Abstracts som fremlægges ved årsmødet for DSGH 2023

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Abstract nummer 9-24 i den første ePoster session (2 min fremlæggelse)

Abstract nummer 25-41 i den anden ePoster session (2 min fremlæggelse)

Indhold

1. Increasing use of biologics in Denmark 2019-2023 – a quality control study from Gastrobio

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Background and aim: Since the introduction of anti-TNF therapy at the beginning of the millennium, the use of biologics in inflammatory bowel disease (IBD) has been on the rise. Despite many studies from various centers in Denmark, no combined registries on a patient level exist. We aimed to describe the use of biologics at four centers in Denmark from 2019-2023.

Methods: Patients treated with biologics from 2019-2023 at four centers in Denmark (Bispebjerg, Hvidovre, Odense, Aalborg) and registered in the clinical treatment database, Gastrobio, were included in this quality control study. We assessed the total number of patients treated and the number of patients on a specific treatment each year.

Results: The total number of patients receiving biological treatment from January 2019 to May 2023 increased from 1228 to 2314. While most patients received infliximab (748 in 2019 and 1048 in 2023), the proportion infliximab usage decreased from 65% to 45% during this period, Figure 1.

Conclusion: In this quality control study from Gastrobio representing four large university centers in Denmark, we found increasing numbers of patients receiving biologics and while infliximab is still the most used biologic, other biologics constitute a growing proportion of the total number of treatments.

2. The effect of ReFerm® versus Fresubin® on hepatic stellate cell activity in patients with advanced alcohol- related liver disease: A 24 week randomized controlled trial

Authors: Johanne K. Hansen[1,2], Camilla D. Hansen[1,2], Jane Møller[1], Mads Israelsen[1,2], Maria Kjærgaard[1,2], Katrine Thorhauge[1,2], Katrine P. Lindvig[1,2], Nikolaj Torp[1,2], Stine Johansen[1,2], Peter Andersen[1], Gitte H. Jensen[3], Sönke Detlefsen[2,3], Ida F. Villesen[1], Morten Karsdal[4], Diana J. Leeming[4], Hans Israelsen[5], Maja Thiele[1,2], Aleksander Krag[1,2] on behalf of the GALAXY consortium

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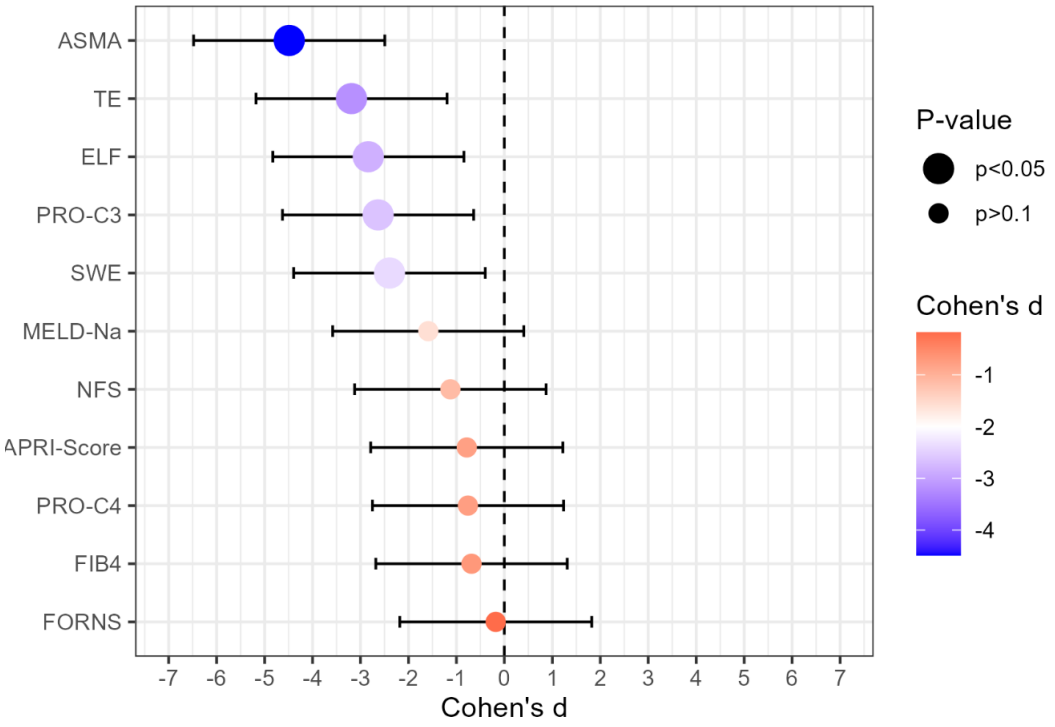
Background: Gut dysbiosis and permeability are suggested treatment targets for alcohol-related liver disease (ALD). ReFerm®, a post-biotic drink made from oat fermented with *Lactobacillus plantarum 299v*, improves the gut barrier in patients with irritable bowel syndrome. We investigated the effect of ReFerm® on formation of liver fibrosis by hepatic stellate cell activity in patients with compensated advanced chronic liver disease (cACLD) related to alcohol.

Methods: We randomized 56 patients with cACLD 1:1 to receive ReFerm® or Fresubin® for 24 weeks. Liver biopsies were collected at baseline and after 24 weeks. We assessed hepatic stellate cell activity by immunohistochemistry of liver biopsies for quantification of α-smooth muscle actin (α-SMA) using automated digital imaging analysis. Primary outcome was ≥10% reduction in α-SMA.

Results: Median age was 63 years (57-67), mainly males (83%) with cirrhosis (F2/F3/F4=4/15/33). Baseline alcohol intake was 36 grams/day, comparable between groups during the study. In the Referm® group, 8/21 (38%) of patients improved ≥10% in α-SMA compared to 4/19 (21%) in the Fresubin® group (OR = 2.3; 95%CI 0.6-9.5; p=0.246). In the adjusted model the ReFerm® group reduced α-SMA by -9.6% (95% CI -16.1 to -3.1, p=0.005) compared to the Fresubin® group (fig.1 A+B).

Conclusion: Treatment with ReFerm® did not reduce α-SMA by ≥10%. However, our results show that ReFerm® improved several markers of fibrosis compared to Fresubin®.

A



B

Name	Effect	Cohen's d	Low	High	P value
ASMA	-9.63	-4.49	-6.48	-2.49	0.00003
TE	-8.66	-3.19	-5.18	-1.20	0.002
ELF	-0.56	-2.84	-4.83	-0.84	0.006
PRO-C3	-3.93	-2.63	-4.63	-0.64	0.010
SWE	-5.54	-2.40	-4.39	-0.40	0.019
MELD-Na	-0.71	-1.59	-3.58	0.41	0.117
NFS	-0.18	-1.13	-3.12	0.87	0.264
APRI-Score	-0.12	-0.78	-2.79	1.22	0.436
PRO-C4	-31.7	-0.76	-2.75	1.23	0.450
FIB4	-0.33	-0.69	-2.68	1.31	0.495
FORNS	-0.05	-0.18	-2.18	1.82	0.858

Fig. 1: A) Forest plot showing Cohen's d effect sizes of ReFerm® compared to Fresubin® on markers of liver fibrosis. B) The effect size of each variable and the corresponding Cohen's d value.
Data are adjusted for age, sex, fibrosis stage at baseline, alcohol intake at baseline, and compliance.

3. Resolution of non-alcoholic fatty liver disease through bariatric surgery restores urea cycle function and reduces ammonia levels

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Background: Non-alcoholic fatty liver disease (NAFLD) impairs urea cycle function which may precipitate hyperammonaemia and contribute to cognitive dysfunction. Bariatric surgery is an effective treatment for NAFLD that resolves liver steatosis and inflammation. We investigated the effect of bariatric surgery on urea cycle function, ammonia levels, and cognitive function.

Methods: Twelve obese patients referred for bariatric surgery were studied before and 2 years after surgery. We examined *in vivo* ureagenesis by the functional hepatic nitrogen clearance (FHNC) and plasma ammonia levels, performed psychometric testing and liver biopsy. Plasma ammonia levels were measured in a validation cohort of bariatric patients.

Results: Bariatric surgery led to a 30% weight loss and the resolution of NAFLD in all patients. In parallel, FHNC increased by 39% (33 ± 16 to 46 ± 21 L/h; $p = 0.03$), while plasma ammonia levels decreased by 38% (21 ± 5 to 13 ± 7 µmol/L; $p = 0.01$) after surgery. Performance in the Portosystemic Encephalopathy and Continuous Reaction Time tests were unchanged. Plasma ammonia levels decreased also in the validation cohort, but only in patients with prior NAFLD ($p = 0.004$, n = 14), and not those without ($p = 0.5$, n = 9).

Conclusion: Bariatric surgery restored urea cycle function and reduced plasma ammonia levels along with the resolution of NAFLD, whereas no cognitive improvements were observed. Our findings substantiate the role of urea cycle dysfunction and its implications for hyperammonaemia in patients with NAFLD.

4. Patients with Eosinophilic Oesophagitis in Denmark have higher use of psychotropic drugs: a Danish Nationwide Study of Psychotropic Drug Use in 3,367 Patients and 16,835 Matched Comparators

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Background: Eosinophilic oesophagitis (EoE) is a chronic, immune-mediated disease of the oesophagus. EoE is associated with a substantial disease burden affecting the quality of life and impact mental health. There are limited data describing the incidence of psychiatric disorders and the use of psychotropic drugs (PDs) in EoE patients.

Objectives: The aim was to investigate whether EoE patients in Denmark, after being diagnosed, have a higher incident use of psychotropic drugs and more psychiatric comorbidity compared to the general population.

Methods: This study is a nationwide, population-based register study including 3,367 EoE patients and 16,835 age- and sex-matched comparators. A register-based EoE definition was used to identify cases. Incident PD use was extracted from the prescription register and information regarding psychiatric contacts was retrieved from the Danish Psychiatric Central Research Register.

Results: The five-year incidence of PD use in EoE patients was 13.8% compared to 7.1% of the matched comparators (HR 1.83; CI 1.6-2.0; P ≤ 0.001). Antidepressants were the most frequently prescribed PD, whereas antipsychotics were the least prescribed PD. **Increasing age, lower educational level, and comorbidity (Charlson Comorbidity Index score ≥1) were associated with the prescription of PDs. The risk of PD use was lower in men compared to women with EoE.**

Conclusion: Treatment with PDs were 94% more common in EoE patients after they were diagnosed than in the general Danish population, indicating that EoE patients have an increased risk of psychiatric disorders.

5. Prevalence of bile acid diarrhoea in patients with active microscopic colitis; preliminary results of a prospective study

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Introduction; Coexistence of bile acid diarrhoea (BAD) and microscopic colitis (MC) has been suggested, and treatment with sequestrants and could reduce the need for budesonide. Fasting plasma 7α-hydroxy-4-cholesten-3-on (C4) values > 46 ng/mL are specific for BAD with a sensitivity of 47% (37-57%) versus SeHCAT.

Aim: To assess the prevalence of BAD in active MC.

Methods: Patients with MC fulfilling the Hjortswang diarrhoea criteria (≥ 3 stools or ≥ 1 watery stool per day) had fasting C4 sampled before and during the last of 6 weeks treatment with budesonid 9 mg once daily. Remission was defined as a daily mean of < 1 watery bowel movement and < 3 total bowel movements. Fasting C4 was collected again during the last treatment week [EudraCT: 2019-002762-12].

Results: 49 patients screened at four centers were included; 26 (53%) with collagenous colitis. Mean number of stools/day declined from 7.9 to 1.9 and watery stools from 3.7 to 0.3 during budesonide treatment. Thus 45 obtained remission; however, 29 had relapsed four weeks after end of budesonide treatment. BAD was diagnosed in 6 (12%), C4 was >33and <46 ng/mL (intermediate) in 3. C4 values were unaffected by treatment.

Conclusion: During active MC, 12% had C4-defined BAD. However, C4 only identifies about half of patients with BAD compared with SeHCAT, meaning about 25% of patients with MC could have coexisting BAD. Bile acid diarrhoea should be considered in patients with relapsing MC.

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6. Quantification of alcohol intake in clinical trials on alcohol-related liver disease

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Background: The quantification and monitoring of alcohol intake are crucial in clinical trials of alcohol-related liver diseases (ALD), but it is unknown if self-reported alcohol intake is reliable. We therefore aimed to compare the diagnostic and prognostic utility of self-reported alcohol intake with the blood-based biomarkers of alcohol intake, phosphatidylethanol (PEth) and carbohydrate-deficient transferrin (CDT).

Methods: We included 192 participants from two randomized clinical trials, who all had a current or former alcohol overuse (≥1 year with ≥24 g/day for women and ≥36 g/day for men) and biopsy-proven ALD. We assessed self-reported alcohol intake, PEth, and CDT at four visits, while follow-up data on hepatic decompensation and death were collected through electronic medical records.

Results: Most participants were male 161 (84%) with a median age of 60 (55-66) years. At baseline, participants with a current alcohol intake had a median consumption of 43 g/day (24-69), and 27 of 32 (84%) who reported ≥6 months abstinence had PEth levels below 0.05 µmol/L, indicating abstinence. At inclusion, self-reported alcohol intake correlated with PEth levels (r=0.617, p<0.001), which remained consistent during follow-up visits. All three alcohol assessment methods predicted hepatic decompensation or death (Figure), with PEth demonstrating predictive superiority over self-reported alcohol intake (p=0.026).

Conclusion: Self-reported abstinence is reliable when recruiting to clinical trials on ALD, but PEth is superior to predict hepatic decompensation or death.

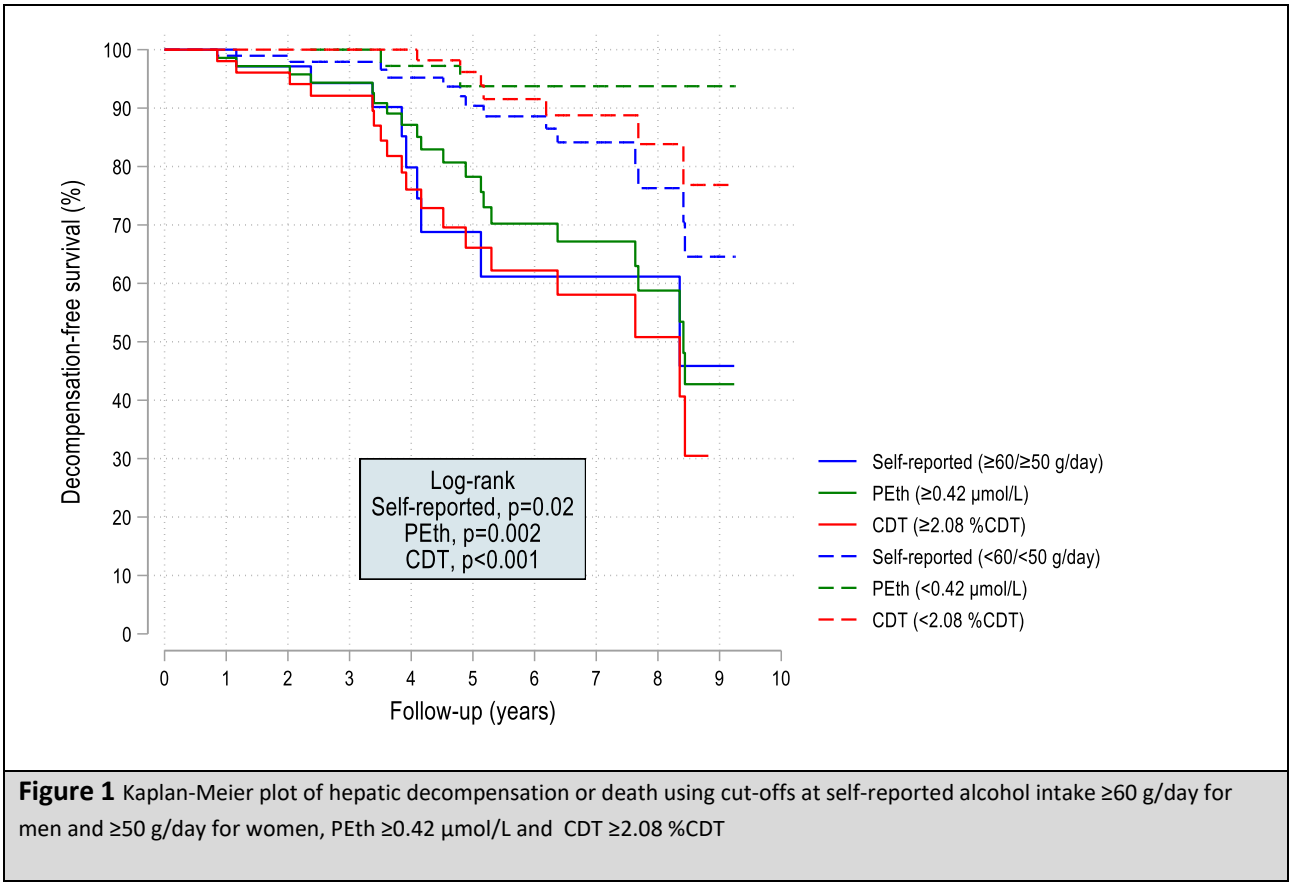

Figure 1 Kaplan-Meier plot of hepatic decompensation or death using cut-offs at self-reported alcohol intake ≥60 g/day for men and ≥50 g/day for women, PEth ≥0.42 µmol/L and CDT ≥2.08 %CDT

7. Validation of Deep Learning-Based Real-Time Video Analysis for Disease Severity Classification in Ulcerative Colitis

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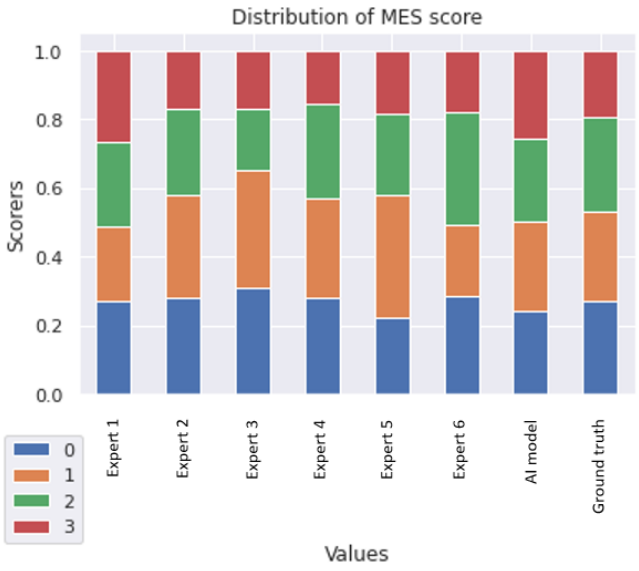
Introduction Endoscopic ulcerative colitis (UC) severity classification shows high interobserver variance. Our prior study proved AI matches central reading scoring still images. To be clinically useful, assessing longer segments is vital. Our aim: a new model for real-time or video-based severity evaluation.

Methods Data was Mayo Endoscopic Subscore (MES)-scored using 2561 images and 53 videos from 645 patients to train a convolutional neural network. Through open-set-recognition, the model differentiated scoreable from unscoreable endoscopy sections. Validation included 140 videoclips from 44 UC patients. Six IBD-experts and 16 non-IBD experts independently rated these clips, with the majority IBD-expert score serving as ground truth. We assessed its value as a second opinion for non-IBD experts and conducted an alpha test with real-time endoscopic support on a real-world patient.

Results The model achieved 0.82 accuracy, with no notable distinction from individual experts (figure 1). When employed as a trigger for second opinions, non-IBD experts' performance improved by 10-15%. The alpha test, integrating the model into the endoscopic column for real-time classification, was successful. It accurately discerned MES 0 and MES 1 frames, aligning with the endoscopist's assessment.



Conclusion Our innovative AI model exhibits significant potential for enhancing UC severity classification accuracy, rivalling IBD-experts and notably improving non-specialists' proficiency. It is designed for clinical implementation and has demonstrated clinical feasibility in an alpha test.

8. Adverse health outcomes in offspring of parents with alcohol-related liver disease: registry-based cohort study from Denmark

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Background: Offspring of parents with alcohol-related liver disease (ALD) may be vulnerable to adverse health outcomes. We compared the risk of adverse health outcomes in such offspring to that of controls.

Method: We used nationwide healthcare registries to identify offspring of parents diagnosed with ALD in Denmark 1996–2018 and age- and gender-matched controls (20:1). We compared the incidence rates of adverse health outcomes in these offspring with that of the matched controls.

Results: There were 60,708 offspring of parents with ALD and 1,213,380 matched controls. Offspring had a median age of 31 years when their parent was diagnosed with ALD; 51% were male. The risk of being diagnosed with ALD peaked at age 55 years for offspring and age 57 years for comparators with 10-year risks of 1.66% (95% CI 1.16–2.30) in offspring and 0.81% (95% CI 0.68–0.97) in comparators at these ages. Offspring also had a higher incidence rate of hospital contacts with alcohol-specific diagnoses, other abuse than alcohol, psychiatric disease, fractures or injury, poisoning and death compared to comparators. Offspring aged 13–25 years were most likely to have their first admission for poisoning in the first year after their parent's ALD diagnosis than at any other time (IRR = 1.25, 95% CI: 1.01-1.55).

Conclusion: Offspring of parents with ALD have a higher risk of adverse health outcomes and the first year after a parent's ALD diagnosis is a particularly vulnerable time for the offspring of a young age with respect to hospitalization with poisoning.

9. Risk factors for acute myocardial infarction in patients with alcohol-related liver cirrhosis - a nationwide nested case-control study

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Background and Aims: Alcohol-related cirrhosis (ALD cirrhosis) has a weaker effect on acute myocardial infarction (MI) than its effect on other arterial or venous thromboses, and the reasons for this pattern are unclear. The aim of this study was to describe risk factors of MI amongst patients with ALD cirrhosis.

Method: This nationwide register-based nested case-control study included all Danish patients diagnosed with ALD cirrhosis in 2000-2019. Patients with first-time MI after diagnosis of ALD cirrhosis were identified as cases and matched cases with cohort members with no history of MI were selected as controls. We used conditional logistic regression to study the association between risk factors and adjusted incidence rate ratio (aIRR) of MI.

Results: 373 cases with MI were included and matched with 3,730 controls. Identified risk factors were history of atherosclerosis (aIRR 1.83 [95% CI 1.35-2.48]), cardiac ischemia (aIRR 6.09 [95% CI 4.25-8.70]), heart failure (aIRR 2.64 [95% CI 1.78-3.93]) chronic obstructive pulmonary disease (COPD) (aIRR 2.26 [95% CI 1.61-3.15]) or hospitalization for infection (aIRR 2.21 [95% CI 1.35-3.62]) or recent surgery (aIRR 1.80 [95% CI 1.17-2.78]).

Conclusion: Among patients the ALD cirrhosis, the incidence rate of MI was higher for those who had history of cardiovascular disease or COPD, were hospitalized because of infection or had surgery in the previous 30 days. Our findings contribute to the understanding of risk factors for MI in patients with ALD cirrhosis. They may have clinical implications e.g., for the decision to offer thromboprophylaxis.

10. Changing prescription patterns of first line biologic in IBD in Denmark 2019-2023 – a quality control study from Gastrobio

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Background and aim: Anti-TNF therapy for inflammatory bowel diseases (IBD), is still the backbone of the biological treatment algorithm. However, with new biologics and small molecules being introduced, a change in prescription patterns for first line biologics is likely to take place. We aimed to describe the first line biologic in IBD patients from 2019-2022 at four IBD centers in Denmark.

Methods: The clinical database, Gastrobio, containing biologic treatments from Bispebjerg, Odense, Hvidovre and Aalborg, was used to examine the number of bio-naïve patients initiating biological or small molecule therapy from January 2019 to December 2022. In addition, the numbers of terminated treatments during the same period were calculated.

Results: Of the 309 initiated treatments in 2019 and 380 in 2022, 83% (255) and 53% (202) were infliximab. Of the 372 and 443 terminated therapies in 2019 and 2022, respectively, 66% (244) and 52% (230) were infliximab. For adalimumab there was a substantial increase in the proportion of this drug as first line therapy (9% in 2019 and 38% in 2022), while the proportion of termination of therapy for this drug was almost the same (16% and 19% in 2019 and 2022, respectively).

Conclusion: In this quality control study from Gastrobio, the distribution of drugs used as first-line biologic or small molecules in IBD patients shows that infliximab is still widely used, but there is an increase in the use of adalimumab as first line therapy. Reflecting current Danish guidelines, other biologics as first-line therapy are still not widely used.

11. PRO-C6 is associated with cardiovascular events in patients with alcohol-related liver disease.

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Background and Aims: Patients with alcohol-related liver disease (ALD) face a high risk of developing cardiovascular disease (CVD), lacking accurate prognostic biomarkers. We investigate the prognostic value of PRO-C6, a fibrosis biomarker of type VI collagen formation, on CVD in patients with ALD.

Method: A prospective study of 459 ALD patients serum samples with matching liver biopsy. Data were obtained from electronic medical records including baseline PRO-C6 and liver fibrosis stage. The CVD events were as defined by the World Heart Federation. PRO-C6 levels were divided into quartiles to assess if there were a difference in risk. The prognostic value of PRO-C6 on CVD events was evaluated using multivariable Cox regression.

Results: The studied cohort covered the full disease spectrum of ALD (F0-1/2/3-4 = 57%/23%/20%) and were followed for a median of 4.4 years (IQR 2.8-6.2). In total, 70 patients (15.3%) developed at least one CVD event. Baseline PRO-C6 were borderline significantly higher in patients who developed a CVD event as compared to patients who did not: 9.9 ng/mL (IQR 8.7- 13.9) vs 9.2 ng/mL (IQR 7.2-12.7), p = 0.055. Intermediate and high

levels of PRO-C6 showed a correlation with the development of CVD in the multivariable analysis (HR 2.87, CI: 1.58-15.70, p= 0.033) and (HR 3.59, CI: 1.16-11.07, p = 0.026).

Conclusion: ALD patients showed a marked risk of developing CVD. While those who developed CVD had a borderline significantly higher PRO-C6 at baseline, intermediate and high values of PRO-C6 did show prognostic value in identifying CVD in ALD patients.

12. Lactulose use among patients with alcohol-related liver cirrhosis: prevalence and association with mortality - a Danish nationwide cohort study

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Background & Aims: Hepatic encephalopathy (HE), one of the most serious prognostic factors in alcohol-related cirrhosis (ALD cirrhosis), is not recorded in Danish healthcare registries. However, treatment of HE with lactulose, the universal first-line treatment, can be identified through data on filled prescriptions. The aim of this study was to investigate if lactulose can be used as a surrogate marker of HE.

Methods: We used Danish healthcare registries to establish a cohort of patients with ALD cirrhosis diagnosed in 2000-2018. Lactulose users were identified using data on filled prescriptions. We computed prevalence of lactulose use, and then matched lactulose users with cohort members who were not using lactulose. This matched dataset was used to identify predictors of lactulose initiation, and to examine the association between lactulose use and all-cause mortality.

Results: We included 23,089 patients, among whom we identified 4,789 first-time lactulose users. The prevalence of lactulose usage rose to 11% within the first 6 months and reached 19% 5 years after inclusion. Predictors of initiating lactulose use were history of severe liver disease (history of at least one complication of liver disease) or hepatocellular carcinoma. Lactulose use was associated with higher mortality (adjusted hazard ratio 1.61 [95% confidence interval 1.53; 1.69]).

Conclusions: Lactulose is used by 10–20% of patients with ALD cirrhosis, primarily those with severe cirrhosis, and lactulose users have a markedly higher mortality than nonusers. These findings are consistent with the hypothesis that lactulose use is a surrogate marker of hepatic encephalopathy.

13. Second line biologics in IBD in Denmark 2019-2023, a quality control study from Gastrobio

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Background and aim: In the early years of biological therapy for inflammatory bowel diseases (IBD), treatment strategies and possibilities of changes in the therapy were limited. However, with the numerous new biologics and small molecule therapy, treatment options and possible second line therapies have increased. In this quality control study, we aimed to evaluate the trends in choice of second line therapy from January 2019 to May 2023 at four large Danish centres.

Methods: Patients treated with biologics from 2019-2023 at four centers in Denmark (Bispebjerg, Hvidovre, Odense, Aalborg) and registered in the clinical treatment database, Gastrobio, were included in this quality control study. For all changes in therapy, we calculated proportions of different drugs as second line therapy.

Results: Of the 1102 patients treated with infliximab as first line therapy from 2019 to 2023, 393 (36%) received a second biologic agents. Of those, 42% (167) received adalimumab, 8% (32) received golimumab, 35% (139) received vedolizumab, 12% (49) received ustekinumab, and 2% (6) received tofacitinib.

Conclusion: In this quality control study from four large university centers in Denmark, we found that the majority of patients remained on infliximab as first line therapy during a five-year period. The preferred second line drugs were adalimumab and vedolizumab. This reflects current official Danish treatment recommendations.

14. Titel: IBS-IUS

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Introduction: Inflammatory bowel disease (IBD) necessitates effective strategies for disease management. Intestinal ultrasound (IUS) has emerged as a potential tool for assessing disease activity and guiding treatment

decisions in IBD patients. This historical cohort aims to evaluate the utilization of IUS and its impact on disease management, while comparing the findings to previous studies.

Methods: 179 patients diagnosed with IBD, who underwent Point-of-Care IUS at the outpatient clinic or medical department were identified. The medical records were reviewed to identify indications for IUS, IUS findings and changes in disease management following IUS. The results were compared to previous studies to assess similarities and discrepancies.

Results: 179 patients with 256 IUS procedures between 2018 and 2022 were included in the study. Among the performed IUS, 73% exhibited symptoms of active disease, while 69% had elevated levels of fecal calprotectin (>50 µg/g). Ultrasonic signs of inflammation were observed in 49% of IUS performed in

patients with Crohn's disease (CD) and in 52% of IUS performed in patients with ulcerative colitis (UC). Following IUS, changes in disease management were made in 63% of CD patients and 74% of UC patients.

Conclusion: This study highlights the significant impact of IUS on the management of IBD. IUS enables the detection of disease activity, even in asymptomatic patients, facilitating timely adjustments to treatment plans.

Keywords: IBD, intestinal ultrasound, monitoring, disease management, point-of-care.

15. Dissektion af truncus coeliacus med miltinfarkt associeret til øget intraabdominalt tryk og methylphenidat

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Indledning: Dissektion af truncus coeliacus er en sjælden erkendt tilstand med symptomatologi fra asymptomatisk til akut abdomen. Diagnosen stilles ved CT. Risikofaktorer er mandligt køn, arteriosklerose, hypertension, rygning, overvægt, graviditet, vaskulitis, bindevævssygdomme, traume, tidligere operative abdominale indgreb og øget intraabdominalt tryk.

Denne kasuistik omhandler to cases med dissektion af truncus coeliacus videre ud i a. lienalis med miltinfarkt. I begge cases var der tale om mandlige patienter, ikke rygere og henholdsvis 39 og 43 år gamle. Det ene tilfælde opstod ved øgning af det intraabdominale tryk i forbindelse med defækation, den anden var associeret til opstart af methylphenidat.

Diskussion Baseret på 43 publicerede cases er en beskrevet risikofaktor øget intraabdominalt tryk, som blev set i den første case, i forbindelse med defækation.

Det andet tilfælde opstod kort efter opstart med methylphenidat, som har en virkningsmekanisme, der ligner amfetamins. Der er i forbindelse med amfetaminbrug beskrevet dissektioner i koronararterier, aorta og ekstracerebrale arterier. Det må formodes, at det er øget arterielt tryk induceret af disse stoffer der er medvirkende til dissektioner.

Der findes ingen fast behandlingsalgoritme for dissektion af truncus coeliacus. Konservativ behandling er ofte den initiale behandling, og omfatter smertebehandling, antikoagulerende og antihypertensiv behandling. Der findes indikation for endovaskulær terapi ved cirkulatorisk ustabile patienter eller ved manglende effekt af konservativ behandling

Konklusion I begge tilfælde blev patienterne behandlet konservativt. Der blev ikke observeret komplikationer under indlæggelsen.

16. Helkrops clearance og produktion af ammonium kvantificeret ved ammoniuminfusion – effekterne af skrumpelever og "ammoniumsænkende" behandling

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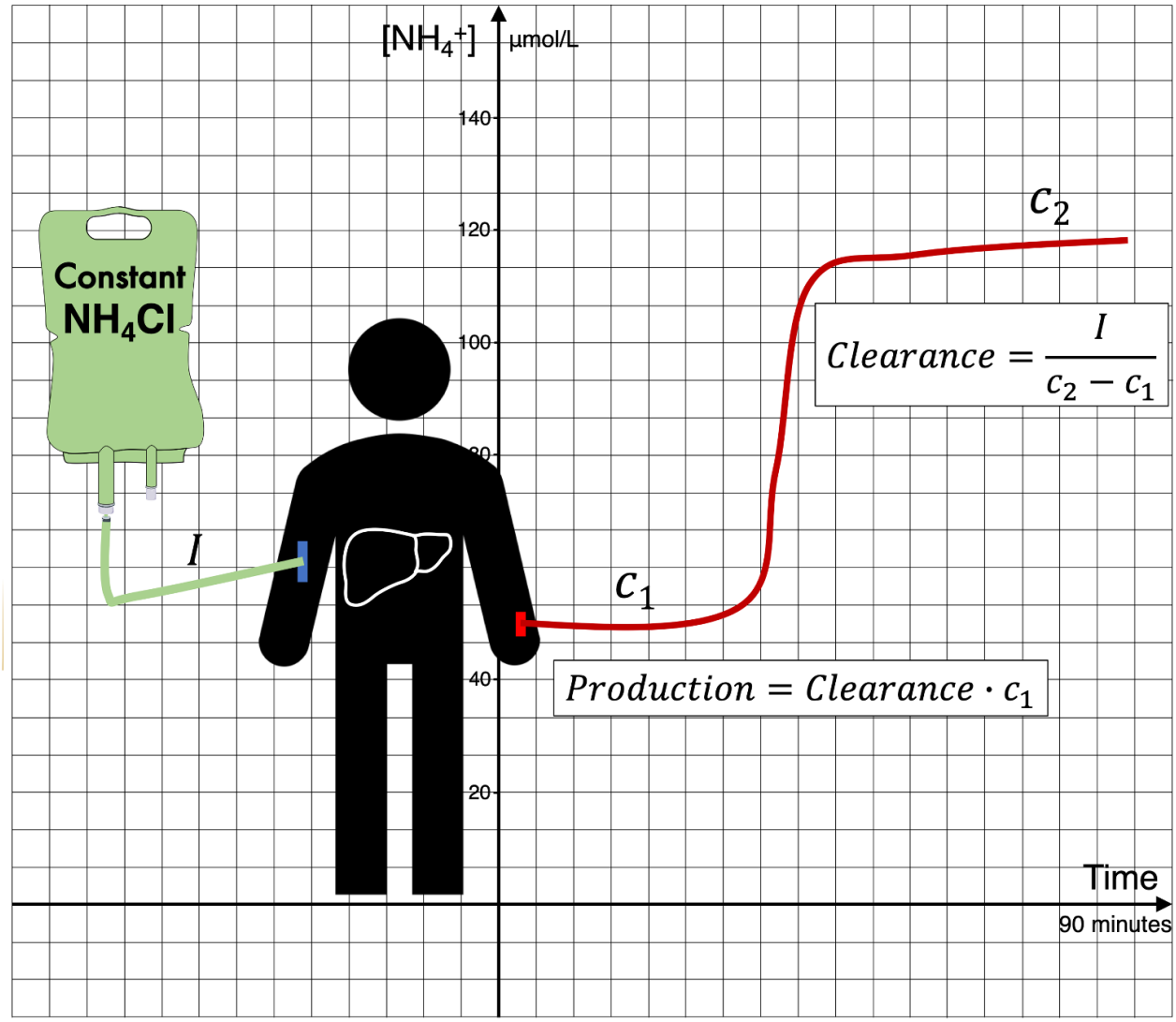
Baggrund: Hyperammoniæmi er et patofysiologisk karakteristika ved leversygdom og spiller en hovedrolle i udviklingen af hepatisk encefalopati (HE). Det relative bidrag til hyperammoniæmi fra hhv. øget ammoniumproduktion og nedsat ammoniumclearance og effekten af "ammonium-sænkende" HE-behandlinger er dårligt belyst.

Formål: At kvantificere helkrops ammoniummetabolisme i raske og patienter med skrumpelever samt at validere metoden ved at undersøge effekten af behandling med glycerol fenylbutyrat og laktulose+rifaximin.

Metoder: 10 raske mænd og 10 mandlige patienter med skrumpelever undersøgt med en 90 minutter konstant ammoniuminfusion til steady-state plasma-ammoniumkoncentration. Ammoniumclearance og -produktion beregnes (figur). Forsøgsdeltagere undersøgtes før og efter "ammoniumsænkende" behandling.

Resultater: Raske havde ammoniumclearance på 3.5 (3.1–3.9) L/min og ammoniumproduktion på 49 (35-63) µmol/min. Fenylbutyrat øgede clearance med 12% (4–19%, p=0.009). Patienter med skrumpelever havde 20% nedsat ammoniumclearance til 2.7 (2.1–3.3) L/min (p = 0.02) og næsten trefold øget produktion på 131 (102–159) µmol/min (p<0.0001). Laktulose+rifaximin reducerede produktionen med 20% (2–37%, p=0.03). Ammoniuminfusionen var generelt veltolereret udover i en allerede hyperammonæmisk skrumpeleverpatient med mulig gastrointestinal blødning, som udviklede HE; reverteret efter afbrydelse af infusion.

Konklusion: Helkrops ammoniummetabolisme kan måles med den præsenterede metode. Ved brug af metoden påvistes nedsat ammoniumclearance og øget -produktion hos skrumpeleverpatienter samt at fenylbutyrate øger clearance, mens laktulose+rifaximin reducerer produktion. Metoden vil kunne bruges til at undersøge en række spørgsmål indenfor normal- som patofysiologi samt belyse effekterne af "ammoniumsænkende" behandlinger.



17. Risikoen for udvikling af interstitiel nefritis under 5-ASA-behandling

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Baggrund: 5-aminosalicylsyre (5-ASA) er et hyppigt anvendt præparat til behandling af colitis ulcerosa. En sjælden bivirkning hertil er interstitiel nefritis, hvorfor det aktuelt anbefales, at man monitorerer nyrefunktionen under behandlingen med måling af denne allerede 14 dage efter opstart, herefter hver 4.uge i 12 uger, efterfulgt af hver 3.måned de næste 5 år, hvorefter man, såfremt der ikke er indtrådt påvirkning af nyrefunktionen, kan overgå til årlig kontrol. Anbefalingen beror primært på case-studier. Blodprøvetagning er forbundet med omkostninger og til gene for patienterne. Ligeledes er det uklart, om man ved regelmæssig blodprøvetagning forebygger udvikling af interstiel nefritis.

Metode: Via registerudtrækning har vi identificeret alle patienter, som siden 2010 har været i behandling med 5-ASA på Lever-, Mave- og Tarmsygdomme, AUH, og registreret alle målinger af kreatinin og eGFR. Journalerne er blevet gennemgået mhp. at finde de patienter, der i perioden har udviklet 5-ASA-betinget nefrotoksicitet.

Resultater: 2432 patienter har siden 2010 været i 5-ASA-behandling. Heraf udviklede 194 (7,9 %) forbigående eller vedvarende kreatininforhøjelse. 4 cases blevet tolket som udløst af 5-ASA svarende til 0,16 %. De 4 cases bestod af 3 unge mænd og en ung kvinde i alderen 23-26 år ved opstart af 5-ASA. Kreatininpåvirkningen (median 159) opstod mellem 3 måneder og 6 år efter opstart, i tre af tilfældene fundet ved tilfældig blodprøvetagning. Diagnosen blev verificeret med nyrebiopsi hos 3. Ingen opnåede normaliseret kreatininen efter ophør af 5-ASA.

Konklusion: Klinisk betydende 5-ASA-betinget nyresygdom er yderst sjældent, og med baggrund heri kan det betvivles om nuværende anbefaling skal opretholdes.

18. An improved guideline adherence and PPI efficacy has been accompanied by a decrease in diagnostic delay, and strictures before diagnosis of eosinophilic oesophagitis in the North Denmark Region - a retrospective registry study of the DanEoE cohorts

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Background: In the North Denmark Region an increased awareness of eosinophilic oesophagitis (EoE) was observed after 2011 where a regional biopsy guideline was implemented. This resulted in an increased awareness of EoE and a 50-fold increase in the incidence of EoE patients between 2007-2017.

Aims: The aims of this study were to examine the progress in diagnostic delay, complications, PPI treatment, and follow up since 2017 in Danish patients with eosinophilic oesophagitis.

Methods: This was a retrospective registry- and population-based cohort study (DanEoE2 cohort) including 346 adult patients with oesophageal eosinophilia diagnosed between 2018-2021 in the North Denmark Region. The DanEoE2 cohort included all possible EoE patients by using the Danish Patho-histology registry based on the SNOMED-system. The data was analysed and compared to the DanEoE cohort (2007-2017).

Results: The diagnostic delay of EoE patients diagnosed between 2018-2021 in the North Denmark Region had decreased to a median of 1.5 (5.5 (2.0;12) versus 4.0 (1.0;12), p=0.03) years. Strictures before diagnosis had

decreased (12% versus 4%, p=0.003). The number of patients started on high-dose PPI increased (56% versus 88%, p<0.001). An intensified awareness regarding national guidelines and follow-up was observed as an increase in the number of histological follow up (67% versus 74%, p=0.05).

Conclusions: Comparisons of the DanEoE cohorts showed a decrease in diagnostic delay, a decrease in stricture formation before diagnosis, and an improved guideline adherence after 2017. Future studies are needed to assess if symptomatic or histological remission on PPI treatment is more capable of predicting a patient's risk of developing complications.

19. There is a long way from current clinical practice in Denmark compared to recent published English guideline on management of children with eosinophilic oesophagitis

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Abstract

Background: A low incidence of eosinophilic esophagitis (EoE) in children in the North Denmark Region (NDR) were measured in 2007-2017. Few of the children diagnosed before 2017 were treated to remission suggesting a lack of awareness. While there currently are no guidelines for treating EoE in Denmark, a new English guideline was published in 2022 renewing focus on the disease.

Objective: The aim of this study was to measure the difference of current Danish clinical practice for treatment and follow-up of EoE children in the NDR with the new English guideline from the British Society of Gastroenterology (BSG) and the British Society of Pediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN).

Methods: This retrospective, register-based DanEoE cohort study included 31 children diagnosed with EoE between 2007–2021 in NDR. Medical records were reviewed and information about treatment and follow-up were collected.

Results: In 32% of the children with EoE in the NDR, first-line treatment initiated corresponded with the recommendations in the new English guideline. One in 6 children were never started on any treatment even though treatment always is recommended. Symptomatic follow-up was completed in 77% (24/31) of children and 85% (11/13) of the children after 2017. Histologic follow-up within 12 weeks was completed in 13% (4/31)

of the children and 15% (2/13) of the children after 2017. Combined symptomatic and histologic remission after first-line treatment was achieved in 6% (2/31).

Conclusions: In Denmark focus on improving EoE treatment and follow-up for children is needed, as there is a significant difference between current clinical practice and the recommendations in the new English guideline.

20. Oesophageal food bolus obstruction in the North Denmark Region in 2021 - More than half of patients were never diagnosed with a cause, or biopsied in the oesophagus

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Background: Danish national guidelines recommend a diagnostic upper endoscopy within 2 weeks after food bolus obstruction (FBO). Firstly to search for possible upper gastro-intestinal (GI) cancer (national cancer guideline), and if cancer is excluded to sample 8 biopsies to exclude eosinophilic oesophagitis (EoE) (EoE guideline). In the clinical work in our Department of Emergency Medicine in Denmark there is a growing suspicion that these nationale guidelines are not always followed.

Aims and Methods:

The aims of this study were to 1) describe the causes of FBO, 2) to determine the proportion of patients who underwent upper endoscopy with biopsies according to guideline, and 3) to identify ICD10 diagnosis and procedure codes applied to the hospital visits due to FBO in the North Denmark Region (NDR). This was a registry based study og the entire population of the North Denmark Region of 580,000 citizens. For all acute hospital visits in the NDR in 2021, medical registries were used to find patients with FBO, and their medical records were reviewed. All hospital visits with ICD 10 codes possibly reflecting FBO, and a sample of 14400 hospital visits with unspecific ICD codes (R and Z codes) were screened for possible FBO. Diagnosis, follow up, and treatment were recorded for all patients with FBO.

Results: Of 1886 hospital visits where registry ICD codes possibly reflected FBO 8.4% were due to FBO, while FBO were present in 0.028% in a sample of 14400 hospital visits with ICD codes of unspecific nature. The median age for a patient presenting with FBO at the hospital was 66.0 (49.8-81.0) years, and 55 % had experienced FBO before. Effective treatment of FBO only involved endoscopic removal in half of patients.

Thirty percent did not undergo upper endoscopy within 2 weeks of the hospital visit (upper cancer guideline), and 51% were never biopsied in the oesophagus (EoE guideline). Most patients (65.1%) were never diagnosed with a cause of FBO.

Conclusion: More than half of patients hospitalized due to FBO in NDR in 2021 were never diagnosed with a cause. In one third the national cancer guidelines were not followed, and in half of the cohort EoE guidelines were not followed. There is a real risk of undetected upper GI cancers and EoE as consequence and the area needs focus in Denmark to improve patient treatment and prevent new FBO.

21. Hyperuricemia as a prognostic factor in alcohol-related cirrhosis

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Background and aims Hyperuricemia is suggested as a potential risk factor for the progression of chronic liver disease towards cirrhosis. We recently demonstrated increased prevalence of hyperuricemia in patients with alcohol-related (ALD) cirrhosis. Yet, the role of uric acid (UA) in disease progression at the stage of cirrhosis remains unclear. We investigated hyperuricemia as a prognostic factor in patients with ALD cirrhosis.

Methods We included 92 patients with ALD cirrhosis (Child Pugh A-B). Hyperuricemia was defined as having a serum-UA of ≥8.07 mg/dL or ≥6.62 mg/dL for men/women at inclusion. Events of hepatic decompensation, hospitalization and death were registered from patient records. Outcomes were analyzed using the Cox proportional hazard model. Hazard ratios (HRs) were adjusted for sex, age, kidney function, and alcohol-consumption (AUDIT-C).

Results During a median follow-up period of 750(IQR: 394-1032) days, hepatic decompensation, hospitalization, and death occurred in 42, 59, and 25 patients, respectively. Hyperuricemia was not associated with decompensation (HR 1.01 [95% CI: 0.44;2.23]), hospitalization (HR 1.50 [95%CI: 0.79;2.86]), or mortality (HR 1.26 [95% CI: 0.42;3.82]). Regarding specific decompensations, hyperuricemia was insignificantly associated with increased risk of ascites (HR 2.40 [95 CI: 0.93;6.18]) and variceal bleeding (HR 1.57 [95%CI: 0.42;5.89]), but not hepatic encephalopathy (HR 0.83 [95%CI: 0.28;2.48]).

Conclusions Hyperuricemia was not associated with poor clinical outcomes in patients with ALD cirrhosis when adjusting for kidney function and alcohol consumption, except for a trend of increased ascites risk. Our findings may have clinical implications as hyperuricemia is easily treated but require validation in larger patient cohorts.

22. Low-dose liraglutide with pragmatic dose escalation achieves remission in more than half of 27 patients with sequestrant-refractory bile acid diarrhoea: a case series

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Introduction. Bile acid diarrhoea (BAD) is a common cause of chronic watery diarrhoea. Sequestrants and liraglutide are efficacious, but the treatment algorithm is not settled.

Aim. To describe the effect of second-line liraglutide on remission of sequestrant-refractory BAD.

Methods. A case series of consecutive BAD patients refractory or intolerant to colestyramine and/or colesevelam and fulfilling the Hjortswang diarrhoea criteria (≥3 stools or ≥1 watery stool per day) were included. We initiated 0.6 mg/day of liraglutide and increased it by 0.6 mg/day at follow-up until remission or a maximum dose of 1.8 mg/day. Remission was defined as a daily mean of < 1 watery bowel movement and < 3 total bowel movements.

Results. Of 27 patients, 21 had BAD diagnosed by SeHCAT (4%, range 0-11%) and 6 patients by a history of ileum resection. Fifteen (56%, 95%CI: 35-75%) achieved remission; 4 of 5 on 0.6 mg, 7 of 9 on 1.2 mg, and 4 of 13 on 1.8 mg liraglutide/day. Mean total bowel movements of 6.5 (95% CI: 5.1-8.3) at baseline reduced to 2.8 (2.2-3.5) at the end of follow-up (paired t-test, $p < 0.0001$); the baseline number of watery bowel movements of 5.1 (3.7-7.0) reduced to 0.8 (0.6-1.1, $p < 0.0001$). Two patients not in remission on 1.8 mg liraglutide/day obtained remission on combination therapy with colestyramine.

Conclusion. Second-line liraglutide achieved remission of sequestrant-refractory BAD in 15 (56%) of 27 patients; 11/15 did not need maximum dosing. In this case series, second-line liraglutide seemed efficacious in treating sequestrant-refractory BAD.

23. PROPHYLAXIS OF POST-OPERATIVE RELAPSE IN PATIENTS WITH CROHN'S DISEASE; INDICATIONS AND PRACTICE

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Introduction: In order to reduce risk of recurrence after surgery, initiation of medical prophylaxis based on assessment of risk of relapse is generally recommended in Crohn's disease (CD).

Aims: to assess adherence to guideline recommendations as regards post-operative prophylaxis (POP) and to evaluate efficacy of POP.

Methods: Single-centre, retrospective study of all CD patients undergoing intestinal resection between February 1st, 2017, and January 31st, 2022. Based on medical records, patients were classified as either high (HR) or low risk (LR) of relapse. Treatment received and outcome of treatment was registered and correlated to known prognostic factors such as smoking status, age, previous surgical resection.

Results: Two-hundred-and sixteen (104 HR and 112 LR) patients were included in the study. Only 61% of the HR patients received POP. There was no significant difference in relapse (clinical, endoscopic and/or MR) rates between those who received POP (67%) and those who did not (53%), *p=0.218*.

Sixty-six % of LR patients received POP in spite of being low risk. There was no significant difference in relapse rates between patients receiving POP (66%) and those not receiving POP (47%), p=*0.067.*
Relapse risk in patients not receiving POP was only non-significantly smaller for LR patients (47%) compared to HR patients (54%).

Conclusion: Adherence to recommendations for POP in CD was relatively low. Effect of POP was unconvincing. Risk-stratification was a poor predictor of relapse. These findings question the clinical usefulness of current risk stratification as well as currently used medications for POP.

24. Prevalence of hyperuricemia in patients with alcohol-related liver cirrhosis

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Background Uric acid (UA) increases inflammation and has been implicated in the disease progression of chronic liver disease. Established risk factors for hyperuricemia are common in patients with cirrhosis, but whether cirrhosis is intrinsically associated with hyperuricemia remains unclear. This study aimed to determine the prevalence of hyperuricemia and investigate risk factors for hyperuricemia in patients with cirrhosis.

Methods We measured serum UA levels in a prospectively included cohort of 86 Danish patients with alcohol-related cirrhosis (ALD cirrhosis) and compared them with background population data from the Nordic Reference Interval Program (NORIP) and National Health and Nutritional Examination Survey (NHANES). Group differences were assessed using the students T-test and by using the clinical cutoffs for hyperuricemia. Known risk factors for hyperuricemia were correlated to UA levels in the patient cohort.

Results Mean(±SD) UA levels were increased in cirrhosis patients (6.28 ±2.01) compared with both NORIP (4.93 ±1.24, p <0.0001) and NHANES (5.34 ±1.46, p <0.0001). The prevalence of hyperuricemia 22.1%/40.7% for men, and 10.5%/17.4% for women, based on cut-offs from the NORIP and NHANES populations, respectively. Cirrhosis was independently associated with a UA increase between 1.00 mg/dL and 0.61 mg/dL, adjusted for sex and age. eGFR was inversely correlated with UA (ρ = -0.5, p< 0.001), while there was no association with age, BMI, alcohol consumption, or MELD score.

Conclusions Patients with ALD cirrhosis had increased prevalence of hyperuricemia, which was particularly evident in women. Poor kidney function was the only risk factor associated with UA levels in cirrhosis patients.

25. Type VII collagen degradation biomarker (C7M): a new marker of alcohol-induced gut injury and bacterial translocation in steatotic liver disease

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Conflict of interest: Ida Lønsmann, Diana Leeming and Morten Karsdal are full-time employees at Nordic Bioscience A/S. Diana Leeming and Morten Karsdal are stock owners of Nordic Bioscience

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Background: The gut barrier is a treatment target in alcohol-related liver disease (ALD) and metabolic dysfunction-associated steatotic liver disease (MASLD), but biomarkers to assess gut injury and bacterial translocation are lacking. Type VII collagen is essential for the integrity of the extracellular matrix (ECM). We therefore aimed to investigate markers of type VII collagen and IL-6 in response to acute alcohol intoxication as markers of gut injury and bacterial translocation.
Method: In a pathophysiological intervention study with 39 participants, including healthy controls, ALD, and MASLD, we administered 2.5 mL/kg of 40% ethanol in 9 mg/mL NaCl through a nasogastric tube over 30 minutes. Blood samples were collected simultaneously during a 180-minute study period. We measured markers of type VII collagen degradation (C7M) and formation (PRO-C7), as well as IL-6 levels.
Results: Mean age was 53 (±11) years with 61.4% males. In all groups, hepatic venous C7M concentration increased during the first 90 minutes and returned to near baseline after 180 minutes. AUCALD for C7M was significantly higher than AUCHC ($p = 0.0074$, 95% CI: 495 - 2846). We observed no significant difference between other groups. Hepatic and systemic IL-6 significantly increased after 180 minutes, while PRO-C7 remained unchanged.
Conclusion: Acute alcohol intake rapidly increases hepatic type VII collagen degradation, suggesting gut-driven ECM damage, along with elevated IL-6 indicating potential increased bacterial translocation.

26. Clinical and biochemical characteristics of a Danish and Turkish cohort of incident and prevalent patients with primary biliary cholangitis.

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Introduction: Primary biliary cholangitis (PBC) is a progressive chronic inflammatory liver disease. Environmental triggers, individual genetic predisposition, and epigenetic factors influence disease development and progression. Although it is observed in all races and regions, its incidence and prevalence vary. In our study, we compared cohorts of Danish and Turkish PBC patients with different genetic backgrounds.

Methods: We compared basic demographic and biochemical data of four cohorts; 1) 155 Danish prevalent patients, 2) 77 Danish incident patients, 3) 103 Turkish prevalent patients, and 4) 101 Turkish incident patients. We evaluated cirrhosis rates and compared response rates to ursodeoxycholic acid (UDCA) treatment in prevalent PBC patients.

Results: More than 90% of the included patients were female, except in the Danish incident cohort with 75% female. Turkish patients had lower median age in both the prevalent and incident cohorts. Median alkaline phosphatase levels were higher in the Turkish cohorts than in the Danish, when comparing incident with incident and prevalent with prevalent, respectively; and more patients were AMA positive. Other biochemical data were similar in the cohorts. Around 15% of the patients in all the cohorts had cirrhosis. More patients in the Turkish prevalent cohort were complete responders to UDCA than in the Danish prevalent cohort.

Conclusion: Turkish and Danish patients have similar age at diagnosis, and the same proportion have cirrhosis, but Turkish patients have higher ALP than Danish. More Turkish than Danish patients have a complete to UDCA treatment.

27. The systemic inflammation in patients with cirrhosis and ascites is acutely affected by terlipressin

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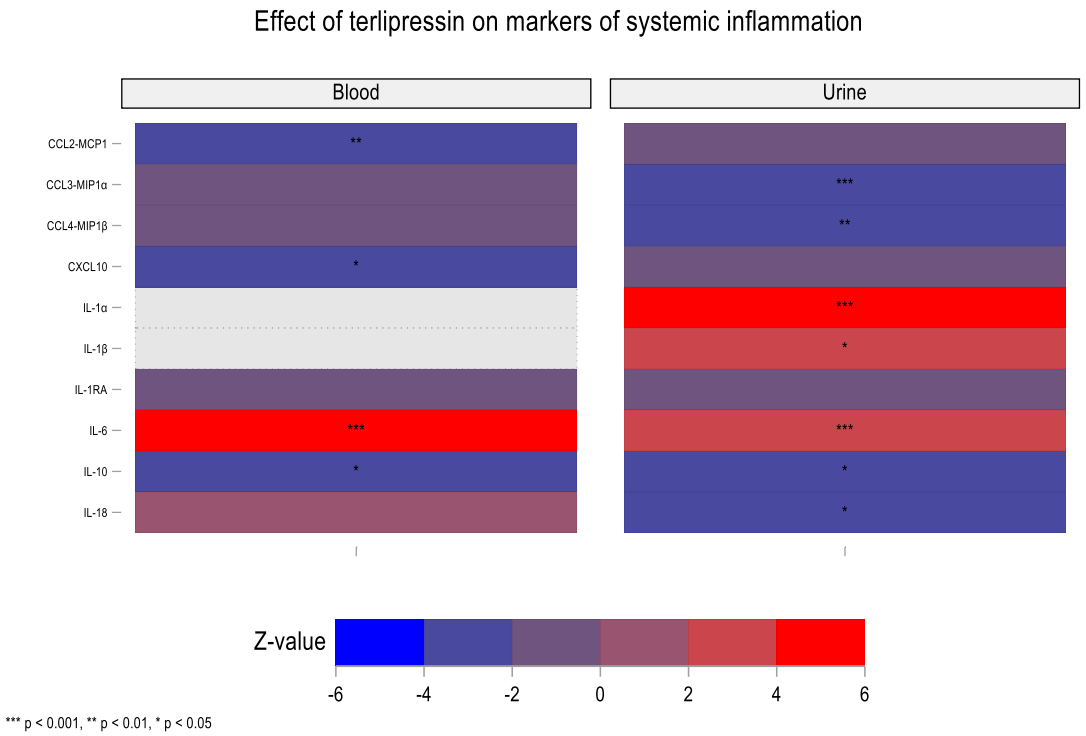
Background: Terlipressin is widely used in the management of complications to cirrhosis but has been shown to increase the risk of sepsis and respiratory failure. Since both adverse events are associated with systemic inflammation, we aimed to investigate the acute effect of terlipressin on inflammation markers in patients with cirrhosis and ascites.

Method: We included 25 patients with cirrhosis and ascites from a pathophysiological intervention study. We compared patients receiving terlipressin (n=20) to patients receiving corresponding placebo (n=5). We compared changes in circulating and urine systemic inflammation markers before and after treatment. Urine measurements were corrected for GFR changes, as assessed by ^{51}Cr-labeled clearance.

Results: Mean age was 57, majority were male (68%) with alcohol-related cirrhosis (92%) as the dominant etiology with median MELD-Na = 10. Terlipressin treatment led to a rapid increase in both blood and urine IL-6 levels relative to placebo (Figure). A selective decrease of chemokines was observed in the blood (CCL2-MCP1 and CXCL10) and urine (CCL3-MIP1α and CCL4-MIP1β). As expected, GFR improved upon terlipressin treatment, but changes were not associated with changes in blood inflammation markers. Similarly, none of the baseline levels of inflammatory markers predicted the renal effect of terlipressin.

Conclusion: Terlipressin induces rapid changes in blood and urinary inflammation markers, including an increase in IL-6. The findings indicate that terlipressin serves as an activator of a systemic inflammation response.



28. Metformin Treatment is Associated with Reduced Risk of Hypoglycemia, Major Adverse Cardiovascular Events, and All-Cause Mortality in Patients with Post-pancreatitis Diabetes Mellitus: A Nationwide Population-Based Cohort Study

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Objective: Post-pancreatitis diabetes mellitus (PPDM) is a frequent complication of pancreatitis and is associated with an increased risk of adverse outcomes. Metformin is recommended for the treatment of

PPDM, but evidence of its risk-benefit profile is limited. In a pharmaco-epidemiologic study, we investigated the association between metformin and adverse outcomes in patients with PPDM.

Research Design and Methods: In a Danish nationwide population-based cohort study, we included adults (>18 years) with incident PPDM or type 2 diabetes between 2009 and 2018. PPDM was categorized into acute and chronic subtypes (PPDM-A and PPDM-C). Associations between metformin treatment and severe hypoglycemia, major adverse cardiovascular events (MACE), and all-cause mortality were examined across the diabetes subgroups using Cox regression analysis, with metformin and insulin treatment handled as time-varying exposures.

Results: We included 222,337 individuals with new-onset type 2 diabetes and 3,781 with PPDM, of whom 2,305 (61%) were classified as PPDM-A and 1,476 (39%) as PPDM-C. Exposure to metformin was associated with a lower risk of severe hypoglycemia (adjusted hazard ratio (HR) 0.42, 95% confidence interval (CI) 0.27-0.64, *P* <0.001), MACE (HR 0.59, 95% CI 0.41-0.85, *P* = 0.048), and all-cause mortality (HR 0.57, 95% CI 0.50-0.65, *P* <0.001) in patients with PPDM. In sensitivity analyses and among individuals with type 2 diabetes, metformin exposure exhibited comparable trends of risk reduction.

Conclusions: Metformin is associated with a lower risk of adverse outcomes, including all-cause mortality in patients with PPDM, supporting the use of metformin as a glucose-lowering therapy for these patients.

29. Risk of primary liver cancer in patients with alcohol-related cirrhosis is similar in England and Denmark

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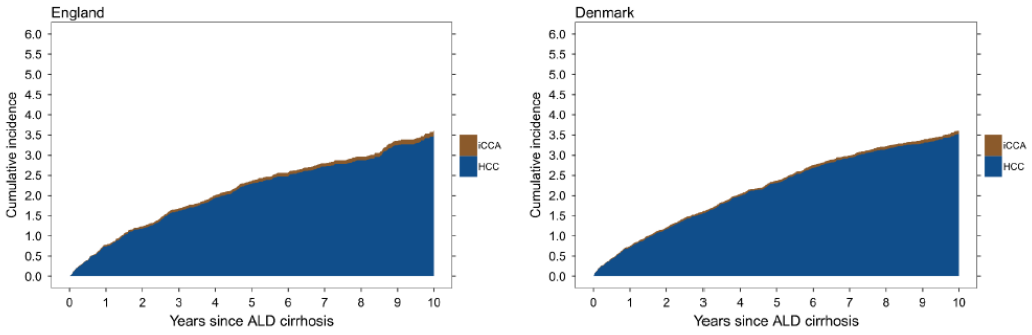
Background: Patients with alcohol-related cirrhosis (ALD cirrhosis) have an increased risk of primary liver cancer (hepatocellular carcinoma [HCC] or intrahepatic cholangiocarcinoma [iCCA]). Imaging-based surveillance for HCC is recommended in England, but not Denmark.

Methods: We included 17,085 English patients (2000-2016) and 22,121 Danish patients (1994-2022) with ALD cirrhosis using healthcare registries. We computed incidence rates (IR) and cumulative incidence of primary liver cancer (including HCC and iCCA separately) and, additionally, mortality from diagnosis of primary liver cancer.

Results: The IR of primary liver cancer per 100,000 person-years was 636 (95% CI 580-698) in England and 676 (630-726) in Denmark. The 5-year risk of primary liver cancer was 2.36% (2.12-2.63) in England (iCCA 0.07%, HCC 2.29%) and 2.37% (2.16-2.58) in Denmark (iCCA 0.05%, HCC 2.31%). In both countries, the risk of primary liver cancer was below 4% in all subgroups, increased in males and with increasing age. The 1-year mortality after a diagnosis of primary liver cancer was 56.7% (52.1-61.5) in England and 60.8% (57.3-64.4) in Denmark.

Conclusion: The risk of and the mortality with primary liver cancer is the same in English and Danish patients with ALD cirrhosis, thus questioning the impact of HCC surveillance guidelines. The risk of primary liver cancers increased with age and was higher for men. In both countries, HCCs constituted >97% of primary liver cancers.

Figure: (next page)



30. Inflammatorisk respons ved cirrose og styrketræning

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Baggrund Patienter med levercirrose er præget af lokal og systemisk inflammation, der er en risikofaktor for udvikling af komplikationer til cirrose. Fysisk aktivitet inklusive styrketræning styrker immunsystemet og har bl.a. en antiinflammatorisk effekt. På kort sigt øges mængden af flere cytokiner i blodet lige efter træning hos raske personer. Men også på den lange bane ses en gavnlig effekt på immunsystemet ved fast ugentlig træning af moderat intensitet.

Formålet med studiet er at undersøge effekten af 12 ugers styrketræning på en række inflammationsmarkører inklusive myokiner (IL-6, IL-8, IL-10) blandt cirrosepatienter.

Metode 39 personer med cirrose Child-Pugh A/B blev randomiseret til enten en trænings- eller en kontrolgruppe. I 12 uger styrketrænede træningsgruppen 3 x 1 time ugentligt. Blodprøver blev indsamlet før og efter interventionen.

Resultater

	Træning (n = 19)			Kontrol (n = 15)			
	Wilcoxon - Median (min.-max.)						Mann-Whitney
	Baseline	Follow-up		Baseline	Follow-up		Δ Grupper
IL-6, pg/mL	2,0 (0,4-9,2)	1,7 (0,4-13,0)	p = 0,85	1,8 (0,6-19,8)	1,4 (0,7-6,1)	p = 0,40	p = 0,66
IL-8, pg/mL	34 (5-118)	36 (9-91)	p = 0,60	26 (6-270)	29 (12 –91)	p = 0,15	p = 0,11
IL-10, pg/mL	0,3 (0,1-1,6)	0,3 (0,1-2,2)	p = 0,14	0,5 (0,2-7,1)	0,4 (0,2-2,3)	p = 0,15	p = 0,84
IL-12p70, pg/mL	0,1 (0,01-0,7)	0,1 (0,02-0,3)	p = 0,38	0,1 (0,02-2,0)	0,2 (0,03-6,0)	p = 0,54	p = 0,52
IL-13, pg/mL	0,7 (0,03-1,3)	0,1 (0,02-0,3)	p < 0,01	1,1 (0,1-4,8)	0,1 (0,0-6,0)	p < 0,05	p = 0,72
TNF-α, pg/mL	2,3 (1,0-5,0)	2,3 (0,8-4,6)	p =0,59	3,6 (1,9-6,1)	2,8 (1,5-6,8)	p = 0,85	p = 0,54
IFN-γ, pg/mL	6,6 (2,4-23,9)	5,3 (1,4-213)	p = 0,62	7,6 (2,3-35,2)	5,4 (2,2-121)	p = 0,15	p = 0,52
CD163 mg/l	4,7 (1,2-14,5)	4,4 (1,4-16,4)	p = 0,19	5,1 (2,6-14,5)	4,6 (2,2-16,0)	p = 0,46	p = 0,78
CD206 mg/l	0,4 (0,2-0,8)	0,4 (0,2-0,7)	p = 0,27	0,4 (0,1-1,9)	0,4 (0,1-0,8)	p = 0,55	p = 0,95

Konklusion Vi fandt ingen effekt af 12 ugers styrketræning på de undersøgte inflammationsmarkører. Det er fortsat uvist, hvorledes inflammationsmarkørerne påvirkes lige efter en enkelt træningssektion hos cirrosepatienter.

31. Effect of continuous glucose monitoring on hypoglycaemia in adults with post-pancreatitis diabetes mellitus

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Background and aim: Post-pancreatitis diabetes mellitus (PPDM) is a frequent complication of acute and chronic pancreatitis and constitutes approximately 1.5% of all adult diabetes cases. Compared to type 2 diabetes, PPDM is characterized by poorer glycaemic control, frequent hypoglycaemic episodes and increased mortality rates. This poorer prognosis is related to multiple underlying complex mechanisms unique to PPDM that remain incompletely understood. Thus, means to decrease the risk of hypoglycaemia and improve the outcome for patients with PPDM are urgently needed.

In people with type 1 diabetes and those with type 2 diabetes on insulin therapy, continuous glucose monitoring (CGM) improves glycaemic control and reduces the risk of hypoglycaemia. These effects are also assumed to be present in PPDM patients, but this has never been investigated. This project aims to examine

the effect of CGM (vs self-monitored blood glucose (SMBG) based on capillary blood samples from finger-pricking) on hypoglycaemia and glycaemic control in PPDM patients.

Methods: An open-label crossover randomized controlled trial will be conducted at Aalborg University Hospital. Thirty adult chronic pancreatitis patients with insulin-treated diabetes will be randomized to receive 50 days of CGM monitoring followed by 50 days of SMBG or *vice versa*. Each study period is preceded by 20 days of masked CGM assessment, which also serves as the washout period between the two study periods. Furthermore, the self-monitoring group will use masked CGM for the last 20 days of the study period to monitor glucose levels for comparison with the unmasked CGM period. Participants fill in questionnaires at baseline and follow-up; at follow-up, adverse events related to CGM or other study activities are registered. The primary endpoint is the difference (CGM vs. SMBG) in time spent with glucose value <3.0 mmol/l during the last 20 days of each study period. Secondary endpoints include CGM time in range (glucose value 3.9 - 10.0 mmol/l), CGM time below range (glucose value <3.9 mmol/l), CGM time above range (glucose value >10 mmol/l), and CGM metrics of glucose variability (standard deviation and coefficient of variation of mean glucose, mean amplitude of glycemic excursions and continuous overall net glycemic action).

Discussion: This trial aims to evaluate continuous glucose monitoring as a novel way to monitor chronic pancreatitis patients with insulin-treated diabetes, with the potential benefit of improved glycemic control and reduced time spent in hypoglycemia.

32. The Role of NT-proBNP, Chromogranin A, and 5-Hydroxyindoleacetic Acid in Screening for Carcinoid Heart Disease

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* Shared first authorship, ° Shared last authorship

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Background & Aim: Carcinoid heart disease (CHD) is a serious complication for patients with neuroendocrine tumors (NETs), and early detection is crucial. We aimed to investigate N-terminal pro-brain natriuretic peptide (NT-proBNP), Chromogranin A (CgA), and plasma 5-Hydroxyindoleacetic acid (P-5-HIAA) as a screening tool for detection of CHD.

Methods: We prospectively included patients with disseminated small-intestinal NETs (SI-NETs) and performed trans-thoracic echocardiography, questionnaires, and biochemical assessment of NT-proBNP, CgA, and P-5-HIAA. The presence and severity of CHD was assessed using a scoring system based on echocardiographic characteristics.

Results: Ninety-three patients were included in the final analysis. Fifteen (16%) were diagnosed with CHD. The median NT-proBNP (219 ng/l vs. 124 ng/l, p=0.05), CgA (3930 pmol/l vs. 256 pmol/l, p<0.0001), and P-5-HIAA

(1160 nmol/l vs. 210 nmol/l, p<0.0001) were significantly higher in patients with CHD compared to non-CHD patients. For NT-proBNP, the area under the receiver operating characteristic (AUROC) curve for detection of CHD was 0.67 (95% CI: 0.50–0.84), and at a 260 ng/l cut-off level, the sensitivity and specificity were 46 % and 79%. For CgA, the AUROC was 0.91 (95% CI: 0.84-0.97), and at a cut-off level of 598 pmol/l, the sensitivity and specificity were 100 % and 69 %. For P-5-HIAA, the AUROC was 0.89 (95% CI: 0.80-0.98), and at a cut-off level of 752 nmol/l, the sensitivity and specificity were 92 % and 85 %.

Conclusion: CgA and P-5-HIAA proved excellent markers of CHD while NT-proBNP lacked the required diagnostic accuracy to be used as a screening tool.

33. Real-world effectiveness of faecal microbiota transplantation (FMT) for first or second *Clostridioides difficile* infection (CDI)

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Introduction: *Clostridioides difficile* infection (CDI) is a life-threatening disease with high mortality. Faecal microbiota transplantation (FMT) is established for recurrent CDI but its use for first or second CDI is investigational. We aimed to assess the effectiveness of FMT for early CDI in a real-world clinical setting.

Methods: This was a multi-site, cohort study including patients with first or second CDI treated with FMT in Denmark from June 2019 to February 2023. The primary outcome was cure of *Clostridioides difficile* associated diarrhea (CDAD) at week 8 following FMT treatment. Secondary outcomes were cure at week 1 and week 8 following the first FMT treatment, and 90-day mortality following positive *Clostridioides difficile* test.

Results: 458 patients with median age 73 years (IQR 57-81 years) received FMT; 154/416 (37%) had antibiotics-refractory CDI, 255/458 (56%) had severe CDI, and 88/458 (19%) had fulminant CDI. Cure of CDAD following one or more FMT treatments was achieved in 367/458 patients (80%, 95% CI 76-84%). The 90-day mortality was 10% (95% CI 8-14%). Following the first FMT treatment, cure of CDAD was achieved in 349/430 patients at week 1 (81%, 95% CI 77-85%), and 256/436 patients (59%, 95% CI 54-63%) had sustained effect at week 8 without further treatment.

Conclusion: FMT effectively treats first and second CDI. Repeating FMT improves the effect. The 90-day mortality rate is substantially lower than reported in comparable cohorts where FMT was not used regularly.

34. Primary biliary cholangitis increases mortality irrespective of the histological stage at diagnosis

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***Background**:* Primary biliary cholangitis (PBC) is an autoimmune liver disease whose effect on long-term survival remains unclear. We aimed to compare the prognosis of PBC patients, based on the histological stage at diagnosis, with population comparators.

***Methods**:* We used nationwide healthcare registries to include all Danish patients diagnosed with histologically confirmed PBC in 1998-2020. We estimated the prevalence of PBC and the incidence in 2016-2019. We used the cumulative incidence function to estimate 1-, 5-, and 10-year risk of death and 10-year risk of HCC while treating liver transplantation as a competing risk. We included 5:1 age- and gender-matched population comparators.

***Results**:* We included 1,163 PBC patients (88.1 % women, median age at diagnosis = 59.7 years) where patients with cirrhosis were older (median 63.9 vs. 59.0). Patients had more comorbidity at diagnosis than comparators, especially connective tissue disease. On January 1st 2021, the prevalence of PBC was 22.3 per 100,000 population. The incidence rate in 2016-2019 was 2.80 (95%CI: 2.58-3.02) per 100,000 population per year. PBC

patients with cirrhosis had a higher 10-year risk of death than their matched comparators, adjusted relative risk = 2.41 (95%CI: 1.89-3.09). For patients with non-cirrhotic PBC the 10-year risk of death was 18.5% (95%CI: 15.5-21.7) vs. 14.3% (95%CI: 13.0-15.6) for their comparators, adjusted relative risk = 1.22 (95%CI: 1.03-1.47). Patients with cirrhotic PBC had a 10-year risk of HCC at 2.6% (95%CI: 0.8-6.0).

***Conclusion**:* Patients with PBC have worse prognosis than age- and gender-matched comparators irrespective of their histological stage at diagnosis.

35. The long term disease course of microscopic colitis – a 5 years prospective European incidence cohort (PRO-MC)

The European Microscopic Colitis Group, presented by Lars K Munck

Fourteen European centers incl. Departments of Gastroenterology, Region of Zealand hospitals

Background The long-term disease course of microscopic colitis (MC) is unknown.

Methods Incident European cases of MC were followed prospectively annually for 5 years.

Results Of the 501 incident cases, 422 accepted inclusion, and 220 completed follow-up. Mean age 63 years and 73% female, 46% collagenous colitis (CC), 41% lymphocytic colitis (LC) and 13% incomplete microscopic colitis. At baseline, 82% reported urgency, 44% nightly defecation, 39% faecal incontinence, and 47% moderate to severe functional impairment; 67% had active disease according to Hjortswang criteria.

Only 5% of the patients followed a quiescent course, *i.e*. no disease activity or treatment after diagnosis. Sustained clinical remission was obtained by 21%, 35% and 55% after 1, 3, and 5 years, respectively, 33% had a relapsing disease course, and 7% a chronic active course with continuous activity and/or treatment. The disease course did not differ between CC and LC.

Stool frequency at baseline did not predict the disease course. A quiescent disease course or achieving sustained clinical remission during the first or second year was associated with a 70% chance of being in clinical remission after 5 years ($p<0.001$). In contrast, 57% of cases with a chronic active disease course in the first year had a chronic active or relapsing disease course throughout 5-year follow-up ($p=0.02$).

Conclusions MC is a relapsing or chronic active disease course with an impaired quality of life 5 years after diagnosis in 40%. Disease activity at 1 and 2 years after diagnosis was predictive of activity after 5 years.

36. Effects of tetrathiomolybdate on copper distribution and biliary excretion: a $^{64}CuCl_2$ PET/MRI study.

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Background: Wilson Disease (WD) patients experience hepatic copper accumulation due to reduced biliary copper excretion. Bis-choline tetrathiomolybdate (TTM) is an experimental copper chelator believed to induce biliary copper excretion in WD patients. We used ^{64}Cu-PET imaging to examine the effects of TTM on copper distribution and hepatic excretion in patients with WD.

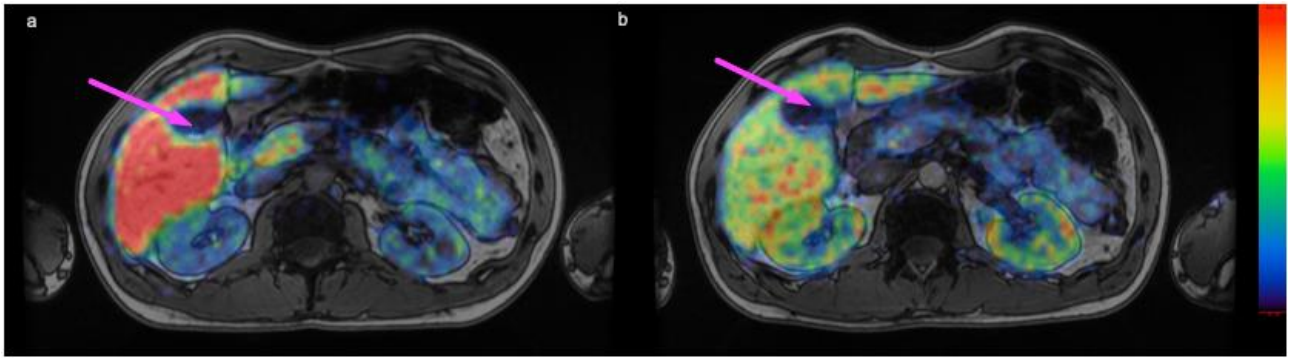
Method: Four WD patients were examined using intravenous ^{64}Cu-PET/MRI before and after TTM. Venous blood was collected for radiocopper measurement. Patients were scanned 20 minutes post ^{64}Cu-dose and 7 more times until 68h post dose. We compared ^{64}Cu content before and after TTM treatment, with each patient serving as their own control.

Results: TTM increased ^{64}Cu levels by 5-700% in blood samples during the first 6H after ^{64}Cu administration. Hepatic ^{64}Cu content was reduced by 59% - 27% (20 min - 68h post dose, respectively). This suggests immediate strong binding of ^{64}Cu in blood by TTM with retention of ^{64}Cu in plasma, leading to reduced uptake in organs.

There were no signs of biliary copper excretion before or after TTM (Figure).

Conclusion: TTM did not enhance biliary excretion of ^{64}Cu after TTM administration to patients with WD. TTM initially acted to reduce exposure of the liver and other organs to Cu by retaining ^{64}Cu in the plasma, but with time the copper may be redistributed.

Figure:



Fused axial abdominal PET/MRI showing the liver, kidneys and gallbladder (arrow), 6 hours after i.v. ^{64}Cu injection. a) Pre-treatment. b) After 7 days of treatment with TTM. 64Cu concentration is expressed as Standard uptake Value (SUV). Scale 2.5 (black) – 20 (red).

37. Effects of tetrathiomolybdate, trientine, and penicillamine on intestinal copper uptake: a randomized placebo-controlled ^{64}Cu PET/CT study

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Background: In Wilson Disease (WD) leads to pathological copper accumulation. Treatments include D-penicillamine (PEN) and trientine (TRI), which reduce copper by induction of cupriuresis, and the investigational bis-choline tetrathiomolybdate (TTM). We hypothesized that inhibition of intestinal uptake of copper could be an additional mechanism of action for these drugs.

Method: Thirty-two healthy subjects underwent ^{64}Cu-PET/CT before treatment and after 7 days of treatment with TTM, TRI, PEN or PLA, each serving as their own control. Participants were scanned 1h and 15h after oral ^{64}Cu. If a drug were to reduce intestinal copper absorption, less copper would be detected in the blood and liver.

Results: Hepatic ^{64}Cu levels 1h post-^{64}Cu dose were reduced by 92% on TTM ($p<0.02$), 53% on TRI ($p<0.02$), 23% on PEN ($p=0.16$), and 3% on PLA ($p=1.00$) (Figure 1). At 15h post-^{64}Cu, hepatic ^{64}Cu levels were reduced by 82% on TTM ($p<0.02$), 50% on TRI ($p<0.02$), 31% on PEN ($p<0.04$) and increased 12% on PLA ($p=0.16$).

TRI, PEN and PLA did not significantly change blood ^{64}Cu at 1h and 15h post ^{64}Cu. Despite TTM reducing hepatic ^{64}Cu by 80-90%, blood activity was only 40% less at 15h, indicating reduced hepatic clearance.

Conclusion: TTM markedly reduced hepatic ^{64}Cu uptake, thus reducing intestinal absorption. A similar, but smaller effect was seen with TRI, but not PEN and PLA.

Figure:

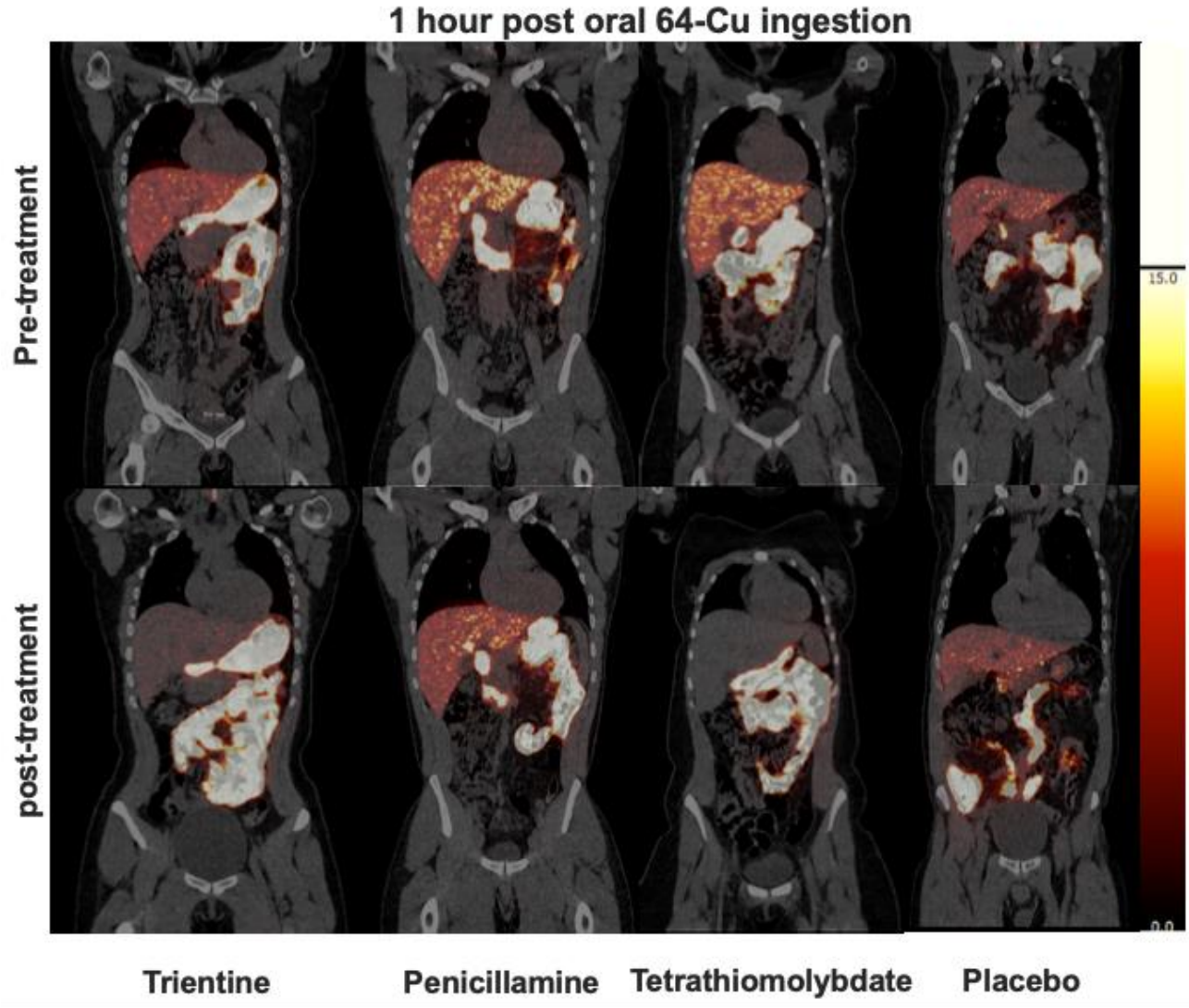

Figure 1 Fused coronal paired, representative images from one subject in each group of eight individuals, whole-body PET/CT images showing ^{64}Cu activity in the liver, heart and parts of the small intestine and colon. 1 hour after ^{64}Cu ingestion. Radioactivity scale 0 (black) – 15 (white).

38. Incidence and disease course of pouchitis in patients with ulcerative colitis and an ileal pouch-anal anastomosis (IPAA)– A Danish population-based cohort study

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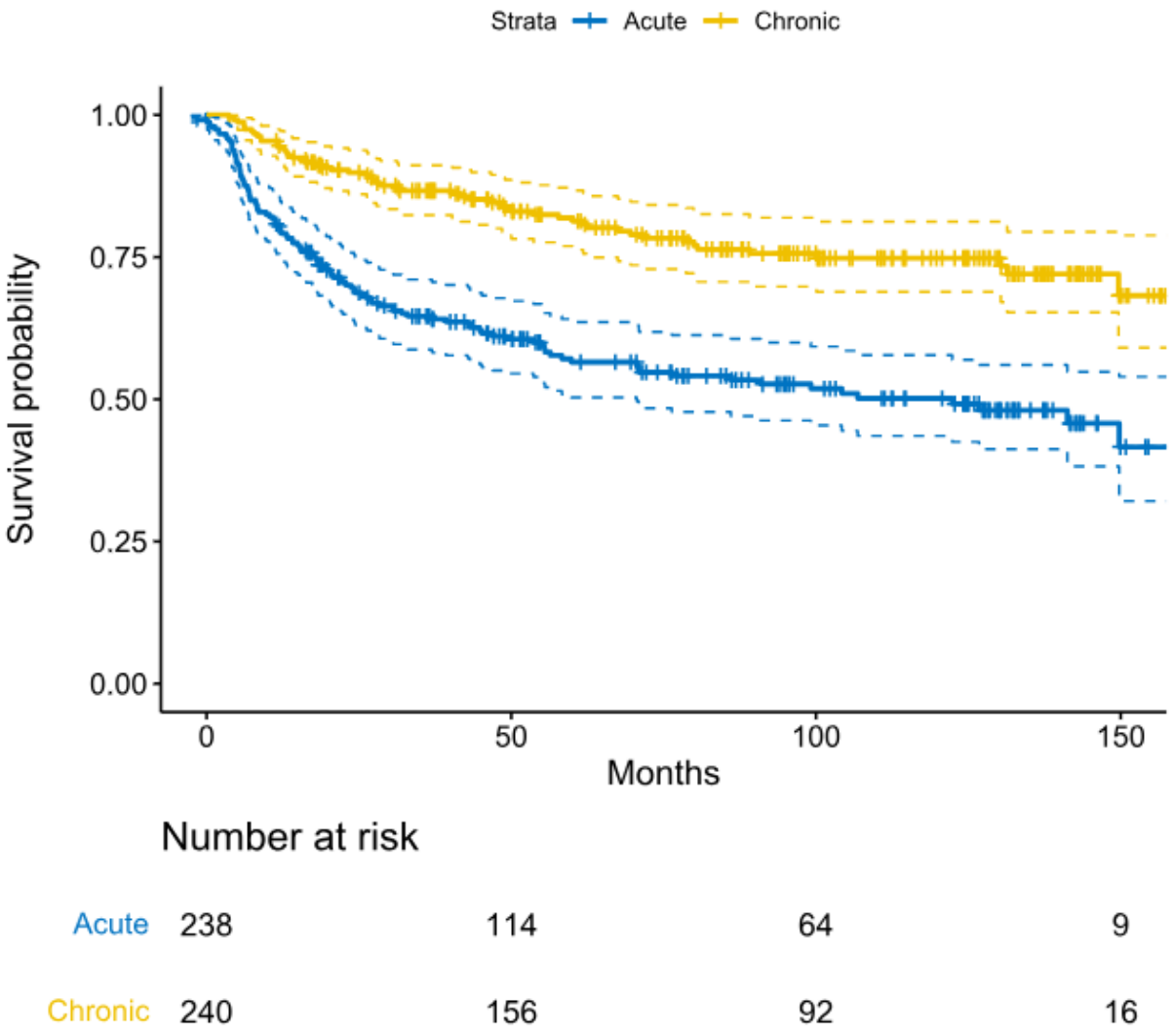
Introduction: Ulcerative colitis (UC) is a chronic inflammatory bowel disease affecting the colon and rectum. Surgical intervention like colectomy may be needed. Ileal pouch-anal anastomosis (IPAA) offers an alternative, but pouchitis, a recognized complication, lacks data on incidence and course. We explore pouchitis in UC patients with IPAA performed at Copenhagen University Hospital Hvidovre Gastrounit between 11th November 1993 and 26th April 2021

Methods The cohort covers approx. 46% of Denmark. Patients screened via electronic records. Pouchitis events and durations documented.

Results In total, 233 UC patients who underwent IPAA (11 Nov 1993 – 26 Apr 2021) were analysed. Median follow-up: 8.36 years (IQR: 4.33–11.16). 122 (52.36%) patients had 421 pouchitis events (1-25 episodes). 329 (78.15%) were acute, 92 (21.85%) were chronic. 311 (73.87%) were episodic, and 110 (26.13%) were relapsing. Time to first pouchitis were 27.24 months (SD: 36.20). Days before remission for episodic were 25.69 days (SD: 59.70). Time between episodes were 373.53 days (SD: 620.14). Survival rate at different time intervals shown.



Conclusion Study reveals high pouchitis incidence post-IPAA in UC patients. About half experienced pouchitis; first episode emerged around 2 years post-IPAA, lasting roughly 3 weeks. Quarter had relapsing pouchitis emphasizing the need for prevention and treatment strategies for better outcomes.

39. The treatment and treatment outcomes of pouchitis in patients with Ulcerative Colitis Following IPAA – A Danish population-based cohort study

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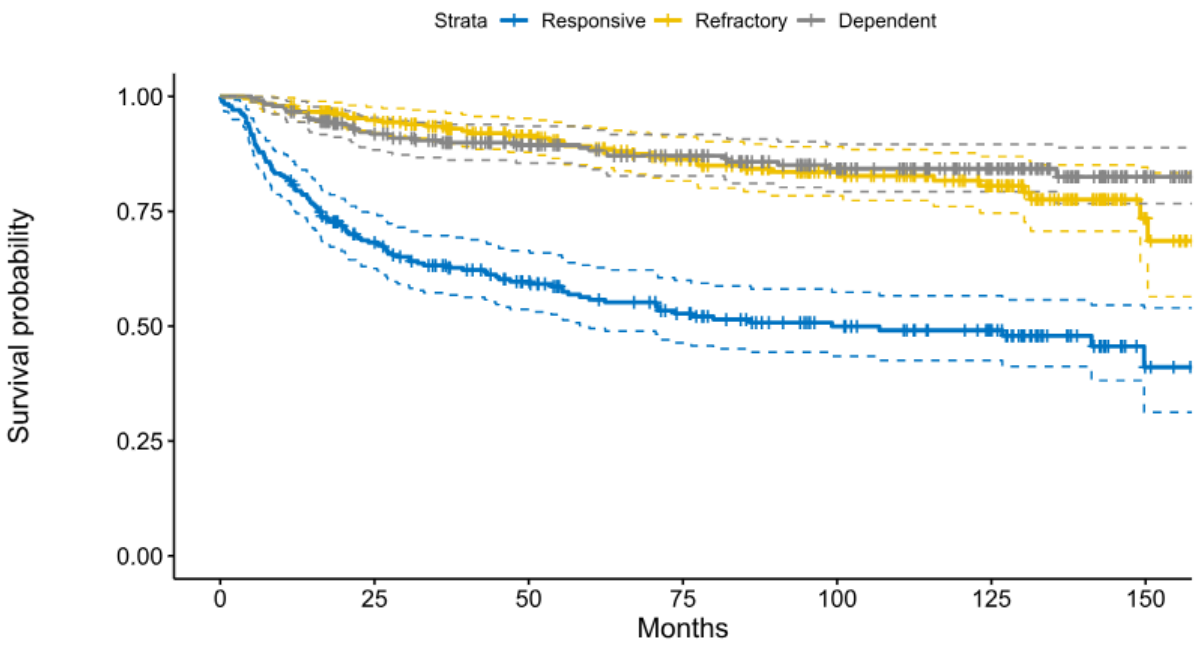
Introduction: Ulcerative colitis (UC), a chronic inflammatory bowel disease, often requires colectomy. Ileal pouch-anal anastomosis (IPAA) can replace ostomy. Up to 50% of IPAA patients experience pouchitis. More real-world data is needed regarding treatments efficacy. The aim was to investigate the choice of treatments, effectiveness, and pouch failure rates.

Methods All patient who underwent IPAA at Copenhagen Univ. Hospital from 1993–2021 were included. Antibiotic responses categorized: dependent, refractory, responsive.

Results: A total 233 IPAA operated patients were analyzed over a median follow-up of 8.36 years. Of these, 118 patients (50.64%) received a total of 529 pouchitis treatments, with 474 (89.6%) involving antibiotics, primarily ciprofloxacin and metronidazole, with a median duration of 11 days. Antibiotic courses exhibited 66% responsiveness and 34% refractoriness/dependency, resulting in patient rates of 46.4% responsive, 14.6% dependent, and 16.3% refractory.

Survival rates are shown in figure 1.



Pouch failure was observed in 13.8% (32) and had various causes: sepsis (33.33%), poor function (52.78%), inflammation (8.33%), and neoplastic transformation (5.56%). Notably, prior to pouch failure, 50.8% of patients experienced responsive pouchitis, 21.9% had dependent pouchitis, and 18.8% had refractory pouchitis.

Conclusion: Study sheds light on pouchitis treatments, effectiveness, failure in UC patients with IPAA. The majority of pouchitis treatments were antibiotics. Antibiotic responsiveness varied among patients, with pouch failure observed in 13.8% of cases.

40. Antibiotic use increases the risk of relapse – A population-based nested case-control study using the Danish National patient registry

Bobby Lo[1,2], Luc Biederman[3], Gerhard Rogler[3], Barbara Dora[3], Andrea Kreienbühl[3], Ida Vind[1,2,4], Flemming Bendtsen[1,2,4], Johan Burisch[1,2]

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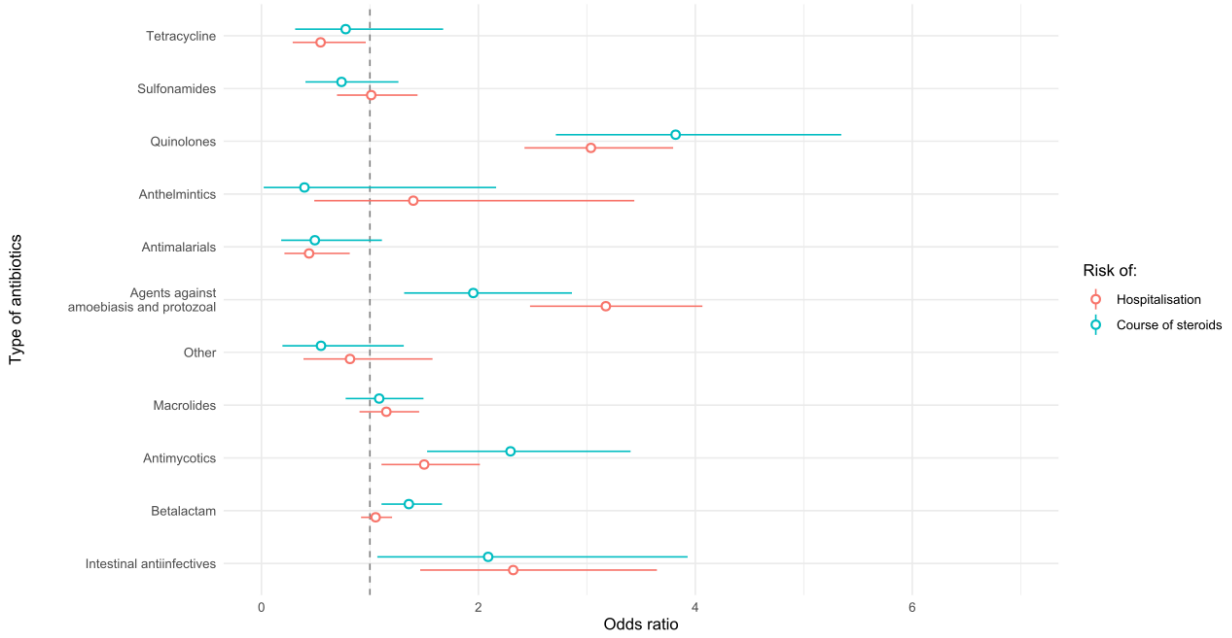
Introduction: Inflammatory bowel disease (IBD) presents chronic gastrointestinal symptoms, e.g., abdominal pain and bloody diarrhea. We investigated environmental factors, including antibiotics, triggering IBD flare-ups using the Danish Nationwide Patient Registry (DNPR).

Methods: DNPR data from 1994-2018, including socioeconomic data, were used. We identified IBD patients from a prior study by Lo et al. Two cohorts, one for steroid use and one for hospitalization, were created. Logistic regression analyzed antibiotic groups' risk for flares, presented as odds ratios (OR) with 95% confidence intervals (95% CI).

Results: In the hospitalization and steroid use cohorts, 15,636 and 5,178 patients were included, respectively. Multivariate logistic regression revealed increased ORs for specific antibiotics. For steroid use, quinolones (OR:3.83), antimycotics (OR:2.30), agents against amoebiasis and protozoal (OR:2.06), betalactam (OR 1.35), and intestinal anti-infectives (OR:2.12) had all an increased risk. For hospitalization, agents against amoebiasis and protozoal (OR:3.48), quinolones (OR:3.10), intestinal anti-infectives (OR:2.42), and antimycotics (OR:1.58) had in increased risk (figure 1).



Conclusion: Certain antibiotics increase IBD flare-up risk. Quinolones, antimycotics, agents vs. amoebiasis/protozoa, betalactam, and intestinal anti-infectives show elevated odds ratios for hospitalization and steroid use. This emphasizes prudent antibiotic use in IBD patients and underscores the need for further research on antibiotic effects in disease progression.

41. Antibiotics are predictive in foreseeing relapse using machine learning methods – A population-based nested case-control study using the Danish National patient registry

Bobby Lo[1,2], Luc Biederman[3], Gerhard Rogler[3], Barbara Dora[3], Andrea Kreienbühl[3], Ida Vind[1,2,4], Flemming Bendtsen[1,2,4], Johan Burisch[1,2]

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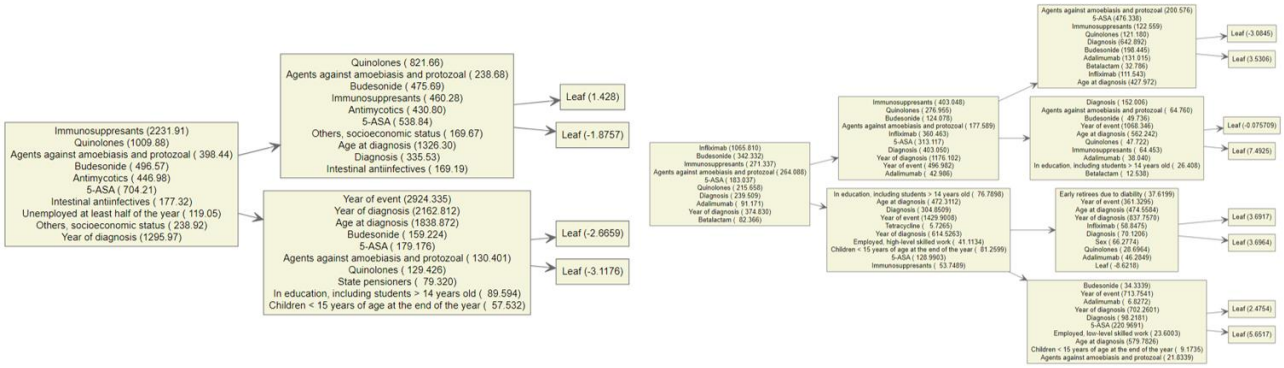
Introduction: Inflammatory bowel disease (IBD) causes chronic gastrointestinal distress. Environmental triggers, like antibiotics , are poorly understood. We used the Danish Nationwide Patient Registry (DNPR) to evaluate antibiotics predictive value for IBD flare-ups.

Methods: DNPR data from 1994-2018, including socioeconomic data, were used. We identified IBD patients from a prior study by Lo et al. Two cohorts, one for steroid use and one for hospitalization, were created. We

employed an 80/20 training/testing split and 5-fold cross-validation with eXtreme Gradient Boosted decision tree (GBDT) models. Model performance was assessed using AUROC, ACC, PPV, and NPV.

Results: 15,636 and 5,178 patients were included in the hospitalization and steroid use cohorts, respectively. GDBT models achieved AUROCs of 0.71 (SD: 0.03) and 0.85 (SD: 0.008) for predicting steroid courses and hospitalization in the training set. On the test-set, ACC was 82.72% for predicting steroid course and 85.23% for predicting hospitalization, with PPV and NPV values provided. Quinolones, agents against amoebiasis and protozoal infections, and other antibiotics emerged as top predictors (figure 1).



Conclusion: This study highlights antibiotics, especially quinolones and agents against amoebiasis and protozoal infections, as valuable for predicting IBD-related flares. GDBT models demonstrated high accuracy, suggesting the potential of antibiotics in forecasting IBD flare-ups and guiding future microbial factor research.