methods
This abstract presents an overview of patients with PM referred and treated in two prospective OPC protocols (PIPAC-OPC1 and -2) between November 2015 and April 2019.

Results
240 patients were referred for protocolled treatment during the inclusion period, and 107 (45%) patients (64F, 43M, mean age 60.2 years, range 31-85) fulfilled the inclusion criteria. Primary diagnosis was mainly gastric, colorectal, ovarian and pancreatic cancer, and 53 patients (49.5 %) had their primary tumor in situ. Extra-peritoneal disease was allowed in the second protocol and represented 20% (14/71). Ninety-five percent of the patients were pretreated with systemic chemotherapy, and 19-45% had ≥ 2 lines of palliative treatment depending on the type of cancer. ECOG performance status at first PIPAC procedure was 0 in 24%, 1 in 73% and 2 in 3% of the patients A total of 288 PIPAC procedures were performed (mean 2.7 procedures/patient, range 1-9) with a median postoperative stay of 1 day (range 0-4). Only 3 patients experienced D-C complications ≥ grade 2. The mean tumor score (PRGS) was reduced from 2.2 to 1.7 in patients having at least 3 PIPAC procedures.

Conclusions
PIPAC is a safe, well tolerated and repeatable procedure in heavily pretreated patients with PM. PIPAC induces a decrease in the objective tumor score between the first and third procedure.

Emerging treatments

#79 Pressurized IntraPeritoneal Aerosol Chemotherapy (PIPAC) directed treatment of peritoneal metastasis from colorectal cancer - A descriptive cohort study.

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Abstract
Introduction
Pressurized IntraPeritoneal Aerosol Chemotherapy (PIPAC) represents a novel approach to intraperitoneal chemotherapy. Hereby results, obtained with PIPAC in patients with advanced peritoneal metastasis (PM) from colorectal cancer (CRC), are presented.

Materials and methods
Data from CRC patients (n=24) included in the prospective PIPAC-OPC1 and PIPAC-OPC2 studies are reported. Oxaliplatin 92 mg/m2 was administered at 4-6-week intervals. Outcome criteria were objective tumor response, survival and adverse events.

Results
Retrospective analysis of 74 PIPAC procedures carried out in 24 consecutive patients with PM from CRC. Five patients had still the primary tumor in situ and 22 patients had received palliative systemic chemotherapy. Nineteen patients completed more than two PIPAC procedures, and objective tumor response according to the histological Peritoneal Regression Grading Score (PRGS) was observed in 67 % of the patients, while 21 % had stable disease. Four patients (21 %) had complete response (mean PRGS=1 and negative cytology).
We recorded a median survival of 37.6 (range 10.2-47.0) months from the time of PM diagnosis, whereas it was 20.5 (range 0.13-34.7) months following the first PIPAC session. Minor postoperative complications were noted, and few were considered related to the PIPAC treatment. Two cases of severe complications were recorded (urosepsis and iatrogenic bowel perforation).

Conclusions
PIPAC with low-dose oxaliplatin can induce objective tumor regression in the majority of selected patients with advanced PM from colorectal cancer, offering survival prospects that are encouraging but need to be further explored.

The study protocols have been approved by The Regional Committees on Health Research Ethics (Project-ID:S-20140211 and S-20160100), Danish Medicines Agency (Code number: 2016083464) and the Danish Data Protection Agency (14/52603,16/23653). ClinicalTrials.gov identifier: NCT02320448 and NCT03287375. EudraCT number 2016-003394-18.

Emerging treatments

#80 First clinical experiences with a high field 1.5 T MR Linac

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Abstract
Introduction
A 1.5 T MR Linac (MRL) has recently become available. MRL treatment workflows (WF) include online plan adaptation based on daily MR images (MRI). This study reports initial clinical experiences after five months of use in terms of patient compliance, cases, WF timings, and dosimetric accuracy.

Materials and methods
Two different WF were used dependent on the clinical situation of the day; Adapt To Position WF (ATP) where the reference plan position is adjusted rigidly to match the position of targets and OARs, and Adapt To Shape WF (ATS) where a new plan is created to match the anatomy of the day using deformable image registration. All WFs included three 3D MRI scans for plan adaptation, verification before beam on, and validation during IMRT delivery. Patient compliance and WF timing were recorded. Accuracy in dose delivery was assessed using a cylindrical diode phantom.

Results
25 patients have started treatment on the MRL of which 19 patients have completed their treatment receiving a total of 176 fractions. Cases vary from prostate treatments (60 Gy/20F) to SBRT treatments of lymph nodes (45 Gy/3F) and castration by ovarian irradiation (15 Gy/3F).
Results on the first 19 patients is presented here: The median session time (patient in to patient out) for 127 ATPs was 26[21-78]min, four fractions lasted more than 45 minutes due to additional plan adaptation. For the 49 ATSs a median time of 12[1–24] min was used for contouring resulting in a total median session time of 42[29-91] min. One SBRT fraction lasted more than an hour due to beam interruption. The time on the MRL couch was well tolerated by the patients. The median gamma pass rate (2mm,2% global max) for the adapted plans was 99.2[93.4-100]%, showing good agreement between planned and delivered dose.

Conclusions
MRL treatment, including daily MRIs, plan adaptation and accurate dose delivery is possible within a clinically acceptable timeframe and is well tolerated by the patients.

Emerging treatments

#81 Stereotactic radiotherapy as treatment for localized relapse of NSCLC after previous surgery or radiotherapy

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Abstract
Introduction
Stereotactic radiotherapy (SBRT) is efficient as treatment for early stages NSCLC. SBRT may, however, also be used as treatment for relapsed recurrent disease. We here report the outcome of patients previously treated with surgery radiotherapy (RT).

Materials and methods
All cases of NSCLC at our institution treated with RT with curative intent are prospectively recorded. We here report the results of 183 cases treated at our institution July 2009 to June 2018 with SBRT for relapsed NSCLC. The doses used for peripheral located tumors was 45-66 Gy (central doses) in 3 fractions (F) while centrally located tumors have been treated with 50 Gy/5F or 80 Gy/ 8 F. The patients have been treated with IMRT or VMAT. A group of 124 patients had previously surgery: Resection 30 (24%), lobectomy 87 (70%), and pneumonectomy 7 (6%). Another group of 59 patients had previous RT: SBRT 34 (58%) and conventional or chemo-RT 25 (42%). All patients had more than 9 mo. potential follow-up.

Results
The median time from the primary treatment to the SBRT was 38.5 (1.6; 273) mo. in the surgical treated group, and 21.2 (2.5; 126) mo. in the RT treated group ($p<0.001$) 70% of the patients in the surgical group were in PS 0-1 compared with 42% the RT group ($p<0.001$).
The median, 1, 2, 3, 4 , and 5 year overall survival was 51.8 mo., 90%, 73%, 64%, 53%, and 44% in the previously surgical treated group and 22.2 mo., 71%, 47%, 37%, 28%, and 22% in the previously RT treated group ($p=.0001$).

In Cox regression analyses previous RT, male gender and PS >1 was associated with poor survival while age, FEV1, and time from primary treatment to SBRT was not.

Conclusions
The survival after SBRT for relapse was significantly better after previous surgery than after previous radiotherapy.

Emerging treatments

#82 Survival in patients with non-small cell lung cancer with brain metastases treated with whole brain radiotherapy

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Abstract
Introduction
Patients with non-small cell lung cancer (NSCLC) are in high risk of developing brain metastases. The prognosis for this patient group is poor. In case of five or less brain metastases, guidelines recommend stereotactic radiosurgery, if more whole brain radiation therapy (WBRT). Multiple studies have shown WBRT to be associated with neurocognitive side effects and to reduce quality of life significantly. For patients with a short life expectancy it is important to consider treatment with supportive care alone. In this retrospective study we want to examine the overall survival (OS) of patients after treatment with WBRT. Furthermore, we want to examine how many patients receive futile WBRT (defined in this study as patients dying within 8 weeks from WBRT start).

Materials and methods
Patients with NSCLC and brain metastases referred to WBRT 2016-2018 at Herlev Hospital are included. Clinical information regarding patient characteristics, status of primary lung cancer, treatment side effects and survival are retrieved. OS was estimated using Kaplan-Meier from WBRT start. Variables possibly influencing OS are calculated using Cox proportional hazards regression model.

Results
138 patients are included in the study. At the present, recording of patient data is ongoing. So far we have preliminary results for a selected number of the variables for 40 patients. The median OS is approx. 13 weeks. 30% of the patients died within 8 weeks after WBRT. ECOG Performance Status 2 (p=0.006) and shorter fractionation schedule (p=0.028) were found to have a significant negative impact on survival.

Conclusions
Preliminary results from 40 patients have shown that a significant part of patients with NSCLC and brain metastases are treated with futile WBRT. Treatment with supportive care alone could be considered for patients with a high performance status. Data analysis on the full cohort of patients is pending and will be presented.

Emerging treatments

#83 Trimodal treatment of locally advanced non-small cell lung cancer: Model-based comparison with chemoradiation only

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Abstract
Introduction
Standard treatment for patients with locally advanced non-small cell lung cancer is chemoradiation (CRT). Some patients with minimal N2 disease in good general condition are offered surgery after CRT (trimodal treatment) but evidence is sparse.
We evaluate the outcome of trimodal treatment compared to CRT alone using two statistical methods.

Materials and methods
Patients treated with CRT with a radiation dose of 60-66 Gy from 2013-18 were eligible. We registered patient and disease characteristics, treatment outcome, survival and eventual surgical details.
A multivariable model was generated based on data from CRT treated patients to provide an expected survival given the covariables: Age, T- and N-stage, histology, performance status and Charlson Comorbidity Score. The model provided expected survival and observed outcome was compared to CRT.
A propensity score match (PSM) analysis was generated based on the same baseline characteristics: Cases were matched 1:1 witch controls with corresponding propensity scores. Outcome in the two groups was compared.

Results
266 patients were included. 43 received trimodal treatment. VATS was performed in 39.5% and open surgery in 60.5% of cases. Complication rate was 48.8%, most commonly infection (27.9%) and bleeding (11,6%). Reoperation rate was 16.3%. 30-day mortality was 7.0%. Complete pathological response after CRT was seen in 27.9% of cases.
In univariate analysis, trimodality patients had improved survival (p=0.01) as compared to CRT. Adjusting for available covariables, the observed survival tended to remain superior to the expected survival if CRT was given. In the multivariate model thirty-six patients including two cases were excluded as comorbidity score was missing.
In PSM analysis trimodality patients also had improved survival compared to the matched controls.

Conclusions
Trimodal treatment appears to improve survival, but residual confounding from case selection is a limitation.

Emerging treatments

#84 Survival after stereotactic radiosurgery for brain metastasis - A single institution experience

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Abstract
Introduction
Advances in cancer treatment result in improved median survival. Consequently, the number of patients (pts) presenting with brain metastasis (BM) is increasing. For pts with limited metastatic disease to the brain, stereotactic radiosurgery (SRS) is increasingly used instead of whole brain radiotherapy (WBRT). The benefit of SRS to WBRT is better local control and reduction in toxicity. However, despite advances in treatment the prognosis for pts with BM remains poor. The aim of this study was to evaluate survival after first treatment with SRS for BM.

Materials and methods
This is a single institution study. All consecutively pts with different primary cancer diagnosis with at least one BM treated from Apr 2011 to Feb 2018 were included. The pts were prospectively registered and clinical data retrospectively gathered. After treatment, pts were followed with regular MRI. In case of a new lesion or local progression the pt were evaluated if SRS, WBRT, surgery, systemic treatment or best supportive care would be the best option for the individual pt. No pts were lost to follow up. Dose to the edge of the Gross Tumor Volume was 20 Gy/ 1 F. All pts were planned with CT- and MR scan. The treatment was performed with three arcs on a linac.

Results
In total 285 pts were treated with SRS. Median overall survival (OS) was 8 months. OS after 1 and 2 years was 35% and 18% respectively. Median OS for breast cancer pts was 13.6 months, 9.8 months for malignant melanoma, and 8.2 months for lung cancer pts. In a cox regression analysis age <70 years, PS, and breast cancer diagnosis had a statistically significant impact of improved survival, whereas number of targets (1 vs. 2-4) did not.

Conclusion
SRS performed with VMAT improve survival compared to WBRT (historical data). It is an effective treatment for BM, but factors such as age, poor PS, and primary cancer diagnose may be considered in pt selection. Despite SRS the majority of the pts with BM still have a poor prognosis.

Emerging treatments

#85 Stereotactic Body Radiotherapy strategy for Oligometastatic disease/advanced disease

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Abstract
Introduction
Stereotactic Body Radiotherapy (SBRT) for oligometastatic disease (OMD)/advanced disease is rapidly emerging into standard practice. However, in most cases, it is still considered investigational and not without risk. The literature is scarce in respect to the optimal dose fractionation scheme, and the optimal imaging work-up, is not yet clearly defined. At ASTRO 2018, two prospective, phase II, randomized trials were presented (OLIGOMEZ and SABR-COMET), documenting acceptable toxicity and improved overall survival after SBRT for OMD. Local control rates in the published international studies generally exceed 80% at 1 year. The use of SBRT to treat Oligo-progressive disease is likewise increasingly being investigated in trials. Our goal is to ensure an SBRT-based treatment option for patients with solid tumours in all metastatic sites.

Materials and methods
We present seven studies that are currently including or will start including patients in 2019. Bony-M: SBRT for bony metastases, STAR-Lung: Stereotactic daily adapted radiation therapy in centrally located lung tumors, ReTreat: Reirradiation of brain metastases with stereotactic radiosurgery (SRS), SRS XL: SRS treatment of brain metastases > 3 cm, SOFT: A phase II study of MR-based SBRT of infra-diaphragmatic soft tissue metastases. SAPR-trial: SBRT for primary RCC. SBRT vs. MWA for CRC: SBRT vs. percutaneous microwave ablation for colorectal cancer patients with metastatic disease in the liver – a randomized phase II trial.
We are in the process of inviting all Danish radiotherapy centers to participate in the studies.

Conclusions
We foresee that the demand for SBRT treatments in the OMD/advanced setting will increase significantly in near future. The initiated studies will facilitate safe implementation of this treatment modality in Denmark. The studies will be performed in close collaboration between the Danish radiotherapy centers

Emerging treatments

#86 Inter-observer variations in evaluation of radiotherapy dose plan quality

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Abstract
Introduction
The primary objective of radiotherapy (RT) is to maximize target coverage (TC) and minimize doses to organs at risk (OAR). This is evaluated using fixed guideline radiation dose constraints. Secondary characteristics of the radiation dose distributions, such as dose fall-off or dose homogeneity, are evaluated qualitatively by the doctor. Qualitative evaluation is subjective and can vary between observers. The aim of this study was to compare consistency in qualitative vs. quantitative evaluation of RT plans.

Materials and methods
Two strategies for radiation treatment plan optimization were used for 20 head-and-neck cancer pts: either using a manual optimization or the knowledge-based semi-automated planning software RapidPlan (RP, v13.7 Varian Medical Systems). Four radiation oncologists performed blinded clinical evaluations of the plans and chose which plan they preferred for each pt, evaluating TC and OAR doses. They also gave scores for the importance of five different secondary qualitative plan characteristics. Corresponding quantitative metrics describing these characteristics were calculated. Consistency between score-metric pairs was evaluated.

Results
All plans complied with critical OAR and TC dose constraints. Physicians tended to choose the plan they gave the better OAR score, but in only six cases did all prefer the same plan. A Friedman's ANOVA test showed significant ($p<0.05$) variations between doctors for all subjective scores except OAR in non-RP plans. Little to no correlation was seen using Spearman's ρ for each score-metric pair, including scores from all doctors (-0.34 to 0.20, median -0.07).

Conclusions
There were substantial inter-observer variations in subjective scores. Little to no consistency was seen between qualitative scores and corresponding quantitative metrics. Consistent use of quantitative metrics in addition to subjective plan evaluation should be investigated as a way of increasing consistency of RT plan quality evaluation.

Emerging treatments

#87 Reconstruction of delivered dose based on in vivo dosimetry in prostate brachytherapy

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Abstract
Introduction
Novel in vivo dosimetry (IVD) systems for brachytherapy (BT) have enabled source tracking (ST) with a sub-millimetre precision. We have used ST to reconstruct dose volume histogram (DVH) parameters in HDR prostate treatments. Reconstructed DVH parameters are compared to the treatment plans to investigate, if current applicator reconstruction uncertainties lead to clinically relevant deviations in dose.

Materials and methods
IVD was performed during 9 fractions of HDR prostate BT. Patients were treated with two HDR fractions of 8.5Gy delivered after 46Gy EBRT. The needles were implanted under trans-rectal ultrasound guidance and the treatment planned on MRIs. A small in-house developed dosimeter was placed inside the prostate in a dedicated needle. Dose rates for each source dwell were recorded during the dose delivery and analysed post-treatment. The position of each needle relative to the dosimeter was determined based on the recorded dose rate. The tracked needle positions were registered to the patient anatomy on the planning MRI and used to reconstruct the delivered DVH parameters.

Results
A total of 149 needles were analysed and showed needle offsets with a spread (1SD) of 1.6 mm in the caudal-cranial direction and 0.4 mm towards-away from the dosimeter. The resulting changes in the dose distributions lead to a mean±1SD fractional change of -0.07±0.1Gy in prostate D90, -0.0±0.01Gy in urethra D0.1cm3, 0.02±0.19 Gy in rectum D2cm, and 0.56±1.57 Gy in bladder D0.1cm3

Conclusions
IVD can be used to provide feedback on a reconstructed BT dose distribution. The observed needle shifts confirm a precise reconstruction of the needles on MR images and only limited discrepancies in the position of treatment needles (1SD < 2mm). The dosimetric impact of the needle movements relative to the dosimeter was small.

Emerging treatments

#88 Workshop vedrørende projektet DEPeNDS – Danish nEurooncology ProtoN Decision Support

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Abstract
Patienter med hjernekræft har siden januar 2019 haft mulighed for at blive behandlet med protonterapi på Dansk Center for Partikelterapi. Især patienter med lavgradsgliomer kan have stor fordel af protonterapi, da de har en lang levetid efter behandling. Det er imidlertid svært at afgøre, hvilke patienter der har størst gavn af behandlingen, da der indtil nu er meget begrænset kendskab til, hvilke bivirkninger forskellige stråledoser giver. Beslutningen bliver dermed ofte taget ud fra en subjektiv vurdering af bl.a. patientens alder, diagnose, sygdomshistorie og generelle helbredstilstand. For at gøre denne beslutningsproces mere objektiv, vil vi med dette projekt forsøge at finde frem til de vigtigste parameter, når læger skal vælge mellem enten foton- eller protonterapi. Projektet er nationalt og involverer læger og fysikere fra de fire henvisende afdelinger i Danmark. DCCC bidrager med økonomisk støtte til projektet.
Tolv læger og ni fysikere mødtes i starten af april til en workshop, hvor hovedformålet var at vælge mellem foton- og protonterapi for 25 patienter med lavgradsgliomer. De 25 patienter havde fået lavet nye struktursæt i overensstemmelse med gældende retningslinjer samt nye foton- og protonplaner. Der var endvidere indsamlet kliniske parametre på alle patienter. Efter en kort introduktion til dagens program, kastede deltagerne sig over arbejdet med stor entusiasme. Da workshoppen var slut, var der nogle få af de 25 patienter, som lægerne var helt enige om, men ellers var det meget forskelligt hvad der blev lagt vægt på. Der var dog generel enighed om at en sådan workshop med god tid til at gennemgå mange forskellige planer grundigt og systematisk var en rigtig god idé, og at dette ville være en fordel for flere diagnosegrupper, da der i en ellers travl hverdag er meget begrænset tid til den slags opgaver.
Efter planen skal i alt 100 patienter indgå i projektet, og der vil med finansieringen fra DCCC blive afholdt yderligere én til to workshops.

Emerging Treatments

#89 Strategi for adaptiv strålebehandling af hovedhalskræftpatienter i protonstrålebehandling

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Abstract
Introduktion
I maj 2019 påbegyndes behandling af hovedhalskræftpatienter med protonbestråling på DCPT. Protoner er følsomme overfor forandringer i væv forårsaget af fx vægttab eller tumorsvind. På DCPT foretages en ugentlig CT til evaluering af anatomiske ændringer samt konsekvens for dosisfordelingen og evt. tilpasset stråleplan. Der optages dagligt i forbindelse med selve strålebehandlingen en conebeam-CT (CBCT) til brug ved lejring af patienten. Hypotesen er, at en kunstig CT-skanning, genereret fra den daglige CBCT, er tilstrækkelig til genberegning af dosis og evaluering af stråleplan når som helst i forløbet.

Materialer og metoder
En kunstig CT genereres ud fra dagsaktuel CBCT og dosisfordeling genberegnes. Aktuel stråledosis genberegnes endvidere på ugentlig CT, som tidsmæssigt matcher CBCTen. Endelig sammenlignes dosisfordeling på kunstig CT med dosisfordeling på ugentlig CT og det evalueres om den kunstige CT-skanning præcist nok kan evaluere behovet for eventuel tilpasning.

Resultater
Metoden er testet retrospektivt på (CB)CT-skanninger fra fotonstrålebehandling. Der er 4 uger mellem CT-skanningerne og udtalte anatomiske forandringer og tumorsvind. Der er udarbejdet en protondosisplan på oprindelig CT-skanning. Planen er genberegnet på 4 ugers-skanningen og på kunstig CT baseret på CBCT fra samme dag som ny CT. Begge genberegninger afslører nedsat dosis til behandlingsområde og helt parallelt ændrede normalvævsdoser.

Konklusioner
Den omtalte metode er testet med lovende resultater på skanninger med store anatomiske forandringer. Det planlægges således at anvende og teste metoden på de første 10 kliniske hovedhalskræftpatienter på DCPT. Målet er fleksibel stråledosistilpasning under behandlingsforløbet, hurtig evaluering af anatomiske forandringer og deres konsekvenser samt anvendelse af eksisterende information (CBCT) til at nedsætte antallet af CT-skanninger til at omfatte de tilfælde hvor strategien afslører et behov for en ny tilpasset protondosisplan.

Emerging treatments

#90 Automatic detection of heart irradiation during breast cancer radiotherapy

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Abstract
Introduction
Heart irradiation during radiotherapy of breast cancer can lead to late cardiac morbidity and increased mortality for long-time survivors. For tangential left-sided treatments, continuous portal images (cine MV images) may be used to monitor the heart exposure at each treatment, but the monitoring is challenged by low image contrast and the location of the heart edge in or near the field penumbra. Here, we develop and test automated heart detection in cine MV images.

Materials and methods
Cine MV portal images of 302 tangential field deliveries were recorded at 7.7Hz for ten left-sided breast cancer patients who received deep-inspiration breath-hold radiotherapy in 15-18 fractions. An algorithm for fully automatic detection of the heart edge in cine MV images was developed and tested for all available images. The algorithm exploits that the intensity of pixels at the heart edge will change cyclically with frequencies of 1-3 Hz due to heartbeat and that the intensity changes of all pixels at the heart edge will be highly correlated with each other because they have the same physical origin (heartbeat). The algorithm generates an enhanced heart edge image, in which the heart edge is segmented and the exposed heart area is calculated.

Results
Part of the heart was unintentionally exposed at 169 out of 302 field deliveries. The heart edge was correctly identified in all cine MV series. Large interfraction variations in the exposed heart area occurred, while intrafraction variations were smaller with high correlation between heart exposure at the two opposing tangential fields at a fraction ($r = 0.85$, $p < 0.001$).

Conclusions
An algorithm for automatic identification of pixels at the heart edge in cine MV images was proposed, developed and shown to be highly efficient for heart exposure detection in tangential breast fields. The algorithm may be used in a surveillance program with automated heart exposure monitoring of all breast cancer treatments in a clinic.

Emerging treatments

#91 Immune Checkpoint Inhibitors (ICI) in a Danish real life Non-Small Cell Lung Cancer (NSCLC) Population. A retrospective cohort study from Odense University Hospital

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Abstract
Introduction
Real life data of Danish NSCLC patients treated with ICI are lacking. The aim of the study was to investigate effect and toxicity of ICI in an unselected NSCLC population, including patients underrepresented in clinical trials (patients with brain metastasis (BM), higher age, autoimmunity, more comorbidity and poorer performance status (ECOG)).

Materials and methods
Real life data were gathered from 118 consecutive NSCLC patients with incurable NSCLC treated with ICI at the Department of Oncology at the University Hospital of Odense, Denmark from September 2015-April 2018. Immune related Adverse Events (irAE) grade 3-5 were registered prospectively during the same period. Additional patient related data were obtained retrospectively from patients' files. Overall survival (OS) and progression free survival (PFS) were calculated using Kaplan Meier estimates, the log-rank test and cox regression analysis was performed for factors affecting survival.

Results
Median age for patients was 66 years [IQR 59-71] and 62 years [range: 55-64] for those with BM. Females 63%; adenocarcinoma/squamous/others 69%/23%/8%; ECOG ≥ 2 10%; bone/brain/liver metastases 36%/18%/15%; PD-L1 (TPS) <1%/ ≥1%≤ 49%/≥50%/NR: 3%/14%/68%/15%; baseline autoimmunity 10%, Charlsons Comorbidity Index Score (CCIS) ≥ 2 39%, treatment line: 1st/2nd/ ≥3rd 39%/30%/31%. Median OS for patients receiving ICI in ≥ 2 line was 11.5 months versus not reached in first line (HR 2.6, [95% CI; 1.3-5.0], p=0.005). For patients with BM, the median OS was 8.2 months (HR 1.38, [95% CI; 0.7-2.5], p=0.37]. Twenty-four percent of patients terminated ICI due to irAE grade 3-5 alone (grade 5, n=1), which were not associated with higher age or BM.

Conclusions
OS and PFS were comparable to clinical trial reports. Long-lasting remission is also possible in patients with BM. Real life populations have higher rates of irAE grade 3-4 than reported in clinical trials, but it does not seem to impact median OS.

Emerging treatments

#92 Treatment with immune checkpoint inhibitors for advanced NSCLC in elderly and frail patients. A real-life experience

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Abstract
Introduction
Immune checkpoint inhibitors (ICIs) have changed the standard treatment in advanced stage NSCLC. However, patients above 75 years and patients in performance status (PS) 2 are underrepresented in randomized clinical trials. Hence, efficacy and safety of treatment in these large subgroups of patients remains unclear. We report a real-life study of such patients treated with ICIs in a 2nd line setting.

Materials and methods
Data from consecutive patients with advanced NSCLC who had 2nd line treatment with ICIs at the University Hospitals in Copenhagen during November 2015 to May 2018 were obtained from medical records. Treatment efficacy and safety was evaluated, and treatment related adverse events (AEs) were registered.

Results
A total of 224 NSCLC patients were treated with either nivolumab or pembrolizumab: The median follow up time of was 12.3 months. Median progression free survival (PFS) was 4.9 months, and median overall survival (OS) was 12.9 months CI [9.7-14.6]. Median age was 67.7 years, while 45 patients (20%) were ≥75 years. There were no significant difference when comparing patients ≥ 75 years vs. < 75 years with respect to PFS (5.3 vs. 4.9 months, p=0.81) nor OS (14.2 vs. 12.8 months, p=0.93). PFS and OS were correlated with PS: PFS was 7.7, 4.7 and 2.0 months (p=0.0003) in PS 0, PS 1 and PS 2, respectively. OS was 20.9, 12.0 and 3.0 months (p>0.0001) in PS0, PS1 and PS 2, respectively. AEs were reported in 175 patients (79%), among whom 30 patients (13%) experienced grade 3-5. There were no difference in AEs in younger patients compared to older ≥ 75 years (p=0.34). The incidence of grade 3-5 AEs was significantly higher among patients in PS 2 (26%) compared to PS 0-1 (11%), (p<0.0001).

Conclusions
Patients ≥ 75 years had efficacy and safety profiles comparable to those of younger patients. However, treatment with ICIs in patients with PS 2 was associated with a significant lower PFS and OS as well as a high risk of seriously AEs.

Emerging treatments

#93 Exercise regulation of tumor immunogenicity and combination with immune checkpoint therapy

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Abstract
Introduction
Mouse studies have shown that access to running wheels lead to >50% reduction of tumor growth along with increased immune cell infiltration of the tumors. Actions of the infiltrating cytotoxic immune cells is inhibited by checkpoint molecules such as PD-1/PD-L1 expressed on inflammatory cells and in some cases also the tumor cells, and blockade of this axis has proven effective in cancer patients with high immune cell infiltration and PD-L1 expression.

Materials and methods
B16 melanoma tumors from control mice and mice with access to running wheels were submitted to mRNA expression analysis of PD1, PD-L1 and PD-L2, and markers of antigen presenting cells (APCs). The potentially synergistic effect between exercise and αPD-L1 treatment was investigated by combining running wheels with αPD-L1 -or placebo treatment followed by evaluation of tumor growth. Tumor biopsies from patients with gastro-esophageal adenocarcinoma were analyzed by IHC for PDL1 -and CD8 expression. The results were correlated to muscle expression of the exercise adaptation marker PGC1α.

Results
Expression of PD1 (2.9-fold $p<0.01$), PDL1 (2.3-fold $p<0.01$) and PDL2 (3.1-fold $p<0.05$) increased with voluntary wheel running, and so did the tumor infiltration by APCs of the cDC1 dendritic cell type identified by CD103 (2.38-fold, $p<0.01$), XCR1 (2.54-fold, $p<0.01$) and Clec9A (3.66-fold, $p<0.001$). We find a significant reduction of tumor growth with exercise ($p<0.05$), but no significant effect of adding αPD-L1 treatment to the exercise intervention. In patients, PDL1 -and CD8 expression in tumors show correlation with muscle expression of PGC1α ($p<0.05$).

Conclusions
In mice, access to running wheels increased tumor expression of immune checkpoint markers and tumor infiltration by cDC1 dendritic cells. Future experiments include a mouse study combining αPD-1 treatment with voluntary wheel running. Cancer patient data indicated correlation between physical fitness and increased tumor immunogenicity.

Emerging treatments

#94 Incidence and initial treatment of brain metastases (BM) in patients with locally advanced non-small cell lung cancer (NSCLC) treated with radiotherapy with curative intend

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Abstract
Introduction
Patients diagnosed with NSCLC are at high risk of developing BM and the risk increases with stage. Guidelines recommend brain MRI before chemoradiation for locally advanced NSCLC to avoid futile therapy, but this have just recently been implemented in our region.
We investigate the incidence of early (< 6 months) symptomatic BM in patients with stage III NSCLC treated with radiotherapy with curative intend, the overall risk and initial treatment of BM. Furthermore, we investigated the impact of histological subtype on the risk of BM.

Materials and methods
Patients with stage IIb-III NSCLC treated with radiotherapy with curative intend at Rigshospitalet (2009-17) and Herlev Hospital (2015-17) were eligible for analysis. In this period brain MRI or contrast enhanced brain CT was not part of the diagnostic work-up. Patients were followed with CT of the thorax and (upper) abdomen every three months for two years and hereafter every six months till five years. Diagnosis of BM was registered as the date of first brain imaging with BM.

Results
411 patients, 233 with adenocarcinoma (AC), 152 with squamous-cell carcinoma (SSC) and 26 with other histology (not specified or adeno-squamous) were included for analysis.
Within the first six months 14 (3,4%) patients developed BM.
Within five years follow-up 81 patients developed BM. The incidence was highest for AC with 58 cases (25%) compared to SCC with 15 cases (10%). Median (range from 2 to 56 months) time to BM was 13 months. 47 of the 81 patients had BM as their first relapse location.
The primary treatment of BM was surgery for 23 (29%), stereotactic radiosurgery for 19 (23%) or whole brain irradiation for 29 (37%) patients. 10 (13%) patients did not receive surgery or radiotherapy for BM.

Conclusions
We found a high incidence of BM for patients with stage IIb-III NSCLC after radiotherapy, especially for patients with adenocarcinoma for whom follow-up with brain MRI should be considered.

Emerging treatments

#95 Relative dose-intensity of adjuvant chemotherapy in early stage non-small cell lung cancer

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Abstract
Introduction
Platinum-based adjuvant chemotherapy is the standard treatment for radically operated patients with early stage non-small cell lung cancer (NSCLC). Only 50% of patients complete four recommended series of chemotherapy resulting in low relative dose intensity (RDI). In adjuvant setting for breast cancer patients, it has been shown that the number of delayed cycles, number of delayed days and RDI less than 85% affects disease-free survival (DFS). This paper evaluates whether similar effects can be seen in the setting of adjuvant cisplatin-based chemotherapy in NSCLC patients.

Materials and methods
95 patients with NSCLC treated with adjuvant cisplatin-based chemotherapy (CHT) in our department between January 2007 and December 2014 were retrospectively included in the study. 12 patients were excluded due to non-radical surgery or synchronous malignancy. RDI was calculated according to Hryniuk's model as a ratio of received to planned dose intensity. The cut-off of 85% of RDI was chosen to divide the cohort into low and high RDI groups. The primary endpoint was DFS and OS at one year.
DFS and OS were analyzed using Kaplan-Meier method. Comparisons between DFS and OS between the groups were done using the log-rank test, $p < 0.05$ being statistically significant.

Results
One year DFS in the low RDI group was 74% in comparison to 82% in the high RDI group. The difference in OS between the groups was statistically significant (p=0.04) also when stratified by Charlson comorbidity index (95% CI: 0.16-0.79, p=0.02). DFS analysis was not statistically significant (95% CI: 0.33-1.24, p=0.2).

Conclusions
Patients who received RDI of ≥ 85% of adjuvant cisplatin for NSCLC showed better OS independently of their comorbidities. However, the received RDI did not have any influence on DFS. Our results suggest that further studies would be relevant.

Emerging treatments

#96 Histology remains the Strongest Predictor of First Failure Site for Locally Advanced Non-Small Cell Lung Cancer in a Competing Risk Model after inclusion of Volumetric Data

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Abstract
Introduction
We hypothesized that gross tumor volume (GTV) of primary tumor (GTVT) and nodal volumes (GTVN) were predictors of first failure site in non-small cell lung cancer (NSCLC). We aimed at also comparing the prognostic model's complexity to its ability to generate absolute risk predictions with emphasis on variables available at the time of diagnosis.

Materials and methods
342 patients treated with definitive chemoradiotherapy (CRT) for adenocarcinoma (AC) or squamous cell carcinoma (SCC) in 2009-2017 were analyzed. Clinical data, standardized uptake values on FDG-PET/CT, GTVT and GTVN were analyzed using multivariate competing risk models.

Results
137 patients had SCC. As first site of failure 49 had locoregional failure (LRF), 40 had distant metastasis (DM) and 24 died with no evidence of disease (NED). In 205 patients with AC, 34 had LRF, 118 had DM as first failure site and 17 died with NED.
Performance status predicted LRF ($p = 0.02$) and UICC stage risk of DM ($p = 0.05$ for stage 3, $p < 0.001$ for stage 4). Adding histology changed predictions with much reduced risk of LRF in AC compared to SCC (HR = 0.5, 95% CI: [0.3-0.75], $p = 0.001$). Conversely, AC had a higher rate of DM than SCC (HR = 2.1, 95% CI: [1.5-3.0], $p < 0.001$).

Addition of FDG metrics and tumor/nodal volume data predicted DM risk ($p = 0.001$), but with smaller impact on absolute risk compared to histology. Separation of GTV in nodal and tumor lesions did not improve risk predictions.

Conclusions
We quantified the effect of adding volumetric and quantitative imaging to competing risk models of first failure site, but did not find tumor volume components to be important. Histology remains the simplest and most important factor in prognosticating failure patterns in NSCLC.

Emerging treatments

#97 Surgical Management of IIIA/N2 Non-Small Cell Lung Cancer; A Systematic Review

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Abstract
Introduction
Non-Small Cell Lung Cancer (NSCLC) stage IIIA/N2 (cT1-3N2M0) represents a heterogenic group, and prognosis varies depending on the level of lymph node involvement, within this group. Optimal treatment is debated, and patients may have benefit from combined treatment modalities. The aim of this study was to assess the evidence regarding surgical treatment of stage IIIA/N2 NSCLC diagnosed before commencement of treatment.

Materials and methods
A systematic literature search on stage IIIA/N2 NSCLC for randomized, controlled trials comparing various combinations of treatments with surgery. Extraction of relevant data was performed, including study characteristics, patient characteristics, quality of trials and survival outcomes.

Results
Five randomized, controlled trials with a total of 1166 patients were included. Treatment modalities varied substantially. None of the included studies found a statistically significant improved median overall survival, and only one study found an improved progression free survival when patients received chemotherapy, radiotherapy and surgery. Results, however indicates better locoregional control with surgery, and one study did report one N2 nodal station positive at diagnosis vs. more than one as a statistically significant independent predictor of outcome.

Conclusions
Current clinical guidelines are not based on high-quality evidence. Results of statistical significance on survival are lacking, and studies show poor methodological quality. Based on the evidence available, surgery is not superior compared to other treatment modalities. Further subgroup analyses are needed, as evidence points toward surgery being beneficial for only a subgroup of patients, possibly those with single-station N2 disease. Randomized, controlled trials of high methodological quality with thorough staging of N2 disease are needed to determine the optimal chemotherapy, radiotherapy and concomitant surgical intervention.

Emerging treatments

#98 Comparison of 5-aminolevulinic acid and Na-fluorescein for peroperative tumor visualization in patients with high-grade gliomas: A single-centre retrospective study

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Abstract
Introduction
High-grade gliomas are the most common malignant primary brain tumor in adults. Maximal safe surgical resection is an important surgical goal. Fluorescent dyes help the surgeon to distinguish malignant tissue from healthy.

Materials and methods
209 patients with high-grade gliomas were included in this retrospective study. Resections were performed in the period 2012-2017 using 5-ALA or Fluorescein. Resection rates were assessed as tumor volume differences early postoperative MRI scans and preoperative MRI scans. Tumor progression-free survival and overall survival were analysed using an adjusted Cox proportional hazards model.

Results
158 patients were operated with 5-ALA and 51 with Fluorescein. Median follow-up time was 46.7 and 21.2 months respectively. Co-variables were evenly distributed. There was no significant difference in resection rate (96.9% for 5-ALA, 97.4% for Fluorescein, p=0.46). Adjusted median overall survival was 14.8 months for 5-ALA, 19.7 months for Fluorescein (p=0.06). Adjusted median progression-free survival was 8.7 months for 5-ALA, 9.2 months for Fluorescein (p=0.03). Residue below 0.175 cm3: 29.5% for 5-ALA, 36.2 % for Fluorescein (p=0.39)

Conclusions
This study represents the first larger comparative study of 5-ALA and Fluorescein. Fluorescein can be used as a viable alternative to 5-ALA for intraoperative fluorescent guidance in brain tumor surgery. Future comparative, prospective and randomized studies are highly needed.

Emerging treatments

#99 Perioperative hypercoagulability state in upper gastrointestinal cancers patients

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Abstract
Introduction
Cancer-associated venous thromboembolism often connects to a hypercoagulable state in cancer patients. This hypercoagulability could reverse in case of surgical removal of the tumor. Since upper gastrointestinal cancer is prone to induce VTE, Radical resection, and chemotherapy may reduce the procoagulant response.

Materials and methods
Enrollment of eligible patients with operable upper gastrointestinal cancer were performed in a study with consecutive blood samples and screening for venous thromboembolism at discrete time points starting at admission (pretreatment), during treatment, postoperatively and in 18 months of follow-up.

Results
In 151 upper gastrointestinal cancer patients (61 pancreatico-biliary and 90 esophago-gastric cancer) plasma levels of prothrombin fragment 1 +2 (F12), thrombin-antithrombin complex (TAT) and D-dimer were analyzed. We found normal pretreatment levels of the markers in the cancer groups and in benign diseases. Surgical response in the markers declined adequately during the follow-up period. A small group of the cancer patients had sustained elevated levels of coagulation markers postoperatively despite radical resection of the tumor. This was not associated with a higher risk of VTE, as 10 of 15 VTE events in the gross study population occurred in the group with normal pretreatment and postoperative levels of markers. Chemotherapy prior to surgery raised the frequency of VTE despite normal coagulation markers before treatment.

Conclusions
The study found no association between levels of D-dimer, F1+2, and TAT before surgery or during follow-up. Perioperative Chemotherapy raises the frequency of VTE, even in patient with normal plasma levels of coagulation markers.

Emerging treatments

#100 Preliminary results of multiparametric magnetic resonance scan in combination with liquid biopsies performed on men suspected of prostate cancer

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Abstract
Introduction
Prostate cancer (PC) is one of the most frequent malignancies among men, with approximately 4500 new cases diagnosed every year in Denmark. PC is responsible for more than 1000 deaths every year in Denmark. Pivotal to the successful treatment of PC is establishing an early diagnosis, which is currently performed by transrectal ultrasound guided biopsy from the prostate. Biopsies are associated with discomfort and severe complications. Some of these complications can, in rare cases, prove fatal. As the biopsies are taken randomly throughout the gland, the procedure has a high risk of false negative result. Multiparametric magnetic resonance imaging (mpMRI) has shown promising results in curbing some of these inadequacies. Combined with advances in the field of liquid biomarkers we seek to establish a new predictive model significantly reducing the need for prostate biopsies.

Materials and methods
We plan to randomize a total of 456 men to either standard pathway (SP) or “mpMRI pathway (MP) in a 1:7 fashion. Blood and urine samples are taken prior to biopsies. We will perform a new type of biomarker sampling (liquid biopsy) on the collected urine and blood specimens. If suspicions lesions are found on the mpMRI additional targeted biopsy cores will be taken.

Results
41 men have completed the study with 37 randomised to MP and 4 to the standard pathway. 27.8% of men in MP had negative biopsy results compared with 50,0% in the SP. The negative predictive value of mpMRI was 80,0% (CI 59,3%- 93,17%) for Gleason Score > 6 PC, when using combined standard and targeted biopsies are reference test. The results of the liquid biopsies are still pending.

Conclusions
Our preliminary results suggest that mpMRI adds important additional information that could better help select patients for biopsy. Combined with the results from the ´liquid biopsy´ we expect to be able to reduce the number of needed biopsies significantly.

Emerging treatments

#101 Repurposing cationic amphiphilic drugs (CADs) for cancer treatment: Role of GPCR mediated cAMP signaling

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Abstract
Introduction
Repurposing cationic amphiphilic drugs (CADs) for cancer treatment is emerging as an attractive means to enhance the efficacy of chemotherapy. Many commonly used CADs, including several antihistamines and antidepressants, induce cancer-specific, lysosome dependent cell death and sensitize cancer cells to chemotherapy. CAD-induced inhibition of lysosomal acid sphingomyelinase is necessary, but not sufficient, for the subsequent lysosomal membrane permeabilization and cell death, while other pathways regulating this cell death pathway are largely unknown.

Materials and methods
In this study, we performed mRNA sequencing analysis of parental MCF7 and CAD resistant MCF7 to analyze the role of calcium and GPCR pathways in the process of CAD induced lysosomal cell death. Pathways were studied by cAMP assay cell death assay, cytoplasmic and lysosomal calcium release assay.

Results
mRNA sequencing analysis reveals the involvement of Ca2+ and cyclic AMP (cAMP) signaling pathways in CAD resistant MCF7 breast cancer cells, we identified here an early lysosomal Ca2+ release through P2X purinergic receptor 4 (P2RX4) and subsequent Ca2+ and adenylyl cyclase 1 (ADCY1)-dependent synthesis of cAMP as a signaling route mediating CAD-induced lysosomal membrane permeabilization and cell death. Importantly, pharmacological and genetic means to increase cellular cAMP levels either by activating cAMP-inducing G-protein coupled receptors (GPR3 or ß2 adrenergic receptor) or ADCY1, or by inhibiting cAMP-reducing guanine nucleotide-binding protein G(i) subunit a2, C-X-C motif chemokine receptor type 4 or cAMP phosphodiesterases, sensitized cancer cells to CADs.

Conclusions
These data reveal a previously unrecognized lysosomal P2RX4- and ADCY1-dependent signaling cascade as a pathway essential for CAD-induced lysosome-dependent cell death, and encourage further investigations to find the most potent combinations of CADs and cAMP-inducing drugs for cancer therapy.

Emerging treatments

#102 Risk of Invasive Cancer and use of Sentinel Node in Women with Preoperative Diagnosis of Ductal Carcinoma in Situ – a Multicenter Study

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Abstract
Introduction
Ductal carcinoma in situ (DCIS) diagnosed by biopsy implies a risk of upstaging to invasive carcinoma (IC) upon final pathology. These patients require a sentinel lymph node biopsy (SLNB) for axillary staging. A two-stage procedure is not always feasible, thus, precise selection of DCIS patients offered SLNB is crucial. The aim of this study was to determine upstage rate and use of redundant/required SLNB in women with a preoperative diagnosis of DCIS and to identify patient and tumor characteristics associated with the risk of upstaging.

Materials and methods
The Orbit Operation Planner was used to identify a total of 1368 women with DCIS who were treated between 2008 and 2016. In total, 975 patients were included. Upstage rates and proportion of redundant/required SLNB were calculated. The associations between clinicopathological characteristics and upstaging were analysed in uni- and multivariate analyses.

Results
Of 975 patients initially diagnosed with DCIS, 246 (25.2%) were upstaged to IC. Redundant SLNB were performed in 392 (40.2%) DCIS patients. Forty-four patients (4.5%) with a final IC diagnosis were not offered a SLNB and were thus potentially undertreated. In adjusted analysis, DCIS size, palpability and mass-formation on breast imaging were associated with upstaging. Van Nuys classification was not associated with upstaging to IC.

Conclusions
One fourth of patients treated for DCIS were upstaged. Most patients with IC on final pathology underwent SLNB. A considerable number of patients with only DCIS underwent a redundant SLNB. Lesion size, palpability and mass-formation but not Van Nuys classification group are suggested risk factors for upstaging. This should be considered in future DCIS treatment guidelines.

Emerging treatments

#103 CT-guided percutaneous cryoablation of renal cancer, a retrospective study of clinical and oncological outcome

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Abstract
Introduction
CT-guided percutaneous cryoablation (PCA) appears to be an effective treatment of renal cell carcinoma (RCC) and can be used in patients selected for nephron sparing procedures after a multidisciplinary conference. The aim of this study was to investigate the clinical and oncological outcome after PCA of pathologically verified RCC at Odense University Hospital (OUH), Denmark.

Materials and methods
In this retrospective study, we included all patients with biopsy proven RCC treated with PCA between 2012-2017. Follow-up imaging was performed after 3 and 6 months and annually up to 5 years. Complications were defined according to the Clavien-Dindo Classificiation. We defined residual tumor as malignant enhancement detected <3 months after treatment, while recurrent tumor was detected in later follow-ups.

Results
A total of 147 RCC in 140 patients were included. The population included both healthy and comorbid patients with a mean age of 66.2 years (range 27-91). Mean tumor diameter was 27.4 mm (range 10-70). Mean follow-up length was 439 days (range 84-2215) with 141 tumors in follow-up longer than 3 months. PCA was performed during general anesthesia in 120 procedures (82%) or sedation in 27 procedures (18%).
Six patients (4%) had complications that were classified as major (Clavien-Dindo classification).
We found treatment success (no residual or recurrent tumor) in 93% (131 tumors). Residual tumor or recurrence was found in 7% (10 patients). Two patients with treatment failure underwent total nephrectomy. The remaining 8 residual/recurrent tumors were treated with re-cryoablation with success of re-treatment in 88% (7 tumors), hereof one patient needed a third cryoablation for success. We found metastases in 2% (3 patients). Hereof, 67% (2 patients) also had residual or recurrent tumor.

Conclusions
Patients treated with PCA had a high rate of successful treatment and few patients experienced significant complications.

Treatment morbidity and late effects:
Poster #104-123

Treatment morbidity and late effects

#104 Præ-diagnostiske biokemiske markører for kræftsenfølger: Et populations-baseret studie-setup

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Abstract
Introduktion
Der er over 325.000 kræftoverlevere i Danmark, som i større eller mindre omfang har somatiske, psykologiske eller sociale senfølger. Behandlingens betydning for senfølger er i mange tilfælde dokumenteret, men vi ved forsvindende lidt om betydningen af tidligere sygdomshistorie for senfølgers forekomst og alvorlighed. Prædiagnostiske parakliniske data kunne være indikatorer på eksisterende, ikke erkendt sygdom, eller markører for sårbarhed. I denne populations-baserede undersøgelse vil vi belyse om rutinemæssigt indsamlede præ-diagnostiske biokemiske markører kan prædiktere risiko for en række kræftsenfølger.

Materialer og metoder
CopLab er en unik database, der indeholder resultater af over 170 millioner biokemiske undersøgelser foretaget for praktiserende læger i et område tilsvarende det tidligere Københavns Amt fra 2000 til 2015 i en population på ca. 1,3 millioner personer. Vi vil igennem Cancerregisteret identificere alle kræftpatienter bosiddende i området, der blev diagnosticeret med deres første primære cancer mellem 2004 og 2015, og koble deres prøvesvar fra CopLab med information om senfølger fra Landspatient- og Lægemiddelstatistikregisteret. Vi vil undersøge hvordan biokemiske fund forud for cancerdiagnosen prædikterer senfølger sammenholdt med en kontrolgruppe. Vores første undersøgelser belyser betydningen af prædiagnostiske HbA1c niveauer for udvikling af diabetes, og inflammatoriske markører for udvikling af psykologiske senfølger (depression og angst), og søvnsygdomme.

Resultater
Populationen er ved at blive etableret og der foreligger endnu ikke resultater af studiet.

Konklusioner
Denne registerkobling giver en unik ny mulighed for at undersøge hvordan kræftpatienters sygdomshistorik og biokemiske fund før kræftdiagnosen påvirker risikoen for senfølger, og kan danne grundlag for fremtidige studier af en lang række markører og senfølger. Tidlige biokemiske markører vil kunne bidrage til at skræddersy opsporing og behandling.

Treatment morbidity and late effects

#105 Do pain, fatigue and dyspnoea impact on everyday activities in people with advanced cancer?

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Abstract
Introduction
Pain, fatigue and dyspnoea are symptoms commonly experienced by people with advanced cancer, but it is not known whether these symptoms impact their everyday activities. The primary objective of the present study was to study the impact of pain, fatigue and dyspnoea on performance of everyday activities over time in people with advanced cancer. A secondary objective was to examine the correlation between pain, fatigue and dyspnoea and performance of everyday activities.

Materials and methods
A cohort study was conducted including 242 people with advanced cancer assessed at baseline (T1) and after six (T2) and 12 weeks (T3). This study is a secondary analysis of data from a previously completed randomised, controlled trial. Exposures were pain, fatigue and dyspnoea at T1 and outcomes were performance of everyday activities at T2 and T3. Spearman's rank-order test and mixed linear models were performed.

Results
The correlation between pain, fatigue and dyspnoea and performance of everyday activities at baseline spanned from trivial to moderate (Spearman's rho: -0.004 to 0.34). Only pain had a statistically significant impact on performance of everyday activities over time (p = 0.01). Participants with no pain problems at T1 had the largest decrease in performance of everyday activities (-0.24 logits (95%-CI: -0.37 to -0.12)), but the decrease was not clinically relevant (≥-0.30).

Conclusions
Pain, fatigue and dyspnoea had little influence on performance of everyday activities both at baseline and over time.

Treatment morbidity and late effects

#106 Follow-up strategies after primary cancer treatment in adult cancer survivors: a systematic review and meta-analysis

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Abstract
Introduction
The impact of different follow-up strategies after cancer treatment on prognostic and patient-reported outcomes remains unclear. In this Cochrane review, we compared the effects of: 1) Non-specialist-led versus specialist-led follow-up; 2) Less intensive versus more intensive follow-up; and 3) Follow-up integrating patient symptom education or survivorship care plans versus usual care, on overall survival, time-to-detection of recurrence, health-related quality of life (HQoL), anxiety and depression.

Materials and methods
We followed standard Cochrane methodology and included randomized trials comparing different follow-up strategies for adult cancer survivors following completion of curatively intended primary treatment. We excluded studies that did not report at least one of our outcomes. A random effects model was used in the meta-analysis. Current results are based on a search done on 19 December 2016. Updated results will be presented at the conference.

Results
We screened 6943 references and included 46 trials (15,795 participants, 11 cancer sites). Non-specialist-led follow-up may decrease overall survival (Hazard ratio, HR 1.34, 95%CI 0.97 to 1.86, P=0.07) but makes little or no difference at 12 months to HQoL (Mean difference, MD 1.06, 95%CI -1.83 to 3.95, P=0.47), anxiety (MD -0.03, 95%CI -0.73 to 0.67, P=0.94) and depression (MD 0.03, 95%CI -0.35 to 0.42, P=0.86). Less intensive follow-up probably makes little or no difference to overall survival (HR 1.05, 95%CI 0.94 to 1.18, P=0.39) but increases time-to-detection of recurrence (HR 0.83, 95%CI 0.75 to 0.91, P=0.0002). We could not synthesize results for the other comparisons and outcomes due to the lack of data.

Conclusions
Evidence regarding the effects of the different follow-up strategies on prognostic and patient-reported outcomes vary substantially. More research is needed.

Treatment morbidity and late effects

#107 Senfølger efter tyktarmskræft

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Abstract
Introduktion
Det anslås, at mere end 23.000 nulevende danskere har haft tyktarmskræft, og med en stigende incidens og en fortsat forbedret overlevelse er prævalensen stigende. Trods det store antal berørte danskere, er senfølger efter behandling af tyktarmskræft imidlertid ringe belyst, og der er betydelig risiko for, at en stor gruppe patienter lever med invaliderende senfølger, som ikke er identificeret i opfølgningsforløbet, og derfor ikke er sufficient behandlet.

Materialer og metoder
I et stort dansk multicenterstudie, p.t. involverende 4 centre i Region Midt og Nord, og planlagt til at ekspandere til de øvrige regioner, besvarer tyk- og endetarmskræftpatienter elektroniske spørgeskemaer (ePROMs) 3, 12, 24 og 36 måneder efter deres operation. Patienter som angiver senfølger, samt ønske om behandling, henvises til relevante specialister. Dette studie fokuserer på det første år efter operation for tyktarmskræft, og data fra 3- og 12-måneders besvarelser vil blive analyseret.

Resultater
Der inkluderes fortsat patienter i studiet, som har opnået en responserate på 82 %. Foreløbig har 199 tyktarmskræftpatienter besvaret spørgeskemaet 12 mdr. postoperativt, og 9 % er henvist til behandling af senfølger, primært diarré, som behandles i gastroenterologisk regi. Analyser af kliniske og demografiske faktorers betydning for udvikling af senfølger efter tyktarmskræft er påbegyndt, og vil kunne præsenteres til Danske Kræftforskningsdage 2019.

Konklusioner
De foreløbige resultater viser, at 9 % af tyktarmskræftpatienterne ønsker henvisning til behandling af senfølger, primært diarré, 12 mdr. efter operationen. Analyser af de indsamlede data vil afsløre hvilke faktorer der har betydning for udvikling af senfølger efter tyktarmskræft, samt hvordan senfølgerne udvikler sig fra 3 til 12 mdr. postoperativt.

Treatment morbidity and late effects

#108 International Consensus Definition of Low Anterior Resection Syndrome (LARS)

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Abstract
Introduction
Low Anterior Resection Syndrome (LARS) is pragmatically defined as disordered bowel function after rectal resection leading to a detriment in quality of life. This broad characterisation does not allow for precise estimates of prevalence. The LARS score was designed as a simple tool for clinical evaluation of LARS. Although the LARS score has good clinical utility, it may not capture all the important aspects that patients experience.

Materials and methods
This international patient provider initiative employed an online Delphi survey, regional patient consultation meetings, and an international consensus meeting. Three expert groups participated; patients, surgeons, and other health professionals from five regions (Australasia, Denmark, Spain, United Kingdom, and North America) and in three languages (English, Spanish, and Danish).

Results
325 participants (156 patients) registered. The response rates for successive rounds of the Delphi survey were 86%, 96%, 99%. Eighteen priorities emerged from the Delphi survey. Patient consultation and consensus meetings refined this to eight symptoms and eight consequences that capture essential aspects of the syndrome.

Conclusions
This is the first definition of LARS developed with direct input from a large international patient panel. The involvement of patients in all phases of the study has ensured that the definition presented encompasses the vital aspects of the patient experience of LARS. The novel separation of symptoms and consequences may enable greater sensitivity to detect changes in LARS over time and with intervention.

Treatment morbidity and late effects

#109 Behandling af funktionsforstyrrelser i tarmen efter kræftbehandling i bækkenorganerne

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Abstract
Introduktion
Hvert år får ca 40.000 danskere konstateret kræft og ca 300.000 lever med en kræftdiagnose. Det skønnes at mindst 50 % oplever senfølger efter behandlingen.
På nationalt plan har Kræftens Bekæmpelse etableret 3 forskningscentre for senfølger, hvoraf centeret for "Senfølger til Kræft i Bækkenorganerne" er tilknyttet Aarhus- og Aalborg Universitetshospitaler. I centeret har man fokus på kortlægning samt forbedret behandling af senfølger. Patienterne oplever ofte senfølger i form af problemer med deres tarmfunktion, blærefunktion og deres seksualliv samt kroniske smerter.

Materialer og metoder
I Senfølgeklinikken behandles størstedelen af patienter med tarmdysfunktion af specialsygeplejersker, som initierer en basisbehandling. Patienter som ikke responderer på dette, bliver set af en læge. Vi har udarbejdet en standardiseret behandlingsalgoritme indeholdende intervention og pædagogisk strategi, samt patientforløbsbeskrivelser. Algoritmen består af en basisdel, bestående af pædagogiske og non-invasive tiltag f.eks. fibertilskud, toiletvaner, tømningsforbedrende tiltag og stoppende midler. Ved behov kan patienterne tilbydes avanceret behandling; f.eks. skyllebehandling.
Til systematisk monitorering af behandlingen anvendes elektroniske spørgeskemaer (patient reported outcome measures/ e-PROMs).

Resultater
Siden juni 2018 har vi i Aalborg og Aarhus inkluderet 78 patienter i et monitoreret behandlingsforløb for tarmdysfunktion i Senfølgeklinikken. Der inkluderes løbende nye patienter og analysen af de foreløbige data er i gang, og vil kunne præsenteres på Danske Kræftforskningsdage 2019.

Konklusion
Foreløbig har projektet afsløret et stort behov for specialiseret behandling af senfølger efter kræft i bækkenorganerne. Analysen af de indsamlede data vil belyse effekten af de behandlingstiltag vi tilbyder.

Treatment morbidity and late effects

#110 Correlation between bowel- and sexual function after treatment for rectal cancer in female patients

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Abstract
Introduction
In females radiotherapy and permanent stoma are known risk factors for sexual inactivity and sexual problems after treatment for rectal cancer.
The aim was to measure the impact of bowel dysfunction after low anterior resection (LAR) and poor stoma function after abdominoperineal resection (APR) on female sexuality.

Materials and methods
Danish rectal cancer patients diagnosed between 2001-2014 were invited to the survey. Patients were identified through the Danish Colorectal Cancer Group registry.
They responded to a bowel-questionnaire (LARS score), a stoma-questionnaire (Colostomy-Impact score), and a questionnaire about sexual function and activity (Rectal-Cancer-Female-Sexuality score).

Results
Some 813 female patients completed the questionnaires (49.2%). Mean follow up time was 6.4 (SD 3.8) years.
After LAR, patients with major LARS did not show increased risk of sexual inactivity (OR 1.28(0.84-1.93)), but revealed increased risk of overall sexual dysfunction (OR 3.09(1.69-5.66)). Most distinct problems were dyspareunia and inability to complete intercourse.
Contrarily after APR, major stoma dysfunction were significantly associated with sexual inactivity (OR 2.27(1.16-4.43)), but not with overall sexual dysfunction (OR 0.74(0.27-1.99)). Major stoma dysfunction was highly related to dissatisfaction with own physical appearance.

Conclusions
Comparing female rectal cancer patients with and without bowel-and stoma dysfunction, we found an increased risk of sexual inactivity among patients with poor stoma function, while risk of overall sexual dysfunction was found among patients with major LARS.

Treatment morbidity and late effects

#111 Genitourinary function after sigmoid resection for cancer: A population-based cross-sectional study

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Abstract
Introduction
Sigmoid resection (SR) for cancer is associated with long-term bowel dysfunction. However, the long-term genitourinary function after sigmoid resection is unknown.

Materials and methods
After excluding patients who had recurrence, metastasis or had received previous radiotherapy, all survivors of sigmoid colon cancer treated with a SR or polypectomy (controls) between 2001 and 2014 within Denmark received the International Consultation on Incontinence Questionnaire for Male/Female Lower Urinary Tract Symptoms (ICIQ-MLUTS/FLUTS) to assess their urinary function. The International Index of Erectile Function (IIEF) and female sexuality score were used to assess their sexual function.

Results
In males, erectile dysfunction was 56% in the SR group versus 51% in the control group (p0.238), similarly there were no significant differences in the voiding or incontinence scores between the 2 groups. The mean voiding score was 7.25 and 7.35 (p=0.717) and mean incontinence score was 3.73 and 3.53 (p=0.334) for the SR and controls respectively. In females, 32% suffered from sexual dysfunction after SR versus 28% after polypectomy (p =0.554), also there were no differences between the 2 groups in filling, voiding and incontinence scores (p=0.884, 0.246, 0.971) respectively.

Conclusions
Unlike bowel function, sigmoid resection is not associated with an increased risk of long-term genitourinary dysfunction.

Treatment morbidity and late effects

#112 Abnormal neuronal response to rectal and anal stimuli in patients treated for distal rectal cancer with high-dose chemoradiotherapy followed by watchful waiting

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Abstract
Introduction
Watchful waiting in rectal cancer patients with complete clinical response after chemoradiation therapy (CRT) has gained increased popularity to avoid morbidity and mortality associated with surgery. Irradiation of the pelvis causes bowel dysfunction, but the effect on ano-rectal sensory function remains obscure in this patient category. The aim of this study was to characterize the sensory pathways of the gut-brain axis in rectal cancer patients treated solely with CRT and compared with healthy volunteers.

Materials and methods
Sensory evaluation by rectal distension was performed and cortical evoked potentials (CEPs) were recorded during rapid balloon distensions of the rectum and anal canal in patients (n=13) and healthy volunteers (n=13). Latencies and amplitudes of CEPs were compared, and the relative amplitude of five spectral bands from recorded CEPs was used as an additional proxy of neuronal processing.

Results
Patients had 35% lower rectal capacity at maximum tolerable volume (p=0.007). We found no differences in rectal CEP latencies (p=0.09) and amplitudes (p=0.38) between groups. However, spectral analysis of rectal CEPs showed decrease in theta (4-8 Hz) and increase in beta (12-32 Hz) band activity in patients (all $p<0.001$). Anal CEPs showed increase in alpha (8-12 Hz) and beta- and decrease in gamma (32-70 Hz) band activity (all $p<0.001$) in patients compared to controls.

Conclusions
CRT for distal rectal cancer causes abnormal cortical processing of both anal and rectal sensory input. Such central changes may play a role in symptomatic patients, especially when refractory to local treatments.

Treatment morbidity and late effects

#113 Risk factors for anastomotic leak in patients undergoing rectal resection for cancer. A retrospective, population-based study

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Abstract
Introduction
Anastomotic leak is a feared complication seen after rectal cancer resection. There is constant development in surgical treatment; hence it is crucial to monitor surgical complications, such as anastomotic leak, and evaluate any risk factors of this. Our aim was to examine patient-related, surgical, and postoperative risk factors for anastomotic leak after rectal cancer resection.

Materials and methods
In a population-based setting of 1.3 mill inhabitants, a retrospective two-center study was conducted in patients undergoing rectal cancer resection with a primary anastomosis between January 2013 and October 2017. Anastomotic leak was detected with CT-scan, endoscopy, or surgery if clinical symptoms. Data on demographics, preoperative treatment, surgery, and postoperative complications were retrieved from the Danish Colorectal Cancer Group Database and supplied with data from review of medical records. Differences in variables were tested by Chi-square test. Risk factors of leak were examined by logistic regression analysis, adjusting for covariates.

Results
Data collection is still ongoing. Expected number of patients: 650. Preliminary results of 292 patients operated at one center during 2013-2015 have shown a leak rate of 16.4% with comparable rates after TME (total mesorectal excision) and PME (partial mesorectal excision). In descriptive analyses, the anastomotic leak rate differed according to gender (male/female: 23.9%/3.7%), body mass index (BMI≥30.0/BMI 18.5-24.9: 24.4%/12.8%), and smoking status (current smokers/non-smokers: 24.4%/14.2%).

Conclusions
The anastomotic leak rate was unexpectedly high at one center during 2013-2015. Results of the entire study will be ready August 2019.

Treatment morbidity and late effects

#114 Nurse-led personalized conservative treatment in patients with Low Anterior Resection Syndrome

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Abstract
Introduction
To study the need for treatment for Low Anterior Resection Syndrome (LARS) and to show the effect of personalized conservative treatment (PCT).

Materials and methods
Electronic medical records of patients undergoing low anterior resection (LAR) for rectal cancer in a single surgical center between 2012 – 2016 were examined.

Results
329 patients received a LAR. 86 patients (26,1%) were referred to nurse-led PCT for LARS. 81 of these patients (94,2%) had major LARS at the time of referral. The patients receiving PCT had a mean change in LARS score of -7 (range -32 to +9) with a significant improvement in LARS score ($p<0.05$). The patients had an average of 1.7 (range 1-7) visits in the clinic and 2.1 (range 0-6) telephone consultations. The patients received an average of 3.7 (range 0-7) treatment modalities ranging from dietary advice to biofeedback (8 patients) and transanal irrigation (18 patients). One patient was treated with sacral nerve stimulation and four patients had a stoma created.

Conclusions
Patients with major LARS can significantly improve their LARS score with PCT and the majority can be managed conservatively.

Treatment morbidity and late effects

#115 Late persistent and substantial patient reported symptoms (LAPERS) after definitive radio-chemotherapy and MRI image-guided adaptive brachytherapy for locally advanced cervical cancer in the EMBRACE study

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Abstract
Introduction
A method to identify patients with LAte, PERsistent, Substantial and likely treatment related symptoms (LAPERS) is applied on patient reported outcomes (PRO) from the prospective, observational, and longitudinal study on MRI image-guided, adaptive brachytherapy in locally advanced cervical cancer (EMBRACE study).

Materials and methods
PRO (EORTC QLQ-C30 + CX24) were analyzed in 657 out of 1416 patients who had a valid baseline, 3 months' assessment and at least 3 late follow ups (6 months and ongoing). A LAPERS event for an individual patient was defined if the median over late follow-ups was more than "a little" representing "quite a bit" or "very much" (substantial symptoms). For organ-related symptoms (e.g. urinary frequency), baseline condition was taken into account by requiring the median to be worse than the minimum of baseline and 3 months scoring (treatment-related); whereas for more unspecific symptoms (e.g. tiredness) baseline correction was not applied. LAPERS was contextualized with crude incidences of substantial symptoms via ratio calculations.

Results
Median follow-up was 42 months (IQR 30-59). A LAPERS event occurred in 0% to 20% of patients depending on symptom. The proportion of patients experiencing a LAPERS event was more than 10% in 11 out of 31 symptoms (e.g. “swelling in one or both legs”) and below 2% in 8 symptoms (e.g. “pain/burning feeling passing urine”. LAPERS/crude incidence ratios were 0.4 or lower for all symptoms; which indicates that ≤ 40% of patients experiencing substantial symptoms did so persistently. For 7 symptoms (e.g. “blood in stools”) the ratios were 0.1 or lower.

Conclusions
Incidence methods capture the first occurrence of an event; LAPERS in contrast excludes transient symptoms and identifies patients with persisting symptoms. When analyzing longitudinal morbidity data, a complementary approach combining incidence methods and LAPERS improves the understanding of extent and duration of toxicity.

Treatment morbidity and late effects

#116 Risk factors for bladder fistula, bleeding and cystitis after Image-guided Adaptive Brachytherapy in cervix cancer: an EMBRACE analysis

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Abstract
Introduction
Embrace I is a prospective, multi-institutional, observational study that enrolled 1416 patients with locally advanced cervical cancer (LACC) treated with chemo(radio)therapy and Image-Guided Adaptive brachytherapy (IGABT) from 2008 to 2015. The present study aim to identify risk factors for bladder fistula, bleeding and cystitis within EMBRACE I.

Materials and methods
Bladder fistula, bleeding and cystitis (CTCAEv.3) were analysed in 1237 patients without bladder involvement at time of diagnosis. Adverse events arising during the course of follow-up were considered. Patient, disease and treatment characteristics were tested with univariate (UVA) and multivariable (MVA) analyses (Cox proportional hazard). Moderate grade G≥2 fistula was analysed individually, while G≥2 cystitis and bleeding were pooled. UVA and MVA were also performed for severe G≥3 morbidity pooling the endpoints. Cumulative minimal dose to the most exposed 2cm3 of the bladder (D2cm3) and ICRU Bladder point dose were considered as continuous variables.

Results
Crude incidences for G≥2 fistula, bleeding and cystitis were 0,5%(n=5), 1,8%(n=23) and 6,7%(n=83), respectively. Pooled G≥3 incidence was 1,1%(n=13). Mean bladder D2cm3 was 75,8±9,7Gy. Median follow-up was 35(range:1-97) months, median age was 49(range:22-91) years, and 31% were smokers.
Bladder D2cm3 was significant (p<0,1) on MVA for all endpoints. ICRU bladder point dose was significant on UVA for G≥2 fistula and G≥3 pooled incidence, but was less predictive than D2cm3 on MVA. Smoking status was predictive for G≥2 bleeding and cystitis and pooled G≥3 incidence, with smokers at higher risk. Younger patients had higher risk for G≥2 bleeding and cystitis.

Conclusions
In the present study, bladder D2cm3 was the most independent risk factor for bladder fistula, bleeding or cystitis after IGABT in LACC patients. Risk of bleeding and cystitis was higher in smokers. Age was predictor for cystitis, with younger patients with higher risk.

Treatment morbidity and late effects

#117 DCCL - Danish Breast Cancer Group Center and Clinic for Late effects

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Abstract
Introduktion
Brystkræft er den hyppigste kræftform hos kvinder. Der er i dag mere end 60.000 danske kvinder, der lever med diagnosen. Et betydeligt antal af brystkræftoverlevere oplever efter behandling livskvalitetssænkende senfølger til behandlingen. I øjeblikket er der ikke veletablerede procedurer for identifikation af brystkræftpatienter med senfølger og ingen nationale retningslinjer for forebyggelse og behandling for de fleste af disse. Formålet med DCCL er, i samspil med Den Danske Brystkræftgruppe (DBCG), at etablere et nationalt center med fokus på tidligt at identificere patienter, der risikerer at udvikle klinisk betydende senfølger, at identificere evidensbaserede forebyggende foranstaltninger og tilbyde behandlingstiltag på baggrund af disse samt løbende at registrere omfanget af senfølger og effekten af de iværksatte interventioner.

Materialer og metoder
De vigtigste tiltag i projektet vil omfatte:

1) Udvikling af interaktiv patientapp, der støtter patienten under og efter et behandlingsforløb ved hjælp af feedback, skræddersyet ud fra patientens spørgeskemasvar.
2) Samkørsel af de indsamlede patientdata og data fra nationale registre, som skal danne datagrundlag for avancerede maskinlæringsalgoritmer, der har til formål at identificere brystkræftpatienter med risiko for senfølger, samt bidrage med konkrete forslag til forebyggelse og interventioner.
3) Initiering og koordinering af og støtte til nye og pågående forskningsprojekter med det formål at udvikle, evaluere og implementere nye forebyggende behandlingstiltag over for brystkræftsenfølger.

Resultater
Grundlæggende funktionalitet for hhv. kliniker- og patientapplikation er færdigudviklet og klar til brugertests med patienter.

Konklusioner
Projektets indsats bidrager til at adressere et betydeligt problem i forbindelse med at identificere, forebygge og behandle senfølger for en voksende gruppe af kræftoverlevende. Den innovative tilgang til projektet er overførbar til andre kræftgrupper.

Treatment morbidity and late effects

#118 Corrective surgeries following prophylactic and therapeutic mastectomy with immediate breast reconstruction

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Abstract
Introduction
Mastectomy and immediate breast reconstruction often require multiple operations in order to achieve aesthetic acceptable outcomes and breast symmetry. The number of corrective operations relies on the individual satisfaction and amount of effort the women are willing to accept. This might be associated with the indication for the mastectomy. The aim of this study was to compare number of corrective surgeries following therapeutic and prophylactic mastectomy with direct to implant breast reconstruction.

Materials and methods
A review of 122 women, including 67 cancer patients and 55 women with high risk of breast cancer was undertaken. All women had a mastectomy and direct to implant breast, were followed and received corrective surgery by the same surgeon during 2014-2017. Demographics, indications and type of corrective surgery were obtained from medical charts.

Results
More cancer patients (69%) than prophylactic treated women (57%) had no additional corrective surgeries. Mean number of corrective surgeries were 0.4 and 0.6 (p= 0.1193) for the cancer patients and prophylactic treated women, respectively. Asymmetry was the main indication for corrective surgery in cancer patients, whereas thin skin flaps/visible implants were the main indication in prophylactic treated women.

Conclusions
Multiple surgeries following direct to implant breast reconstruction is frequent. Women receiving prophylactic mastectomy were more likely to have corrective surgery compared to women receiving therapeutic mastectomy. This is important information in the consultation process prior to the reconstructive surgery.

Treatment morbidity and late effects

#119 Effect of progressive resistance training on persistent pain after axillary dissection in breast cancer– a randomized controlled trial

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Abstract
Introduction
Persistent pain is a known challenge, affecting 1 in 5 breast cancer survivors. We examined the effect of progressive resistance training on persistent pain after surgery with axillary lymph node dissection and radiotherapy.

Materials and methods
Women, aged 18 – 75 years, diagnosed with primary unilateral breast cancer and treated with surgery including axillary lymph node dissection and radiotherapy were eligible. Participants were randomized (1:1) to usual care or exercise intervention, which included progressive resistance training three times weekly throughout the first post-operative year; supervised in groups in the first 20 weeks, and self-administered in the following 30 weeks. The individual exercise load was decided from baseline maximum strength tests, and progressed from low to moderate. Pain was assessed at baseline, 20 weeks and 12 months by a questionnaire covering intensity and frequency of pain, neuropathic pain, and the influence of pain on aspects of daily life. The effect was analyzed using linear mixed models and multinomial logistic regression models.

Results
158 women participated, 76 randomized to control and 82 to intervention. The proportion of women experiencing pain and neuropathic pain declined and did not significantly differ between groups during follow-up. However, in terms of intensity of pain, a consistent tendency favored the exercise group, with the intervention group scoring significantly lower for neuropathic pain (p=0.049), and having significantly lower odds for moderate/severe pain at 20 weeks (p=0.02) and affected sleep at 12 months (p=0.03).

Conclusions
We found favourable effects of progressive resistance training on pain in women treated for breast cancer with surgery including axillary lymph node dissection and radiotherapy. These results affirm that the health benefits of progressive resistance training can be made available without increasing the risk of post treatment pain.

Treatment morbidity and late effects

#120 Functional assessment of late toxicity and quality of life after radiation therapy of sinonasal carcinoma

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Abstract
Introduction
Radiation of sinonasal tumours introduces a risk of permanent late side effects. Proton therapy may spare normal tissue and thus reduce late toxicity. In order to evaluate the demand and potential effect of proton therapy for sinonasal cancer, we aimed to determine the incidence and severity of late toxicity.

Materials and methods
All patients who were treated with radiotherapy for sinonasal cancer in three Danish institutes, who were alive without a recurrence were eligible for this cross sectional study. So far, 18 participants from one center have accepted inclusion, inclusion from the two additional centers will start later in 2019. Toxicity were evaluated with an ophthalmologic examination, blood samples including synachten test, neuropsychological tests, MRI of the brain and the Brief Smell Identification Test. Quality of life (QoL) was assessed with questionnaires.

Results
Results from the first center are currently available (n=18). Median age was 70.5 years (range 47-83). Compared with normative data, patients evidenced poorer neurocognitive functioning in several cognitive domains up to 1.5 SD below the norm. Late toxicity from the optical pathway were present in 5 patients (28%), one were enucleated due to toxicity. Six patients (33 %) revealed hypopituitarism, one with panhypopituitarism. Olfaction test showed age-adjusted impaired smell identification in 13 patients (72 %). Regarding QoL, the most affected domains were social, emotional and physical functions. Increased anxiety were reported in 15 patients (83 %), significantly related to a poorer global QoL score (p=0.029). Symptoms that affected QoL most were lack of smell or taste, thick nasal discharge, need to blow the nose, and blocked nose.

Conclusions
The results indicate substantial late radiation induced morbidity with a significant impact on QoL. Based on the results, a larger, nationwide prospective study of toxicity after radiotherapy for sinonasal cancer is now planned.

Treatment morbidity and late effects

#121 A randomized phase III trial for alleviating radiation-induced xerostomia with chewing gum

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Abstract
Introduction
Xerostomia is frequent complaint after radiotherapy (RT) for head and neck cancer (HNC), and is affecting quality of life (QOL). The aim of this study was to reduce symptoms of radiation-induced xerostomia in HNC survivors in a randomized trial, in which the experimental arm used chewing gum for a month. Primary endpoint was changes in scoring of xerostomia as defined by EORTC QLQ-H&N35 between the two arms.

Materials and methods
HNC survivors treated with curative intended primary RT and without loco-regional failure were recruited from the follow-up clinic. Inclusion criteria were physician-assessed xerostomia, sufficient dental health, and minimum six months follow-up. Subjects were randomized 2:1 to one month of chewing gum or standard care. Intervention was a customized experimental sugar-free chewing gum without flavors. Xerostomia-related QOL was assessed using EORTC QLQ-H&N35 and GRIX questionnaires. Unstimulated and stimulated sialometry were performed to measure saliva flow, and viscosity was tested with the Inclined Plane Test by recording the saliva transit time on vertical plate.

Results
Ninety-one subjects were eligible for analysis and randomized to intervention (Arm A, n=55) or standard care (Arm B, n=36). When comparing categorized scores for xerostomia symptoms between arms, a reduction in symptoms was significantly higher for Arm A than Arm B (p=0.05). For the GRIX questionnaire, symptoms were likewise reduced for Arm A, however not significantly different from Arm B. Salivary flow increased and viscosity decreased upon immediate stimulation within both arms ($p<0.001$, respectively), however no significantly difference was observed when comparing the two arms.

Conclusions
Intervention with chewing gum found the reduction in categorized scores of dry mouth to be significantly higher in Arm A than Arm B. Increase in salivary flow and reduction of viscos saliva was seen with immediately stimulation by the chewing gum for both arms.

Treatment morbidity and late effects

#122 Long term morbidity after radiation therapy for brain tumours

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Abstract
Introduction
The extent of knowledge on radiation therapy (RT) induced cognitive dysfunction is limited. So is the knowledge regarding the parts of the brain needed to be spared to prevent cognitive dysfunction. This study was designed to determine the cognitive domains most affected by RT.

Materials and methods
A cross-sectional study assessing cognitive function in 110 adult patients with a primary brain tumour grade I-III or medulloblastoma treated at Aarhus University Hospital, Denmark, between 2006 and 2016. Two cohorts were established: A cohort of 81 patients who had received neurosurgery followed by RT (RT+), and a cohort of 29 patients who had only received neurosurgery (RT-). The patients completed questionnaires and underwent neuropsychological assessment. RT dose-volume histogram (DVH) of specific areas in the brain were extracted from the treatment plans to explore correlations between dose-volume parameters and cognitive scores.

Results
Mean age was 53.5 years with an average time since diagnosis of 7.3 years. Compared to RT- patients, RT+ patients scored lower on domains concerning processing speed (p=0.036) and executive function (p= 0.048) and had higher impairment frequency on verbal fluency (p=0.019) with 16% of patients exceeding 1.5 SD below the normative mean. Preliminary data indicate that higher dose to the left hippocampus correlates with the number of people with impaired scores on Hopkins Verbal Learning Test (HVLT), a test assessing verbal learning and memory.

Conclusions
Our results indicate that treatment, including RT, for a primary brain tumour may have negative long-term impact on cognitive function. Preliminary data suggest that higher RT dose to the left hippocampus is associated with greater verbal learning and memory impairment.

This study is followed by a national prospective study in association with DNOG (Danish Neuro-Oncology Group) assessing cognitive function in brain tumour patients before and after RT.

Treatment morbidity and late effects

#123 Exploring the role of protein intake on maintaining muscle mass in patients with non-small cell lung cancer

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Abstract
Introduction
Muscle wasting in cancer patients is prevalent and the role of protein intake in muscle maintenance remains unknown. The aim of the current study was to explore the role of protein intake in relation to muscle mass during anti-neoplastic treatment in patients with non-small cell lung cancer (NSCLC).

Materials and methods
A longitudinal observation study was conducted in NSCLC patients during the first three cycles of anti-neoplastic treatment. Nutrient intake was assessed by a 24-hour recall at the 1st and 2nd cycle of treatment. Skeletal muscle mass (cm2) was calculated as absolute change by routine CT scans (baseline and after 3 cycles of treatment) at the 3rd lumbar vertebrae landmark (VikingSlice software). Independent t-tests and chi-square test were conducted to assess differences in protein intake in muscle maintainers (±5.9 cm2) and muscle wasters (>6 cm2 loss). Univariate and multivariate linear regression analyses were performed to determine the role of protein intake on changes in muscle mass.

Results
Sixty-two patients were included in the study of which 52 had both pre- and post chemotherapy CT scans performed. Most patients had stage IV disease and received palliative anti-neoplastic treatment. Twenty-seven out of 52 patients maintained muscle mass and had a significantly higher total protein intake (1.2 vs. 1.0g protein/kg body weight/d, p=0.023) as well as a higher protein intake per meal (1.1 vs 0.7g protein/kg body weight/meal, p=0.038) compared to muscle wasters (n=25). The protein intake explained 9.2% of the variation in muscle mass which increased to 14.4% when the inflammatory score was added in the model ($p<0.05$). Muscle wasting was not detectable by weight loss.

Conclusions
Total protein intake daily and protein quantity per meal were higher in muscle maintainers compared to muscle wasters. Muscle wasting occurs early in the treatment course and effective interventions to maintain skeletal muscle mass are warranted.

Patient involvement: Poster #124-148

Patient involvement

#124 Patient reported outcomes during immunotherapy for metastatic melanoma – Patients' and clinicians' experience

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Abstract
Introduction
Using electronic Patient-Reported Outcome questionnaires has proven feasible in many settings. However, it remains to be investigated how melanoma patients and clinicians experience the electronic self-reporting of symptoms. Thus the primary objective of the study was to examine melanoma patients' and clinicians' experiences with an e-health intervention to monitor symptoms during immunotherapy.

Material and methods
An e-Health intervention based on questions from the PRO-CTCAE library was used in a randomized clinical trial with melanoma patients receiving immunotherapy. Patients reported their symptoms weekly during treatment. The electronic patient reports were available to clinicians in the out-patient clinic. A mixed methods approach was applied to investigate patients' and clinicians' experience with the intervention. Data from patients' experiences was collected in a short survey. Moreover, a subset of the patients participating in the survey was interviewed and one focus group interview with clinicians was carried out.

Results
57 patients completed the Patient Feedback Form, and 14 patients were interviewed. The focus group interview included five clinicians. Overall, patients and clinicians were satisfied with the tool. They believed it enhanced patients' awareness of symptoms and increased the feeling of involvement. However, a minority of the patients did not experience that the clinicians had seen their reports when they came to the clinic. Moreover, the patients did not believe that they were more in contact with the department due to the reporting.

Conclusion
Overall, the satisfaction with the e-Health intervention was high among patients and their treating clinicians.
The tool was easy to use and contributed to greater symptom awareness and patient involvement.

Patient involvement

#125 Patient-reported outcomes in nurse led consultations – A potential tool for proactive symptom management during chemotherapy

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Abstract
Introduction
Patient reported out comes in symptom management during chemotherapy is a focus of international studies. The potential of PRO for proactive symptom management and limited investigated. The aim of present study was to investigate the types of interventions prompted by a PRO questionnaire in a prostate cancer population.

Materials and methods
In an explorative qualitative study, patients reported their symptoms via an electronic population specific PRO questionnaire. The questionnaire was comprised of 25 PRO-CTCAE™ symptoms and an open "write in" section. Data were collected once a week via semi-structured interviews based on the PRO-CTCAE™ data from patients with metastatic prostate cancer treated with chemotherapy at Rigshospitalet, Denmark. The data collection focused on the grade/experience of each symptom and which of the following 6 types of intervention they prompted, 1) self-management 2) consultation by nurse 3) consultation by physician 4) acute visit at out patient clinic 5) admission to hospital ward 6) others. The interviews were conducted by a nurse who assessed the symptoms, the need for intervention and relevant actions were taken.

Results
7 patients were included and followed for 9-19 weeks observational period. Out of the 25 PRO-CTCAE™ symptoms the patients reported 23 types of symptoms. There were no acute visits to outpatient clinic or admissions to hospital ward, 1 referral to rehabilitation clinic and 2 consultations by physicians. The remaining symptoms were handled either by nurse consultation or self-management. In the observational period a trend appeared regarding type of intervention in the individual patient pathway, from nurse consultation to self-management.

Conclusions
The study indicates that systematic use of a population specific PRO-questionnaire can support symptom management and implies that nurse consultations can lead to self-management. However, this type of intervention requires resources for nurses.

Patient involvement

#126 Management of side effects in head and neck cancer by systematic use of Patient Reported Outcome during radiotherapy. Design of a national PRO study- DAHANCA 38

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Abstract
Introduction
We here describe the design of a national DAHANCA (Danish Head and Neck Cancer Group) Patient Reported Outcome (PRO) study that will investigate the effects of active use of PROs during radiotherapy (RT) for head and neck cancer (HNC).

Materials and methods
The study is a prospective nationwide sequential cohort study, NCT ID No. NCT03918382, DAHANCA 38. The study will include patients ≥ 18 years diagnosed with HNC and planned for RT (primary or postoperative) at the University Hospitals of Aalborg, Aarhus, Herlev, Naestved, Odense and Rigshospitalet.
The management of side effects in standard clinical counselling (control group) versus clinical counselling based on PRO (PRO group) will be investigated. Quality of life (QoL) in the two groups will be recorded.
In the first phase, 97 patients will be included in the control group. In the second phase 194 patients will be included in the PRO group. The intervention is active use of electronic Patient Reported Outcomes. Patients in the PRO group report their symptoms on a tablet at baseline, weekly during RT until week 2 after RT completion. The PRO answers will be presented graphically and used as part of the consultation. The PRO questions consist of HNC relevant items from PRO-CTCAE™ and EORTC item library. QoL (EORTC QLQ-C30 and EQ-D5-L5) questionnaires will be answered in both groups at baseline, week 4 of treatment, at completion of RT and 2 months after RT completion.

Results
Primary endpoint is health-related quality of life at end of RT. Data on secondary endpoints will include time to start opioid treatment, time to tube-feeding/other feeding, weight loss, DAHANCA toxicity and compliance to treatment.

Conclusions
In collaboration with DAHANCA a national study on active use of PROs during RT for HNC has been established. The results will generate evidence on the use of PROs versus standard counselling during RT. Inclusion of patients will begin May 2019.

Patient involvement

#127 Patient-reported outcomes item selection for bladder cancer patients in chemo- or immunotherapy

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Abstract
Introduction
Selection of specific patient-reported outcomes (PROs) for cancer patients requires careful consideration to the purpose and population at aim. Here we report the process of choosing which items to include in a bladder cancer(BC) population in chemo- or immunotherapy, based on the Patient-Reported Outcomes Version of the Common Terminology Criteria of Adverse Events (PRO-CTCAE).

Materials and methods
Initial PRO-CTCAE symptoms were chosen through 1)medical record audit 2)patient interviews 3)SPCs from European Medicines Agency and Food and Drug Administration for the applied chemotherapies, and 4)toxicity reporting from Phase 2&3 trials for immunotherapies applied in patients with urothelial cancer. The selected questions were applied in a prospective cohort of 78 BC patients receiving chemo- or immunotherapy at Rigshospitalet and Herlev Hospital. Symptoms tested in this population were selected for the final module if they appeared in ≥3 of the following groupings a)the most prevalent PRO-CTCAE symptoms grade ≥2 overall during treatment b)the PRO-CTCAE symptoms reported in conjunction with hospital admissions or mentioned in focus group interviews discussing which symptoms were prevalent in this patient group with specialized c)nurses or d)physicians. The authors also included symptoms in the final module if they were present in 2 of the above groups and defined as actionable by clinicians.

Results
From the initial selection of PRO-CTCAE symptoms, a total of 45 PRO-CTCAE symptoms explored by 84 PRO-CTCAE questions were retrieved. Through the second selection process based on the described criteria, the study group agreed on 15 PRO-CTCAE symptoms explored by 30 PRO-CTCAE items to be appropriate and relevant for the bladder population during medical oncological treatment.

Conclusions
The selection of disease specific PROs in a BC population was feasible. The process revealed several steps of selection needed to reach a final module for clinical application.

Patient involvement

#128 First acute patient-reported toxicity and change in health-related quality of life after magnetic resonance guided radiotherapy – preliminary results from the MR-linac at Odense University Hospital

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Abstract
Introduction
MR-guided radiotherapy (RT) on the MR-linac (MRL) is a new technology using real-time MR images for daily RT plan adaption. To evaluate clinical effectiveness, patient-reported outcomes (PRO) are valuable as incidence and severity of symptoms often are higher when reported by patients than by clinicians. 25 patients have been treated on the MRL at our local clinic since October 2018. This is a study reporting PRO results from the 14 patients having had a 4-week follow-up.

Materials and methods
All patients at the MRL reported health-related quality of life (HRQL) and health state (EQ-VAS 0-100) with EQ-5D at baseline and at their 4-week follow-up. In addition, prostate cancer patients treated on the MRL (60 Gy/20 F) reported acute toxicity (I-PSS (scale 0-35), EPIC-26 (scale 0-100)) at baseline, end of RT and at the 4-week follow-up.

Results
All patients at the MRL reported health-related quality of life (HRQL) and health state (EQ-VAS 0-100) with EQ-5D at baseline and at their 4-week follow-up. In addition, prostate cancer patients treated on the MRL (60 Gy/20 F) reported acute toxicity (I-PSS (scale 0-35), EPIC-26 (scale 0-100)) at baseline, end of RT and at the 4-week follow-up.

Conclusions
HRQL for all patients treated on the MRL was similar at baseline and follow-up. Patients treated for prostate cancer on the MRL primarily reported acute urinary irritative symptoms at the end of RT, however, at the 4-week follow-up the symptom scores improved.

Patient involvement

#129 Handling of symptomatic adverse events in breast cancer patients receiving adjuvant chemotherapy in a cluster randomized trial with electronic Patient-Reported Outcomes as intervention

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Abstract
Introduction
The present study is based on a national cluster randomized trial investigating the effect of electronic patient-reported outcomes (ePRO) on treatment outcomes in breast cancer patients receiving adjuvant chemotherapy. The purpose of the present study was to investigate the handling of symptomatic adverse events (AE) in the two study arms.

Materials and methods
A 10% sample of patients enrolled in the cluster randomized trial was randomly selected for a medical record audit. Information on documentation of symptomatic AE and handling (medication, counselling or referral to other specialists/programs) were extracted from electronic medical symptomatic AE. A substantially higher number of patients in the ePRO arm compared to patients in the usual care arm had counselling for patients' self-management of symptomatic AE records.

Results
In total, 45 patients (ePRO) and 35 patients (usual care) were randomly selected for the audit. In the ePRO arm, 44 patients had 196 documented symptomatic AE (mean 4.6) and in the usual care arm, 34 patients had 175 documented symptomatic AE (mean 5.1) in the medical records. Totally, 26 patients (ePRO) and 21 patients (usual care) had medication prescribed for symptomatic AE. Eight patients in the ePRO arm were referred to a specialist/program compared to two patients in the usual care arm. Counselling for patient's self-management was documented in 22 patients (51 symptomatic AE) in the ePRO arm compared to one patient (one symptomatic AE) in the usual care arm.

Conclusions
There were no difference between the two study arms in the number and type of documented symptomatic AE. A substantially higher number of patients in the ePRO arm compared to patients in the usual care arm had counselling for patients' self-management of symptomatic AE documented.

Patient involvement

#130 Investigator-perceived facilitators and barriers for the implementation of electronic patient reported outcomes as an intervention in clinical cancer trials in Denmark

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Abstract
Introduction
Electronic patient reported outcomes (ePROs) are increasingly used as an active intervention in clinical cancer trials. However, the use of ePROs as an intervention is complex and dependent on many factors.
The aim of the study was to describe facilitators and barriers perceived by investigators during the implementation of Danish clinical cancer trials using ePROs.

Materials and methods
All primary investigators of clinical cancer trials using ePRO as an intervention and attending the 2019 Danish annual PhD course in oncology and hematology, were invited to participate in a semi-structured interview. All interviews were analyzed using thematic text analysis and sub-themes were identified.

Results
All six investigators agreed to participate. Four out of six participants used the AmbuFlex PRO software for their trial. The most emphasized facilitators were the presence of individual clinical pioneers, management support, software usability, support by clinical research units and appointment of nurses as key figures for logistic implementation. Rigorous and non-consistent interpretations of the Danish data and health legislation were perceived as the main barriers for clinical trials that used an electronic interaction with the patient.
Also, different regional software complicates national studies by troublesome login solutions for the PRO systems. Other barriers were skepticism among clinicians regarding the validity of the PRO tool and clinicians´ belief in patients' ability to comply with the intervention.

Conclusions
Diverging legislative interpretations was perceived as the largest system-barrier for national research collaboration. Facilitators are often dependent on individual commitment and software-usability. Patients' compliance was not seen as a barrier by the investigators. We suggest that health-administrators are involved to address these issues before attempts are made to implement ePRO as an active intervention in routine clinical care.

Patient involvement

#131 Patientrapporterede oplysninger (PRO) relateret til akutte bivirkninger og oplevelser ved strålebehandling med protoner

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Abstract
Introduktion
DCPT er et nationalt center, der tilbyder strålebehandling med protoner til kræftpatienter. Behandlingen er i visse tilfælde mere skånsom end konventionel strålebehandling, da det formodes at kunne reducere bivirkninger på lang sigt. De akutte bivirkninger til protonbehandling er imidlertid ikke veldokumenterede, hverken nationalt eller internationalt. Ved systematisk PRO registrering i DCPT dokumenteres akutte bivirkninger under og efter behandlingsforløbet, hvilket kan danne grundlag for evidensbaseret patientinformation. Desuden kan PRO anvendes aktivt som dialogstøtte ved læge-og sygeplejesamtaler under behandlingsforløbet. Herved registreres den nuværende status og udviklingen kan følges over tid. Besvarelserne giver mulighed for aktiv anvendelse af PRO, således at behandling af bivirkninger kan iværksættes og justeres rettidigt.

Materialer og metoder
Relevante items er selekteret fra det generiske spørgeskema EORTC QLQ-C30 samt fra de diagnosespecifikke EORTC spørgeskemaer gældende for patienter med hjernetumorer og hoved-hals kræft. Der er desuden suppleret med spørgsmål relateret til patienternes oplevelser i forbindelse med protonstrålebehandling. I takt med at behandling til andre diagnosegrupper implementeres på DCPT, udvælges relevante diagnosespecifikke spørgsmål.
Baseline PRO besvares elektronisk før behandlingsstart, herefter ugentligt forud for samtaler samt månedligt i follow up perioden på seks måneder.
Med henblik på at sikre relevansen af de udvalgte spørgsmål inddrages 10-20 patienter til at vurdere spørgsmålene samt omfanget af det samlede spørgeskema. Fremgangsmåden til patientinddragelse i testen af spørgeskemaet er inspireret af EORTCs manual for oversættelse af spørgeskemaer.

Resultater
Dataindsamling er pågående, som en del af daglig klinisk praksis, og på sigt forventes det at kunne indsamle data fra 1200 patienter årligt.

Patient involvement

#132 Patientinvolvering i udvikling af patientforløb for brystkræft. Et aktions-forskningsprojekt

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Abstract
Introduktion
Patientinvolvering er på dagsordenen hos politikere, patientorganisationer og sundhedsprofessionelle internationalt. Studier har undersøgt metoder til patientinvolvering i udvikling af sundhedsvæsenets ydelser, men evidensen er sparsom for hvilke metoder, der er hensigtsmæssige. Formålet med studiet var at udvikle, afprøve og evaluere en metode til patientinvolvering i udvikling af det kirurgiske patientforløb for brystkræft.

Materialer og metoder
Det overordnede design var aktionsforskning. Patienter opereret for brystkræft og deres pårørende blev inviteret til at deltage i fokusgrupper med henblik på at afdække deres oplevelser og forslag til forbedringer i patientforløbet. Dette blev diskuteret på dialog møder med patienter, pårørende og personale. På denne baggrund planlagde og udførte personalet indsatser og metoden til patientinvolvering blev evalueret.

Resultater
Patienter og pårørende oplevede patientforløbet hurtigt, gennemskueligt og veltilrettelagt og lagde vægt på betydningen af empati og støtte fra personalet. Desuden pegede de på fem situationer i forløbet, der havde særlig betydning. Forslag til forbedringer var relateret til information, kommunikation, valg af behandling, fleksibilitet og let adgang til klinikken. Affødt heraf deltog patienter og pårørende i udvikling af et beslutningsstøtteværktøj. Alle deltagere var tilfredse med at deltage i projektet og havde anbefalinger til yderligere kvalificering af patientinvolvering. Anbefalingerne var rettet mod opfølgning, facilitator, de sundhedsprofessionelles attitude samt ressourcer hos patienter og pårørende.

Konklusioner
Studiet viste, at metoden til patientinvolveret var velegnet til at involvere patienter og pårørende i udvikling af patientforløb for brystkræft. Anbefalingerne fra studiet har potentiale i forhold til at tilpasse metoden til andre kliniske områder. Derudover viste aktionsforskning sig at være et velegnet design til at udvikle viden om metoder til patientinvolvering.

Treatment morbidity and late effects

#133 Patterns in detection of recurrence among patients treated for early breast cancer

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Abstract
Introduction
Danish patients with early breast cancer are now offered fewer outpatient visits following curative treatment, but knowledge on how this may impact detection of recurrence is lacking. We aim to evaluate detection patterns of recurrence among breast cancer patients in order to clarify the proportion of recurrences that may be detected with delay in future follow-up programs.

Materials and methods
We conducted a cross-sectional study among 310 patients with recurrent breast cancer in the departments of oncology at Aarhus and Copenhagen University Hospitals. Information on tumor characteristics, type of visit when recurrence was detected, localization of recurrence, symptoms reported and duration of symptoms leading to detection of recurrence were retrieved from DBCG and medical records.

Results
The 310 recurrences were locoregional (26%), locoregional and distant (15%) or distant (59%). Among the 205 patients still in outpatient follow-up at time of recurrence, recurrence was detected at: patient-initiated consultations (61%; 15% in the outpatient clinic and 46% by the general practitioner (GP) or other specialist), planned follow-up visits (31%; 20% in the outpatient clinic and 11% at scheduled mammography), or at unclear visit type (8%). Among patients with recurrence detected at planned outpatient visits, the majority reported symptoms related to recurrence. Most frequent symptoms were pain (37%), dyspnea (15%) and fatigue (12%). Only five patients were asymptomatic. For patients with recurrence after end of follow-up (n=105), 96% of recurrences were detected by GP or other specialist.

Conclusions
Most breast cancer recurrences detected at scheduled outpatient visits are symptomatic, and these recurrences will not be detected with delay, if patients learn to react on relevant symptoms.
Still, for the few asymptomatic recurrences detected at scheduled outpatient visits, we may expect delayed detection as the number of scheduled visits has decreased.

Patient involvement

#134 A study in optimizing follow up for postmenopausal women with breast cancer treated with adjuvant endocrine therapy

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Abstract
Introduction
New clinical guidelines concerning follow up care after cancer were launched by the Danish Health and Medicines Authority in February 2015. Women treated for early breast cancer were recommended to be followed at the oncological department if they receive specific oncological treatment, such as endocrine therapy. Yet, there is no evidence for routine examinations to improve overall survival. Mammography is the only examination to be offered to asymptomatic women attending follow-up. This study aims to investigate how follow-up care can be optimized by an individualization of the program and whether the active use of patient reported outcomes (PROs) is a feasible tool for this individualization.

Materials and methods
We designed a randomized clinical trial in which postmenopausal women treated for hormone receptor positive early breast cancer were randomly assigned to standard follow up care or individualized follow-up with the use of PROs to customize the care. PROs were used as screening tools for the patients' needs for clinical encounters and as tools to focus the dialogue in the meeting with health professionals. During a two-year study period, we examined feasibility, patient reported experience measures and the impact on the use of resources.

Results
From a cohort of 207 newly diagnosed postmenopausal women with hormone receptor positive early breast cancer, 134 were randomized during the inclusion period from April 2016 through June 2017. By the end of June 2019, all participants have been followed for two years. Currently sixteen (25%) of the sixty-five women allocated for individual follow-up have not been in need of a single consultation at any time point and patients report to be equally satisfied.

Conclusions
This study will contribute with experiences of, and perspectives on, the active use of PROs as screening tools and dialogue tools to individualize follow-up care after treatment for breast cancer.

Patient involvement

#135 Impact of Patient Involvement on a Clinical Study: Experiences from a Study Analyzing FDG-PET/CT in Women with Advanced Breast Cancer

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Abstract
Introduction
Patient involvement in health care research has become of increasing interest in recent years. Researchers, however, may be unclear about the gain of involving patients in clinical studies. We aimed to evaluate the impact of patient involvement in a clinical study of FDG-PET/CT in women with advanced breast cancer with regard to patient recruitment and change of attitude within our research team.

Materials and methods
The patient partners were asked to contribute to participator information as well as to evaluate ethical aspects. The impact of patient involvement on patient recruitment was evaluated by comparing expected versus actual number of patients recruited, and by relating it to the patient recruitment from a previous comparable study performed without patient involvement in the same institution.

Results
The expected number of patients recruited was 135 patients per year. This number was based on patient recruitment in a previous study in which only 33 patients were enrolled per year. Compared to this, 199 patients have been enrolled during the first year in the current study - i.e. 147 % of the expected number. Having patients as partners in the study led to a major revision of the participator information material and the way ethical issues were addressed. An initial resistance within the research team was observed against inviting patients as partners. The resistance resolved gradually during the process, and hence the most reluctant researchers from the beginning applauded the collaboration and the ideas generated by patient representatives in a later phase.

Conclusions
Inviting and involving patients as partners in the research team resulted in major changes of the patient participator information material and had a significant, positive impact on patient recruitment for the study. Involving patients as partners changed the researchers' attitudes towards patient involvement in research in a positive direction.

Patient involvement

#136 Nephspare PRO - Patient involvement in choosing the relevant instrument to measure patient reported quality of life after nephron sparing treatment of small renal tumors in a Danish setting

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Abstract
Introduction
Partial nephrectomy(PN) is the gold standard in nephron sparing treatment of small renal tumors. Percutaneous cryoablation(PCA) is a less invasive treatment with similar oncological outcome. To both achieve clinically relevant results and increased end user value, it has become increasingly common to involve patients in the research process. The overall aim of this study is to assess and compare patient reported quality of life and self-reported health status after PN and PCA. Our specific objective in this study is to identify the relevant instrument to measure the quality of life according to the patients' perspectives.

Materials and methods
Three validated questionnaires covering the aim of the study were chosen: a generic (SF-36), a cancer specific (EORTC QLQ C-30) and a renal cancer specific (RQRC (only locally validated)). Testing was done in two phases, i) preliminary testing with experts and layman ii) cognitive interviews with patients from the study population. The test included: comprehension of items, adequacy of response categories, duration, overlapping of items and whether the questionnaires cover important and relevant concepts. A total of 10 patients were telephone interviewed; eight male age 38-79 and 2 women age 61-82 reflecting the study population. The interviews were based on the 'think aloud' method initiated by pre-formulated probes.

Results
After preliminary testing, it was evident that both the length of the questionnaire and overlapping items posed challenges. Thus, SF-36 was replaced with SF-12. Minor adjustments were made in the RQRC and we changed time for follow-up. The interviews provided valuable insight into patients' interpretation of both the total questionnaires and the single items – useful for both understanding and interpreting data and for implementation of the results.

Conclusions
Patient involvement contributes vital knowledge for both choosing the relevant instrument and for optimizing the study method.

Patient involvement

#137 Couple counselling and pelvic floor muscle training to men operated for prostate cancer and their partners. Preliminary results from the ProCan pilot randomized controlled trial

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Abstract
Introduction
Radical prostatectomy (RP) is often followed by long-term erectile and urinary dysfunction, which has proven to affect quality of life and intimate relationship of patients and partners. In order to ameliorate sexual and urological dysfunctions after RP, we developed and tested the effect of couple counselling and pelvic floor muscle training on sexual and urological outcomes.

Materials and methods
The ProCan intervention consisting of up to six couple counselling sessions and up to three individual instructions in pelvic floor muscle training including a DVD home training program was evaluated in a pilot randomized controlled study (RCT). Couples in both groups filled out baseline and follow-up questionnaires at 8 and 12 months. The primary outcome was erectile functioning in patients, while secondary outcomes included urinary function in patients only and sexual functioning, dyadic functioning, health related quality of life, anxiety and depression in both patients and partners.

Results
Between January 2016 and December 2018, all 319 candidates to RP at the Clinic of Urology at Rigshospitalet were invited to fill in the baseline questionnaires and 104 returned the questionnaire (33%) and were evaluated for eligibility. Sixty-one sexually active couples were invited to participate in the pilot RCT and 35 couples accepted participation (57%) and were randomized to either standard care (n=19) or the ProCan intervention (n=16) In total 67 couple counselling sessions (median 4 per couple) and 34 individual sessions with pelvic floor muscle training (median 2 per patient) were carried out. Results will be presented on data from the baseline, 8 and 12 months follow-up questionnaires from 16 couples in the intervention and the control group respectively.

Conclusions
Our results will be important for how to improve sexual and urological dysfunctions in prostate cancer patients and their partners.

Patient involvement

#138 Fælles beslutningstagning for patienter med recidiv af højgradsgliom – hvordan gør vi og er det overhovedet relevant?

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Abstract
Introduktion
Højgradsgliomer (HGG) er aggressive og infiltrerende hjernetumorer. Trods optimal kirurgisk og onkologisk behandling vil størstedelen af patienterne opleve recidiv.
Der er begrænset viden om patienters og pårørendes oplevelse af denne situation og hvordan og i hvilket omfang de ønsker at blive inddraget i beslutningen om den videre behandling og pleje.
Formålet med dette PhD-projekt er at undersøge patienter og pårørendes perspektiver på beslutningsprocessen. Herudover at udvikle et beslutningsstøtteværktøj, der kan styrke patientinddragelse i beslutningstagningen.

Materialer og metoder
PhD-projektet består af tre delstudier:

I. Systematisk review. Afdække eksisterende viden om beslutningstagning for patienter med HGG.
II. Kvalitativt studie. Belyse patienter og pårørendes oplevelser og perspektiver på beslutningsprocessen omkring behandling og pleje ved recidiv af HGG. Belyse relevante klinikeres perspektiv på beslutningstagning og patientinddragelse for patienter med recidiv af HGG.
III. Udvikling af beslutningsstøtteværktøj.

Resultater
Projektet forløber fra 2019-2022.
Via semistrukturerede interviews med patienter, pårørende og klinikere genereres data om de forskellige perspektiver på beslutningsprocessen.
Der indsamles demografiske data på alle deltagere samt journaldata omhandlende sygdoms- og behandlingsforløb på deltagende patienter.
Ovennævnte vil, sammen med evidensbaseret viden om de tilgængelige muligheder for behandling og pleje, indgå i udviklingen af et beslutningsstøtteværktøj målrettet den specifikke situation.

Konklusioner
Projektet vil bidrage til øget viden om patienter og pårørendes perspektiver på beslutningstagning ved recidiv af HGG.
Fælles beslutningstagning og anvendelse af beslutningsstøtteværktøjer forventes at kunne støtte patienter til at afklare egne præferencer for den videre behandling og pleje samt styrke inddragelsen af patienter og pårørende i beslutningstagningen.

Patient involvement

#139 Hvad har betydning for patienters behov og præferencer for transport og ophold under et nationalt ambulant behandlingsforløb ved Dansk Center for Partikelterapi (DCPT)?

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Abstract
Introduktion
DCPT er et nationalt center, der tilbyder strålebehandling med protoner til danske kræftpatienter. Behandlingen foregår i Aarhus over 5-6 uger. Størstedelen af DCPT's patienter vil kunne modtage behandlingen ambulant. Regler for transport, ophold og ledsagelse varierer tværregionalt, hvilket potentielt kan betyde geografisk ulighed for adgang til behandlingstilbuddet. Det vil være hensigtsmæssigt at udvikle nationale kriterier for transport, ledsagelse eller ophold ved længerevarende ambulante behandlingstilbud, der udelukkende tilbydes ét sted i Danmark. Kriterierne kunne bero på behandlingsfrekvens og – længde, klinisk vurdering, afstand til behandlingscentret samt geografisk beliggenhed.
Udenlandsk forskning viser, at geografisk afstand har betydning for adgang til behandling. Sammenhængen er ikke veldokumenteret i dansk kontekst, hvorfor det ønskes belyst i dette studie. Endvidere er det relevant at afdække patienters behov og præferencer for transport, ophold og ledsagelse relateret behandlingsforløbet. Dette kan danne grundlag for informationsmateriale, der kan støtte patienter i at træffe valg mellem forskellige bo muligheder, samt forslag til, hvordan hverdagen under behandlingsforløbet planlægges og indholdsmæssigt struktureres.

Materialer og metoder
Undersøgelsen består af en spørgeskemaundersøgelse med fokus på geografisk ulighed. Spørgeskema besvares ved behandlingsstart og -afslutning. Det forventes at inkludere 350 patienter på DCPT over 2 år. Desuden foretages en interviewundersøgelse med fokus på patientens behov og præferencer for transport, ophold og ledsagelse under behandlingsforløbet. Inklusion fortsætter til purposeful sampling og datamætning er opfyldt.

Resultater
Dataindsamling er ikke afsluttet. De kvantitative data præsenteres deskriptivt. Desuden sammenholdes den geografiske patientfordeling med registerdata over kræftpatienter i de respektive regioner. I den kvalitative analyse genereres temaer ud fra den indsamlede empiri.

Patient involvement

#140 Når højt specialiseret, kirurgisk kræftbehandling ikke kan gennemføres - en undersøgelse af muligheder for patientinvolvering i det videre forløb

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Abstract
Introduktion
Tidligere forskning har dokumenteret, at patienter henvist til højt specialiseret, centraliseret kirurgisk behandling for peritoneal cancer udgået fra tarmsystem og ovarier opfatter kirurgisk behandling som deres mulighed for helbredelse. De og deres pårørende accepterer derfor behandlingstilbuddet uden at stille spørgsmålstegn ved det. Imidlertid kunne kirurgisk behandling kun gennemføres i syv ud af de 15 patientforløb, vi har undersøgt. På den baggrund ønsker vi at afdække muligheder for patientinvolvering når højt specialiseret, kirurgisk kræftbehandling ikke kan gennemføres.

Materialer og metoder
Sekundær analyse af 31 semistrukturerede forskningsinterview og 37 kliniske feltobservationer i relation til 15 patienter og pårørendes forløb, samt to fokusgruppeinterview med fire kirurger og fem sygeplejersker fra deltagende afdelinger.
Igangværende supplerende feltobservationer og forskningsinterviews med fokus på efterforløbet, når beslutning om at opgive den planlagte kirurgiske behandling er truffet.

Foreløbige resultater
Patientforløbet er i udgangspunktet planlagt med en række stopklodser indlejret, hvor der sker en gradvis selektion ved både diagnostisk laparoskopi og under selve operationen. Beslutning om ikke at operere tages først under operationen og baserer sig på kliniske parametre.
Patient og pårørende ønsker bedre overblik over forløbet, og at blive støttet i at stille spørgsmål.
I udgangspunktet er patienterne ikke nødvendigvis sårbare, men mødet med systemet, det komplekse behandlingsforløb, og den store usikkerhed frem til det viser sig, om behandlingen kan gennemføres, kan skabe sårbarhed.

Foreløbig konklusion
Komplekse kirurgiske behandlingsforløb kan være forbundet med betydelig uforudsigelighed, der strækker sig helt frem til operationstidspunktet. Den professionelle indsats skal derfor balanceres mellem standard og individ, og justeres fremadrettet i forhold til patientens aktuelle behov og personlige præferencer.

Patient involvement

#141 Program committees for cancer treatment is a succes, which ensure a high organizational quality of standardized patient courses at Odense university Hospital (OUH)

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Abstract
The concept of the program committees for cancer treatment at Odense University Hospital (OUH):

- Establishment of program committees took place in May 2011 at OUH
- One director is chairman of the 13 program committees - important program committees have decision-making power. 7 of the 13 program committees are covering the region of Southern Denmark
- All players in a cancer package course participate in the program management (data controllers, secretaries, nurses, specialized doctor managers, department management and staff-supporters which make the program management quorum)

Results

- Great effort in the research area
- The Region of Southern Denmark has long maintained a leading position in respect of compliance cancer pathways in Denmark
- General improvement in overall compliance time for cancer treatment
- The clinics can talk about the challenges - where it is given a forum where they possible to discuss and initiating cross-cutting initiatives that are necessary to comply the time requirements in relation to cancer treatment
- Progress on clinical cancer quality databases
- Focus on correct coding

Conclusions
The concept of the program committees at OUH works:

- Because the areas where a program management is established are high on the managerial agenda at both OUH and the region
- Because a broad support is ensured from all the departments that have shares in the patient programs that belong to the individual program management
- Because larger implementation tasks can be anchored - for example implementation of follow-up programs after finishing treatment
- Because there can be established anchoring of the regional cooperation between the hospitals - for example organizing multidisciplinary conferences (MDT)

Future

- Proactive monitoring of cancer programs
- Pathology response on time
- MR accelerator
- PET / MR scanner
- Personal medicine
- Patient responsible doctor

Patient involvement

#142 Bringing patients and health researchers closer together: patient involvement in a study on patient-reported outcomes in cancer consultations

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Abstract
Introduction
Patient involvement in health research may improve quality and relevance. However, little is known about how and when patients are best involved. We aimed to gain knowledge and experience with the impact of patient involvement on both process and results of a clinical study investigating the effect of using patient-reported outcomes (PRO) as a dialogue-based tool in oncology consultations.

Materials and methods
A steering group with two patients and six researchers was established in 2017. In the design phase, the steering group selected relevant PRO measures and composed a patient information sheet. In the analysis phase, the steering group received training in order to analyze audiotaped consultations using the Verona Coding Definitions of Emotional Sequences (VR-CoDES). The analysis was done individually before consensus-meetings were hold. Additionally, the steering group will be involved in the dissemination phase.

Results
In the design phase, patients advocated for inclusion of PRO measures to enable discussions with both clinicians and relatives in the consultation, which was not considered by the researchers beforehand. The title and wording of the information sheet were adjusted in light of the patients' suggestions. In the analysis phase, patients contributed with new perspectives on how the physician-patient relationship determines the way emotional expressions and responses are articulated in the consultations. Arranging meetings, additional expenses, and death of involved patients were challenging elements in the process.

Conclusions
Bringing researchers and patients closer together in co-production of research is feasible and beneficial but also time-consuming. Ethical discussions about the appropriate extent of involvement, the harms of patients and how to avoid tokenism are needed. Knowledge and experiences about involving patients in research can be applied to other settings where patients are partners in the research process.

Patient involvement

#143 Communication in Oncologist-Patient Encounters from the Patients' Point of View – a qualitative study

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Abstract
Introduction
The aim of the study was to explore patients' perspective on communication during Oncologist-Patient encounters.

Materials and methods
We conducted a qualitative study with data collected from the Department of Oncology, Odense University Hospital, Denmark. Data was collected through video recorded encounters and semi-structured interviews with patients in their own home approximately one week after they have visited the Oncology Department.
Between the encounter and the interview; the videos were transformed into written text and reviewed by EI and PG. The semi-structured interview was based on open-ended questions followed by targeted questions from the reviewing of the encounters. During the interview, the video was shown to the patient who was instructed to pause the video having any comments. The interviewer was also allowed to pause the video if it seemed necessary. A systematic text condensation was performed on the transcribed interviews.

Results
A total of six encounters and interviews were included for the systematic text condensation. In general, patients were very satisfied with the oncologist and all stated they wished to consult the same physician for their next appointment. During the analysis, we looked for patients' perspectives aiming to improve communication and found four themes; Patients found it disturbing if it was a non-familiar physician, lack of opportunity to talk about worries, confusions from logistics, inadequate information about examinations, tests, and plans for the next step.

Conclusions
Altogether, the patients were very satisfied with the communication at the Oncology Department however there is still room for improvement. Especially; all patients requested to see the same physician for every visit as this may avoid inadequate information and make it easier to talk about feelings. The next step for our research is to compare the patient´s statements to what happened in the encounters.

Patient involvement

#144 The meaning of health literacy and participation in cancer survivorship care – An Interpretive Description of experiences and perspectives of patients and health professionals

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Abstract
Introduction
The number of cancer survivors is increasing, thus the need for cancer survivorship care (CSC). Dialogue and communication is crucial for patients, to make informed choices in relation to participate in CSC. Health literacy (HL) is a patient's prerequisites of competencies to meet with the complexity of communication in the health care system. Many cancer patients do not get sufficient information on CSC and a great number of patients do not participate in CSC.

The overall aim of this PhD-project is to establish research-based knowledge on the meaning of HL, in relation to informed decisions on participation in CSC, by exploring the experiences and perspectives from patients and health care professionals.

Materials and methods
This PhD-project comprises two overall studies: A systematic literature review and an ethnographic study with design and methodology of Interpretive Description, guided along with Symbolic Interactionism. Data will be generated at four settings, through participant observations, individual interviews with 16 cancer patients and 4 focus group interviews with a total of 32 health professionals. Data will be recorded, transcribed and analyzed. Patient and public involvement will help qualify the research. The PhD-project will be conducted at: Department of Oncology, Regional Hospital of West Jutland, Department of Oncology, Aarhus University Hospital, The public health center, the municipality of Aarhus, The public health center, municipality of Ringkøbing Skjern.

Results
The knowledge and experiences gained from this PhD-project, will contribute to focus on barriers and facilitators of HL in CSC and thereby help to promote HL by ensure dialog, encourage patient centered communication and thereby improve an informed decision towards participating in CSC.

Conclusions
More knowledge on HL may enhance patients' knowledge on CSC and possibly ensure a more systematic and equal initiative towards participation in CSC.

Patient involvement

#145 Adherence to preventive swallowing exercises for head and neck cancer patients undergoing (chemo)radiotherapy treatment

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Abstract
Introduction
In recent years, preventive swallowing exercises have been investigated as a means to limit dysphagia in head and neck cancer patients. However, adherence to exercise regimes has been poorly documented limiting the conclusions drawn on the effects of the interventions. We investigated adherence to a preventive swallowing exercise program and identified possible associations between adherence and four selected baseline factors: HPV status, partner status, concomitant chemotherapy and tumour site, and between adherence to swallowing exercises and attendance to supervised training sessions.

Materials and methods
Forming part of an ongoing RCT (clinicaltrials.gov NCT02385929) adherence to intervention was based on participant provided training-logs. The exercise program consisted of 3 weekly supervised sessions of 30 minutes each and a home-based exercise program to be performed 3 times daily. Adherence was calculated as percentage of prescribed exercises completed and dichotomously as high (≥80 %~median) and low (<80 %~median) adherence. Associations between adherence and the four clinical/demographic factors and attendance level were explored by logistic regression analyses.

Results
Full adherence data were available from 45 (76 %) participants. The total cohort median adherence to exercises was 78 %. No associations were found between any of the tested factors and adherence.

Conclusion
The study found a high adherence to preventive swallowing exercises in HNC patients undergoing (chemo)radiotherapy, both in home-based exercises and in supervised sessions, when compared to other studies, although median adherence to home-based exercises was below the defined 80 % threshold. We acknowledge, that adherence in an RCT may be higher than in the everyday clinical situation due to surveillance bias. However, we find it reassuring that HNC patients comply with a preventive swallowing program, which requires some time investment from the patients.

Patient involvement

#146 Development of a nurse-led follow-up model after curatively intended treatment for esophageal cancer

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Abstract
Introduction
Cancer in the esophagus is an aggressive disease affecting more than 500 people in Denmark annually. About one third are offered surgical treatment with curative intent. Due to the extensive surgery, many patients experience complications such as dysphagia, change in tasting sensation, dumping syndrome, pain and fatigue. Patients describe a negative impact from these problems on quality of life (QoL). Furthermore, psychological distress is more prevalent in this patient group than in patients with other gastrointestinal cancers.
Patients and health professionals request improved information and supportive care during follow-up. The Danish Health Authorities (2015) recommends improved initiatives for information, rehabilitation, palliative care, health promotion initiatives, psychological efforts and a special focus on individual follow-up programs with patient involvement.
Nurse-led follow-up for patients treated for cancer in the esophagus has been studied in few, minor studies suggesting increased patient satisfaction and fewer expenses.

The aim of this preparatory project is to develop a systematic, nurse-led follow-up model for patients treated for esophageal cancer with curative intent, as an alternative to traditional surgeon-led follow-up.

Materials and methods
The model will be developed with close involvement of patients and health professionals, and the development process will follow the principles for implementation and testing of complex interventions. Patient representatives from all four participating centers are invited to participate in a reference group, which is closely involved in several stages of the development process. The purpose is to prepare a follow-up model ready for pilot-testing and subsequently evaluation in a national clinical trial (randomized and controlled), where the nurse-led model is compared to traditional surgeon-led follow-up, with quality of life as primary outcome.

No results or conclusions available yet.

Patient involvement

#147 Highly motivated, but deceived and exhausted by repeated, abrupt complications: Implications for rehabilitation when treated with allogeneic non-myeloablative stem cell transplantation

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Abstract
Introduction
NMA-HSCT can cure patients with malignant blood diseases, but subsequently the majority of patients suffer from recurrent serious side effects and complications. Hence, it is a major challenge for patients treated with NMA-HSCT to rehabilitate. The objective was to explore patients' experiences and perspectives of their challenges and needs regarding their return to everyday life after allogeneic non-myeloablative haematopoietic stem cell transplantation (NMA-HSCT).

Materials and methods
The design was qualitative using the Interpretive Description methodology, and the theoretical framework Symbolic Interactionism inspired the interview guide and analysis. Between April to May 2017, five focus group interviews were conducted with 15 outpatients in a haematological ward in DK treated with NMA-HSCT 8–30 months prior to the interviews.

Results
The impaired functioning was the overarching theme and seemed to be the trigger entailing rehabilitation needs related to the following main themes: realising decline, adapting to changes, the meaning of motivation and reliance on relations. These findings seemed to affect and influence the patients' struggle for a return to an acceptable everyday life.

Conclusions
Based on our findings, a rehabilitation programme should encompass: extensive variation regarding how to address the impaired functioning through individualised approaches, multimodal interventions through several months with varying intensity, an interdisciplinary team approach supporting motivation and visualisation of progress by tangible goal setting, communication regarding hope, extended supportive care for patients living alone and increased adherence through social sessions.

Patient involvement

#148 Safety first: Older women's experiences with colposcopy and preferences for follow-up after abnormal cervical cytology

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Abstract
Introduction
Research on psychological effects of colposcopy indicates both pre- and post-colposcopy distress. Examination of older women can be challenging due to age-retraction of the transformation zone. One treatment strategy for older women with a not fully visible transformation zone is ‘See and treat’ which is a procedure that allows women to be diagnosed and treated in one visit. However, the procedure involves high risk for overtreatment.
In this study we aimed to explore older women's experiences with colposcopy and preferences for follow-up after abnormal cervical cytology, including attitudes to 'See and treat'.

Materials and methods
We conducted a focus group interview study with HPV positive women above 60 years of age who had undergone a colposcopy, some also a cone biopsy. A dynamic semi-structured interview guide was used, and the interviews were audio-recorded and transcribed verbatim. A thematic analysis was conducted, based on an interpretive tradition of ethnography.

Results
Attitudes towards referral from the general practitioner to colposcopy were highly positive, and the ‘See and treat’ approach at the gynecological department was preferred if the transformation zone was not visible. The women emphasized that getting a certain diagnosis was important to them even though a certain diagnosis was associated with considerable risk of overtreatment. Many underlined the importance of getting thorough oral and written information before the colposcopy to reduce psychological distress associated with the procedure and to feel prepared to make an informed decision about follow-up procedures including 'See and treat'.

Conclusions
Certainty about diagnosis is pivotal for these women and the 'See and treat' approach may be preferred over repeated follow-up colposcopies despite the risk for overtreatment. Oral and written information before colposcopy should include thorough information about pros and cons of 'See and treat'.

Palliation, psychosocial support: Poster #149-156

Palliation, psychosocial support

#149 Udvikling af palliativ indsats i den danske hospitalssektor – et tværfagligt palliativt samarbejde mellem den multidisciplinære cancer gruppe for palliation (DMCG-PAL) og de sygdomsspecifikke DMCG'er

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Abstract
Introduktion
Internationalt er der stigende evidens for og fokus på at integrere den palliative indsats i hele forløbet med fremskreden kræft, således at den forløber parallelt med den antineoplastiske behandling. I Danmark findes der ingen samlet national viden om palliation på de kliniske afdelinger (fx onkologiske, gynækologiske og kirurgiske), der ikke har palliation som deres primære arbejdsopgave.
Med etablering af DMCG.DK's 'Udvalg for Tværfaglig Palliativt Samarbejde' er det formålet at etablere et formaliseret samarbejde mellem DMCG-PAL/Dansk Palliativ Database og de sygdomsspecifikke DMCG'er/databaser. Samarbejdet skal omfatte kvalitetsudvikling af og forskning i den palliative indsats i hele forløbet med fremskreden kræft.

Materialer og metoder
Arbejdet vil blandt andet omfatte følgende områder:
1. Etablering af en 'dobbeltforankret, national database for palliativ indsats', som vil indgå i både de sygdomsspecifikke DMCG'ers databaser og i Dansk Palliativ Database
2. National koordinering af forskning og kvalitetsudvikling vedrørende palliativ indsats, herunder etablering og gennemførelse af forskningsprotokoller for afprøvning af modeller for tidlig palliativ indsats
3. Udvikling og implementering af kliniske retningslinjer for palliativ indsats i hele det danske sundhedsvæsen (i første omgang med vægt på hospitalssektoren)

Resultater
Udvalget for Tværfagligt Palliativt Samarbejde blev nedsat i foråret 2019, og består af medlemmer fra DMCG-PAL og følgende sygdomsspecifikke DMCG'er: hæmatologi, gynækologi, urologi, sarkomer, kolorektal, lunge og hoved-hals samt REHPA og forskere fra det palliative felt.

Konklusioner
Interessen for 'Udvalg for Tværfagligt Palliativt Samarbejde' fra flere forskellige sygdomsspecifikke DMCG'er tyder på, at der i den kliniske hverdag er et behov for og et ønske om sammen at skabe kvalitetsudvikling af og forskning i den palliative indsats i hele forløbet med fremskreden kræft.

Palliation, psychosocial support

#150 Kommunal rehabilitering og palliation til socialt sårbare patienter med fremskreden kræft

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Abstract
Introduktion
Rehabilitering og palliation kan forbedre livskvalitet, funktionsevne og reducere følger af kræft og kræftbehandling. Viden om socialt sårbare patienter med fremskreden kræft og deres behov for rehabilitering og/eller palliation er begrænset; både i forhold til forløb og indsatsernes indhold og leveringsform. Projektets overordnede formål er at udvikle en generisk model, der kan guide kommunale rehabiliterende og palliative interventioner til målgruppen. Projektet er en del af COMPAS-studiet, som udgår fra Nationalt Center for Lighed i Kræft.

Materiale og metode
Projektet består af seks delstudier. Studie 1 og studie 2 er epidemiologiske registerkoblingsstudier af kræftpatienter i Danmark fra 2015-2018. Studie 3 er et beskrivende surveystudie vedrørende eksisterende kommunale tilbud til målgruppen. Studie 4 er et eksplorativt og beskrivende interviewstudie vedrørende 1) socialt sårbare kræftpatienters behov og problemer samt mulige indsatser og 2) social- og sundhedsprofessionelles erfaringer med gavnlige indsatser til målgruppen. Studie 5 er et modelleringsstudie, hvor to workshops afholdes med deltagere fra projektgruppen og fra et brugerpanel. Her skal indholdet af interventionen og leveringsformen udvikles. Studie 6 er et feasibility-studie af den udviklede intervention i kommunalt regi.

Resultat
Resultaterne fra de første 4 studier skal danne grundlag for studie 5 og 6. Den udviklede generiske model fra studie 5 vil blive afprøvet i studie 6. Såfremt modellen er anvendelig kan den danne grundlag for et implementeringsstudie i form af et cluster-randomiseret studie i kommunalt regi af målrettede rehabiliterende og/eller palliative interventioner til målgruppen.

Konklusion
Afklaring af sygdomsforløb og erfaringer med muligheder og barrierer i sundhedssystemet for socialt sårbare kræftpatienter er forudsætninger for at kunne nå ud til og tilbyde målgruppen deltagelse i kommunal rehabilitering og/eller palliation.

Palliation, psychosocial support

#151 High admittance to palliative care team and low admittance to hospice for immigrants from non-Western countries. A nation-wide register-based study of patients with cancer

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Abstract
Introduction
The population of immigrants in Europe is aging. Accordingly, the number of immigrants with chronic and life-threatening diseases and a need of specialised palliative care (SPC) will increase. Admittance to SPC for immigrants has rarely been investigated in Europe and the aim was to investigate whether country of birth was associated with admittance to SPC, overall and type specific (hospital-based palliative care team and hospice).

Materials and methods
The data sources were the nation-wide clinical database, Danish Palliative Care Database and several other nation-wide registers. The associations between country of birth and admittance to SPC, overall and type specific, were investigated in adjusted logistic regression analyses.

Results
In 2010-16, 104,611 patients died from cancer in Denmark: 96% were born in Denmark, 2% in other Western and 2% in non-Western countries. Overall admittance to SPC was higher for immigrants born in other Western (OR=1.13; 95%CI:1.03-1.24) and non-Western countries (OR=1.22; 95%CI:1.08-1.37) than for Danish born. Similar results were found for admittance to hospital-based palliative care team. No difference in admittance to hospice was found for immigrants born in other Western countries (OR=1.04; 95%CI:0.93-1.16) compared to Danish born, while lower admittance was found for non-Western immigrants (OR=0.70; 95%CI:0.60-0.81).

Conclusions
Immigrants born in other Western and non-Western countries had higher admittance to hospital-based palliative care team, and immigrants from non-Western countries had lower admittance to hospice, compared to Danish born. To ensure that admittance to SPC is based on the patient's wish health care professionals should have the knowledge and skills to handle cultural differences.

Palliation, psychosocial support

#152 Emotion regulation therapy for psychologically distressed caregivers of cancer patients - a randomized controlled trial

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Abstract
Introduction
Previous cognitive behavioral therapies (CBTs) for informal caregivers (ICs) of cancer patients have produced negligible effects. The primary purpose of the current study was to evaluate, in a randomized controlled trial (RCT), the efficacy of Emotion Regulation Therapy (ERT-C) on psychological and inflammatory outcomes in psychologically distressed ICs and the cancer patients cared for.

Materials and methods
81 ICs with elevated psychological distress were randomized to ERT-C or a waitlist (WL) condition, and assessed pre-, mid-, and post-treatment. In 52 cases, the patient cared for by the IC was included. Patients were assessed but never received therapy. Both the ERT-C and WL groups were followed 3 and 6 months post-treatment.

Results
Compared with ICs in the waitlist condition, ICs in the ERT-C condition experienced medium to large statistically significant reductions in psychological distress (HADS; p<.001, g=0.85), worry (PSWQ; (p<.001, g=0.96), and caregiver burden (CRA; p=.007, g=0.53). No effects were found for rumination (RRS-B; p=.220, g=0.24). Results concerning caregiver burden were maintained through follow-up. Although the effects on psychological distress and worry diminished, their end-point effects were medium to large. No effects on systemic inflammation were detected. Patients with ICs in ERT-C experienced a large increase in quality of life (EORCT-QLQ-C30; p=.017, g=0.89).

Conclusion
This is the first RCT evaluating the efficacy of ERT-C for ICs. Given the previous disappointing effects of other CBTs for this population, the present findings are very encouraging.

Palliation, psychosocial support

#153 Strengthening young adult cancer survivors' participation in everyday activities: development and feasibility of a rehabilitation programme

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Abstract
Introduction
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Aim
To develop and feasibility test a rehabilitation programme aiming to strengthen participation in everyday activities in YACS after completing cancer treatment.

Materials and methods
This study is designed in accordance with the British Medical Research Council guideline for developing and evaluating complex interventions. The present project is designed to encompass the first two phases: 1) development phase and 2) feasibility/pilot phase.

Three studies will be performed in the development phase: 1) A Group Concept Mapping study where YACS together with relatives, representatives from YACS' environments and professionals will identify and prioritise ideas on how to enhance participation in everyday activities among YACS; 2) A systematic review which will identify and synthesize scientific evidence of interventions for YACS; and 3) a modelling study describing the development process and content of a rehabilitation programme. The modelling of the programme will be informed by the results from study 1 and study 2 together with input from two expert workshops. In the feasibility/pilot phase, a feasibility study will be performed investigating acceptability of the intervention components (study 4).

Results
None yet.

Conclusions
The project provides fundamental knowledge to underpin a future full-scale randomized, controlled trial to evaluate effectiveness, process, and cost-effectiveness of the programme. Furthermore, the project is expected potentially to impact future organisation and development of rehabilitation for YACS, nationally and internationally.

Palliation, psychosocial support

#154 Effect on parental distress of a home-based psychological intervention for families of children with cancer (FAMOS): a nationwide randomized controlled trial

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Abstract
Introduction
No convincing evidence-based model has been developed to relieve psychological symptoms in families of children with cancer. We evaluated the effect of a new psychotherapeutic intervention FAMily-Oriented Support (FAMOS), targeting the whole family after end of childhood cancer treatment on symptoms of post-traumatic stress, depression and anxiety among parents in a nation-wide randomized controlled trial (RCT).

Materials and methods
Families of children (aged 0-6 years) with cancer who were treated at one of the four pediatric oncology departments in Denmark were invited after end of intensive medical treatment. Families were randomly assigned using a computer-generated randomization (1:1) to care as usual or to FAMOS, a cognitive-behavioural manualized home-based intervention with up to six sessions over a six months period for the whole family. We assessed symptoms of post-traumatic stress, depression and anxiety in parents using the Harvard Trauma questionnaire and the Symptom Checklist-90 at baseline, 6, and 12 months follow-up and estimated intervention effects in mixed method models.

Results
The FAMOS trial enrolled 109 families (204 parents). The intervention significantly reduced symptoms of depression at 6 months follow-up (estimated difference, -0.18; 95% CI -0.32 to-0.04 Cohen's d, 0.22). Intervention reductions in symptoms of post-traumatic stress (estimated difference, -0.10; 95% CI -0.20 to 0.01 Cohen's d, 0.18) and anxiety (estimated difference, -0.16; 95% CI -0.33 to 0.01 Cohen's d, 0.23) did not reach statistical significance.

Conclusions
This is the first psychotherapeutic family intervention targeting families of children with cancer after end of treatment, which in a randomized controlled design has shown that symptoms of depressions in the parents may be attenuated.

clinicaltrials.gov: NCT02200731

Palliation, psychosocial support

#155 Kliniske effekter af moderne parenteral ernæring hos patienter med avanceret kræft, et systematisk review

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Abstract
Introduktion
Indikation for parenteral ernæring (PN) hos patienter med kræft diskuteres stadig, mens fordele og ulemper er uafklaret. I nyere meta-analyser af PN indgår studier med uddateret PN såsom hyperkalorisk infusion og glukoserige opløsninger. Formålet er at evaluere effekten af moderne PN på livskvalitet, fysisk funktion, ernæringsstatus, overlevelse og komplikationer hos patienter med avanceret kræft.

Materialer og metoder
Systematisk litteratursøg i Ovid MEDLINE, EMBASE og CINAHL EBSCOhost (18. Maj 2018). Søgeord: advanced cancer AND parenteral nutrition, inklusive synonymer. Reviewet var udført ifølge PRISMA guidelines (PROSPERO ID: 4201707915). 1042 studier identificeret, 85 fuldtekst artikler gennemlæst, 64 artikler ekskluderet pga. inklusions- og eksklusionskriterier og 13 artikler ekskluderet grundet kritisk høj risiko for bias.

Resultater
To randomiserede og seks observationsstudier inkluderet (n=894). Hos patienter i onkologisk behandling, hvor PN var eneste ernæringsmulighed, sås signifikant gevinst i livskvalitet (+4 til +24 points, EORTC QLQ-C30) og subjektiv fysisk funktion (+4 til +17 points, EORTC QLQ-C30), men ikke hos patienter som kunne ernæres oralt/enteralt. Ernæringsstatus var forbedret hos patienter uafhængig af kræftbehandling og gastrointestinal funktion (+6.4 kg fedtfri masse, $p<0.05$; +1.5 til +4.6 kg kropsvægt, $p<0.05$). PN gav hverken bedre overlevelse sammenlignet med væskebehandling hos terminale patienter eller kostvejledning hos patienter som kunne ernæres oralt/enteralt. Forekomst af komplikationer var lav (incidens kateterrelaterede infektioner: 0-9 %; 0,33/1000 kateterdage).

Konklusioner
Moderne PN behandling hos patienter med avanceret kræft er ikke tilstrækkeligt undersøgt. Vidensgrundlaget for de kliniske effekter af PN er mangelfuld, hvorfor RCT studier med homogene patientgrupper og tilstrækkeligt antal ønskes. Nuværende PN behandling ser ud til at give færre komplikationer end tidligere rapporteret.

Palliation, psychosocial support

#156 Knogleantiresorptiva i behandlingen af metastaserende brystkræft

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Abstract
Introduktion
Retningslinjer for brug af knogleantiresorptiva (BMA) anbefalet af Danish Breast Cancer Cooperative Group (DBCG) for behandling af metastatisk brystkræft (BCBM) synes at være uspecifik vedr. behandlingsvalg, varighed og doseringsinterval. Mål: Udforske evidensen for brug af denosumab, zoledronsyre (ZA) og ibandronsyre (IA) for behandling af BCBM mhp. virkning, defineret som skeletrelaterede hændelser (SRE), med fokus på doseringsinterval, behandlingsvarighed og bivirkninger.

Materialer og metoder
25 artikler var inkluderet i dette review med søgninger i PubMed og en national survey om BMA-behandling for BCBM.

Resultater
Et 12-ugers ZA doseringsinterval var non-inferior ift. hver 4. uge, mens denosumab synes lovende med doseringsintervaller længere end hver 4. uge. Denosumab var signifikant mere effektiv end ZA mht. at reducere SREs, ZA var signifikant mere effektiv end placebo, og po./iv. IA var signifikant og non-signifikant sammenlignet med ZA eller placebo. BMAs er generelt veltolereret når brugt med forsigtighed. Kæbeosteonekrose (ONJ) forekommer sjældent hos alle uafhængig af lægemiddel, men med forudgående dental vurdering og god tandhygiejne kan reducere forekomsten. Survey viste at BCBM-patienter behandles forskelligt på danske hospitaler, bl.a. med hensyn til førstevalgspræparat, dosisinterval og indikation for seponering.

Konklusioner
DBCG anbefales at tydeliggøre retningslinjerne med hensyn til indikation for seponering af BMA, præcisere behandlingsprocedurer i tilfælde af ONJ og begrunde rationalet for doseringsinterval længere end fire uger ved IA-behandling.
Alle præparater har få alvorlige bivirkninger. Denosumab er den mest effektive behandling, mens po. IA-behandling er et naturligt valg at kombinere med po. kemoterapi eller endokrinbehandling. Endelig, ZA er næsten ligeså effektiv som denosumab, og er en billigere behandling.

Screening:
Poster #157-167

Screening

#157 Risikostratificeret mammografiscreening – It's personal

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Abstract
Introduktion
Danske kvinder i alderen 50-69 år tilbydes mammografi hvert andet år. Dette redder livskvalitet og liv. Mange faktorer har betydning for personlig risiko for brystcancer: Almindelige genetiske varianter, brystvævets udseende på mammogrammet, livsstil og reproduktions- samt familiehistorie. Det er klarlagt hvordan disse faktorer kan kombineres til ét samlet personligt risikoestimat. Vi hypotiserer, at det vil reducere ulemperne og fastholde eller øge de gavnlige effekter af mammografiscreening, hvis man stratificerer mammografiscreeningen på basis af individuel risikomåling. Dette koncept skal forinden testes i et randomiseret klinisk forsøg.

Materialer og metoder
1:1 randomisering af 20.000 50-51 årige samtykkende førstegangsmammograferede kvinder til to grupper: Kontrolgruppen, der fremover får tilbud om det nuværende mammografiprogram og interventionsgruppen, der fremover får tilbud om mammografiprogram på baggrund af personlig risikomåling. Denne udregnes på baggrund af måling af 313 hyppige genetiske varianter, billedanalyse af første mammogram, og kortlægning af livsstil, reproduktions-, og familiær anamnese. Efterfølgende vil kvinderne blive fulgt i 5 år.

Resultater
Personlig risikomåling identificerer kvinder med høj, mellem og lav forhåndsrisiko. Med forventede 165 tilfælde af brystcancer blandt alle 20.000 kvinder, vil studiet have 80% styrke til at detektere en ændring af 1) hyppigheden af falsk positive fra 2,4% til 1,9%, 2) andel af tumorstørrelse < 10mm fra 35% til 57%, 3) forekomst af positive lymfeknuder fra 21% til 6% og 4) halveret risiko for intervalcancer i interventionsgruppen. Styrken til at detektere reduktion af den psykosociale påvirkning er endnu højere.

Konklusioner
Personlig risikomåling som basis for stratificeret mammografiscreening vil kunne reducere ulemperne og fastholde eller øge gevinsterne ved mammografiscreening. Mange spørgsmål skal endnu afklares førend denne mere intelligente screening kan tilbydes som rutine.

Screening

#158 Screening for lungekræft i Herlev/Østerbroundersøgelsen

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Abstract
Introduktion
I et nyligt publiceret Hollandsk-Belgisk lungecancerscreenings studie (NELSON) med ca. 16.000 deltagere randomiseret 1:1 til regelmæssig thorax CT og almindelig opfølgning, var der 10 år efter studiestart markant lavere dødelighed af lungecancer i interventionsgruppen. Overført til danske forhold, vil op mod 10% af befolkningen mellem 50 og 75 år opfylde NELSON kriterierne, der er baseret på subjektive rygeinformationer. Lungecancerscreening i Danmark med disse kriterier vil betyde en stor belastning af sundhedsvæsnet og risiko for overdiagnostik og utilsigtede fund. Det er derfor vigtigt at udvikle algoritmer til yderligere selektion af screeningspopulationen.
Nye, men uafprøvede, biomarkører i blod, repræsenterer en mulighed for dette.

Materialer og metoder
Deltagere af Herlev/Østerbroundersøgelsen, der opfylder NELSON kriterierne, bliver inviteret til at deltage. Eksisterende blodprøve anvendes til at måle AHRR methylering i leukocyt-DNA, der er en stærk – og objektiv markør for rygevaner, og bedre end subjektiv rygeinformation til at prædiktere risiko for lungecancer. Målinger af cellefrit DNA fra blodet vil blive testet for om de bidrager yderligere til prædiktion af risiko.

Resultater
Af 48.000 inviterede, deltager ca. 20.000 individer i Herlev/Østerbroundersøgelsen på to år. Af disse, opfylder 2600 NELSON kriterierne. Nye rygekriterier og AHRR methylering vil kunne reducere dette tal til 1330, der får tilbudt thorax CT. Med forventede 24 tilfælde af lungecancer, vil studiet have 80% styrke til at detektere en reduktion af 1) behov for CT scan fra 2600 til under 2470, 2) antal usikre scanninger fra 500 til under 450, 3) antal falsk positive scanninger fra 44 til under 28, men fastholde antallet af lungecancer.

Konklusion
Personlig – og objektiv - risikomåling inden thorax CT vil forhåbentlig kunne reducere ulemperne og fastholde gevinsterne ved lunge cancer screening. Dette vil hjælpe med til at indføre et sundhedstilbud, der redder menneskeliv.

Screening

#159 Does Dynamic Spectral Imaging (DSI) Colposcopy improve the diagnostic accuracy of cervical dysplasia?

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Abstract
Introduction
New adjunctive colposcopy technologies are available to assist with colposcopy. It has been suggested that Dynamic Spectral Imaging (DSI) colposcopy improves diagnostic accuracy of the colposcopy exam. However, none of the previous studies have compared the diagnosis of the cervical biopsies with the final excisional procedure diagnosis. The purpose of our study was to examine how well the diagnosis of the different biopsies taken from the cervix, agree with the final excisional procedure diagnosis, and evaluate if DSIcolposcopy will improve the diagnostics of cervical dysplasia.

Materials and methods
In a prospective clinical study 105 women were included at Randers Regional Hospital. All women were examined by DSIcolposcopy and 4 biopsies were taken from the cervix according to the national guideline. Colposcopy was performed by trained nurses, residents and consultants. Only women with fully or partly visible transformation zones (TZ) of the cervix were included.
The first biopsy taken was the colposcopic directed biopsy (CDB) and marked by the colposcopist before the DSImap was revealed. The second biopsy was marked from the worst area indicated by the DSImap. Furthermore, 2 random biopsies were taken. All 4 biopsies had to be representative of the TZ. If any of these biopsies indicated cervical dysplasia of such a degree that an excisional procedure was indicated the patient was referred for a loop electrosurgical excision procedure (LEEP). The diagnosis of the biopsies was compared to the LEEP diagnosis.

Results
The CDB agreed with the worst area indicated by the DSI map in 62.9% of cases. Overall agreement between the CDB and LEEP diagnosis was 61.9%. For the DSI indicated biopsy overall agreement was 63.8%. Combining all 4 biopsies there was agreement in 83.8% of cases.

Conclusions
These preliminary results indicate that there probably is no difference in the diagnostic ability between the CBD and the biopsy indicated by the DSI technology.

Screening

#160 Early blood-based detection of colorectal cancer by methylation-specific droplet digital PCR - A clinical biomarker discovery and validation study

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Abstract
Introduction
Early detection plays an essential role to reduce colorectal cancer mortality. However, current screening strategies are either invasive or suffer from low compliance. Here, we describe the development of TriMeth, a blood-based test for detection of early-stage colorectal cancer. The test is based on assessment of three tumor-specific DNA methylation markers in circulating cell-free DNA.

Materials and methods
The markers were identified in a thorough multi-step biomarker discovery process based on DNA methylation profiles of more than 5,000 tumors and blood cell populations. Using methylation-specific droplet digital PCR, the TriMeth test was applied to plasma from 113 primarily early-stage CRC patients and 87 age and gender matched controls. The scoring algorithm of the test was locked, and results were validated in an independent cohort comprising 143 CRC patients and 91 controls.

Results
We identified three DNA methylation markers, which efficiently discriminated plasma from colorectal cancer patients from that of healthy individuals (area under the curve = 0.86-0.91). The three markers were combined in the TriMeth test, which showed an average sensitivity of 85% (217/256) at 99% (176/178) specificity in two independent plasma cohorts.

Conclusions
We show that colorectal cancer can be detected in plasma from early-stage colorectal cancer patients with high sensitivity and specificity using the TriMeth test. These results underline the potential utility of DNA methylation markers as non-invasive markers for early detection of colorectal cancer. These results are currently being further validated in approximately 900 asymptomatic individuals enrolled in the Danish colorectal cancer screening program.

Screening

#161 HPV self-sampling as a tool to reduce social inequality in cervical cancer screening participation

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Abstract
Introduction
Social inequality in cervical cancer screening participation exists. Self-sampling for high-risk human papillomavirus testing (HPV self-sampling) improves participation among non-participants. We evaluated if all socioeconomic groups of non-participants benefit from self-sampling and if the invitation strategy for offering self-sampling influences participation in various socioeconomic groups.

Materials and methods
The study was based on registry data applied to data from a randomized controlled trial (N= 9,791) measuring the effect of self-sampling on participation among Danish women aged 30-64 due to receive their second screening reminder. The women received either: 1) self-sampling kit mailed directly to their homes (directly mailed group), 2) invitation to order the kit (opt-in group), or 3) a standard second reminder to attend routine cytology screening (control group). Women offered self-sampling could also attend routine cytology screening if wanted. Participation was analyzed as intention-to-treat and linked to registry data on socioeconomic factors.

Results
Women in the directly mailed group participated more often than women in the control group, regardless of their socioeconomic status. The largest effects occurred in Western immigrants (participation difference (PD): 18.1%, 95%CI:10.2-26.0%) and social welfare recipients (PD: 15.2%, 95%CI:9.7-20.6%). Compared with the control group, opt-in self-sampling increased participation in most socioeconomic groups, but immigrants or less educated women had no significant effect.

Conclusions
All socioeconomic groups benefitted from the directly mailed strategy in terms of higher participation, but Western immigrants and social welfare recipients benefitted the most, indicating that this intervention may be a promising tool to reduce social inequality in participation. As immigrants and some lower socioeconomic groups had only insignificant effect of opt-in self-sampling, the directly mailed strategy may be favored.

Screening

#162 Ethnic minorities are more likely neither to be HPV vaccinated nor to participate in cervical cancer screening – results from a Danish register-based cohort study.

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Abstract
Introduction
Today, the Danish population consists of 11% ethnic minorities, mostly from Middle-Eastern and North African countries (MENA). By 2060, it is predicted that the ethnic minority population will rise to 26 %. Ethnic minorities attend HPV-vaccination (HPVV) and cervical cancer screening (CCS) at a lower rate than native Danish women. Women reaching screening age today have also been offered HPVV. At present, it is unknown whether the same groups of women attend both HPVV and CCS or some overrepresentation in combined none-attendance exists in some ethnic minorities. Our aims were to investigate regional and country specific differences in combined non-attendance among ethnic minorities. Further, to analyze the association between country of origin and combined non-attendance among women from MENA countries compared to native Danish women.

Methods and materials
Using logistic regression, the crude and adjudged odds ratio (OR) of being combined non-attender was examined for women from MENA countries compared to native Danish women.

Results
Combined non-attendance was overrepresented among women from the region of MENA (30%) compared to other regions of origin (ranging from 16-21%) and native Danish women (10%). Within MENA, Somali women had the highest combined non-attendance rate (52%) while Iranian women had the lowest combined non-attendance rate (16%). Women from Somalia had seven times higher odds of being combined non-attender compared to native Danish women. While women from Iran had one and a half times higher odds compared to native Danish women. These differences were significant regardless of socio-economic status.

Conclusion
Our results emphasize that a fast-growing sub-population exists that neither attend HPVV nor CCS, leaving these women at a considerably higher risk of developing cervical cancer.

Screening

#163 Skræddersyede tilbud om kræftscreening til kvinder med indvandrerbaggrund i socialt udsatte boligområder

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Abstract
Introduktion
I Danmark deltager kvinder med indvandrerbaggrund sjældnere i systematisk screening for kræft, og de får ofte stillet kræftdiagnoser i et senere stadie, sammenlignet med danske kvinder. Formålet med studiet var at undersøge barrierer for kræftscreening blandt kvinder med indvandrerbaggrund i socialt udsatte boligområder, samt udforme en skræddersyet intervention til at øge kendskabet til kræftscreening i målgruppen.

Materialer og metoder
Studiet var baseret på etnografisk feltarbejde i et socialt udsat boligområde i Danmark. Gennem snowball-sampling blev kvinder med indvandrerbaggrund inviteret til fokusgruppeinterviews, gruppeinterviews med tolk samt individuelle interviews. Data bestod af transskriberede interviews og feltnoter fra flere forskere, og blev kodet og kategoriseret efter etnografiske principper med inspiration fra aktionsforskning.

Resultater
Barrierer inkluderede: mistillid til det danske sundhedssystem; manglende tradition for at bruge det danske sundhedssystem til sygdomsforebyggelse; angst for brist i jomfruhinden ved screening for livmoderhalskræft; samt opfattelser af at kræft ikke kan behandles, selv hvis den opdages tidligt. Kvinderne efterspurgte viden om kræft og screening, formidlet af en lokal aktør, samt mulighed for skriftligt materiale/invitation, oversat til flere sprog. I studiet udformes en intervention med tillidsskabende oral undervisning i lokale kulturfællesskaber/foreninger, der anvender sproglig og kulturel tilpasset informationsmateriale.

Konklusioner
Kvinder med indvandrerbaggrund kan bidrage aktivt til udformning af en intervention, der skal udbrede kendskab til kræftscreening og potentielt højne deltagelse i kræftscreening blandt kvinder med indvandrerbaggrund. En intervention kan centreres om at skabe viden og opmærksomhed på emnet i et tillidsfuldfuldt forum med henblik på at overkomme barrierer, som kvinderne oplever i forhold til kræftscreening.

Screening

#164 Differentiated effectiveness of colorectal cancer screening according to socioeconomic status - A nationwide cohort study

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Abstract
Introduction
Even though evidence of social disparity in colorectal cancer (CRC) incidence is inconsistent, the risk of dying from CRC is higher among people with low socioeconomic position. The aim of this study was to analyse if the effectiveness of CRC screening regarding removal of adenomas and detection of CRC was modified by socioeconomic and demographic factors.

Materials and methods
A register-based retrospective cohort study with a study period from 1 March 2014 to 30 June 2015. The study population included all men and women resident in Denmark and aged 50-72 years on 1 January 2014. To determine if the effectiveness of the programme was modified by age, gender, ethnicity, marital status, educational attainment and income, stratified relative risks (RR) were calculated and differences were tested with the Mantel–Haenszel test for homogenity.

Results
The effectiveness regarding removal of adenomas was lower for women (RRwomen 4.7, RRmen 5.7), non-Western immigrants (RRnon-Western 3.6, RRWestern 5.5, RRDanish 5.3), people living alone (RRAlone 4.8, RRCohabiting 5.5) and those with lowest income (RRLow 4.8, RRMiddle 5.6, RRHigh 5.3). The effectiveness regarding detection of CRC tended to be lower for the young (ranging from RR50-59 1.7 to RR70-72 2.2), women (RRWomen 1.8, RRMen 2.2), non-Western immigrants (RRnon-western 1.3, RRWestern 1.9, RRDanish 2.0) and those with lowest income (RRLow 1.8, RRMiddle 2.0, RRHigh 2.2).

Conclusions
Effectiveness of screening depends on the underlying prevalence of undiagnosed CRC and actual participation. Even though women are more likely to participate in CRC screening, this study shows that the effectiveness is higher among men than women which is consistent with the slightly higher risk of CRC among men. Further the results are consistent with the lower screening participation in the groups with lowest effectiveness of screening stressing the need for interventions increasing screening participation in vulnerable groups.

Screening

#165 Social inequalities in colorectal cancer screening

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Abstract
Introduction
Colorectal cancer (CRC) screening was implemented in Denmark in 2014 for citizens aged 50-74. To participate citizens had to complete a fecal immunochemical test (FIT) sample. If the test was positive, the participant would be invited for a colon examination (by default an optical colonoscopy (OC)). There is a risk of social inequalities when uptake relies on the citizens to take action. If sociodemographic subgroups do not participate equally, inequalities in CRC mortality are feared as cancers in non-participating individuals will likely be identified at a later stage causing higher numbers of colorectal cancer deaths and bowel resections in non-screened population, whereas screened population may to a higher extent benefit from polypectomy. We aimed to investigate social inequalities in participation in the Danish CRC screening.

Materials and methods
More than 800,000 citizens were invited in 2014-15. Inequalities were investigated in two stages; participation by submitting FIT sample and by undergoing follow-up colon examination. Odds of non-participation were estimated in each stage based on marital status, country of origin, gender, age, income and education by univariate and multivariate logistic regression models. Socioeconomic and demographic variables included.

Results
In both stages social inequalities were found. Age, gender, educational level, income and immigration status were all independent predictors of non-participation (Odds Ratios (OR) varying from 0.51 to 2.80) when submitting FIT samples. In individuals with a positive FIT, social inequalities in colon examination uptake were also evident (OR from 0.54 to 2.04).

Conclusions
Large social inequalities exist in CRC screening uptake. The inequalities are evident at first invitation for FIT and they are evident at follow-up colon examination in population submitting a positive FIT. When inequalities are evident at each stage the overall inequalities are enhanced and should be addressed.

Screening

#166 The LEAD trial. The effectiveness of a decision aid on decision making among citizens with lower educational attainment who have not participated in FIT-based colorectal cancer screening in Denmark: a randomised controlled trial

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Abstract
Introduction
This trial sought to test the effectiveness of a self-administered web-based decision aid, targeted at citizens with lower educational attainment, on informed choice about colorectal cancer screening participation as assessed by group levels of knowledge, attitudes and uptake.

Materials and methods
The randomized controlled trial was conducted among 2,702 screening-naïve Danish citizens, 53-74 years old, with lower educational attainment. Baseline questionnaire respondents (62%) were allocated to intervention and control groups. Intervention group citizens received the decision aid.
The primary outcome was informed choice as assessed by knowledge, attitudes and uptake. Secondary outcomes were worries and decisional conflict.

Results
Analyses were conducted among 339 eligible citizens. The mean difference in knowledge score change between intervention and control groups was 0.00 (95% confidence interval (CI): -0.38;0.38). The intervention group tended to have more positive screening attitudes (mean difference in score change: 0.72, 95% CI: -0.38;1.81) and a higher screening uptake was observed (7.6%, 95% CI:-2.2;17.4%), however, both tendencies were statistically insignificant. Worries (-0.33, 95% CI: -0.97;0.32) and decisional conflict (mean difference: -3.5, 95%CI: -7.0;-0.1) were slightly reduced.

Conclusions
The decision aid had no overall effect on informed choice. No changes were observed in knowledge or attitudes, but the screening uptake was slightly but not significantly higher in the intervention group as compared to the control group, however.
Being a simple intervention and easily administered, the decision aid could represent a cost-effective way of enhancing some elements of informed decision-making among citizens with lower educational attainment.

Trial registration
ClinicalTrials.gov NCT03253888. Registered 17 August 2017

Screening

#167 Sammenhængen mellem sundhedskompetencer og deltagelse i samt bekymringer relateret til tarmkræftscreening

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Abstract
Introduktion
Viden om hvilke befolkningsgrupper der er særligt svære at inkludere i organiserede screeningsprogrammer, åbner muligheden for specifikt at målrette information og intervention til disse grupper.

Formålet med dette studie var at undersøge associationen mellem sundhedskompetencer og deltagelse i tarmkræftscreening, samt at undersøge betydningen af sundhedskompetencer for borgernes bekymringer om tarmkræft og tarmkræftscreening.

Materialer og metoder
I en spørgeskemaundersøgelse blandt 10.030 53-74-årige ikke tidligere screenede borgere blev sundhedskompetencer samt bekymringsniveau vurderet. Data på screeningsdeltagelse blev indhentet fra Dansk Tarmkræftscreening Database, og socioøkonomiske og -demografiske data blev koblet fra Danmarks Statistik efter endt dataindsamling.
Sammenhængen mellem sundhedskompetencer og screeningdeltagelse blev estimeret ved logistisk regression, mens sammenhængen mellem sundhedskompetencer og bekymringsniveau blev estimeret ved lineær regression.

Resultater
I alt blev 7.142 (71,2%) spørgeskemaer besvaret. OR for screeningsdeltagelse var 1,07 (95% CI: 0.96;1,19) blandt borgere med middel niveau af sundhedskompetencer samt 1,01 (95% CI: 0,87;1,17) blandt borgere med lavt niveau af sundhedskompetencer i sammenligning med borgere med et højt niveau af sundhedskompetencer.
Den samlede bekymringsscore steg med faldende sundhedskompetencer fra 8,67 (95% CI: 8,57;8,76) blandt dem med de højeste sundhedskompetencer til 9,75 (95% CI: 9,58;9,91) blandt dem med de laveste sundhedskompetencer.

Konklusioner
Vi fandt ikke nogen association mellem sundhedskompetencer og deltagelse i screening for tarmkræft, men borgere med færre sundhedskompetencer blev mere bekymrede i forbindelse med tilbuddet.