NVGE
NEDERLANDSE VERENIGING VOOR GASTRO-ENTEROLOGIE

DIGESTIVE DISEASE DAYS - DDD

Het programma werd samengesteld met inbreng van de volgende verenigingen en secties:
Nederlandse Vereniging voor Gastroenterologie
Nederlandse Vereniging voor Gastrointestinale Chirurgie
Nederlandse Vereniging voor Hepatologie
Nederlandse Vereniging van Maag-Darm-Leverartsen

Secties:
Netherlands Society of Parenteral and Enteral Nutrition
Sectie Experimentele Gastroenterologie (DEG)
Sectie Gastrointestinale Endoscopie
Sectie Neurogastroenterologie en Motiliteit
Sectie Gastrointestinale Oncologie
Sectie Inflammatoire Darmziekten IBD
Sectie Kinder-MDL
Verpleegkundigen & Verzorgenden Nederland – MDL

INHOUDSOPGAVE **pag.**

Tijdstippen diverse ledenvergaderingen woensdag:

Nederlandse Vereniging voor Hepatologie	20 maart	09.30 uur – Auditorium
Sectie Inflammatoire Darmziekten	20 maart	11.15 uur – Brabantzaal
Nederlandse Vereniging voor Gastroenterologie	20 maart	11.30 uur – Baroniezaal
NVMDL i.o.	20 maart	12.00 uur – Zaal 63

Tijdstippen diverse ledenvergaderingen donderdag:

Nederlandse Vereniging van Maag-Darm-Leverartsen	21 maart	08.00 uur – Zaal 82-83
V&VN MDL	21 maart	09.30 uur - Brabantzaal

Belangrijke mededeling
over de aanwezigheid van farmaceutische industrieën

Aan alle deelnemers tijdens de Digestive Disease Days op 20 en 21 maart 2019

De Nederlandse Vereniging voor Gastroenterologie kent een jarenlange samenwerking met de farmaceutische industrie. De vereniging stelt de farmaceutische industrie in de gelegenheid aanwezig te zijn bij de wetenschappelijke vergaderingen met een stand. Mede hierdoor kan de vereniging haar wetenschappelijke bijeenkomsten organiseren.

De Geneesmiddelenwet zegt dat - onder strikte voorwaarden - de farmaceutische industrie alleen reclame mag maken voor receptgeneesmiddelen voor personen die bevoegd zijn om dergelijke geneesmiddelen voor te schrijven. Alle andere personen (inclusief bijvoorbeeld verpleegkundigen, endoscopie-assistenten en biochemici) worden beschouwd als "publiek". De farmaceutische industrie mag geen reclame maken voor receptgeneesmiddelen voor publiek.

De Nederlandse Vereniging voor Gastroenterologie is een wetenschappelijke vereniging voor personen die beroepsmatig betrokken zijn bij zorg, onderwijs en onderzoek ten behoeve van patiënten met maag-, darm- en leveraandoeningen. Dat betekent dat ook personen die geen arts zijn, lid van de NVGE zijn.
De aanwezigheid van artsen, niet-artsen en farmaceutische industrieën tijdens het congres kan de NVGE ongewild in aanraking brengen met de inspectie voor de gezondheidszorg, sectie reclametoezicht, en daarmee in diskrediet worden gebracht. Dat willen wij uiteraard voorkomen.

In verband met de Gedragscode Geneesmiddelenreclame van de CGR en de aan het NVGE-congres verbonden expositie van farmaceutische producten, medische instrumenten en voedingsmiddelen, zal bij uw congresregistratie via de NVGE-website worden gevraagd naar uw bevoegdheid om medicijnen voor te schrijven.

Alle congresdeelnemers dragen verplicht een congresbadge waarop behalve de naam ook beroep/functie staat aangegeven. Farmaceutische standhouders benaderen uitsluitend congresdeelnemers die de bevoegdheid hebben om receptgeneesmiddelen voor te schrijven of ter hand te stellen. Om dit extra te verduidelijken zal wederom worden gekozen voor verschillende kleuren congresbadges.

Uit het bovenstaande volgt dat aanwezige reclame-uitingen en merkproductinformatie van farmaceutische industrieën alleen gericht zijn op personen die bevoegd zijn om de betreffende geneesmiddelen voor te schrijven. Wij maken u erop attent dat het voor niet-artsen dan ook niet is toegestaan de stands van de aanwezige farmaceutische industrieën te bezoeken.

De NVGE en farmaceutische industrie (sponsoren) vertrouwen erop u met bovenstaande voldoende te hebben geïnformeerd.

Het bestuur van de NVGE

Post ECCO — Brabantzaal

Voorzitter: *A.E. van der Meulen*

10.00 Nieuws in de IBD Immunologie
Dr. C.S. Horjus, MDL-arts, Rijnstate Ziekenhuis, Arnhem

10.15 Update Fase II en III trials M. Crohn en colitis ulcerosa
Dr. M. Löwenberg, MDL-arts, Amsterdam UMC (loc. AMC), Amsterdam

10.30 Nieuws huidige IBD medicatie
Dr. P.W.J. Maljaars, MDL-arts, LUMC, Leiden

10.45 Update kanker risico in de IBD patiënt
Dr. B. Oldenburg, MDL-arts, UMCU, Utrecht

11.00 Nieuws over het microbioom
Prof. dr. R.K. Weersma, MDL-arts, UMCG, Groningen

11.15 Ledenvergadering sectie IBD

11.30 Ledenvergadering en uitreiking van de multidisciplinaire onderzoekssubsidie NVGE in Baroniezaal

NVGE symposium — Brabantzaal

Voorzitters *: B.G.P. Koot en P.B.F. Mensink*

Symposium: Jong gekregen, oud gehouden

13.00 'Gastro-oesofageale reflux; van wieg tot graf'
Dr. M.P. van Wijk, kinderarts-MDL, Amsterdam UMC, (loc. VUmc), Amsterdam
Prof. dr. A.J.P.M. Smout, MDL-arts, Amsterdam UMC, (loc. AMC), Amsterdam

13.40 Transitiezorg voor patiënten met fecale incontinentie.
Dr. M. Groeneweg, kinderarts-MDL, Maasstad Ziekenhuis, Rotterdam
Dr. C.I.M. Baeten, chirurg, Groene Hart Ziekenhuis, Gouda
A.M.C. Baven-Pronk, MDL-arts, Groene Hart Ziekenhuis, Gouda

14.20 Cystic fibrosis, ziektebeeld in transitie: van pancreasenzymen naar colon carcinoom screening.
Dr. F.A.J.A. Bodewes, kinderarts-MDL, UMCG, Groningen
C. Hoge, MDL-arts, MUMC, Maastricht

15.00 Theepauze expositiehal

NVGE symposium **Brabantzaal**

***Voorzitters** : P.D. Siersema en W.H. de Vos tot Nederveen Cappel*

Symposium: Op het grensvlak van pathologie en endoscopie

Slokdarm

15.30 Introductie casus door aios

15.35 De endoscopische behandeling van een vroegcarcinoom in de oesophagus.
Dr. R.E. Pouw, MDL-arts, Amsterdam UMC (loc. AMC), Amsterdam

15.45 Commentaar
Prof. dr. I. Nagtegaal, patholoog, Radboudumc, Nijmegen

15.50 Discussie + Uitkomst casus aios

Maag

16.00 Introductie casus door aios

16.05 Het vroegcarcinoom: onderschat en overschat
Dr. A.D. Koch, MDL-arts, Erasmus MC, Rotterdam

16.15 Commentaar
Prof. dr. I. Nagtegaal, patholoog, Radboudumc, Nijmegen

16.20 Discussie + Uitkomst casus aios

Colon IT

16.30 Introductie casus door aios

16.35 De endoscopische behandeling van een T1 in het colon
Dr. L.M.G. Moons, MDL-arts, UMCU, Utrecht

16.45 Commentaar
Prof. dr. I. Nagtegaal, patholoog, Radboudumc, Nijmegen

16.50 Discussie + Uitkomst casus aios

Colon IBD dysplasie

17.00 Introductie casus door aios

17.05 IBD gerelateerde dysplasie
Dr. A.C. de Vries, MDL-arts, Erasmus MC, Rotterdam

17.15 Commentaar
Prof. dr. I. Nagtegaal, patholoog, Radboudumc, Nijmegen

17.20 Discussie + Uitkomst casus aios

President Select — Brabantzaal

Voorzitters : *P.D. Siersema en C.J. van der Woude*

17.30 **State of the art lecture**
How to recognize acute on chronic liver failure: tips for the attending physician
Prof. dr. J. Wendon, Kings College Hospital, Institute of Liver Sciences, London

18.00 Robot-assisted pancreatoduodenectomy in the Netherlands: a multicenter analysis of the first 100 procedures (p. 35)
C.L.M.A. Nota[1], J. Hagendoorn[1], M.J.W. Zwart[2], I.H.M. Borel Rinkes[1], P.P.L.O. Coene[3], E.W. van der Harst[3], W.W. te Riele[4], T. Tran[5], H.C. van Santvoort[4], B. Groot Koerkamp[5], I.Q. Molenaar[1]. [1]Dept. of Gastrointestinal Surgery, UMC Utrecht, Utrecht. [2]Dept. of Gastrointestinal Surgery, Amsterdam UMC (loc. AMC), Amsterdam. [3]Dept. of Gastrointestinal Surgery, Maasstad Hospital, Rotterdam. [4]Dept. of Gastrointestinal Surgery, St. Antonius Hospital, Nieuwegein. [5]Dept. of Gastrointestinal Surgery, Erasmus MC, Rotterdam, The Netherlands.

18.10 Early endoscopic retrograde cholangiography with biliary sphincterotomy or conservative treatment in predicted severe acute biliary pancreatitis (apec): a multicenter randomized controlled trial (p. 36)
N.J. Schepers[1,2], N.D.L. Hallensleben[2], M.G.H. Besselink[3], M.P.G.F. Anten[2], T.L. Bollen[4], F. van Delft[2], H.M. van Dullemen[2], M.G.W. Dijkgraaf[2], C.H.J. van Eijck[2], G.W. Erkelens[2], N.S. Erler[5], P. Fockens[2], E.J.M. van Geenen[2], H.G. Gooszen[2], J. van Grinsven[3], J.E. van Hooft[2], R.W.M. van der Hulst[2], J.M. Jansen[2], F.J.G.M. Kubben[2], S.D. Kuiken[2], R. Laheij[2], R. Quispel[2], R.J.J. de Ridder[2], M.C.M. Rijk[2], T.E.H. Romkens[2], C.H.M. Ruigrok[2], E.J. Schoon[6], M.P. Schwartz[2], B.W.M. Spanier[2], A.C.I.T.L Tan[2], W.J. Thijs[2], R. Timmer[2], N.G. Venneman[2], R.C. Verdonk[2], F.P. Vleggaar[2], W. van de Vrie[2], B.J. Witteman[2], H.C. van Santvoort[2], O.J. Bakker[2], M.J. Bruno[2]. [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Gastroenterology and Hepatology, [3]Dept. of Surgery[4]. Dept. of Radiology, [5]Dept. of Clinical Epidemiology, Erasmus University Medical Center,. [6]Dept. of Gastroenterology and Hepatology, Catharina Ziekenhuis, Eindhoven,. [7]Dept. of Gastroenterology and Hepatology,St. Antonius Hospital, Nieuwegein, The Netherlands.

18.20 Miltefosine decreases visceral hypersensitivity through modulation of the gut microbiome and mycobiome in a rodent model of Irritable Bowel Syndrome (p. 37)
I.A.M. van Thiel[1], S. Botschuijver[1], S.A. van Diest[1], T.B.M. Hakvoort[1], F.H.J. Schuren[2], W.J. de Jonge[1], R.M. van den Wijngaard[1]. [1]Dept. of Gastroenterology, Tytgat Institute for Liver and Intestinal Research, Amsterdam UMC (loc. AMC), Amsterdam. [2]Dept. of Microbiology and Systems Biology, The Netherlands Organization for Applied Scientific Research (TNO), Zeist.

Uitreiking prijzen — Brabantzaal

Voorzitters : *P.D. Siersema en C.J. van der Woude*

18.30 Uitreiking Gastrostart subsidies

18.35 Uitreiking NVGE Gastrointestinale Research Award 2019 door voorzitter van de jury
Gevolgd door voordracht door de prijswinnaar

18.45 Promotiefilm GastrOlympics

18.50 Congresborrel in de expositiehal.

19.30 Diner in de Beneluxzaal

Nederlandse Vereniging voor Hepatologie **Auditorium**

09.30 Ledenvergadering NVH

Symposium – Nederlandse Vereniging voor Hepatologie **Auditorium**

***Voorzitters** : J.I. Erdmann en J.M. Vrolijk*

Symposium: Do's en don'ts van chirurgie bij levercirrose

10.00 Een hepatologische kijk op leverfunctie, leverfalen en mortaliteit bij leverchirurgie
Prof. dr. H.J. Metselaar, MDL-arts, Erasmus MC, Rotterdam

10.20 Een chirurgische kijk op leverfunctie, leverfalen en mortaliteit bij leverchirurgie
Dr. J.I. Erdmann, chirurg, Amsterdam UMC (loc. AMC), Amsterdam

10.40 Consequenties van operaties anders dan leveroperaties bij patiënten met cirrose
Prof. dr. G. Kazemier, chirurg, Amsterdam UMC (loc. VUmc), Amsterdam

11.00 En erna? Postoperatieve zorg bij patiënten met levercirrose
Dr. C.M. den Hoed, MDL-arts, Erasmus MC, Rotterdam

11.30 Ledenvergadering NVGE in Baroniezaal

12.00 Lunch expositiehal

Symposium – Sectie Gastrointestinale Endoscopie **Auditorium**

***Voorzitters** : M.J.M. Groenen en L.M.G. Moons*

Thema: Future in Endoscopy

13.00 Future Aspects in Barrett's Esophagus
Prof. dr. B.L.A.M. Weusten, MDL-arts, UMCU, Utrecht

13.30 Molecular Imaging in Endoscopy
Dr. W.B. Nagengast, MDL-arts, UMCG, Groningen

13.50 Artificial Intelligence in optical diagnosis
Dr. E.J. Schoon, MDL-arts, Catharina ziekenhuis, Eindhoven

14.10 Future Aspects in ERCP
Dr. A. Inderson, MDL-arts, LUMC, Leiden

14.30 Future of (interventional) Endosonography
Dr. Manuel Perez-Miranda, Head of Gastroenterology & Hepatology, Hospital Universitario Rio Hortega, Spain

15.00 Theepauze in de expositiehal

Symposium – Nederlandse Vereniging van Maag-Darm-Leverartsen **Auditorium**

***Voorzitter** : A.A.M. Masclee*

Symposium: Opioiden gebruik en misbruik

15.30 De stille opioïd epidemie!
Prof. dr. C. Matheï, Dept of Public health and Primary care, KU Leuven

16.00 MDL-artsen: drugsdealers?
Prof. dr. K. Kramers, afd. Interne Geneeskunde en Klinische Farmacie, Radboudumc, Nijmegen

16.30 Het moet beter, maar hoe?
Prof. dr. M. van Kleef, afd. anesthesie en pijnbestrijding, Maastricht UMC, Maastricht

17.00 Ervaringen uit de MDL-praktijk, casuïstiek
Vanuit NGM Task Force

17.30 Plenaire sessie in de Brabantzaal

18.45 Congresborrel in de expositiehal

19.30 Diner in de Beneluxzaal

Meet the expertsessie **Baroniezaal**

Thema: Pancreascarcinoom

10.00 – 11.00

Deze sessie – waarvoor tevoren moet worden ingeschreven - wordt verzorgd door:

Prof. dr. M.J. Bruno, MDL-arts, Erasmus MC, Rotterdam
Dr. M.B.S. Stommel, HPB chirurg, Radboudumc, Nijmegen

Ledenvergadering NVGE **Baroniezaal**

***Voorzitter**: P.D. Siersema*

11.30 Ledenvergadering Nederlandse Vereniging voor Gastroenterologie

12.00 Lunch expositiehal

Abstractsessie - Sectie Inflammatoire Darmziekten **Baroniezaal**

Voorzitters : *A.G.L. Bodelier en B. Oldenburg*

13.00 In-depth characterization of host-genetics and gut microbiome unravels novel host-microbiome interactions in inflammatory bowel disease (p. 38)
S. Hu[1], A. Vich Vila[1], R. Gacesa[1], V. Collij[1], R.J. Xavier[2], C. Stevens[3], M.J. Daly[3], C. Wijmenga[4], H. van Dullemen[1], G. Dijkstra[1], M.C. Visschedijk[1], E. Festen[1], J. Fu[5], A. Kurilshikov[4], A. Zhernakova[4], R. Weersma[1]. [1]Dept. of Gastroenterology and Hepatology, UMC Groningen, Groningen, The Netherlands. [2]Dept. of Gastroenterology, Massachusetts General Hospital, Boston, United States of America. [3]Dept. of Clinical Genetics, Broad Institute, Boston, United States of America. [4]Dept. of Clinical Genetics, UMC Groningen, Groningen, The Netherlands. [5]Dept. of Pediatrics, UMC Groningen, Groningen, The Netherlands.

13.10 Combining absolute quantification of fecal bacteria with metagenomic sequencing data improves the characterization of the gut microbiome of patients with Crohn's disease (p. 39)
A. Vich Vila[1], A.M. Boddeke[1], A. Kurilshikov[2], J.Z.H.V.O Martels[1], V. Collij[1], P. Sureda Horrach[1], A.R. Bourgonje[1], S. Hu[1], A. Zhernakova[2], G. Dijkstra[1], H.J.M. Harmsen[3], R.K. Weersma[1], . [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Clinical Genetics, [3]Dept. of Medical Microbiology, UMC Groningen, Groningen, The Netherlands.

13.20 Detection and monitoring of IBD based on faecal volatile organic compounds (p. 40)
S. Bosch[1], D. Wintjens[2], A. Wicaksono[3], J. Kuijvenhoven[4], R. van der Hulst[4], P. Stokkers[5], E. Daulton[3], M. Pierik[2], J.A. Covington[3], T.G.J. de Meij[6], K.H.N. de Boer[1]. [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. VUmc), Amsterdam, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Maastricht UMC, Maastricht, The Netherlands. [3]School of Engineering, University of Warwick, Coventry, United Kingdom. [4]Dept. of Gastroenterology and Hepatology, Spaarne Gasthuis, Hoofddorp/Haarlem, The Netherlands. [5]Dept. of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis West, Amsterdam, The Netherlands. [6]Dept. of Pediatrics, Amsterdam UMC (loc. VUmc), Amsterdam, The Netherlands.

13.30 Therapeutic drug monitoring in ustekinumab: which factors affect trough levels? (p. 41)
R. Theeuwen[1], N. Provoost[2], C.A.M. de Koning[2], A. van der Meulen-de Jong[2], D.J.A. Moes[3], J. Maljaars[2]. [1]Dept. of Gastroenterology, [2]Dept. of Gastroenterology and Hepatology, [3]Dept. of Clinical Pharmacy and Toxicology, Leiden UMC, Leiden, The Netherlands.

13.40 Higher discontinuation rates of anti-TNF therapy in elderly IBD patients compared to a younger age group: results from a prospective registry (p. 42)
L.J.T. Smits[1], M.E. de Jong[2], N. den Broeder[1], M.G.V.M. Russel[3], T.E.H. Römkens[4], R.L. West[5], J.M. Jansen[6], F. Hoentjen[1]. [1]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen. [2]Dept. of Gastroenterology, Radboudumc, Nijmegen. [3]Dept. of Gastroenterology and Hepatology, Medisch Spectrum Twente, Enschede. [4]Dept. of Gastroenterology and Hepatology, Jeroen Bosch Ziekenhuis, 's Hertogenbosch. [5]Dept. of Gastroenterology and Hepatology, Franciscus Gasthuis & Vlietland, Rotterdam. [6]Dept. of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands.

13.50 Premedication with steroids does not influence the incidence of Infusion Reactions after Infliximab Infusions in paediatric IBD patients - a retrospective case-control study (p. 43)
E.A. van Wassenaer[1], V.L. Meester[2], A. Kindermann[1], B.G.P. Koot[1], M.A. Benninga[1], T.G.J. de Meij[2]. [1]Dept. of Pediatric Gastroenterology, Hepatology and Nutrition, Emma Children's Hospital, Amsterdam UMC, Amsterdam. [2]Dept. of Pediatric Gastroenterology, Hepatology and Nutrition, Emma Children's Hospital, Amsterdam UMC, Amsterdam, The Netherlands.

14.00 Prevalence of cervical dysplasia in women with Inflammatory Bowel Disease: data from the Parelsnoer Institute (PSI) and PALGA database (PAP-IBD study) (p. 44)

R.L. Goetgebuer[1], J.E. Kreijne[1], C.A. Aitken[2], M.J. Pierik[3], F. Hoentjen[4], N.K. de Boer[5], B. Oldenburg[6], A.E. van der Meulen[7], C.I.J. Ponsioen[8], G. Dijkstra[9], F.A. van Kemenade[10], G.M. Nieuwenhuyzen-de Boer[11], A.G. Siebers[12], C.J. van der Woude[1], A.C. de Vries[1]. [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam. [2]Dept. of Public Health, Erasmus MC, Rotterdam. [3]Dept. of Gastroenterology and Hepatology, Maastricht UMC, Maastricht. [4]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen. [5]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. VUmc), Amsterdam. [6]Dept. of Gastroenterology and Hepatology, UMC Utrecht, Utrecht. [7]Dept. of Gastroenterology and Hepatology, Leiden UMC, Leiden. [8]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. AMC), Amsterdam. [9]Dept. of Gastroenterology and Hepatology, UMC Groningen, Groningen. [10]Dept. of Pathology, Erasmus MC, Rotterdam. [11]Dept. of Gynaecologicl Oncology, Erasmus MC, Rotterdam. [12]Dept. of Biomedical Data Sciences, Palga, the nationwide network and registry of histo- and cytopathology in NL, Houten, The Netherlands.

14.10 Increased risk of advanced neoplasia in inflammatory bowel disease patients with recurrent low-grade dysplasia (p. 45)

M.E. de Jong[1], H. Kanne[1], L.H.C. Nissen[2], I.D. Nagtegaal[3], J.P.H. Drenth[1], L.A.A.P. Derikx[1], F. Hoentjen[1]. [1]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen. [2]Dept. of Gastroenterology and Hepatology, Jeroen Bosch Hospital, s' Hertogenbosch. [3]Dept. of Pathology, Radboudumc, Nijmegen, The Netherlands.

14.20 Environmental and lifestyle factors are associated with a divergent effect on the course of Inflammatory Bowel Diseases (p. 46)

H.C. Rijkmans[1], K.W.J. van der Sloot[1], M.C. Visschedijk[1], E.A.M. Festen[1], H.M. van Dullemen[1], R.K. Weersma[1], B.Z. Alizadeh[2], G. Dijkstra[1]. [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Epidemiology, UMC Groningen, Groningen, The Netherlands.

14.32 Treatment of perianal fistulas in Crohn's disease, seton versus anti-TNF versus surgical closure following anti-TNF (PISA): a randomised controlled trial (p. 47)

K.A.T.G.M Wasmann[1], E.J. de Groof[1], M.E. Stellingwerf[1], G.R.A.M. D'Haens[2], C.Y. Ponsioen[2], K.B. Gecse[2], M.G.W. Dijkgraaf[3], W.A. Bemelman[1], C.J. Buskens[1]. [1]Dept. of Surgery, [2]Dept. of Gastroenterology and Hepatology, [3]Dept. of Epidemiology, Amsterdam UMC, The Netherlands.

14.42 Prediction of endoscopic activity in patients with Crohn's disease - systematic review and external validation of published prediction models (p. 48)

E.C. Brand[1], S.G. Elias[2], I.M. Minderhoud[3], J.J. van der Veen[1], F.J. Baert[4], D. Laharie[5], P. Bossuyt[6], Y. Bouhnik[7], A. Buisson[8], G. Lambrecht[9], E. Louis[10], B. Pariente[11], M.J. Pierik[12], C.J. van der Woude[13], G.R.A.M. D'Haens[14], S. Vermeire[15], B. Oldenburg[1]. [1]Dept. of Gastroenterology and Hepatology, UMC Utrecht, Utrecht, The Netherlands. [2]Dept. of Clinical Epidemiology, UMC Utrecht, Utrecht, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, Tergooi Hospitals, Blaricum/Hilversum, The Netherlands. [4]Dept. of Gastroenterology, AZ Delta, Roeselare, Belgium. [5]Dept. of Gastroenterology and Hepatology, Hôpital Haut-Lévêque, Bordeaux, France. [6]Dept. of Gastroenterology, Imelda General Hospital, Bonheiden, Belgium. [7]Dept. of Gastroenterology, Beaujon Hospital, APHP, Paris Diderot University, Clichy, France. [8]Dept. of Gastroenterology, Estaing University Hospital, Clermont-Ferrand, France. [9]Dept. of Gastroenterology, AZ Damiaan, Oostende, Belgium. [10]Dept. of Gastroenterology, Liège University Hospital CHU, Liège, France. [11]Dept. of Gastroenterology, Huriez Hospital, Lille 2 University, Lille, France. [12]Dept. of Gastroenterology and Hepatology, Maastricht UMC, Maastricht, The Netherlands. [13]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, The Netherlands. [14]Dept. of Gastroenterology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands. [15]Dept. of Gastroenterology and Hepatology, University Hospitals Leuven, Leuven, Belgium.

15.00 Theepauze in de expositiehal

Abstractsessie - Sectie Inflammatoire Darmziekten **Baroniezaal**

Voorzitters : *L.J.A.C. Hawinkels en M. Pierik*

15.30 Inleiding
L.J.A.C. Hawinkels

15.40 Two year experience with vedolizumab in inflammatory bowel disease patients: results of the ICC Case Series, a nationwide prospective observational cohort study (p. 49)
V.B.C. Biemans[1], C.J. van der Woude[2], G. Dijkstra[3], A.E. van der Meulen-de Jong[4], B. Oldenburg[5], N.K.H. de Boer[6], M. Löwenberg[7], N. Srivastava[8], J.M. Jansen[9], R. West[10], A.C. de Vries[2], J.J.L. Haans[11], M.J. Pierik[11], F. Hoentjen[12]. [1]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen. [2]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam. [3]Dept. of Gastroenterology and Hepatology, UMC Groningen, Groningen. [4]Dept. of Gastroenterology and Hepatology, Leiden UMC, Leiden. [5]Dept. of Gastroenterology and Hepatology, UMC Utrecht, Utrecht. [6]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. VUmc), Amsterdam. [7]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. AMC), Amsterdam. [8]Dept. of Gastroenterology and Hepatology, Haaglanden MC, Den Haag. [9]Dept. of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam. [10]Dept. of Gastroenterology and Hepatology, Franciscus Gasthuis & Vlietland, Rotterdam. [11]Dept. of Gastroenterology and Hepatology, Maastricht UMC, Maastricht. [12]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, The Netherlands.

15.50 Acetylcholine secreting T-cells contribute to innate immune driven colitis (p. 50)
R.A. Willemze, D.J. Brinkman, O. Welting, H.P. van Hamersveld, M.E. Wildenberg, J. Seppen, W.J. de Jonge. Dept. of Gastroenterology, Tytgat Institute for Liver and Intestinal Research, Amsterdam UMC, Amsterdam, The Netherlands.

16.02 High-dimensional mass cytometry reveals the immune cell landscape in inflammatory bowel disease (p. 51)
L.F. Ouboter[1], V. van Unen[2], N. Li[2], T. Abdelaal[3], Y. Kooy-Winkelaar[2], G. Beyrend[2], T. Höllt[4], M.L. Mearin[5], A.M.C. Witte[6], J.C. Escher[7], B.P.F. Lelieveldt[8], A.E. van der Meulen-de Jong[9], F. Koning[2]. [1]Dept. of Gastroenterology and Hepatology, Leiden UMC, Leiden. [2]Dept. of Immunohematology and Blood Transfusion, Leiden UMC, Leiden. [3]Delft Bioinformatics Lab, Delft University of Technology, Delft. [4]Computer Graphics and Visualization, Delft University of Technology, Delft. [5]Dept. of Pediatrics, Leiden UMC, Leiden. [6]Dept. of Gastroenterology, Alrijne Hospital, Leiderdorp. [7]Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Erasmus MC, Rotterdam. [8]Dept. of LKEB Radiology, Leiden UMC, Leiden. [9]Dept. of Gastroenterology, Leiden UMC, Leiden, The Netherlands.

16.14 Exosomes derived from mesenchymal stromal cells enhance epithelial regeneration in vitro and in experimental colitis induced by DSS in mice (p. 52)
L.G. Plug[1], M.C. Barnhoorn[1], E.S.M. de Jonge-Muller[1], E. Bos[2], A.E. van der Meulen-de Jong[1], H.W. Verspaget[1], L.J.A.C. Hawinkels[1]. [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Cell and Chemical Biology, Leiden UMC, Leiden, The Netherlands.

16.26 Dashboard driven dosing of infliximab is superior to conventional treatment in inflammatory bowel disease: the PRECISION trial (p. 53)
A.S. Strik[1], S.E. Berends[2], D.R. Mould[3], R.A. Mathot[2], C.I. Ponsioen[1], J. van den Brande[4], J. Jansen[5], D.R. Hoekman[6], J.F. Brandse[7], M. Lowenberg[1], G.R. D'Haens[1]. [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands. [2]Dept. of Hospital Pharmacy, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands. [3]Dept. of Hospital Pharmacy, Projections Research Inc., Phoenixville, United States of America. [4]Dept. of Gastroenterology and Hepatology, Tergooi Hospital, Hilversum, The Netherlands. [5]Dept. of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands.

[6]Dept. of Clinical Genetics, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands. [7]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. VUmc), Amsterdam, The Netherlands.

16.38 Faecal calprotectin is an early predictor of endoscopic response and histologic remission after the start of vedolizumab (p. 54)

R.W.M. Pauwels[1], A.C. de Vries[1], J.C. Goet[1], N.S. Erler[2], C.J. van der Woude[1]. [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Biomedical Data Sciences, Erasmus MC, Rotterdam, The Netherlands.

16.50 Prediction model to safely cease anti-TNF therapy in Crohn's disease: individual patient data meta-analysis (IPD-MA) (p. 55)

R.W.M. Pauwels[1], C.J. van der Woude[1], D. Nieboer[2], E.W. Steyerberg[3,12], M.J. Casanova[4], J.P. Gisbert[4], A.J. Lobo[5], C.W. Lees[6], N.A. Kennedy[6], T. Molnár[7], K. Szántó[7], E. Louis[8], J.Y. Mary[9], M. Lukas[10,13], M. Duijvestein[11], S. Bots[11], G.R.A.M. D'Haens[11], A.C. de Vries[1]. [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Health Services Research, Erasmus MC, Rotterdam, The Netherlands. [3]Dept. of Biomedical Data Sciences, Leiden UMC, Leiden, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, Madrid Hospital Universitario de la Princesa, Madrid, Spain. [5]Dept. of Gastroenterology and Hepatology, Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom. [6]Dept. of Gastroenterology and Hepatology, Western General Hospital, Edinburgh, United Kingdom. [7]Dept. of Internal Medicine, University of Szeged, Szeged, Hungary. [8]Dept. of Gastroenterology and Hepatology, Centre Hospitalier Universitaire de Liège, Liège, France. [9]Dept. of Biomedical Data Sciences, Inserm U717, Paris, France. [10]Dept. of Gastroenterology and Hepatology, IBD Clinical and Research Centre, Prague, Czech Republic. [11]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands. [12]Dept. of Public Health, Erasmus MC, The Netherlands. [13]Institute of Medical Biochemistry and Laboratory Diagnostics, 1st Medical Faculty and General Teaching Hospital, Prague, Czech Republic.

17.00 The cytokine milieu in patients with Inflammatory Bowel Disease impacts the phenotype of mesenchymal stromal cells (p. 56)

M.C. Barnhoorn[1], K. Schepers[2], H.W. Verspaget[1], W. Fibbe[2], L.J.A.C. Hawinkels[1], M. van Pel[2], A.E. van der Meulen-de Jong[1]. [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Immunohematology and Blood Transfusion, Leiden UMC, Leiden, The Netherlands.

17.03 PNAd+ and MAdCAM+ High Endothelial Venules correlate with disease activity in ulcerative colitis (p. 57)

B. Roosenboom[1], C.S. Horjus Talabur Horje[1], M.J.M. Groenen[1], C. Smids[1], J. Meijer[2], E.G. van Lochem[3], P.J. Wahab[1]. [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Pathology, [3]Dept. of Immunopathology, Rijnstate Hospital, Arnhem, The Netherlands.

17.15 Mucosal macrophages express elevated levels of HDAC9 in inflamed and uninflamed mucosa of Crohn's disease, but not ulcerative colitis (p. 58)

M. Ghiboub[1], J. de Bruyn[1], C. Wichers[2], T. Radstake[2], K. Reedquist[2], M.E. Wildenberg[1], J. Broen[2], G. D'Haens[3], W. de Jonge[1]. [1]Dept. of Gastroenterology, Amsterdam UMC (loc. AMC), Tytgat Institute for Liver and Intestinal Research, Amsterdam. [2]Dept. of Immunopathology, Utrecht UMC, Utrecht. [3]Dept. of Gastroenterology, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands.

17.30 Voor het plenaire programma kunt u zich begeven naar de Brabantzaal

18.45 Congresborrel in de expositiehal

19.30 Diner in de Beneluxzaal

Meet the expertsessie **Parkzaal**

Thema: IgG gemedieerde ziekte

10.00 – 11.00

Deze sessie – waarvoor tevoren moet worden ingeschreven - wordt verzorgd door

Prof. dr. U.H.W. Beuers, MDL-arts, Amsterdam UMC (loc. AMC), Amsterdam
Dr. H.R. van Buuren, MDL-arts, Erasmus MC, Rotterdam

Abstractsessie - Sectie Gastrointestinale Oncologie **Parkzaal**

Voorzitters : *V.M.C.W. Spaander en N. van Lelyveld*

13.00 Prognostic factors and survival in MEN1 patients with gastrinomas: results from the DutchMEN Study Group (DMSG) (p. 59)
D.J. van Beek[1], S. Nell[1], C.R.C. Pieterman[2], W.W. de Herder[2], A.C. van de Ven[2], O.M. Dekkers[3], A.N. van der Horst-Schrivers[2], M.L. Drent[2], P.H. Bisschop[2], B. Havekes[2], I.H.M. Borel Rinkes[1], M.R. Vriens[1], G.D. Valk[2]. [1]Dept. of Gastrointestinal Surgery, [2]Dept. of Internal Medicine, [3]Dept. of Epidemiology, UMC Utrecht, Utrecht, The Netherlands.

13.10 Endoscopically removed colorectal NETs; a nationwide cohort study (p. 60)
T. Kuiper[1], M.G.H. van Oijen[2], M.L. van Velthuysen[3], N. van Lelyveld[4], M. van Leerdam[5], F.D. Vleggaar[1], H.J. Klumpen[2]. [1]Dept. of Gastroenterology, UMC Utrecht, Utrecht. [2]Dept. of Gastrointestinal Oncology, Amsterdam UMC, Amsterdam. [3]Dept. of Pathology, Erasmus MC, Rotterdam. [4]Dept. of Gastroenterology, St Antonius Hospital, Nieuwegein. [5]Dept. of Gastroenterology, Antoni van Leeuwenhoek, Amsterdam, The Netherlands.

13.20 Effect of perioperative treatment on microsatellite instable gastric cancer in the CRITICS trial (p. 61)
H.D. Biesma[1], K. Sikorska[2], D. Hoek[1], H.F. van Essen[1], B. Ylstra[1], E. Meershoek-Klein Kranenbarg[3], C.J.H. van de Velde[3], H.W.M. van Laarhoven[4], J.W. van Sandick[5], M. Nordsmark[6], M.L. Jespersen[7], M. Verheij[8], A. Cats[9], N.C.T. van Grieken[1]. [1]Dept. of Pathology, Cancer Center Amsterdam - Amsterdam UMC (loc. VUmc), Amsterdam, The Netherlands. [2]Dept. of Biometrics, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands. [3]Dept. of Surgery, Leiden UMC, Leiden, The Netherlands. [4]Dept. of Medical Oncology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands. [5]Dept. of Surgery, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands. [6]Dept. of Medical Oncology, Aarhus University Hospital, Aarhus, Denmark. [7]Dept. of Pathology, Aarhus University Hospital, Aarhus, Denmark. [8]Dept. of Radiotherapy, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands. [9]Dept. of Gastroenterology and Hepatology, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands.

13.30 A comparison of elderly versus non-elderly patients in the CRITICS gastric cancer trial (p.62)
A.E. Slagter[1], B. Tudela[2], R.M. van Amelsfoort[1], K. Sikorska[3], J.W. van Sandick[4], C.J.H. van de Velde[5], N.C.T. van Grieken[6], P. Lind[7], M. Nordsmark[8], H. Putter[9], C. Grootscholten[10], E. Meershoek-Klein Kranenbarg[5], E.P.M. Jansen[1], A. Cats[11], M. Verheij[12]. [1]Dept. of Radiation Oncology, Antoni van Leeuwenhoek, Amsterdam, The Netherlands. [2]Dept. of Radiation Oncology, Universidad de Valparaíso, Valparaíso, Chile. [3]Dept. of Biostatistics, Antoni van Leeuwenhoek, Amsterdam, The Netherlands. [4]Dept. of Surgery, Antoni van Leeuwenhoek,

Amsterdam, The Netherlands. [5]Dept. of Surgery, Leiden UMC, Leiden, The Netherlands. [6]Dept. of Pathology, Amsterdam UMC (loc. VUmc), Amsterdam, The Netherlands. [7]Dept. of Medical Oncology, Karolinska Intitutet, Stockholm, Sweden. [8]Dept. of Medical Oncology, Aarhus University Hospital, Aarhus, Denmark. [9]Dept. of Biostatistics, Leiden UMC, Leiden, The Netherlands. [10]Dept. of Medical Oncology, Antoni van Leeuwenhoek, Amsterdam, The Netherlands. [11]Dept. of Gastrointestinal Oncology, Antoni van Leeuwenhoek, Amsterdam, The Netherlands. [12]Dept. of Radiation Oncology, Radboudumc, Nijmegen, The Netherlands.

13.40 Venous thromboembolism during preoperative chemotherapy in the CRITICS gastric cancer trial (p. 63)

A.E. Slagter[1], K. Sikorska[2], C. Grootscholten[3], H.W.M. van Laarhoven[4], H. Boot[5], E. Meershoek-Klein Kranenbarg[6], C.J.H. van de Velde[6], N.C.T. van Grieken[7], E.P.M. Jansen[1], M. Verheij[8], A. Cats[5]. [1]Dept. of Radiation Oncology, Antoni van Leeuwenhoek, Amsterdam. [2]Dept. of Biostatistics, Antoni van Leeuwenhoek, Amsterdam. [3]Dept. of Medical Oncology, Antoni van Leeuwenhoek, Amsterdam. [4]Dept. of Medical Oncology, Amsterdam UMC (loc. AMC), Amsterdam. [5]Dept. of Gastrointestinal Oncology, Antoni van Leeuwenhoek, Amsterdam. [6]Dept. of Surgery, Leiden UMC, Leiden. [7]Dept. of Pathology, Amsterdam UMC (loc. VUmc), Amsterdam. [8]Dept. of Radiation Oncology, Radboudumc, Nijmegen, The Netherlands.

13.50 Factors associated with the progression of gastric intestinal metaplasia in a low risk population - A multicenter, prospective cohort study (p. 64)

S.A.V. Nieuwenburg[1], M.C. Mommersteeg[1], T.J. Tang[2], M.P. Anten[3], I. Prytz-Berset[4], E. Witteman[5], F. ten Borg[6], G.D. den Hartog[7], M.J. Bruno[1], M.P. Peppelenbosch[1], M. Doukas[8], E.J. Kuipers[1], M.C.W. Spaander[1]. [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, IJsselland Hospital, Capelle a/d IJsel, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, St. Fransiscus Hospital, Rotterdam, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, More and Romsdal Trust, Alesund, Norway. [5]Dept. of Gastroenterology and Hepatology, Canisius-Wilhelmina Hospital, Nijmegen, The Netherlands. [6]Dept. of Gastroenterology and Hepatology, Deventer Hospital, Deventer, The Netherlands. [7]Dept. of Gastroenterology and Hepatology, Rijnstate, Arnhem, The Netherlands. [8]Dept. of Pathology, Erasmus MC, Rotterdam, The Netherlands.

14.00 Patient-reported burden of intensified surveillance and surgery in high-risk individuals under pancreatic cancer surveillance (p. 65)

K.A. Overbeek[1], D.L. Cahen[1], A. Kamps[1], I.C.A.W. Konings[1], F. Harinck[1], M.A. Kuenen[2], B. Groot Koerkamp[3], M.G.H. Besselink[4], A. Wagner[5], M.G.E. Ausems[6], M. van der Vlugt[7], P. Fockens[7], F. Vleggaar[8], J.W. Poley[1], J.E. van Hooft[7], E.M.A. Bleiker[2], M.J. Bruno[1]. [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam. [2]Dept. of Scientific Research, Netherlands Cancer Institute, Amsterdam. [3]Dept. of Surgery, Erasmus MC, Rotterdam. [4]Dept. of Surgery, Amsterdam UMC, University of Amsterdam, Amsterdam. [5]Dept. of Clinical Genetics, Erasmus MC, Rotterdam. [6]Dept. of Clinical Genetics, UMC Utrecht, Utrecht. [7]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam. [8]Dept. of Gastroenterology and Hepatology, UMC Utrecht, Utrecht, The Netherlands.

14.10 12 Years of prospective pancreatic cancer surveillance: results of the Dutch nationwide program in high-risk individuals (p. 66)

K.A. Overbeek[1], I.J.M. Levink[1], I.C.A.W. Konings[1], F. Harinck[1], B. Koopmann[1], M.G.E. Ausems[2], A. Wagner[3], P. Fockens[4], B. Groot Koerkamp[5], M.G.H. Besselink[6], M. van der Vlugt[4], F. Vleggaar[7], J.W. Poley[1], D.L. Cahen[1], J.E. van Hooft[4], M.J. Bruno[1]. [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam. [2]Dept. of Clinical Genetics, UMC Utrecht, Utrecht. [3]Dept. of Clinical Genetics, Erasmus MC, Rotterdam. [4]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam. [5]Dept. of Surgery, Erasmus MC, Rotterdam. [6]Dept. of Surgery, Amsterdam UMC, Amsterdam. [7]Dept. of Gastroenterology and Hepatology, UMC Utrecht, Utrecht, The Netherlands.

14.20 Yield of malignant lymph node detection by EUS and FNA in restaging after neoadjuvant chemoradiotherapy for esophageal cancer (p. 67)

R.D. van der Bogt[1], B.J. van der Wilk[2], J.W. Poley[1], K.K. Krishnadath[3], E.J. Schoon[4], L.E. Oostenbrug[5], P.D. Siersema[6], F.P. Vleggaar[7], K. Biermann[8], J.J.B. van Lanschot[2], M.C.W. Spaander[1]. [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam. [2]Dept. of Surgery, Erasmus MC, Rotterdam. [3]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. AMC), Amsterdam. [4]Dept. of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven. [5]Dept. of Gastroenterology and Hepatology, Zuyderland Medical Center, Heerlen, [6]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen. [7]Dept. of Gastroenterology and Hepatology, UMC Utrecht, Utrecht. [8]Dept. of Pathology, Erasmus MC, Rotterdam, The Netherlands.

14.30 Genomic biomarkers for cancer risk in Barrett's esophagus: an update on the longitudinal dutch barrett's esophagus cohort (p. 68)

K.K. Krishnadath[1,3,7], S.J.M. Hoefnagel[1], W.M. Westra[1], M.R. Timmer[1], P. Martinez[2], E. Klaver[3], C.T. Lau[1], S. Calpe[1], C.M. del Sancho-Serra[1], D. Straub[1], A.M. Baker[2], A.M. Rygiel[1], W.D. Rosmolen[3], S.L. Meijer[5], F.J.W. ten Kate[5], M.G.W. Dijkgraaf[7], R.C. Mallant-Hent[7], A.H.J. Naber[7], A.H.A.M. van Oijen[7], L.C. Blaak[7], P. Scholten[7], C.J.M. Böhmer[7], C.C. Maley[6], T.A. Graham[2], J.J.G.H.M Bergman[3,7]. [1]Center for Experimental and Molecular Medicine, Amsterdam UMC, Amsterdam, The Netherlands. [2]Evolution and Cancer Laboratory, Barts Cancer Institute, London, United Kingdom. [3]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, The Netherlands. [4]Dept. of Oncogenomics, Amsterdam UMC, Amsterdam, The Netherlands. [5]Dept. of Pathology, Amsterdam UMC, Amsterdam, The Netherlands. [6]Biodesign Institute, School of Life Sciences, Arizona State University, Tempe, United States of America. [7]Gastroenterological Association, Amsterdam, The Netherlands.

14.40 Mutational signatures during the preneoplastic cascade towards cholangiocarcinoma in Primary Sclerosing Cholangitis (p. 69)

E.J.C.A. Kamp[1], W.N.M. Dinjens[2], R. van Marion[2], M. Doukas[2], J. Verheij[3], M.J. Bruno[1], B. Groot Koerkamp[4], M.P. Peppelenbosch[1], A.C. de Vries[1]. [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam. [2]Dept. of Pathology, Erasmus MC, Rotterdam. [3]Dept. of Pathology, Amsterdam UMC, University of Amsterdam, Amsterdam. [4]Dept. of Surgery, Erasmus MC, Rotterdam, The Netherlands.

14.50 Trends in incidence, treatment and survival of gallbladder cancer; a nation-wide cohort study (p. 70)

E.A.J. de Savornin Lohman[1], T.J.J. de Bitter[2], R.H. Verhoeven[3], L. van der Geest[3], I.D. Nagtegaal[2], C.J.H.M. van Laarhoven[1], J. Hagendoorn[1], N. Haj Mohammad[5], F. Daams[1], H. Klumpen[4], T.M. van Gulik[1], J.I. Erdmann[1], M.T. de Boer[1], B. Groot Koerkamp[1], A.E. Braat[1], R.J. de Haas[5], P. van der Boezem[1], R.S. van der Post[2], P.R. de Reuver[1]. [1]Dept. of Surgery, [2]Dept. of Pathology, Radboudumc, Nijmegen. [3]Integraal Kankercentrum Nederland (IKNL), Utrecht. [4]Dept. of Medical Oncology, UMC Utrecht, Utrecht. [5]Dept. of Radiology and Nuclear Medicine, Groningen UMC, Groningen, The Netherlands.

15.00 A Functional Assay-Based Procedure to Classify Mismatch Repair Gene Variants in Lynch Syndrome. **(MLDS-voordracht)** (p. 71)

M. Drost[1], Y. Tiersma[1], B.A. Thompson[2,3], A.B. Spurdle[4], J.H. Frederiksen[5], G. Keijzers[5], L. Pappas[6], K.M. Boucher[6], S. Molenkamp[7], J.B. Zonneveld[7], C.J. van Asperen[7], R.H. Sijmons[8], D.E. Goldgar[9], L.J. Rasmussen[5], M.S. Greenblatt[10*], Niels de Wind[1*], S.V. Tavtigian[2*]. [1]Dept. of Human Genetics, Leiden University Medical Center, Leiden, The Netherlands. [2]Dept. of Oncological Sciences, Huntsman Cancer Institute, Salt Lake City, USA. [3]Centre for Epidemiology and Biostatistics, University of Melbourne, Melbourne, Australia. [4]Dept. of Genetics and Computational Biology, QIMR Berghofer Medical Research Institute, Brisbane, Australia. [5]Center for Healthy Aging, University of Copenhagen, Copenhagen, Denmark.*

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15.10 Theepauze expositiehal.

Abstractsessie - Sectie Gastrointestinale Endoscopie — Parkzaal

Voorzitters : *W.B. Nagengast en J. Honing*

15.30 Detection of Barrett's esophagus through exhaled breath using a non-invasive screening tool (p. 72)
Y. Peters[1], R.W.M. Schrauwen[2], A.C. Tan[3], S.K. Bogers[2], B. de Jong[1], P.D. Siersema[1]. [1]Dept. of Gastroenterology and Hepatology, Radboudumc. Nijmegen, [2]Dept. of Gastroenterology and Hepatology, Bernhoven Hospital, Uden. [3]Dept. of Gastroenterology and Hepatology, Canisius Wilhelmina Hospital, Nijmegen, The Netherlands.

15.40 E-Patient Counseling trial (E-PACO): computer based patient education is non-inferior to nurse counseling prior to colonoscopy, a multicenter randomized controlled trial (p. 73)
G. Veldhuijzen[1], M. Klemt-Kropp[2], J.S. Terhaar sive Droste[3], B. van Balkom[4], A.A.J. van Esch[1], J.P.H. Drenth[1]. [1]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen. [2]Dept. of Gastroenterology and Hepatology, Northwest Clinics, Alkmaar. [3]Dept. of Gastroenterology and Hepatology, Jeroen Bosch Hospital, Den Bosch. [4]Dept. of Gastroenterology and Hepatology, Bernhoven Hospital, Uden, The Netherlands.

15.50 EndoRotor ablation of Barrett's esophagus; a safety and feasibility study (p. 74)
A.W. Gotink[1], Y. Peters[2], M.J. Bruno[1], P.D. Siersema[2], A.D. Koch[1]. [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam. [2]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, The Netherlands.

16.00 Predictors of adequate sampling in EUS guided TA of solid pancreatic lesions in a large prospective cohort of Dutch community hospitals (p. 75)
H.M. Schutz[1], R. Quispel[1], S.A. Mulder[1], A.Y. Thijssen[2], L. Brouwer-Hol[3], C.E. Fitzpatrick[4], M.P.G.F. Anten[5], B.J. Veldt[1], L.M.J.W. van Driel[6], M.J. Bruno[6]. [1]Dept. of Gastroenterology and Hepatology, Reinier de Graaf Gasthuis, Delft. [2]Dept. of Gastroenterology and Hepatology, Albert Schweitzer Hospital, Dordrecht. [3]Dept. of Gastroenterology and Hepatology, Maasstad Hospital, Rotterdam. [4]Dept. of Gastroenterology and Hepatology, IJsselland Hospital, Capelle a/d Ijssel. [5]Dept. of Gastroenterology and Hepatology, Franciscus Gasthuis & Vlietland, Rotterdam. [6]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, The Netherlands.

16.10 Guidance for setting alternative competence criteria for optical diagnosis of diminutive colorectal polyps which are easier to implement in daily practice - a simulation study (p. 76)
B.B.S.L. Houwen[1], M.J. Greuter[2], J.L.A. Vleugels[1], Y. Hazewinkel[1], V.H.M. Coupe[2], E. Dekker[1]. [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. AMC) Amsterdam. [2]Dept. of Epidemiology and Biostatistics, Amsterdam UMC (loc. VUmc), Amsterdam, The Netherlands.

16.20 Single-step treatment with endoscopic resection and cryoballoon ablation is feasible and safe in an esophageal porcine model (p. 77)
A. Overwater[1], L.A.A. Brosens[2], B.L.A.M. Weusten[1]. [1]Dept. of Gastroenterology and Hepatology,

St. Antonius Hospital & UMC Utrecht, Utrecht. [2]Dept. of Pathology, UMC Utrecht, Utrecht, The Netherlands.

Woensdag 20 maart 2019

16.30 Clinical outcome of endoscopic treatment of symptomatic sterile walled-off necrosis (p. 78)
L. Boxhoorn[1], J.A. Fritschze[1], P. Fockens[1], J.E. van Hooft[1], P.J.F. de Jonge[2], J.W. Poley[2], M.J. Bruno[2], R.P. Voermans[2]. [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam. [2]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, The Netherlands.

16.40 Feasibility, safety, tolerability and dose-related efficacy of a novel CryoBalloon Swipe Ablation (CbSAS90) device in dysplastic Barrett's esophagus (p. 79)
A. Overwater[1], S.N. van Munster[2], G.M. Raicu[3], C.A. Seldenrijk[3], W.B. Nagengast[4], E.J. Schoon[5], J.J.G.H.M Bergman[2], B.L.A.M. Weusten[1]. [1]Dept. of Gastroenterology and Hepatology, St. Antonius Hospital & UMC Utrecht, Utrecht. [2]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam. [3]Dept. of Pathology, Pathology DNA, St. Antonius Hospital, Nieuwegein. [4]Dept. of Gastroenterology and Hepatology, UMC Groningen, Groningen. [5]Dept. of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven, The Netherlands.

16.50 Deep learning algorithm for characterization of Barrett's neoplasia demonstrates high accuracy on NBI-zoom images (p. 80)
M.R. Struyvenberg[1], A.J. de Groof[1], J. van der Putten[2], F. van der Sommen[2], F. Baldaque Silva[3], R. Bisschops[4], E.J. Schoon[5], W.L. Curvers[5], P.H.N. de With[2], J.J. Bergman[1]. [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, The Netherlands. [2]Dept. of Electrical Engineering, VCA group, Eindhoven University of Technology, Eindhoven, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, Karolinska University Hospital, Stockholm, Sweden. [4]Dept. of Gastroenterology and Hepatology, University Hospitals Leuven, Leuven, Belgium. [5]Dept. of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven, The Netherlands.

17.00 Measuring KRAS mutations in pancreatic cyst fluid by droplet digital PCR and Next-Generation Sequencing (p. 81)
N.C.M. van Huijgevoort[1], F. Dijk[2], J.B.G. Halfwerk[2], S.J. Lekkerkerker[1], R.J. Reinten[2], P. Fockens[1], M.G. Besselink[3], O.R. Busch[3], C.J.M. van Noesel[2], M.J. van de Vijver[2], J. Verheij[2], J.E. van Hooft[1]. [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Pathology, [3]Dept. of Surgery, Amsterdam UMC, Amsterdam, The Netherlands.

17.10 Treatment of disconnected and disrupted pancreatic duct in necrotizing pancreatitis: a systematic review and meta-analysis (p. 82)
S.M. van Dijk[1], H.C. Timmerhuis[2], R.C. Verdonk[3], E. Reijnders[1], M.J. Bruno[4], P. Fockens[5], R.P. Voermans[5], M.G. Besselink[1], H.C. van Santvoort[2]. [1]Dept. of Surgery, Amsterdam UMC (loc. AMC), Amsterdam. [2]Dept. of Surgery, St. Antonius Hospital, Nieuwegein. [3]Dept. of Gastroenterology and Hepatology, St. Antonius Hospital, Nieuwegein. [4]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam. [5]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands.

17.20 Resultaten van survey van de Sectie Gastrointestinale Endoscopie
J. Honing, aios MDL, UMCU, Utrecht

17.30 Plenaire sessie in de Brabantzaal

18.45 Congresborrel

20.00 Diner in de Beneluxzaal

Woensdag 20 maart 2019

Meet the expertsessie **Zaal 80**

Thema: Pancreascarcinoom

13.00 – 14.00

Deze sessie – waarvoor tevoren moet worden ingeschreven - wordt verzorgd door:

Prof. dr. M.J. Bruno, MDL-arts, Erasmus MC, Rotterdam
Dr. M.B.S. Stommel, HPB chirurg, Radboudumc, Nijmegen

Meet the expertsessie **Zaal 81**

Thema: IgG gemedieerde ziekte

13.00 – 14.00

Deze sessie – waarvoor tevoren moet worden ingeschreven - wordt verzorgd door:

Prof. dr. U.H.W. Beuers, MDL-arts, Amsterdam UMC (loc. AMC), Amsterdam
Dr. H.R. van Buuren, MDL-arts, Erasmus MC, Rotterdam

Digitalisering in de zorg **Zaal 80**

Voorzitters : *M.P. Schwartz en J.J. van Dijk-Kuiper*

Thema: Digitalisering in de zorg

15.30 Introductie minisymposium

15.40 MijnIBDCoach
Dr. A.E. van der Meulen- de Jong, MDL-arts Leids Universitair Medisch Centrum

16.00 Versnellingsprogramma Informatie-uitwisseling tussen patiënt en professional (VIPP)
I. van Es, senior beleidsadviseur NVZ

16.20 Wat kunnen we binnen de MDL met een patiëntenportaal?
J.J. van Dijk-Kuiper, MDL-arts Albert Schweitzer ziekenhuis

16.40 Lagerhuisdebat omtrent de digitalisering in de zorg
J. Rijpma, Senior Public Affairs Adviseur NVZ

17.00 Einde programma in deze zaal, vervolg plenaire sessie in de Brabantzaal vanaf 17.30

Symposium – Nederlandse Vereniging voor Gastrointestinale Chirurgie I — Beneluxhal

Voorzitters: *Dr. O. van Ruler en M. Ditzel*

IBD

09.00 IBD voor Dummies/Chirurgen
Prof. dr. G. Dijkstra, MDL-arts, UMCG, Groningen

09.15 IBD-chirurgie in NL: waar zijn we mee bezig?
Dr. J.F.M. Lange, chirurg, UMCG, Groningen

09.30 Registreren, who cares? UR-CARE!
Dr. J.D.W. van der Bilt, chirurg, Flevoziekenhuis, Almere

09.45 TAMIS in IBD-chirurgie
Dr. E.J.R. de Graaf, chirurg, IJsselland ziekenhuis, Capelle a/d IJssel

10.00 Operatieve behandeling Crohnse colitis
Prof. dr. L.P.S. Stassen, chirurg, MUMC, Maastricht

10.15 Medicamenteuze onderhoudstherapie versus chirurgie bij Crohn
Dr. K.B. Gecse, MDL-arts, Amsterdam UMC (loc. AMC), Amsterdam

10.30 Koffiepauze in de expositiehal

Symposium – Nederlandse Vereniging voor Gastrointestinale Chirurgie II — Beneluxhal

Voorzitters: *L.P.S. Stassen en H. Cakir*

Fluorescentie & het colorectaal carcinoom

11.00 Welkom & introductie

11.05 Fluorescentie bij endoscopische screening colorectaal carcinoom
Dr. W.B. Nagengast, MDL-arts, UMCG, Groningen

11.20 Fluorescentie ter beoordeling perfusie colorectale anastomose
Dr. R. Hompes, colorectaal chirurg, Amsterdam UMC (loc. AMC), Amsterdam

11.35 Fluorescentie imaging van de ureter tijdens colorectale chirurgie
M. Al Taher, aios/arts-onderzoeker, Zuyderland ziekenhuis/MUMC

11.50 Imaging technieken voor perioperatieve beoordeling colorectale levermetastasen
Dr. R.J. Swijnenburg, HPB chirurg, Amsterdam UMC (loc. AMC), Amsterdam

12.05 Tumorspecifieke probes, HIPEC, en andere nieuwe ontwikkelingen
Dr. A.L. Vahrmeijer, HPB chirurg, LUMC, Leiden

12.30 Lunchpauze in de expositiehal

Symposium – Nederlandse Vereniging voor Gastrointestinale Chirurgie III — Beneluxhal

Voorzitter: *Dr. E. van der Harst en A.P.T. van der Ploeg*

Highlights from Lowlands

13.30 Adjuvante hypertherme intraperitoneale chemotherapie (HIPEC) bij patienten met coloncarcinoom met hoog risico op peritonitis carcinomatosis (COLOPEC trial)
C.E.L. Klaver, arts-onderzoeker, Amsterdam UMC (loc. AMC), Amsterdam

13.45 SNAPSHOT study betreffende behandeling obstructief linkszijdig coloncarcinoom
F. Amelung, arts-assistent chirurgie, UMCU, Utrecht

14.00 Vroege chirurgische interventie versus huidige stapsgewijze behandeling bij patienten met chronische pancreatitis (ESCAPE)
A.M. Kempeneers, arts-onderzoeker, Amsterdam UMC (loc. AMC), Amsterdam

14.15 Vroege ERC met sfincterotomie versus conservatieve behandeling bij patienten met voorspeld ernstige biliaire pancreatitis (APEC trial)
N.J. Schepers, aios MDL, Albert Schweitzer ziekenhuis, Dordrecht

14.30 Chirurgie versus conservatieve behandeling van recidiverende diverticulitis en persisterende klachten na diverticulitis: 5 jaar uitkomsten van de DIRECT-Trial
H. Bolkenstein, arts-onderzoeker, Meander Medisch Centrum, Amersfoort

14.45 Lange termijn oncologische en funtionele uitkomsten van chemoradiatie gevolgd door orgaansparende transanale endoscopische microchirurgie voor het distale rectum-carcinoom: de CARTS Studie.
Dr. R. Stijns, arts-onderzoeker, Radboudumc, Nijmegen

15.00 Laparascopische cholecystectomie versus percutane catheter drainage bij hoog-risico patienten met acute cholecystitis (CHOCOLATE trial)
Dr. C.S. Loozen, arts-onderzoeker, St. Antonius ziekenhuis, Nieuwegein

15.30 Einde programma, koffie/thee in de expositiehal

Abstractsessie - Sectie Gastrointestinale Oncologie — Auditorium

Voorzitters : *L. van Vlerken en n.t.b.*

09.30 Is decompressing stoma a better alternative than stent as bridge to surgery for left-sided obstructive colon cancer? A nationwide, propensity score matched analysis (p. 83)
J.V. Veld[1], F.J. Amelung[2], W.A.A. Borstlap[1], E.E. van Halsema[3], E.C.J. Consten[2], P.D. Siersema[4], F. ten Borg[5], E.S. van der Zaag[6], P. Fockens[3], W.A. Bemelman[1], J.E. van Hooft[3], P.J. Tanis[1]. [1]Dept. of Surgery, Amsterdam UMC, University of Amsterdam, Amsterdam, [2]Dept. of Surgery, Meander MC, Amersfoort, [3]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, University of Amsterdam, Amsterdam, [4]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, [5]Dept. of Surgery, Deventer Hospital, Deventer, [6]Dept. of Surgery, Gelre Hospital, Apeldoorn, The Netherlands.

9.40 Changes in management of left-sided obstructive colon cancer: national practice and guideline implementation (p. 84)

J.V. Veld[1], F.J. Amelung[2], W.A.A. Borstlap[1], E.E. van Halsema[3], E.C.J. Consten[2], P.D. Siersema[4], F. ten Borg[5], E.S. van der Zaag[6], P. Fockens[3], W.A. Bemelman[1], J.E. van Hooft[3], P.J. Tanis[1]. [1]Dept. of Surgery, Amsterdam UMC, University of Amsterdam, Amsterdam, [2]Dept. of Surgery, Meander MC, Amersfoort, [3]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, University of Amsterdam, Amsterdam, [4]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, [5]Dept. of Surgery, Deventer Hospital, Deventer, [6]Dept. of Surgery, Gelre Hospital, Apeldoorn, The Netherlands.

9.50 Early detection of colorectal cancer and advanced adenomas based on faecal volatile organic compounds (p. 85)

S. Bosch[1], R. Bot[1], A. Wicaksono[2], J. Kuijvenhoven[3], R. van der Hulst[3], P. Stokkers[4], J.A. Covington[2], T.G.J. de Meij[5], N.K.H. de Boer[1]. [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. VUmc), Amsterdam, The Netherlands. [2]School of Engineering, University of Warwick, Coventry, United Kingdom. [3]Dept. of Gastroenterology and Hepatology, Spaarne Gasthuis, Hoofddorp/Haarlem, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis West, Amsterdam, The Netherlands. [5]Dept. of Pediatrics, Amsterdam UMC (loc. VUmc), Amsterdam, The Netherlands.

10.00 Interval cancers after a negative faecal immunochemical test in the first screening round in the Netherlands for two cut-off levels (p. 86)

E. Toes-Zoutendijk[1], A.I. Kooyker[1], E. Dekker[2], M.C.W. Spaander[3], A.W.J. Opstal-van Winden[1], C. Ramakers[4], M. Buskermolen[1], A.J. van Vuuren[3], E.J. Kuipers[3], F.J. Kemenade[5], M.F. Velthuysen[5], M.G.J. Thomeer[6], H. van Veldhuizen[7], M. van Ballegooijen[1], I. Nagtegaal[8], H.J. Koning[1], M. van Leerdam[9], I. Lansdorp-Vogelaar[1]. [1]Dept. of Public Health, Erasmus MC, Rotterdam, [2]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. AMC), Amsterdam, [3]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, [4]Dept. of Clinical Laboratory, Erasmus MC, Rotterdam, [5]Dept. of Pathology, Erasmus MC, Rotterdam, [6]Dept. of Radiology, Erasmus MC, Rotterdam, [7]IQ Healthcare, Erasmus MC, Rotterdam, [8]Dept. of Pathology, Radboudumc, Nijmegen, [9]Dept. of Gastroenterology and Hepatology, Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, The Netherlands.

10.10 Post-colonoscopy mortality in a FIT-based colorectal cancer screening program (p. 87)

A.I. Kooyker[1], E. Toes-Zoutendijk[2], A.W.J. Opstal-van Winden[2], M.C.W. Spaander[3], E. Dekker[4], M. Buskermolen[2], A.J. van Vuuren[3], E.J. Kuipers[3], F.J. van Kemenade[5], H. van Veldhuizen[2], M.G.J. Thomeer[6], I. Nagtegaal[7], C. Ramakers[8], M. van Ballegooijen[2], H. Koning[2], I. Lansdorp-Vogelaar[2], M.E. van Leerdam[1]. [1]Dept. of Gastroenterology, Netherlands Cancer Institute, Amsterdam, [2]Dept. of Public Health, Erasmus MC, Rotterdam, [3]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, [4]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. AMC), Amsterdam, [5]Dept. of Pathology, Erasmus MC, Rotterdam, [6]Dept. of Radiology, Erasmus MC, Rotterdam, [7]Dept. of Pathology, Radboudumc, Nijmegen, [8]Dept. of Cell and Chemical Biology, Erasmus MC, Rotterdam, The Netherlands.

10.20 Joint surgical and gastroenterological assessment to decide on the optimal treatment of early colorectal neoplasia. (p. 88)

K.M. Gijsbers[1], A.K. Talsma[2], R.J.I. Bosker[2], F. ten Borg[1]. [1]Dept. of Gastroenterology, [2]Dept. of Surgery, Deventer Hospital, Deventer, The Netherlands.

10.30 Koffiepauze in de expositiehal

Symposium - Sectie Gastrointestinale Oncologie — Auditorium

Voorzitters : *L. Brouwer-Hol en M. Bigirwamungu-Bargeman*

Shared decision making

11.00 Casuïstiek
Aios MDL

11.10 "De kunst van het samen beslissen"
Dr. A. Pieterse, cognitief psycholoog, UHD medische besliskunde, LUMC

11.35 "Samen beslissen in de dagelijkse praktijk"
Dr. M. van der Kolk, GE-chirurg, Radboudumc, Nijmegen

12.05 "To care or to cure? Behandeling van oudere patiënten met kanker"
Dr. Frederiek van den Bos, internist-ouderengeneeskunde, UMC, Utrecht

12.30 Lunchpauze in de expositiehal

Abstractsessie - Sectie Experimentele Gastroenterologie — Baroniezaal

Voorzitters : *D.M.A.E. Jonkers en L.J.A.C. Hawinkels*

09.00 Discovery and selection of HBV-derived T cell targets for global immunotherapy based on HLA binding, conservation and viral indispensability (p. 89)
M.T.A. de Beijer[1], D.T.S.L. Jansen[1], Y. Dou[1], W.J.E. van Esch[2], J.Y. Mok[2], M.J.P. Maas[2], G. Brasser[2], R.A. de Man[1], A.M. Woltman[1], S.I. Buschow[1]. [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam. [2]Dept. of Research & Development, Sanquin, Amsterdam, The Netherlands.

09.12 Mass spectrometry analysis of HLA class I peptides presented on human hepatocytes and hepatocellular carcinoma to guide antigen-based immunotherapy (p. 90)
M.T.A. de Beijer[1], K. Bezstarosti[2], R. Bouzid[1], P.J. Biesta[1], R.A. de Man[1], A.M. Woltman[1], J.A. Demmers[2], S.I. Buschow[1]. [1]Dept. of Gastroenterology and Hepatology, [2]Proteomics Center, Erasmus MC, Rotterdam, The Netherlands.

09.24 Combined TRC105/PD1 therapy synergistically inhibits tumor growth by targeting immune suppressing cells and activation cytotoxic responses (p. 91)
M.J.A. Schoonderwoerd[1], R. Angela[1], M. Koops[1], C.P. Theuer[2], J.C.H. Hardwick[1], M.F. Fransen[3], L.J.A.C. Hawinkels[1]. [1]Dept. of Gastroenterology and Hepatology, Leiden UMC, Leiden, The Netherlands. [2]Dept. of Scientific Research, TRACON Pharmaceuticals, San Diego, United States of America. [3]Dept. of Immunohematology and Blood Transfusion, Leiden UMC, Leiden, The Netherlands.

09.36 VCAM/Endoglin positive subpopulations of Mesenchymal Stromal (stem) Cells reverse fibrogenesis in experimental liver fibrosis (p. 92)
D. van der Helm, J.J. Habibe, M.C. Barnhoorn, E.S.M. de Jonge-Muller, M.J. Coenraad, B. van Hoek, H.W. Verspaget. Dept. of Gastroenterology and Hepatology, Leiden UMC, Leiden, The Netherlands.

09.48 Pasteurized whey protein improves maturation of the immature intestine of preterm and near-term piglets (p. 93)
M. Navis[1], V. Muncan[1], P.T. Sangild[2], L. Møller Willumsen[2], P. Koelink[1], M.E. Wildenberg[1], E. Abrahamse[3,4], T. Thymann[2], R.M. van Elburg[3,5], I.B. Renes[3,5]. [1]Tytgat Institute for Liver and Intestinal Research, Amsterdam UMC, Amsterdam, The Netherlands. [2]Dept. of Pediatric Gastroenterology, Hepatology and Nutrition, Comparative Pediatrics & Nutrition, University of Copenhagen, Copenhagen, Denmark. [3]Dept. of Gastroenterology and Hepatology, Danone Nutricia Research, Utrecht, The Netherlands. [4]Laboratory of Food Chemistry, Wageningen University, Wageningen, The Netherlands. [5]Dept. of Pediatrics, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, The Netherlands.

10.00 Autophagy regulates Rac1GTP and RhoAGTP activity in dendritic cells and epithelial cell lines (p. 94)
M.M.C. Prins, F.P. Giugliano, P.J. Koelink, G.R. van der Brink, M.E. Wildenberg. Dept. of Gastroenterology and Hepatology, Tytgat Institute for Intestinal and Liver Research, Amsterdam, The Netherlands.

10.12 Whole-exome sequencing in early-onset primary sclerosing cholangitis: first results of the WHELP-study (p. 95)
S.M. Haisma[1], R.K. Weersma[2], M.E. Joosse[3], B.A.E. de Koning[3], T. de Meij[4], B.G.P. Koot[5], V.W. Wolters[6], O. Norbruis[7], M.J. Daly[8], C. Stevens[8], R.J. Xavier[8], M.A. Rivas[9], M.C. Visschedijk[2], H.J. Verkade[1], R. Barbieri[2], B.H. Jansen[2], E.A.M. Festen[2], P.F. van Rheenen[1], C.C. van Diemen[10]. [1]Dept. of Pediatric Gastroenterology, Hepatology and Nutrition, UMC Groningen, Groningen, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, UMC Groningen, Groningen, The Netherlands. [3]Dept. of Pediatric Gastroenterology, Hepatology and Nutrition, Erasmus MC, Rotterdam, The Netherlands. [4]Dept. of Pediatric Gastroenterology, Hepatology and Nutrition, Amsterdam UMC (loc. VUmc), Amsterdam, The Netherlands. [5]Dept. of Pediatric Gastroenterology, Hepatology and Nutrition, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands. [6]Dept. of Pediatric Gastroenterology, Hepatology and Nutrition, UMC Utrecht, Utrecht, The Netherlands. [7]Dept. of Pediatrics, Isala, Zwolle, The Netherlands. [8]Dept. of Biomedical Data Sciences, Broad Institue of Harvard and Massachusetts Institute of Technology, Boston, United States of America. [9]Dept. of Biomedical Data Sciences, Stanford University, Stanford, United States of America. [10]Dept. of Clinical Genetics, UMC Groningen, Groningen, The Netherlands.

10.30 Koffiepauze in de expositiehal

Abstractsessie - Sectie Experimentele Gastroenterologie — Baroniezaal

Voorzitters : *D.M.A.E. Jonkers en N. Festen*

11.00 Loss of intestinal Indian Hedgehog enhances Apc-driven tumorigenesis (p. 96)
B.F. Westendorp, O.N. Karpus, M. van Roest, S. Meisner, N.V.J.A. Büller, M.E. Wildenberg, V. Muncan, G.R. van den Brink. Dept. of Gastroenterology and Hepatology, Tytgat Institute for Liver and Intestinal Research, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands.

11.12 Loss of the Bone Morphogenetic Protein signalling in myofibroblasts initiates polyp formation in the mouse intestine (p. 97)
S. Ouahoud[1], L.R.A. van der Burg[1], P.W. Voorneveld[1], C. Steenkamp[1], J.A.D.E. Erinkveld[1], E.S.M. de Jonge-Muller[1], G.J. Offerhaus[3], L.J.A.C. Hawinkels[1], J.C.H. Hardwick[1]. [1]Dept. of Gastroenterology and Hepatology, Leiden UMC, Leiden, [2]Dept. of Pathology, UMC Utrecht, Utrecht, The Netherlands.

11.24 Inhibition of BMP2 and BMP4 eradicates Barrett's esophagus and enhances the regeneration of squamous epithelium (p. 98)

K.K. Krishnadath[1,2], A. Correia[1], D. Straub[1], S.J.M. Hoefnagel[1], S. Calpe[1], M. Read[3], W. Philips[3]. [1]Center for Experimental and Molecular Medicine, Amsterdam UMC, Amsterdam, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, The Netherlands. [3]Dept. of Experimental Surgery, Peter MacCallum Oncology Center, Melbourne, Australia.

11.36 A chemoradiotherapy treatment response mRNA signature as predictor for esophageal adenocarcinoma treated according to the CROSS regimen (p. 99)

K.K. Krishnadath[1,2,8], S.J.M. Hoefnagel[1,2], J. Koster[3], W.J. Koemans[4], J.M. van Dieren[5], J.W. van Sandick[4], L.L. Kodach[6], S. Calpe[1], S.L. Meijer[7,8], C.M. del Sancho-Serra[1], H.N. Khan[1], H.W.M. van Laarhoven[8], M.I. van Berge Henegouwen[8], S.S. Gisbertz[8], M.C.C.M. Hulshof[8]. [1]Center for Experimental and Molecular Medicine, Amsterdam UMC, Amsterdam, [2]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, [3]Dept. of Oncogenomics, Amsterdam UMC, Amsterdam, [4]Dept. of Surgical Oncology, The Netherlands Cancer Institute, Amsterdam, [5]Dept. of Gastrointestinal Oncology, The Netherlands Cancer Institute, Amsterdam, [6]Dept. of Pathology, The Netherlands Cancer Institute, Amsterdam, [7]Dept. of Pathology, Amsterdam UMC, Amsterdam, [8]Esophagal Cancer Workgroup, Amsterdam UMC, Amsterdam, The Netherlands.

11.48 Genetic variants of innate immunity receptors are associated with mortality but not with bacterial infections in liver cirrhosi (p. 100)

J.J. Schaapman[1], A. Amoros[2], J.J. van der Reijden[3], W. Laleman[4], S. Zeuzem[5], R. Bañares[6], R. Jalan[7], V. Arroyo[2], H.W. Verspaget[3], M.J. Coenraad[3]. [1]Dept. of Gastroenterology and Hepatology, Leiden UMC, Leiden, The Netherlands. [2]Dept. of Hepatology, European Foundation for the study of chronic liver failure, Barcelona, Spain. [3]Dept. of Gastroenterology and Hepatology, Leiden UMC, Leiden, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, UZ Leuven, Leuven, Belgium. [5]Dept. of Gastroenterology and Hepatology, Universitätsklinikum Frankfurt, Frankfurt, Germany. [6]Dept. of Gastroenterology and Hepatology, Gregorio Marañón Hospital, Madrid, Spain. [7]Dept. of Gastroenterology and Hepatology, University College London Hospital, London, United Kingdom.

11.51 The effects of citrus flavonoids on intestinal permeability and inflammation using an in vitro co-culture model (p. 101)

Y. Stevens[1,2], A.A.M. Masclee[1], T. de Bie[2], L. van de Ven[2], D. Jonkers[1]. [1]Dept. of Gastroenterology and Hepatology, Maastricht UMC, Maastricht, [2]Dept. of Scientific Research, BioActor B.V., Maastricht, The Netherlands.

11.54 HNF4A is essential for intestinal epithelial regeneration upon radiation-induced injury (p. 102)

S.P. Montenegro-Miranda[1], J.H.M. van der Meer[1], C. Jones[2], S. Meisner[1], J.L.M. Vermeulen[1], F. Boudreau[2], A. Ribeiro[3], G.R. van den Brink[1], V. Muncan[1]. [1]Tytgat Institute for Liver and Intestinal Research, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands. [2]Département Pavillon de recherche appliquée sur le cancer, Sherbrooke, Canada, [3]Centre de Recherche des Cordeliers, Sorbonne Universités, Université Pierre et Marie Curie, Paris, France.

11.57 Luminal preservation of the human small bowel graft reduces mucosal damage during cold storage P. 103)

G. Trentadue[1], A.M. de Jong[1], J. van Praagh[2], M. Clarysse[3], E. Canovai[4], L. Ceulemans[5], J. Pirenne[5], J.W. Haveman[6], K.N. Faber[1], G. Dijkstra[1]. [1]Dept. of Gastroenterology and Hepatology, UMC Groningen, Groningen, The Netherlands. [2]Dept. of Clinical Pharmacy, UMC Groningen, Groningen, The Netherlands. [3]Dept. of Gastrointestinal Surgery, University Hospitals Leuven, Leuven, Belgium. [4]Dept. of Surgery, Elisabeth-TweeSteden Hospital, Tilburg, The Netherlands. [5]Dept. of Surgery, University Hospitals Leuven, Leuven, Belgium. [6]Dept. of Surgery, UMC Groningen, Groningen, The Netherlands.

Donderdag 21 maart 2019

12.00 Battle (3 presentaties van 5 minuten)

12.15 Abstract en battle prijs

12.30 Lunchpauze in de expositiehal

Abstractsessie - Nederlandse Vereniging voor Gastroenterologie — Parkzaal

Voorzitters: *W.H. de Vos tot Nederveen Cappel en J.M. Conchillo*

09.00 A history of cholecystectomy is associated with higher rates of metabolic syndrome and nonalcoholic fatty liver disease: a population based study (p. 104)
C.S.S. Latenstein[1], L.J.M. Alferink[2], S. Darwish Murad[2], J.P.H. Drenth[3], C.J.H.M. van Laarhoven[1], P.R. de Reuver[4]. [1]Dept. of Surgery, Radboudumc, Nijmegen, [2]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, [3]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, [4]Dept. of Gastrointestinal Surgery, Radboudumc, Nijmegen, The Netherlands.

09.10 Ethnicity and response to primary standard three-dose hepatitis B vaccination in employees in The Netherlands. 1983 through 2017 (p. 105)
Ö.M. Koc[1], C. Menart[2], J. Theodore[2], C. Kremer[3], N. Hens[3], G.H. Koek[2], A.M.L. Oude Lashof[1]. [1]Dept. of Medical Microbiology, Maastricht UMC, Maastricht, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Maastricht UMC, Maastricht, The Netherlands. [3]Dept. of Clinical Epidemiology, Hasselt University, Hasselt, Belgium.

09.20 Serum lipidomics profiling as a diagnostic tool for NAFLD in children: a matched case-control pilot study (p. 106)
L.G. Draijer[1], D. Torenstra[1], A.E. Bohte[2], F.M. Vaz[3], M. van Weeghel[3], M.A. Benninga[1], B.G.P. Koot[1]. [1]Dept. of Pediatric Gastroenterology, Hepatology and Nutrition, [2]Dept. of Radiology and Nuclear Medicine, [3]Dept. of Gastroenterology and Metabolism, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands.

09.30 Risk factors for symptomatic gallstone disease after Roux-en-Y gastric bypass (p. 107)
S. Haal[1], D. Rondagh[2], P. Fockens[1], B.A. Hutten[3], Y.I.Z. Acherman[4], R.P. Voermans[1], V.E.A. Gerdes[2], R. Huijgen[2]. [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. AMC), Amsterdam, [2]Dept. of Internal Medicine, MC Slotervaart, Amsterdam, [3]Dept. of Epidemiology, Amsterdam UMC (loc. AMC), Amsterdam, [4]Dept. of Surgery, MC Slotervaart, Amsterdam, The Netherlands.

09.40 A multicentre randomized non-inferiority trial comparing usual care to restrictive strategy for use of cholecystectomy in patients with gallstones and abdominal pain (SECURE trial) (p. 108)
A.H. van Dijk[1], S.Z. Wennmacker[2], P.R. de Reuver[2], C.S.S. Latenstein[2], O. Buyne[3], S.C. Donkervoort[4], Q.A.J. Eijsbouts[5], J. Heisterkamp[6], K. in t Hof[7], J. Janssen[8], V.B. Nieuwenhuis[9], H.M. Schaap[10], P. Steenvoorde[11], H.B.A.C. Stockmann[5], D. Boerma[12], G.P. Westert[13], J.P.H. Drenth[14], M.G.W. Dijkgraaf[15], M.A. Boermeester[1], C.J.H.M. van Laarhoven[2]. [1]Dept. of Surgery, Amsterdam UMC (loc. AMC), Amsterdam, [2]Dept. of Surgery, Radboudumc, Nijmegen, [3]Dept. of Surgery, Maashospital Pantein, Boxmeer, [4]Dept. of Surgery, Onze Lieve Vrouwe Gasthuis East, Amsterdam, [5]Dept. of Surgery, Spaarne Gasthuis, Hoofddorp, [6]Dept. of Surgery, Elisabeth-Tweesteden Hospital, Tilburg, [7]Dept. of Surgery, Flevohospital, Almere, [8]Dept. of Surgery, Admiraal de Ruyter Hospital, Goes, [9]Dept. of Surgery, Isala, Zwolle, [10]Dept. of Surgery, Treant Zorggroep, Emmen, [11]Dept. of Surgery, Medisch Spectrum Twente, Enschede, [12]Dept. of Surgery, Antonius Hospital, Nieuwegein, [13]Dept. of Research & Development, Radboudumc, Nijmegen, [14]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, [15]Dept. of Clinical Epidemiology, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands.

09.50 Per-oral endoscopic pyloromyotomy for severe refractory gastroparesis: a feasibility and efficacy study in the Netherlands (p. 109)
J.M. Conchillo[1], J.W. Straathof[1], E.L. Venema[1], N.D. Bouvy[2], A.A.M. Masclee[1]. [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Surgery, Maastricht UMC, Maastricht, The Netherlands.

10.00 Long-term follow-up of gut-directed hypnotherapy self-exercises at home using CD versus individual therapy by qualified therapists in children with irritable bowel syndrome or functional abdominal pain (syndrome) (p. 110)
R. Rexwinkel[1], A.M. Vlieger[2], J.F.M. Bovendeert[1], J.M.T.M. Rutten[1], C. Frankenhuis[1], M.A. Benninga[1]. [1]Dept. of Pediatric Gastroenterology, Hepatology and Nutrition, Emma Children's Hospital, Amsterdam, [2]Dept. of Pediatrics, St. Antonius Hospital, Nieuwegein, The Netherlands.

10.10 Reduction in IBS symptom severity does not result in improved quality of life in patients with irritable bowel syndrome (p. 111)
Z.Z.R.M. Weerts, L. Vork, Z. Mujagic, D. Keszthelyi, M. Hesselink, D.M.A.E. Jonkers, A.A.M. Masclee. Dept. of Gastroenterology and Hepatology, Maastricht UMC, Maastricht, The Netherlands.

10.20 Koffiepauze

Abstractsessie - Sectie Neurogastroenterologie en Motiliteit — Parkzaal

Voorzitters : *J.M. Conchillo en F.B. van Hoeij*

11.00 Day-to-day variability in fecal microbiota and its association with stool consistency: do we need repeated sample collection on the short-term? (p. 112)
L. Vork[1], J. Penders[2], S. van Kuijk[3], J. Jalanka[4], M. Rajilic-Stojanovic[5], C. Bojic[5], C. Manichanh[6], M. Pozuelo[6], A.A.M. Masclee[1], D. Jonkers[1]. [1]Dept. of Gastroenterology and Hepatology, Maastricht UMC, Maastricht, The Netherlands. [2]Dept. of Medical Microbiology, Maastricht UMC, Maastricht, The Netherlands. [3]Dept. of Clinical Epidemiology and Medical Technology Assessment, Maastricht UMC, Maastricht, The Netherlands. [4]Dept. of Medical Microbiology, University of Helsinki, Helsinki, Finland, [5]Dept. of Chemical and Biomolecular Engineering, University of Belgrade, Belgrade, Serbia, [6]Dept. of Digestive Diseases, University Hospital Vall d'Hebron, Barcelona, Spain.

11.10 Physiotherapy for children with functional constipation: a pragmatic randomized controlled trial in primary care (p. 113)
J.J.G.T. van Summeren[1], G.A. Holtman[1], B.J. Kollen[1], Y. Lisman-van Leeuwen[1], A.H.C. van Ulsen-Rust[2], M.M. Tabbers[3], J.H. Dekker[1], M.Y. Berger[1]. [1]Dept. of General Practice and Elderly Care Medicine, UMC Groningen, Groningen, [2]Dept. of Physiotherapy, Pelvicum children's pelvic physiotherapy, Groningen, [3]Dept. of Pediatric Gastroenterology, Hepatology and Nutrition, Emma Children's Hospital, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands.

11.20 Opioid usage is significantly associated with rectal hyposensitivity and functional evacuation disorders in patients with chronic constipation (p. 114)
P.F. Vollebregt, S.M. Scott, J. Miller, C.H. Knowles. Centre for Trauma and Surgery and GI Physiology Unit, Queen Mary University of London, London, United Kingdom.

11.30 A prospective evaluation of gastrointestinal symptoms and dysmotility in subjects with and without Hypermobility Spectrum Disorders (p. 115)
L. Vork[1], A.A.M. Masclee[1], A. Beckers[1], J. Conchillo[1], J. Kruimel[1], Q. Aziz[2], D. Keszthelyi[1]. [1]Dept. of Gastroenterology and Hepatology, Maastricht UMC, Maastricht, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Queen Mary University of London, London, United Kingdom.

11.40 Diagnostic value of inflammatory parameters in the work-up of functional abdominal pain (p. 116)
J. Zeevenhooven[1], R. Rexwinkel[1], E. Tromp[2], M.A. Benninga[1], A.M. Vlieger[2]. [1]Dept. of Pediatric Gastroenterology, Hepatology and Nutrition, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Amsterdam, [2]Dept. of Pediatrics, St. Antonius Hospital, Nieuwegein, The Netherlands.

11.50 The socioeconomic burden of IBS in a Dutch population (p. 117)
Z.Z.R.M. Weerts[1], D. Keszthelyi[1], J. Willems[1], D.J.P.A. Janssen[1], B. Essers[2], D.M.A.E. Jonkers[1], A.A.M. Masclee[1]. [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Clinical Epidemiology and Medical Technology Assessment, Maastricht UMC, Maastricht, The Netherlands.

12.00 Prevalence of child abuse in children with functional constipation (p. 118)
M.H. Vriesman[1], T.F. Vrolijk- Bosschaart[2], S.N. Brilleslijper-Kater[2], A.H. Teeuw[2], R.J.L. Lindauer[3], M.A. Benninga[1]. [1]Dept. of Pediatric Gastroenterology, Hepatology and Nutrition, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Amsterdam, [2]Dept. of Social Pediatrics, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Amsterdam, [3]Dept. of Child and Adolescent Psychiatry, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands.

12.10 A smartphone application for symptom assessment and data collection in medical trials: example from an IBS drug intervention trial (p. 119)
Z.Z.R.M. Weerts, A.B.A. Quanjel, L. Vork, D.M.A.E. Jonkers, A.A.M. Masclee, D. Keszthelyi. Dept. of Gastroenterology and Hepatology, Maastricht UMC, Maastricht, The Netherlands.

12.20 Coexistence of fecal incontinence and constipation in adults is an underappreciated clinical problem (p. 120)
P.F. Vollebregt, U. Grossi, R.P. McCaughan, C.H. Knowles, S.M. Scott. Centre for Trauma and Surgery and GI Physiology Unit, Queen Mary University of London, London, United Kingdom.

12.30 Lunchpauze in de expositiehal

Abstractsessie - Nederlandse Vereniging voor Gastrointestinale Chirurgie I — Zaal 80

Voorzitters : *M. Coolsen en J.A.M.G. Tol*

09.30 Proposed method for adequate surgical gallbladder examination (p. 121)
B.J.G.A. Corten[1], W.K.G. Leclercq[1], P.H. van Zwam[2], R.M.H. Roumen[1], G.D. Slooter[1]. [1]Dept. of Surgery, Máxima Medical Center, Veldhoven, [2]Dept. of Pathology, Laboratory for Pathology and Medical Microbiology (PAMM), Veldhoven, The Netherlands.

09.40 Selective histological examination after cholecystectomy; an analysis of current daily practice in the Netherlands (p. 122)
B.J.G.A. Corten, W.K.G. Leclercq, R.M.H. Roumen, G.D. Slooter. Dept. of Surgery, Máxima Medical Center, Veldhoven, The Netherlands.

09.50 Nationwide outcome including long-term quality of life after total pancreatectomy (PANORAMA) (p.123)
A.E.J. Latenstein[1], L. Scholten[1], J.E. van Hooft[2], B.A. Bonsing[3], K. Bosscha[4], P.P.L.O. Coene[5], R.M. van Dam[6], S. van Dieren[1], C.H.J. van Eijck[7], J. Erdmann[8], M.F. Gerhards[8], H. van Goor[8], E. van der Harst[8], I.H. de Hingh[8], G. Kazemier[8], J.M. Klaase[8], S. Mieog[8], I.Q. Molenaar[8], G. Patijn[8], H. van Santvoort[8], J.J. Scheepers[8], G.P. van der Schelling[8], F.J. Snoek[8], B.K. Pranger[8], O.R.C. Busch[1], J.H. DeVries[8], M.G. Besselink[1]. [1]Dept. of Surgery, Amsterdam UMC, Amsterdam, [2]Dept. of

Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, [3]Dept. of Surgery, Leiden UMC, Leiden, [4]Dept. of Surgery, Jeroen Bosch Hospital, Den Bosch, [5]Dept. of Surgery, Maasstad Hospital, Rotterdam, [6]Dept. of Surgery, Maastricht UMC, Maastricht, [7]Dept. of Surgery, Erasmus MC, Rotterdam, [8]Dept. of Surgery, Amsterdam UMC (loc. VUmc), Amsterdam, The Netherlands.

10.00 Textbook outcome as a novel quality measure in pancreatic surgery: a nationwide analysis (p. 124)
S. van Roessel[1], T.M. Mackay[2], S. van Dieren[2], G.P. van der Schelling[2], V.B. Nieuwenhuijs[2], K. Bosscha[2], E. van der Harst[2], R.M. van Dam[2], M.S.L. Liem[2], S. Festen[2], M.W.J. Stommel[2], D. Roos[2], F. Wit[2], I.Q. Molenaar[2], V.E. de Meijer[2], I.H.J.T. de Hingh[2], H.C. van Santvoort[2], B.A. Bonsing[2], O.R.C. Busch[2], B. Groot Koerkamp[2], M.G.H. Besselink[2]. [1]Dept. of Surgery, Amsterdam UMC, Amsterdam, [2]Dept. of Surgery, Reinier de Graaf Gasthuis, Delft, The Netherlands.

10.10 Comparing the revised European, AGA and IAP guidelines on pancreatic cystic neoplasms: accuracy in identifying advanced neoplasia in IPMN (p. 125)
N.C.M. van Huijgevoort[1], S. ten Bokkel-Huinink[1], S.J. Lekkerkerker[1], I. Somers[2], M. Del Chiaro[3], P. Fockens[1], M.G. Besselink[4], J.E. van Hooft[1]. [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, The Netherlands. [2]Dept. of Radiology, Amsterdam UMC, Amsterdam, The Netherlands. [3]Dept. of Surgery, University of Colorado Anschutz Medical Campus, Aurora, United States of America. [4]Dept of Surgery, Amsterdam UMC, Amsterdam, The Netherlands.

10.20 Risk factors for the development of vascular complications after liver transplantation (p. 126)
Y. Li[1], L.M. Nieuwenhuis[2], M.J.M. Werner[2], R.J. Porte[2], O.B. van Leeuwen[2], H. Blokzijl[1], E.A.M. Festen[1], V.E. de Meijer[2]. [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Surgery, UMC Groningen, Groningen, The Netherlands.

10.30 Koffiepauze in de expositiehal

Abstractsessie - Nederlandse Vereniging voor Gastrointestinale Chirurgie II — Zaal 80

Voorzitters : *R.J.J. Verhage en G. Vijgen*

11.00 Palliative gastrectomy for advanced gastric cancer does not result in additional morbidity compared to curative gastrectomy (p. 127)
E.C. Gertsen[1], H.J.F. Brenkman[2], L. Goense[3], N. Haj Mohammad[4], B.L.A.M. Weusten[5], R. van Hillegersberg[1], J.P. Ruurda[1]. [1]Dept. of Surgery, UMC Utrecht, Utrecht, [2]Dept. of Surgery, Diakonessenhuis, Utrecht, [3]Dept. of Surgery, Sint Antonius Hospital, Nieuwegein, [4]Dept. of Medical Oncology, UMC Utrecht, Utrecht, [5]Dept. of Gastroenterology and Hepatology, UMC Utrecht, Utrecht, The Netherlands.

11.10 A national cohort study evaluating the association of short-term outcome indicators with long-term survival after esophageal and gastric cancer surgery (p. 128)
L.R. van der Werf[1], B.P.L. Wijnhoven[2], J.W. van Sandick[3], G.A.P. Nieuwenhuijzen[4], L.A.D. Busweiler[5], R. van Hillegersberg[6], M.W.J.M. Wouters[3], M.I. van Berge Henegouwen[7]. [1]Dept. of Surgery, Erasmus MC, Rotterdam, [2]Dept. of Gastrointestinal Surgery, Erasmus MC, Rotterdam, [3]Dept. of Surgery, Antoni van Leeuwenhoek Hospital, Amsterdam, [4]Dept. of Surgery, Catharina Hospital, Eindhoven, [5]Dept. of Surgery, Amsterdam UMC, Amsterdam, [6]Dept. of Surgery, UMC Utrecht, Utrecht, [7]Dept. of Gastrointestinal Surgery, Amsterdam UMC, Amsterdam, The Netherlands.

11.20 Added value of MRI to endoscopic and endosonographic response assessment after neoadjuvant chemoradiotherapy in oesophageal cancer: a pilot study (p. 129)
S.E. Vollenbrock[1], J.M. van Dieren[2], F.E.M. Voncken[3], S.T. van Turenhout[2], L.L. Peppelenbosch-Kodach[4], K.J. Hartemink[5], B.M.P. Aleman[3], R.G.H. Beets-Tan[1], A. Bartels-Rutten[1]. [1]Dept. of Radiology, [2]Dept. of Gastrointestinal Oncology, [3]Dept. of Radiation Oncology, [4]Dept. of Pathology, [5]Dept. of Surgery, Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands.

11.30 Direct oral feeding following minimally invasive esophagectomy (NUTRIENT II trial): an international, multicenter, open-label randomized controlled trial. (p. 130)
L.F.C. Fransen[1], G.H.K. Berkelmans[1], A.C.P. Dolmans-Zwartjes[1], E.A. Kouwenhoven[2], M.J. van Det[2], M. Nilsson[3], G.A.P. Nieuwenhuijzen[1], M.D.P. Luyer[1]. [1]Dept. of Surgery, Catharina Hospital, Eindhoven, The Netherlands. [2]Dept. of Surgery, Hospitalgroup Twente, Almelo, The Netherlands. [3]Dept. of Surgery, Karolinska Institute and Karolinska University Hospital, Stockholm, Sweden.

11.40 The preoperative fecal lipidome but not fecal microbial diversity predicts postoperative ileus in elective colorectal surgery (p. 131)
D.J. Brinkman[1], J. Lewis[2], S.E. Mason[2], S.J. Cameron[2], Z. Takats[2], A. Darzi[2], W.J. de Jonge[1], J. Kinross[2]. [1]Dept. of Gastroenterology, Amsterdam UMC, Amsterdam, The Netherlands. [2]Dept. of Surgery, Imperial College, London, United Kingdom.

11.50 Adhesion-related hospital readmissions in patients with open or laparoscopic abdominal or pelvic surgery: A nationwide cohort study (SCAR update) (p. 132)
P. Krielen, M.W.J. Stommel, H. van Goor, R.P.G. ten Broek. Dept. of Surgery, Radboudumc, Nijmegen, The Netherlands.

12.00 IMAGINE: Ileus Management International (p. 133)
S.Z. Kuiper. Dept. of Gastrointestinal Surgery, Maastricht UMC, Maastricht, The Netherlands. On behalf of the EuroSurg Collaborative.

12.10 Efficacy and safety of additional autologous Platelet Rich Stroma in transanal mucosal advancement flap repair of complex cryptoglandular anal fistulas (p. 134)
J.H.C. Arkenbosch[1], O. van Ruler[2], W.B. Deijl[2], H.P. Stevens[3], A.C. de Vries[1], C.J. van der Woude[1], E.J.R. de Graaf[2], W.R. Schouten[2,4]. [1]Dept. of Gastroenterology, Erasmus MC, Rotterdam, [2]Dept. of Colorectal Surgery, IJsselland Hospital, Capelle a/d IJssel, [3]Dept. of Plastic and Reconstructive Surgery, Bergman Clinics, Bilthoven, [4]Dept. of Colorectal Surgery, Erasmus MC, Rotterdam, The Netherlands.

12.20 Decline in unnecessary surgery for locally advanced rectal cancer due to adequate multidisciplinary response evaluation following chemo-radiotherapy (p. 135)
J.F. Huisman[1], I.J.H. Schoenaker[2], R.M. Brohet[3], O. Reerink[4], H. van der Sluis[1], F.C.P. Moll[5], E. de Boer[6], J.C. de Graaf[7], G.L. Beets[8], W.H. de Vos tot Nederveen Cappel[1], H.L. van Westreenen[9]. [1]Dept. of Gastroenterology and Hepatology, Isala, Zwolle, [2]Dept. of Gastrointestinal Oncology, Isala, Zwolle, [3]Dept. of Epidemiology, Isala, Zwolle, [4]Dept. of Radiotherapy, Isala, Zwolle, [5]Dept. of Pathology, Isala, Zwolle, [6]Dept. of Radiology, Isala, Zwolle, [7]Dept. of Internal Medicine, Isala, Zwolle, [8]Dept. of Surgery, Antoni van Leeuwenhoek, Amsterdam, [9]Dept. of Surgery, Isala, Zwolle, The Netherlands.

12.30 Randomised clinical trial of selective decontamination of the digestive tract in elective colorectal cancer surgery (the SELECT trial). **(MLDS-voordracht)** (p. 136)
G.S.A. Abis[1,2], H.B.A.C. Stockmann[1], H.J. Bonjer[2], N. van Veenendaal[2], M.L.M. van Doorn-Schepens[2], A.E. Budding[2], J.A. Wilschut[2], M. van Egmond[2], S.J. Oosterling[1]. [1]Dept of Surgery, Spaarne Gasthuis Haarlem/Hoofddorp. [2] Dept of Surgery, Amsterdam UMC, location VUmc, Amsterdam, The Netherlands.

12.40 Lunchpauze in de expositiehal

Cursorisch onderwijs in maag-darm-leverziekten **Brabantzaal**

Cursuscommissie: Dr. B. Oldenburg, MDL-arts, UMCU, Utrecht, voorzitter
Dr. E.J.M. van Geenen, Radboudumc, Nijmegen
Dr. I.L. Holster, aios MDL, Albert Schweitzer, Dordrecht
Dr. M.A.J.M. Jacobs, MDL-arts, VUmc, Amsterdam
Dr. Y. Keulemans, MDL-arts, Zuyderland, Heerlen
Dr. J.F.M. Lange, chirurg, UMCG, Groningen
Dr. A.M.J. Langers, MDL-arts, LUMC, Leiden
Drs. M. Radersma, aios MDL, OLVG, Amsterdam
Dr. B.J. Veldt, MDL-arts, Reinier de Graaf Gasthuis, Delft
Dr. L.G. van Vlerken, MDL-arts, Antoni van Leeuwenhoek Amsterdam

13.30-13.40 uur Opening: Dr. B. Oldenburg, MDL-arts, UMCU, Utrecht
Pre-test vragen

Onderwerp: Dunne Darm I

Voorzitters: *Dr. M.A.J.M. Jacobs, MDL-arts, VUmc, Amsterdam*
Dr. L.G. van Vlerken, MDL-arts, Antoni van Leeuwenhoek, Amsterdam

13.40-14.00 uur Coeliakie en gluten-overgevoeligheid
Prof. dr. G. Bouma, MDL-arts, Amsterdam UMC, VUmc
Leerdoelen: nieuwe inzichten die in de richtlijn zouden moeten komen, de waarheid over gluten overgevoeligheid

14.00-14.20 uur Beeldvorming van de dunne darm: ballon enteroscopie, video capsule of MRI
Dr. S.J.B van Weyenberg, MDL-arts, Spaarne Gasthuis, Hoofddorp
Leerdoelen: aan de hand van casuïstiek duidelijk maken wanneer welke techniek moet of kan worden ingezet

14.20-14.40 uur Bariatrische chirurgie: de chirurg en de endoscopist
J.A. Apers, chirurg, St. Franciscus, Rotterdam
Leerdoelen: overzicht in de verschillende technieken, waarbij de nadruk moet liggen op endoscopische bevindingen, complicaties en beperkingen

14.40-15.00 uur Bariatrische chirurgie: complicaties op langere termijn
Dr. P.J. Wahab, MDL-arts, Rijnstate, Arnhem
Leerdoelen: overzicht geven van complicaties op het gebied van deficiënties, bloedingen, obstructies, galstenen en preventieve en therapeutische handreikingen

15.00-15.30 uur Pauze in de expositiehal

Cursorisch onderwijs in maag-darm-leverziekten **Brabantzaal**

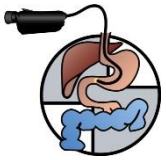
Onderwerp: Pancreatitis

Voorzitters:	*Dr. I..L. Holster, aios MDL, Albert Schweitzer, Dordrecht* *Dr. J.F.M. Lange, chirurg, UMCG, Groningen*
15.30-15.50 uur	Pancreatitis, NIET veroorzaakt door galstenen, alcohol of de endoscopist Dr. H.R. van Buuren, MDL-arts, Erasmus MC, Rotterdam *Leerdoelen: Wanneer dient aan alternatieve diagnoses gedacht te worden, wat is de differentiaal diagnose, welke diagnostiek moet worden ingezet?*
15.50-16.10 uur	Diagnose en therapie van acute pancreatitis Dr. E.J.M. van Geenen, Radboudumc, Nijmegen *Leerdoelen: wat is het standaardbeleid aangaande infusiebeleid, voeding, beeldvorming?*
16.10-16.30 uur	Endoscopische behandeling van complicaties van pancreatitis Prof. dr. F.P. Vleggaar, MDL-arts, UMCU, Utrecht *Leerdoelen: wat zijn de indicaties voor transgastrische benadering of stenting, hoe dient dit te worden verricht, hoe is de verdere follow up?*
16.30-16.50 uur	Chronische pancreatitis: pijn en andere complicaties Prof. dr. M.A. Boermeester, chirurg, UMCA, locatie AMC, Amsterdam *Leerdoelen: indicaties voor interventies (pijn, recidiverende flares ..), keuzes.*
16.50-17.20 uur	Pauze bij de Limburgfoyer

Onderwerp: Dunne Darm II

Voorzitters:	*Prof. dr. M.A. Boermeester, chirurg, Amsterdam UMC, locatie AMC, Amsterdam* *Drs. M. Radersma, aios MDL, OLVG, Amsterdam*
17.20-17.40 uur	Darmischemie revisited Prof. dr. J.J. Kolkman, MDL-arts, Medisch Spectrum Twente, Enschede *Leerdoelen: wanneer opnemen in de differentiaal diagnose, hoe te bevestigen, wanneer verwijzen, hoe te behandelen?*
17.40-18.00 uur	Short Bowel syndroom, TPV en dunne darm transplantatie Prof. dr. G. Dijkstra, MDL-arts, UMCG, Groningen *Leerdoelen: welke behandelstappen moeten worden gezet bij de behandeling van een short bowel. Wanneer TPV, wanneer Groningen bellen?*
18.00-18.20 uur	Quiz en prijsuitreiking, sluiting
18.30-19.30 uur	Indisch buffet in Restaurant Uithof

V&VN ochtendprogramma I — Brabantzaal



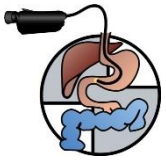
Beroepsvereniging van zorgprofessionals
Maag Darm Lever

Voorzitters : *Mw. T.A. Korpershoek, voorzitter V&VN MDL*

Thema: MDL algemeen

09.30	Algemene ledenvergadering
10.10	#MDLISOVERAL *Dr. M. ter Borg, MDL-arts, Maxima Medisch Centrum, Eindhoven*
10.30	Gastro intestinale stroma tumor (GIST) *P.A. Boonstra, aios MDL, Isala ziekenhuis, Zwolle*
10.50	Voeding *P. Voogt, verpleegkundig specialist voedingszorg, Jeroen Bosch ziekenhuis, 's Hertogenbosch*
11.10	Pauze

V&VN ochtendprogramma II — Brabantzaal



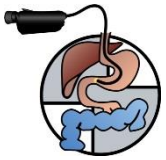
Beroepsvereniging van zorgprofessionals
Maag Darm Lever

Voorzitters : *Mw. T.A. Korpershoek, voorzitter V&VN MDL*

Thema: MDL algemeen

11.40	MDL klachten 1e lijn *Dr. S.J.B van Weyenberg, MDL-arts, Spaarne Gasthuis, Hoofddorp*
12.00	Gastroesophageal reflux disease (GERD) *Dr. D.P. Hirsch, MDL-arts, Rijnstate, Arnhem*
12.20	Leverfunctiestoornissen *Dr. L.C. Baak, MDL-arts, OLVG, Amsterdam*
13.00	Lunchpauze in de expositiehal

V&VN middagprogramma I — Auditorium



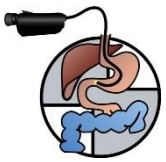
Beroepsvereniging van zorgprofessionals
Maag Darm Lever

Voorzitter: *Mw. M. van Hout*

Thema: Endoscopie

14.00	Flourecense moluculaire endoscopie *Dr. W.B. Nagengast, UMCG*
14.25	Helicobacter Pylori *S. Nieuwenburg, promovendus, Erasmus MC, Rotterdam*
14.50	Endoscopische behandeling van GE-bloedingen *Dr. F. Wolfhagen, MDL-arts, Albert Schweitzer ziekenhuis, Dordrecht*
15.15	T1 coloncarcinoom, endoscopische opties? *Dr. A.U.G. van Lent, MDL-arts, OLVG, Amsterdam*
15.40	Afsluitend drankje foyer bij Auditorium en Parkzaal

V&VN middagprogramma II — Baroniezaal



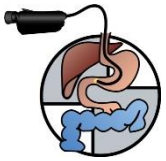
Beroepsvereniging van zorgprofessionals
Maag Darm Lever

Voorzitter: *Mw. M.H. Francois-Verwey*

Thema: IBD

14.00	Refractaire proctitis (IFX falers, stamcellen, surveillance) *Drs. M. Barnhoorn, arts-onderzoeker, LUMC, Leiden*
14.25	Pathologie IBD *Dr. A. Mookhoek, patholoog i.o., VUmc, Amsterdam*
14.50	Basisbegrippen genetica, geneticus, oorzaak genitica *Dr. E.A.M. Festen, MDL-arts, UMCG, Groningen*
15.15	Tofacitinib *Prof. dr. G. Dijkstra, MDL-arts, UMCG, Groningen*
15.40	Afsluitend drankje foyer bij Auditorium en Parkzaal

V&VN middagprogramma III **Parkzaal**



Voorzitter: *Mw. A. Boersen*

Thema: Verpleegkundig endoscopisten

14.00	Irritable Bowel Syndrome *Dr. M.H. Otten, MDL-arts, MC de Veluwe, Apeldoorn*
14.25	Vaatanomalieën *Drs. M.L. Hazen, MDL-arts, Elkerliek, Helmond*
14.50	Juridische kader VE *Mw. mr. A.J.G.M. Janssen*
15.15	Gloucester Comfort Scale *Dr. B. den Hartog, MDL-arts, Arnhem*
15.40	Afsluitend drankje foyer bij Auditorium en Parkzaal

Robot-assisted pancreatoduodenectomy in the Netherlands: a multicenter analysis of the first 100 procedures

C.L.M.A. Nota[1], J. Hagendoorn[1], M.J.W. Zwart[2], I.H.M. Borel Rinkes[1], P.P.L.O. Coene[3], E.W. van der Harst[3], W.W. te Riele[4], T. Tran[5], H.C. van Santvoort[4], B. Groot Koerkamp[5], I.Q. Molenaar[1]. [1]Dept. of Gastrointestinal Surgery, UMC Utrecht, Utrecht, [2]Dept. of Gastrointestinal Surgery, Amsterdam UMC (loc. AMC), Amsterdam, [3]Dept. of Gastrointestinal Surgery, Maasstad Hospital, Rotterdam, [4]Dept. of Gastrointestinal Surgery, St. Antonius Hospital, Nieuwegein, [5]Dept. of Gastrointestinal Surgery, Erasmus MC, Rotterdam, The Netherlands.

Background: Minimally invasive surgery is currently the gold standard for many surgical procedures. Most pancreatoduodenectomies, however, are still being performed through laparotomy. Conventional laparoscopy is limited by the straight visual- and working axis and might be less suited for pancreatoduodenectomy. Potentially, the use of robotic technology offers a solution. The technically enhanced articulating instruments and 3D vision allow for optimal surgical dexterity, as needed during meticulous dissection and construction of the anastomoses in pancreatoduodenectomy. The aim of this study was to determine safety and feasibility of a robotic approach to pancreatoduodenectomy in the Netherlands and compare our results to recent studies reporting on the outcomes of open pancreatoduodenectomies.

Methods: This is a multicenter post hoc analysis of prospective databases from three high volume Hepato-Pancreato-Biliary (HPB) centers in the Netherlands. The first 100 patients undergoing robot-assisted pancreatoduodenectomy were included. Primary endpoint was severe complication, defined as occurrence of one or more of the following complications: ISGPS gr. B/C postpancreatectomy hemorrhage, ISGPS gr. B/C pancreatic fistula, multiple or single organ failure or death. Outcomes were scored during index admission. In addition, we performed a systematic review of observational, monocenter studies reporting on outcomes of > 500 open pancreatoduodenectomies, published in the past 5 years.

Results: A total of 22 (22%) patients suffered from a severe complication. Pancreatic fistula (ISGPS gr. B/C) occurred in 19 (19%) patients and 9 (9%) patients suffered from post-pancreatectomy hemorrhage (ISGPS gr. B/C). Delayed gastric emptying (ISGPS gr. B/C) occurred in 26 (26%) patients. In 8 (8%) patients the minimally invasive procedure was converted to an open pancreatoduodenectomy. There was no postoperative in-hospital or 30-day mortality. The systematic review of 14 studies (n=12.780 patients) reporting on the outcomes of open pancreatoduodenectomy, demonstrated that morbidity occurred in 38% of all patients and reoperations in 7%. The weighted mean mortality was 3%.

Conclusion: These outcomes of the first 100 robot-assisted pancreatoduodenectomies demonstrate that this procedure was introduced safely in three hospitals in the Netherlands without postoperative mortality and acceptable morbidity. Morbidity and mortality in this study were not higher than the morbidity and mortality rates reported in 14 recent, large, international studies on open pancreatoduodenectomies, although this comparison was limited by heterogeneity in used definitions.

Early endoscopic retrograde cholangiography with biliary sphincterotomy or conservative treatment in predicted severe acute biliary pancreatitis (apec): a multicenter randomized controlled trial

N.J. Schepers[1,7], N.D.L. Hallensleben[1,7], M.G.H. Besselink[3], M.P.G.F. Anten[2], T.L. Bollen[4], F. van Delft[8], H.M. van Dullemen[9], M.G.W. Dijkgraaf[2], C.H.J. van Eijck[2], G.W. Erkelens[10], N.S. Erler[5], P. Fockens[3], E.J.M. van Geenen[11], H.G. Gooszen[12], J. van Grinsven[13], J.E. van Hooft[14], R.W.M. van der Hulst[15], J.M. Jansen[16], F.J.G.M. Kubben[17], S.D. Kuiken[16], R. Laheij[18], R. Quispel[19], R.J.J. de Ridder[20], M.C.M. Rijk[21], T.E.H. Romkens[2], C.H.M. Ruigrok[19], E.J. Schoon[6], M.P. Schwartz[22], B.W.M. Spanier[23], A.C.I.T.L Tan[24], W.J. Thijs[25], R. Timmer[7], N.G. Venneman[26], R.C. Verdonk[7], F.P. Vleggaar[27], W. van de Vrie[28], B.J. Witteman[29], H.C. van Santvoort[30], O.J. Bakker[2], M.J. Bruno[1]. [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam. [2]Dept. of Gastroenterology and Hepatology, St. Franciscus Hospital, Rotterdam. [3]Dept. of Surgery, Amsterdam UMC (loc. AMC), Amsterdam. [4]Dept. of Radiology, [5]Dept. of Clinical Epidemiology, [6]Dept. of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven. [7]Dept. of Gastroenterology and Hepatology, St. Antonius Hospital, Nieuwegein. [8]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. VUmc), Amsterdam. [9]Dept. of Gastroenterology and Hepatology, UMC Groningen, Groningen. [10]Dept. of Gastroenterology and Hepatology, Gelre Hospital, Apeldoorn. [11]Dept of Gastroenterology and Hepatology, Radboudumc, Nijmegen. [12]Dept. of Surgery, Radboudumc, Nijmegen. [13]Dept. of Surgery, Tergooi Hospitals, Hilversum. [14]Dept. of Gastroenterology and Hepatology, Amsterdam UMC (loc. AMC), Amsterdam. [15]Dept. of Gastroenterology and Hepatology, Spaarne Gasthuis, Haarlem. [16]Dept. of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam. [17]Dept. of Gastroenterology and Hepatology, Maasstad Hospital, Rotterdam. [18]Dept. of Gastroenterology and Hepatology, Elisabeth TweeSteden Hospital, Tilburg. [19]Dept. of Gastroenterology and Hepatology, Reinier de Graaf Gasthuis, Delft. [20]Dept. of Gastroenterology and Hepatology, Maastricht UMC, Maastricht. [21]Dept. of Gastroenterology and Hepatology, Amphia Hospital, Breda. [22]Dept. of Gastroenterology and Hepatology, Meander MC, Amersfoort. [23]Dept. of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem. [24]Dept. of Gastroenterology and Hepatology, Canisius Wilhelmina Hospital, Nijmegen. [25]Dept. of Gastroenterology and Hepatology, Martini Hospital, Groningen. [26]Dept. of Gastroenterology and Hepatology, Medisch Spectrum Twente, Enschede. [27]Dept. of Gastroenterology and Hepatology, UMC Utrecht, Utrecht. [28]Dept. of Gastroenterology and Hepatology, Albert Schweitzer Hospital, Dordrecht. [29]Dept. of Gastroenterology and Hepatology, Gelderse Vallei Hospital, Ede. [30]Dept. of Surgery, St. Antonius Hospital, Nieuwegein, The Netherlands.

Background: Patients with acute biliary pancreatitis may develop cholangitis, organ failure and other life-threatening complications. Early biliary decompression by endoscopic retrograde cholangiography (ERC) and sphincterotomy may ameliorate the disease course, but previous randomized trials have shown conflicting results. Recent guidelines advise ERC in biliary pancreatitis only in case of cholangitis, and to consider ERC in case of (persistent) cholestasis. Whether early ERC and biliary sphincterotomy is beneficial in patients with predicted severe acute biliary pancreatitis with or without cholestasis, but without cholangitis, remains debated.

Methods: We randomized 232 patients in 26 Dutch hospitals with predicted severe acute biliary pancreatitis (based on an Acute Physiology and Chronic Health Evaluation [APACHE II] score of ≥8, an Imrie score of ≥3 or a C-reactive protein level of >150 mg/L within 24 hours of admission) and without cholangitis, to early ERC with biliary sphincterotomy within 24 hours after presentation at the emergency department or conservative treatment with on-demand ERC in case of cholangitis. The primary end point was a composite of death or major complications (i.e. new-onset persistent organ failure, cholangitis, bacteremia, pneumonia, pancreatic necrosis and pancreatic insufficiency) during 6 months follow-up.

Results: The primary end point occurred in 45 of 117 patients (39%) in the early ERC group compared with 50 of 113 patients (44%) in the conservative group (risk ratio 0.87; 95% confidence interval 0.64-1.18; P=0.37). 112 patients (96%) in the early ERC group underwent ERC at a median of 20 hours after presentation (interquartile range [IQR] 12-23 hours), and after a median of 29 hours after symptom onset (IQR 22-44 hours). Sphincterotomy was performed in 91 patients (81%). In 35 of the 113 patients (31%) in the conservative group, ERC was performed for cholangitis or persisting cholestasis after a median of 8 days (IQR 3-34 days) after randomization. In the early ERC group, cholangitis occurred less often compared with conservative treatment (2% vs. 10%; P=0.01) without significant differences in outcome including new-onset organ failure (19% vs. 15%; P=0.45) or death (7% vs. 9%; P=0.57). In the predefined subgroup of patients with cholestasis, no significant difference in the primary end point was found (32% vs. 43%; risk ratio 0.73; 95% confidence interval 0.47-1.16; P=0.18).

Conclusion: In patients with predicted severe acute biliary pancreatitis without cholangitis, early ERC with biliary sphincteromy within 24 hours after presentation did not reduce the primary end point of death or major complications.

Miltefosine decreases visceral hypersensitivity through modulation of the gut microbiome and mycobiome in a rodent model of Irritable Bowel Syndrome

I.A.M. van Thiel[1], S. Botschuijver[1], S.A. van Diest[1], T.B.M. Hakvoort[1], F.H.J. Schuren[2], W.J. de Jonge[1], R.M. van den Wijngaard[1]. [1]Dept. of Gastroenterology, Tytgat Institute for Liver and Intestinal Research, Amsterdam UMC (loc. AMC), Amsterdam, [2]Dept. of Microbiology and Systems Biology, The Netherlands Organization for Applied Scientific Research (TNO), Zeist, The Netherlands.

Background: Irritable Bowel Syndrome (IBS) is a functional bowel disorder characterized by frequent abdominal pain. In patients and an IBS-like rat model, we have previously shown an association between increased sensitivity to gut stimuli (visceral hypersensitivity) and altered fungal composition in the gut (mycobiome dysbiosis). In rat, antifungal treatment by fluconazole reversed visceral hypersensitivity. Miltefosine, a drug currently used in the therapy of visceral *Leishmaniasis*, is known to have broad fungicidal activity. In this study, we assessed *in vitro* toxicity of miltefosine on fungal or bacterial cultures. Furthermore, we assessed the potential of miltefosine for modulation of the fecal micro- and mycobiome of IBS-like rats.

Methods: Kirby-Bauer assays were used to assess *in vitro* toxicity of miltefosine on *Candida albicans* or *Bacillus subtilis.*

Adult maternal separated (MS) and non-handled (NH) rats were subjected to water avoidance to induce visceral hypersensitivity, and then treated with either vehicle (n=8) or 10 mg/kg miltefosine per os (n=9) for 8 days. Visceral sensitivity to distension (1, 1.5 and 2ml) was assessed pre- and post-water avoidance and post-treatment by quantifying the visceromotor response.

Fecal pellets of MS animals were collected after treatment. Microbial DNA was isolated, amplified, and both bacterial (16S) and fungal-specific regions (*Internal Transcribed Regions* (ITS-1)*)* were sequenced. Differences in micro- and mycobiome composition were visualized based on the Bray-Curtis Dissimilarity Index.

Results: Compared to vehicle, inhibition halos of *Candida albicans* were larger after incubation with miltefosine (n=3; vehicle = 3 mm; 10mM miltefosine = 13 mm; $p<0.001$). The same observation was made for *Bacillus subtilis* (n=3, vehicle = 2.5 mm; 10mM miltefosine = 11 mm; $p<0.05$).

In contrast to NH rats, MS rats developed visceral hypersensitivity, which was reversed upon miltefosine treatment. The MS mycobiomes separated into two distinct clusters; the first cluster contained 7 non-treated and 2 miltefosine-treated animals. The separation of vehicle vs. miltefosine treatment was highly significant, confirmed by non-metric multidimensional scaling ($p=0.0009$). The MS bacterial microbiomes show less clear separation of clusters, but multidimensional scaling did reveal two separate microbiome groups ($p=0.0001$).

Conclusion: Taken together, our data confirm the antimicrobial effects of miltefosine. To this end, miltefosine treatment of IBS-like rats leads to changes in the micro- and mycobiome, and thereby reverses visceral hypersensitivity.

In-depth characterization of host-genetics and gut microbiome unravels novel host-microbiome interactions in inflammatory bowel disease

S. Hu[1], A. Vich Vila[1], R. Gacesa[1], V. Collij[1], R.J. Xavier[2], C. Stevens[3], M.J. Daly[3], C. Wijmenga[4], H. van Dullemen[1], G. Dijkstra[1], M.C. Visschedijk[1], E. Festen[1], J. Fu[5], A. Kurilshikov[4], A. Zhernakova[4], R. Weersma[1]. [1]Dept. of Gastroenterology and Hepatology, UMC Groningen, Groningen, The Netherlands, [2]Dept. of Gastroenterology, Massachusetts General Hospital, Boston, United States of America, [3]Dept. of Clinical Genetics, Broad Institute, Boston, United States Of America, [4]Dept. of Clinical Genetics, UMC Groningen, Groningen, The Netherlands, [5]Dept. of Pediatrics, UMC Groningen, Groningen, The Netherlands.

Background: A large number of host genetic factors, as well as changes in the gut microbiota, are known to determine etiology and pathogenesis of inflammatory bowel disease (IBD). The knowledge on the interaction between these two factors is, however, still limited. In order to characterize these interactions, in depth determination of the host genetics and gut microbiota is necessary. Here we aimed to identify genetic factors relevant for maintenance of the gut microbiome in the context of IBD.
Methods: We performed whole exome sequencing of the host genome, and whole genome shotgun sequencing of fecal samples of 524 IBD patients and 939 controls from population-based cohort. The interaction between exonic variants, microbial taxa and metabolic pathways was explored using a four step approach: 1) Bidirectional meta-analysis between the two cohorts to identify common variants 2) A targeted meta-analyses of IBD risk loci and protein truncating variants (PTVs) 3) A gene-based burden test to detect rare mutations that affect microbial features, and 4) an interaction analysis to identify IBD-specific microbial quantitative trait loci (mbQTLs).
Results: We tested 170,000 protein coding variants and 641 microbial features and identified 26 associations between genetic variants and gut microbial features (FDR<0.05). Among common variants, a strong mbQTL was observed for deletion near the IBD-risk *IL17REL* gene that was correlated to *Alistipes indistinctus* abundance, which is known to be decreased in IBD patients. The gene-based burden test revealed that mutations in an IBD-related gene *CYP2D6*, a major component of phase I drug metabolism, were associated with decreased level of bacterial biosynthesis of vitamin K (PWY-5838). Moreover, *GPR151* gene, known to be protective against obesity and type II diabetes, was found to be associated with a decrease in bacterial degradation of glucose. The interaction analysis revealed another association between *BTNL2* and *Bacteroides* specific to IBD.
Conclusion: We performed the largest, high resolution, genome-microbiome association study to date, that utilizes whole exome sequencing and metagenomics sequencing methods. Disease specific interactions were explored in the context of IBD, including the effect of risk loci and protein truncating variants. These results highlight the importance of host genetics in the maintenance of gut microbiome homeostasis critical for prevention of IBD.

Combining absolute quantification of fecal bacteria with metagenomic sequencing data improves the characterization of the gut microbiome of patients with Crohn's disease

A. Vich Vila[1], A.M. Boddeke[1], A. Kurilshikov[2], J.Z.H.V.O Martels[1], V. Collij[1], P. Sureda Horrach[1], A.R. Bourgonje[1], S. Hu[1], A. Zhernakova[2], G. Dijkstra[1], H.J.M. Harmsen[3], R.K. Weersma[1], . [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Clinical Genetics, [3]Dept. of Medical Microbiology, UMC Groningen, Groningen, The Netherlands.

Background: Increasing evidence has shown the role of the gut microbiota in the development and progression of Crohn's disease (CD). So far, gut microbiome studies in patients with CD have focused on characterizing the changes in bacterial abundances without considering the impact of clinical factors on the bacterial ecosystem. We hypothesize that combining sequencing data with absolute quantification (e.g. the number of bacteria per gram of faeces) of the gut microbiota can provide a better insight of the disease heterogeneity and improves the accuracy of gut microbiome studies in diseases like IBD
Methods: We collected 140 fecal samples from a cohort of 70 patients with CD, taken at two time points with an interval of three weeks. Microbial densities were calculated by fluorescence *in situ* hybridization. Microbiota composition was estimated by shotgun metagenomic sequencing. Phenotypic data, such as medication use or surgery, was obtained from the clinical records. PERMANOVA analysis was used to estimate the explained variance of each phenotype on the microbiome composition. Differences between disease phenotypes and microbial loads were calculated using a Wilcoxon-test. Partial correlations were used to estimate the effect of bacterial load correction in the microbiome-trait associations
Results: Patients with CD showed a large variation in the gut bacterial densities. This variation could not be linked to fecal calprotectin levels (rho=0.05, P=0.53) Differences in microbial loads explained most of the variation in microbiome composition between samples (R2=10%, P = 0.0001). While higher densities were related with an increased abundance of beneficial bacteria, such as *F.prausnitzii* and *R.intestinalis*, lower microbial loads were associated with an expansion of potentially pathogenic bacteria like *E.coli*. Patients with intestinal resections showed lower microbial loads (P= 5.94E-06), although latest resection occurred, on average, 11 years before sample collection. Correcting for bacterial densities in the microbe-trait associations allowed us to increase the specificity and therefore, pinpoint relevant species in CD sub-phenotypes
Conclusion: The number of bacteria in the gut of patients with CD show a large variation between individuals. Lower microbial densities are correlated with the expansion of pathogenic bacteria and associated with intestinal resection. The differences in bacterial loads should be considered when exploring the gut microbiota of patients with CD, both as a separate major indicator of gut health and as correction factor for microbe-phenotype association. Together these results provide a better understanding of the heterogeneity and dynamics of the disease

Detection and monitoring of IBD based on faecal volatile organic compounds

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Background: The gold standard to detect and monitor inflammatory bowel disease (IBD) remains endoscopic assessment which is invasive and costly. Faecal calprotectin (FCP) is the most commonly used non-invasive biomarker to assess IBD but lacks specificity. Faecal volatile organic compounds (VOC) are molecular end-products thought to represent both metabolic processes in the human body and the interaction between microbiota and host. The aim of the current study was to evaluate the potential of faecal VOC patterns to detect IBD and to identify disease exacerbation.
Methods: Patients aged 18 years and older with an established diagnosis of IBD collected a faecal sample prior to their scheduled consult at the outpatient clinic of two tertiary hospitals. The healthy control (HC) group consisted of patients without mucosal abnormalities observed during their scheduled colonoscopy. Active disease was defined as an FCP level of ≥250 mg/g, remission was defined as FCP <100 mg/g combined with a Harvey Bradshaw Index <4 points for Crohn's disease (CD) or Simple Clinical Colitis Activity Index <3 points for ulcerative colitis (UC). Faecal samples were measured by means of gas chromatography-ion mobility spectrometry (G.A.S. Flavourspec). The data were split into three sets, 70% for training and validation and 30% as test set. A Wilcoxon rank-sum test was used to find the 100 most discriminatory features and Random Forest classification was used to provide statistical results.
Results: A total of 497 faecal samples were provided by 281 IBD patients and compared to 224 HC samples. Of these, 294 were CD samples (107 active disease, 84 remission) and 203 were UC samples (83 active disease, 64 remission). IBD, UC and CD could be discriminated from HC with high accuracy both in active state and remission (AUC (95%CI), p-values: UCa vs HC 0.97(0.95-1), p<0.0001; UCr vs HC 0.97(0.95-0.99), p<0.0001; CDa vs HC 0.98(0.96-1), p<0.0001; CDr vs HC 0.97(0.95-1), p<0.0001). No difference was observed between UC and CD, and between active disease state and remission (UC vs CD 0.54(0.49-0.6), p=0.074; UCa vs UCr 0.62(0.43-0.81), p=0.094; CDa vs CDr 0.49(0.36-0.62), p=0.56).
Conclusion: We demonstrated that faecal VOC patterns can discriminate IBD, CD and UC from HC both during active disease state and remission, though there is no difference between UC and CD. These characteristics imply that faecal VOC patterns may hold potential as non-invasive biomarkers for IBD disease detection. Based on clinical activity, active disease could not be discriminated from remission, which hamper its potential to detect disease exacerbation.

Therapeutic drug monitoring in ustekinumab: which factors affect trough levels?

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Background: Ustekinimab (UST) is a fully human monoclonal antibody against the p40 subunit of interleukin-12 (IL-12 and interleukin-23 (IL23). Efficacy of biological drugs can be optimized by ensuring adequate exposure to these drugs, by using trough level- based therapeutic drug monitoring. The aim of our research was to identify (bio)markers that influence UST trough levels. Furthermore, we aimed to assess the relationship between exposure and response to UST.
Methods: An observational study was carried out at our centre. All adult patients with Crohn's disease that received UST treatment between December 2016 and November 2018 were included. Patient were treated with an initial intravenous induction therapy, followed by subcutaneous maintenance therapy. Patients demographics were collected (concomitant medication use, biological uses in the past, disease localization, body weight, BMI), as were disease activity measures (Harvey Bradshaw Index (HBI); fecal calprotectine (FCP); C -reactive protein (CRP) and Albumin). UST dosage and interval, trough levels and antibodies were collected as treatment specific data. Nonlinear mixed effect modelling was used to estimate pharmacokinetic parameters based on the collected UST trough concentrations as implemented in the NONMEM software package (version 7.3.0) using PsN toolkit 4.7.0 and Piraña version 2.9.7 as modelling environment. Plotting of the results was performed using statistical software package R (v3.4.4) and R studio Version. Parameters calculated were Distribution Volume (V; liters) and clearance (CL/ L/Day).
Results: 50 patients (34.6% male, mean age 43 yrs, mean disease duration 17 yrs) with Crohn's disease were included. A total of 365 doses UST were administered, and a total of 196 trough levels were measured. A one compartment model with first order elimination was identified. The typical value of CL 0.28 L/day, V was 6.94 L. The inter-individual variability was estimated 35.1% for CL and 35.2 % for V. Among the evaluated covariates, body weight significantly affected CL. In addition, baseline albumin and a CRP level >10 were found to be significantly affect V. In the exposure response analysis a relationship between HBI , CRP, FCP and UST levels was identified. Patient with higher UST levels had a lower HBI score and lower CRP and FCP levels.
Conclusion: A population pharmacokinetic model for UST was developed. Bodyweight, baseline albumin and CRP had a significant influence on UST pharmacokinetics. Patient with higher UST levels had a lower HBI score, lower FCP and lower CRP. These results show a possible rationale for TDM of UST, however further research is required to establish a clear therapeutic window.

Higher discontinuation rates of anti-TNF therapy in elderly IBD patients compared to a younger age group: results from a prospective registry

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Background: Increasing life expectancy and IBD incidence will result in more elderly IBD patients. There is paucity of data on safety and efficacy of anti-TNF in the elderly since this group is underrepresented in clinical studies. We aimed to compare the long-term effectiveness and safety of first anti-TNF treatment in IBD patients per age group (20-40 years/41-60 years/>60 years), by assessment of drug survival and reasons for discontinuation.
Methods: Patients on first anti-TNF treatment were identified through IBDREAM, a multicenter prospective IBD registry in 5 hospitals in the Netherlands. Data on demographics, medical history, drug survival and adverse events were extracted from IBDREAM. STATA 11.2's competing risk regression was used to study time to drug discontinuation due to adverse events or lack of effectiveness, with discontinuation due to remission as a competing risk. The following predictors were considered in the analysis, corrected for age group: gender, IBD-type, anti-TNF type (infliximab or adalimumab), co-medication at baseline, disease duration, malignancies and surgery in medical history.
Results: A total of 895 patients were included, 679 had Crohn's disease, 200 ulcerative colitis and 16 IBD unclassified. Male represented 42%, median age at diagnosis was 26 years (IQR 19-38) and median follow-up was 46 months (IQR 18-97). 546 patients started anti-TNF at an age between 20-40 (61%), 268 at age 41-60 (30%) and 81 at age >60 (9%). Infliximab was the first anti-TNF in 75%, 71% and 67% of patients respectively per age group. A total of 450 patients discontinued first anti-TNF therapy, 284 (52%), 133 (50%) and 33 (41%) per group. Reasons for discontinuation were adverse events in 27%, 29% and 39% respectively per age group, lack of effectiveness in 40%, 47% and 32% and remission in 15%, 30% and 3%. Competing-risks regression analysis, with discontinuation due to adverse events/ lack of effectiveness as the outcome of interest and discontinuation due to remission as a competing event, showed a shorter drug survival in the two older groups (subhazard rate (SHR) age >60 1.46, SHR age 41-60 1.21; p=0.03, both SHR compared to age <40). Risk factor for discontinuation was prednisone use at baseline (SHR: 2.78; p<0.001).
Conclusion: IBD patients starting the first anti-TNF agent at higher age showed a higher discontinuation rate due to adverse events or lack of effectiveness, with patients >60 years having the highest rate of discontinuation. Prednisone use at baseline was the only other predictor found for discontinuation.

Premedication with steroids does not influence the incidence of Infusion Reactions after Infliximab Infusions in paediatric IBD patients - a retrospective case-control

study.

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Background: Infusion reactions (IR) are common side effects of Infliximab (IFX) infusions, especially in children, and often lead to discontinuation of IFX. Premedication (PM), such as antihistamines and corticosteroids, has been considered to decrease the odds of developing an IR, however evidence to support this strategy is lacking. This study aimed to investigate the effects of PM on the incidence of IR in paediatric Inflammatory Bowel Disease (PIBD) patients receiving IFX. The secondary objectives were to assess risk factors for developing IR and to assess association between PM and development of antibodies against IFX (ATI).
Methods: This was a retrospective case-control study including all PIBD-patients receiving IFX in two tertiary care centres. PM (steroids) was part of standard care in one of the centres (PM-group) and was not routinely given in the other (non-PM group). All acute IR were noted and were divided into mild/severe reactions and also in grade 1/2/3/4 for further detailed exploration (grade 1: no interventions necessary, but observation is desired, grade 2: interruption of infusion and/or oral medication required, grade 3: i.v. medication is necessary, grade 4: infusion was required to stop). Differences between two subgroups were assessed with the T- or Chi-square test and logistic regression was used for assessment of influence of PM on IR, of PM on ATI and for identification of risk factors.
Results: A total of 230 patients (92 PM, 138 non-PM, 50% male, mean age at onset of IBD: 12.7 year), receiving 3476 infusions in total, were included. Three severe IR occurred, all in the PM-group. There was no significant difference between the PM- and non-PM-group in number of patients developing any type of IR (14.1% vs. 17.4% p=0.51) or a grade 3/4 IR (4.1% vs. 4.1%, p=1.0). The odds ratio (OR) of developing any IR when using PM was 1.28 (95% CI: 0.61-2.66, p=0.51) and 1.0 (95% CI: 0.27–3.65, p=1.0) for developing a grade 3/4 IR. The OR of developing ATI when using PM was 0.82 (95% CI: 0.33-2.1, p=0.68). Presence of ATI significantly increased the risk of developing IR (OR: 1.01, 95% CI: 1.0-1.01, p:0.04).
Conclusion: Premedication with steroids was not associated with a decrease in the incidence of IR in this cohort of PIBD patients receiving IFX, while severe IR were rarely observed. PM was not associated with development of ATI. Development of ATI was identified as a risk factor for IR. Our results suggest that PM with steroids is not indicated in PIBD to prevent IR.

Prevalence of cervical dysplasia in women with Inflammatory Bowel Disease: data from the Parelsnoer Institute (PSI) and PALGA database (PAP-IBD study)

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Background: Women with inflammatory bowel disease (IBD) may be at higher risk for cervical intraepithelial neoplasia (CIN). Possible explanations for this elevated risk include increased persistence of high-risk human papillomavirus (hrHPV) and rapid progression of premalignant lesions in immunocompromised individuals. However, data on CIN in IBD are conflicting. The aim of this study is to assess the prevalence of CIN in a large cohort of female Dutch IBD patients as compared to the general cervical screening population.
Methods: We retrieved all cervical cytology and histology records from the nationwide Dutch Pathology Database (PALGA) for women with IBD in the Parelsnoer study; a large multicenter cohort study (Parelsnoer Institute, Dutch IBD Biobank) in which clinical data are prospectively collected. Women in the IBD cohort were frequency matched 1:4 to a control group of women from the general cervical screening population from PALGA, based on age at first smear and year of screening.
Results: Cervical smears were available on 2,098 IBD patients (1,370 Crohn's disease (65.3%), 678 ulcerative colitis (32.3%), median age at IBD diagnosis 28.5 years). We found a significant difference in prevalence of CIN 2 or more severe (CIN 2+) lesions in IBD women (110/2,098, 5.2%) compared to the control group (324/8,439, 3.8%) with an odds ratio of 1.4 (95% confidence interval 1.1 – 1.7, *P = 0.004*). CIN 2 and CIN 3 were found more often in the IBD cohort (2.2% CIN 2, 2.9% CIN 3) than in the control group (1.4% CIN 2, 2.2% CIN 3, *P = 0.002*). Two cervical cancers occurred in our IBD cohort (2/2,098) compared to 20 cervical cancers in the control group (20/8,439) (*P = 0.20*). Possible risk factors associated with CIN, such as disease behavior, smoking and immunosuppressive drugs are currently investigated in this study population.
Conclusion: Women with IBD are at increased risk for CIN2+ lesions compared to their age matched controls. These results underline the current ECCO guideline on HPV vaccination in young IBD women, and the importance of adherence to screening guidelines. In addition, the benefits of more intensive cervical cancer screening, potentially starting at younger age, need to be assessed.

Increased risk of advanced neoplasia in inflammatory bowel disease patients with

recurrent low-grade dysplasia

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Background: A history of low-grade dysplasia (LGD) is a major risk factor for the development of high-grade dysplasia (HGD) and colorectal cancer (CRC) in Inflammatory Bowel Disease (IBD) patients. Consequently, guidelines recommend an intensified surveillance program for these patients. However, it is unknown how a second (recurrent) LGD impacts advanced neoplasia (HGD and/or CRC) risk. We aimed to assess the long-term advanced neoplasia risk in IBD patients with recurrent LGD and compared this to patients without subsequent dysplasia after initial LGD.
Methods: We identified all IBD patients with LGD from 1991 to 2005 in The Netherlands who received at least one follow-up colonoscopy in the subsequent 3 years, using the Dutch nationwide network and registry of histo- and cytopathology in the Netherlands (PALGA). Follow-up data were collected until 2016. Kaplan Meier curves were used to compare the cumulative advanced neoplasia incidence between patients with and without recurrent LGD at first colonoscopy after initial LGD. Patients were censored at the end of surveillance or colectomy.
Results: We identified 1,215 IBD patients with colonic LGD and follow-up colonoscopy within 3 years (923 (76.0%) ulcerative colitis, 214 (17.6%) Crohn's disease and 78 (6.4%) IBD unclassified). Mean time from initial LGD to first follow-up colonoscopy was 1.5 ($\pm$0.6) years in both patients with and without recurrent LGD. A total of 259 patients (21.3%) had recurrent LGD within 3 years, of whom 46 patients (17.8%, 31 CRC and 15 HGD) developed advanced neoplasia (versus 10.9% in patients without recurrent LGD). Patients with recurrent LGD had a higher cumulative advanced neoplasia incidence (HR 1.70; 95% CI 1.20-2.41; p=0.003). The cumulative advanced neoplasia incidence two years after surveillance colonoscopy was 4.4% in patients with dysplasia, versus 1.4% in those without recurrent dysplasia.
Conclusion: Recurrent LGD at follow-up colonoscopy after initial LGD increased the advanced neoplasia risk (HR 1.70). Patients without LGD at follow-up colonoscopy after initial LGD had a cumulative advanced neoplasia incidence of 1.4% in the subsequent 2 years.

Environmental and lifestyle factors are associated with a divergent effect on the course of Inflammatory Bowel Diseases

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Background: The etiology of Inflammatory Bowel Disease (IBD), Crohn's Disease (CD) and Ulcerative Colitis (UC), is complex with an interplay between genetic susceptibility, diet, the microbiome and environmental factors. Once IBD has developed, disease course is divergent between patients, and it is unknown what causes these differences in disease course. Environmental factors could be involved therefore we studied known and possibly involved lifestyle factors influencing the disease course of IBD in a large population-based study.
Methods: IBD patients (n:674) treated at a tertiary referral IBD center in the Netherlands, completed the previously validated Groningen IBD Environmental Questionnaire (GIEQ). The course of IBD was measured using prospectively collected medical records of outcomes during routine outpatient face-to-face follow-up. The adverse outcomes are defined as need for biological therapy, and/or surgery. Here, we focus on nine lifestyle factors measured by the GIEQ. Logistic regression was applied to estimate the multivariable-adjusted effect of lifestyle factors on the course of IBD (odds ratio; OR) and 95% confidence intervals (95%CI), while adjusting for sex, age, disease duration and smoking. The level of significance was set at p-value<0.05.
Results: In CD, active smokers at time of questionnaire have higher odds of needing biologicals (OR1.9, 95%CI 1.1-3.40), whereas a protective trend is seen for UC. The frequency of alcohol consumption does not seem to affect disease course. However, in UC, drinking white (2.1, 1.1-3.9) and red wine (3.6, 1.1-12.5) increases the risk of biologicals use. While having a dog increases risk of biological use (2.4, 1.3-4.4) and surgery (1.8, 1.0-3.2) in UC, no effect is seen for CD. Livingroom-wide carpet decreases odds of having surgery in CD (0.3, 0.1-0.8), whereas bedroom-wide carpet is associated with less chance of using biologicals (0.5, 0.3-0.8). Lastly, UC patients have less chance of surgery when living in an urban environment (0.2, 0.0-0.8), while no effect is seen on the course of CD.
Conclusion: Current lifestyle and living environment factors have a divergent effect on the course of IBD. Smoking in CD, consuming wine, and having a dog increase the risk for severe course in UC but room-wide carpet decreases the risk for complicated disease course in CD. Living in an urban environment yields a protective effect. Further studies in independent cohorts are needed to confirm these findings.

Treatment of perianal fistulas in Crohn's disease, seton versus anti-TNF versus surgical closure following anti-TNF (PISA): a randomised controlled trial

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Background: Most patients with draining perianal Crohn's fistulas receive medical treatment with anti-TNF. So far, outcomes of this medical approach have not been directly compared to long term seton drainage or surgical closure. The aim of this study was to identify the best treatment approach for perianal Crohn's disease. As closure rates were expected to be comparable based on a systematic review, we compared re-intervention rates among these three treatment arms. It was hypothesized that seton drainage would result in fewer re-interventions compared to anti-TNF medication with or without subsequent surgical closure.
Methods: In this multicentre randomised prospective trial, chronic seton drainage was compared to prolonged anti-TNF therapy and surgical closure following anti-TNF induction for the treatment of high perianal Crohn's fistula with a single internal opening. Patients with proctitis, rectovaginal fistulas, and patients who previously failed anti-TNF treatment were excluded. The primary outcome was the number of patients with fistula-related re-intervention(s), defined as surgical and/or (re)start anti-TNF treatment within 1.5 year. Secondary outcomes were the perianal disease activity index (PDAI) and quality of life (QoL). Patients refusing randomisation due to a specific treatment preference were included in a parallel prospective PISA registry cohort.
Results: The study was stopped after inclusion of 44 of the 126 planned patients, based on futility at interim analysis (likelihood to show superiority of chronic seton treatment at the completion of the trial was less than 1%). A follow-up of minimally 6 months was awaited. Seton treatment was associated with the highest re-intervention rate within 1.5 year (10/15 versus 6/15 anti-TNF and 3/14 surgical closure+anti-TNF patients, P=0.02). No substantial differences in PDAI and QoL between the three treatment groups were observed. Interestingly, in the PISA prospective registry (n= 50), inferiority of chronic seton treatment could not be observed for any outcome measure.
Conclusion: The results imply that chronic seton treatment should not be recommended as the sole or superior treatment for perianal Crohn's fistulas. However, the statistical inferiority of seton treatment should be interpreted with caution, due to the crucial aspects of small numbers and as this inferiority could not be confirmed in the PISA registry data.

Prediction of endoscopic activity in patients with Crohn's disease - systematic review and external validation of published prediction models

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Background: Endoscopic healing (EH) is associated with an improved long-term prognosis and is therefore considered a key target in the treatment of Crohn's disease (CD). Assessment of EH requires ileocolonoscopy, which is a costly and burdensome procedure. A non-invasive index, combining several predictors, to predict EH would simplify and improve management of CD in clinical practice. Published non-invasive models predicting EH or endoscopic activity often lack external validation. We reviewed the current literature for prediction models for ileocolonic endoscopic activity and subsequently compared their discriminatory abilities using two datasets.
Methods: We systematically searched PubMed, Embase and the Cochrane libraries until February 14, 2018 for all published diagnostic models based on a combination of at least 3 predictors, e.g. symptoms, serological, or fecal parameters, with as outcome ileocolonic endoscopic activity or EH in CD assessed by ileocolonoscopy. We subsequently evaluated the discriminatory ability (area under the receiver operating characteristic curve [AUC]) of the identified models in two separate cohorts, i.e. the TAILORIX (a randomized controlled trial investigating tailored treatment with infliximab for active luminal Crohn's disease) study (346 colonoscopies in 155 patients), and the development dataset of the Utrecht Activity Index (UAI) (93 colonoscopies in 82 patients). We corrected for clustering of colonoscopies per patient employing the Obuchowski method.
Results: After screening 5303 titles, 21 studies reporting on 27 models with at least 3 predictors were identified. The most commonly used predictors, alongside other predictors in the models, were C-reactive protein (n=18 [67%]) and fecal calprotectin (n=13 [48%]). Twelve models were reported in sufficient detail for validation; of these, 8 models could be validated: 6/8 in the TAILORIX and 6/8 in the UAI dataset. For the threshold of endoscopic activity measured by the CD Endoscopic Index of Severity (CDEIS) of ≥3, the AUCs of the published models ranged from 0.55 to 0.85 in the TAILORIX dataset, and from 0.59 to 0.77 in the UAI development dataset. The discriminative ability (AUC), in the TAILORIX and UAI dataset respectively, of continuous values of fecal calprotectin was 0.82 and 0.79, and of C-reactive protein (CRP) 0.75 and 0.80.
Conclusion: Based on the discriminatory ability published prediction models display limited benefit over the continuous values of fecal calprotectin or CRP in prediction of endoscopic activity in CD.

Two year experience with vedolizumab in inflammatory bowel disease patients: results of the ICC Case Series, a nationwide prospective observational cohort study

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Background: Vedolizumab (VDZ) is approved for the treatment of inflammatory bowel disease (IBD). Prospective data on clinical effect, safety and usage beyond one year of follow-up is scarce. We aimed to study the two year real-life experience with VDZ in IBD patients.
Methods: IBD patients initiating VDZ treatment were prospectively enrolled in a nationwide, web-based registry: the *ICC Case Series*. Clinical activity scores (Harvey Bradshaw Index (HBI) for Crohn's disease (CD), Short Clinical Colitis Activity Index (SCCAI) for ulcerative colitis (UC)), biochemical parameters (C-reactive protein (CRP) and faecal calprotectin (FCP)), VDZ dosage, concomitant medication, and adverse events were documented at week 0, 12, 24, 52, and 104, or when VDZ treatment was discontinued. Clinical remission was defined as HBI ≤4 and SCCAI ≤2. Biochemical remission was defined as a CRP concentration ≤5 mg/L and/or FCP level ≤200 µg/g. Intention-to-treat (ITT) follow-up was determined between first visit and last visit included in the ITT analysis.
Results: In total, 275 IBD (173 CD, 102 UC) patients were included (98.9% and 89.2% anti-tumor necrosis factor (TNF) exposed, respectively), with a median follow-up period of 104.0 weeks (IQR 100.7-104.0) for CD and 104.0 weeks (IQR 56.8-104.0) for UC. The proportion of patients in steroid-free clinical remission at week 52 and 104 was 28.0% and 27.5% for CD and 33.7% and 30.9% for UC, respectively. Between week 52 and 104, 73.7% of the CD and 73.1% of the UC patients remained in steroid-free clinical remission. Clinical effect was comparable for combination of VDZ and immunosuppressive agents versus VDZ monotherapy (week 104: 29.5% vs. 28.4% p=0.86). The proportion of patients in biochemical remission at week 52 and 104 was 26.5% and 21.0% for CD and 30.6% and 22.2% for UC, respectively. An additional infusion at week 10 was given to 83 (48.0%) CD and 17 (16.7%) UC patients, 40 (23.1%) CD and 13 (12.7%) UC patients underwent interval shortening (≤6 weeks). Ten severe infections occurred resulting in hospital admission (3.4 per 100 patients years), 8/10 used concomitant immunosuppressive agents. VDZ was discontinued in 100 (57.8%) CD and 47 (46.1%) UC patients, mainly due to primary non-response (CD: 61%, UC: 85.1%). Nine patients discontinued VDZ due to adverse events (3.1 per 100 patient years). Twenty-six (CD: 22, UC: 4) patients discontinued after the first year.
Conclusion: We assessed clinical outcomes of VDZ in a nationwide, prospective cohort of anti-TNF experienced IBD patients with 104 weeks follow-up. Our data showed persistent effectiveness of VDZ beyond 52 weeks of treatment, as well as frequent dosage optimization and a reassuring long-term safety profile.

Acetylcholine secreting T-cells contribute to innate immune driven colitis

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Background: Chronic complex immune diseases, such as inflammatory bowel diseases (IBD), do not always respond to therapy. Furthermore, treatments can have severe side effects and the diseases have a major impact on life. Currently, there are promising pilot trials indicating that vagus nerve stimulation might be an alternative approach in treating IBD. Earlier research shows that T-cells capable of producing acetylcholine (characterized by the expression of choline acetyltransferase (ChAT), the rate limiting enzyme for acetylcholine synthesis) in the spleen are of crucial importance for this anti-inflammatory effect of vagus nerve stimulation. We showed that this cell is also present in the intestine in high frequencies and the aim of this research was to investigate the role of $ChAT^{+}$ $CD4^{+}$ cells in different experimental colitis models in mice.
Methods: We made use of $CD4^{cre}ChAT^{fl/fl}$ mice (KO), lacking ChAT specifically in CD4 cells. Littermates ($ChAT^{fl/fl}$ mice) served as controls. We used three experimental colitis models: 1) Acute dextran sulfate sodium (DSS)-induced colitis: 7 days of 2% DSS in the drinking water; 2) A resolution model of DSS-induced colitis: 5 days of 2% DSS in the drinking water followed by 7 days without DSS; 3) T-cell transfer colitis: injecting $CD4^{+}CD45RB^{high}$ cells from the $CD4^{cre}ChAT^{fl/fl}$ or $ChAT^{fl/fl}$ mice in $Rag1^{-/-}$ mice. Bodyweight loss, endoscopy and histology score and colon weight/length ratio were measured as well as intestinal cytokine levels (both at protein and mRNA expression level).
Results: In the acute DSS-induced colitis model, KO mice had lower intestinal cytokine levels compared to their littermates. Strikingly, in the resolution model of DSS-induced colitis, KO mice recovered slower compared to littermates concerning bodyweight. In addition to this, histology score and intestinal cytokine levels were higher in the KO mice than in the littermates. $Rag1^{-/-}$ mice receiving T-cells from different donors all developed colitis concerning clinical parameters and intestinal cytokine levels. However, there was no difference between the $Rag1^{-/-}$ mice that received T-cells from the KO mice versus the $Rag1^{-/-}$ mice that received T-cells from the littermates.
Conclusion: Our results indicate that $ChAT^{+}$ $CD4^{+}$ cells aggravate the acute innate immune response in colitis, while they are supporting the later resolution process. Likely, the phenotype of the cell and the cellular targets of acetylcholine depend on the phase of inflammation. This determines the net contribution of the acetylcholine secreting T-cell to the immune response in colitis.

High-dimensional mass cytometry reveals the immune cell landscape in inflammatory bowel disease

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Background: Inflammatory bowel disease (IBD) is characterized by chronic inflammation of the intestine. Studies on individual immune lineages have shown alterations in the innate and adaptive intestinal immune system implicated in IBD. However, a comprehensive analysis of the cell composition in intestinal biopsies from IBD patients across all major immune lineages simultaneously was lacking.
Methods: In patients aged 10-40 years with a clinical suspicion of IBD, we took paired biopsies (N=104) from ileum and colon (both inflamed and uninflamed mucosa if available) and blood samples in 23 IBD patients and in 15 controls with a normal colonoscopy. We generated single cells suspensions from all samples and applied a 36 antibody panel designed to capture the heterogeneity in adaptive and innate immune system simultaneously. We used a mass cytometer to acquire data on single cells from all samples. The generated dataset was analysed with Hierarchical SNE (HSNE) in the Cytosplore analysis and visualisation tool.
Results: In total, we identified 309 distinct cell clusters from the collective intestinal dataset containing 3.4 million cells in a data-driven manner. Here, controls clustered separate from patients, ileum samples separate from colon samples, and affected segments separate from unaffected segments. However, affected samples from the different subgroups of IBD (Crohn's disease, ulcerative colitis, undeterminate colitis) were mostly intermixed, suggesting similarities in the immune profiles. Moreover, we observed a large interindividual variation in the immune cell composition, indicative of unique individual 'immune fingerprints' in the intestinal tract.
In addition, 19 subsets were significantly different between affected-IBD samples and unaffected-IBD samples/controls. Finally, in a Spearman rank correlation analysis, several CD4+ T cell clusters correlated with ILC and myeloid cell clusters and were upregulated in IBD-affected segments, while in particular TCRgd cell clusters and a group of ILC clusters were upregulated in unaffected samples of patients and controls.
Conclusion: Our study provides evidence that a coordinated cellular network of both innate and adaptive immune cell types are implicated in IBD. Together with the evidence for the unique individual-specific composition of the intestinal immune system, this may aid in the development of more (cost-)effective and personalized patient care.

Exosomes derived from mesenchymal stromal cells enhance epithelial regeneration

in vitro and in experimental colitis induced by DSS in mice

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Background: Mesenchymal stromal cells (MSCs) are a promising potential therapeutic alternative for the treatment of Inflammatory Bowel Disease, due to their immune regulatory properties and their ability to actively participate in tissue repair. Previously performed experiments show that MSCs can reduce experimental colitis in mice. However the exact working mechanism is unclear. We investigated if the therapeutic effects of local MSC therapy are possibly generated by MSC-derived exosomes. Exosomes are small vesicles released by cells, which carry parts of the content of the cell, like proteins and microRNAs. MSC-derived exosomes could be a cell free alternative for MSC therapy.
Methods: Exosomes were isolated from the conditioned medium of bone marrow-derived murine MSCs and their presence confirmd by western blot and electron microscopy. Additionally, conditioned medium with and without exosomes was isolated. *In vitro* epithelial cells were damaged with dextran sodium sulfate (DSS) for 24 hours, after which the cells were treated with (non)-conditioned medium with or without different doses of exosomes (CM +/-exosomes). The amount of epithelial cells was measured for 3 days. To study epithelial cell migration and proliferation, a scratch assay and MTS proliferation assay were performed. To investigate the response on epithelial cells *in vivo*, experimental colitis was induced in mice using DSS. The mice received local injections with MSCs ($2x10^6$), exosomes (15ug) or PBS during endoscopy in the distal part of the colon at day 5. Body weights were measured daily and endoscopy was performed at day 5 and 10 to evaluate the murine endoscopic index of colitis severity (MEICS) score. After sacrifice, the colon was micro- and macroscopically analysed.
Results: The amount of surviving epithelial cells after 48 hours was significant higher after treatment with a high dose of exosomes. Epithelial cell proliferation and migration significantly increased after treatment with a high dose of exosomes as well as with conditioned medium+exosomes, compared to non-conditioned medium in scratch and MTS assays. *In vivo*, after treatment with MSCs and exosomes, the relative body weights of the mice increased faster compared to the PBS group. This was also reflected in the MEICS score which was reduced in the MSC- and exosome treatment groups. Microscopic evaluation of the percentage of epithelial damage in the distal colon revealed also a trend towards less epithelial injury after treatment with exosomes.
Conclusion: MSC-derived exosomes can, at least partly, elicit the therapeutic effects of local MSC therapy, most probably caused by increased epithelial proliferation and survival.

Dashboard driven dosing of infliximab is superior to conventional treatment in inflammatory bowel disease: the PRECISION trial

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Background: Loss of response to infliximab (IFX) complicates the management of inflammatory bowel disease (IBD). Up to date, no prospective study has demonstrated a significant benefit of proactive dose adjustment based on serum IFX levels compared to conventional dosing. However, more personalized dosing strategies using a dashboard to achieve and maintain well-defined IFX target trough levels (TLs) may prevent loss of response. The aim of the PRECISION trial was to investigate the efficacy of dashboard driven IFX maintenance dosing in comparison with conventional IFX treatment in IBD patients in clinical remission during one year.
Methods: In this multicenter 1:1 randomized prospective trial, patients in clinical remission (Harvey Bradshaw Index (HBI) ≤4 for Crohn's disease (CD) or partial mayo score (PM) ≤2 for ulcerative colitis (UC)) receiving IFX maintenance treatment were included. Patients in the precision dosing group (PG) received IFX dosing guided by a Bayesian pharmacokinetic model, aiming to achieve and maintain an IFX TL of 3 µg/ml by treatment (de-)escalation as indicated by the dashboard. Patients in the control group (CG) continued IFX treatment regimen given prior to randomization without dose adaptation. Biochemical remission was defined as a fecal calprotectin <250 µg/g and CRP <0.5 mg/L. Clinical loss of response was defined as a HBI >4 or PM score >2 at two consecutive visits. Results: In total, 80 patients were included (66 CD and 14 UC) with a median age ([interquartile range; IQR]) of 37 years [27-51]. Median IFX treatment duration was 3.5 years [2-7.8] in the PG and 4.0 years [1.3-5.8] in the CG. Median TLs were 3.7 µg/ml [1.6-6.4] and 3.0 µg/ml [1.9-5.2] in the PG and CG respectively. Fifteen out of 80 patients (37.5%) in the PG and 17 out of 40 patients (42.5%) in the CG were treated in combination with an immunomodulator. Clinical loss of response was observed in 14/39 (36%) patients in the CG compared to 4/32 (13%) patients in the PG (p=0.03). Three patients (7.5%) in the PG were considered failures because of re-opening of their perianal fistula after dose de-escalation to achieve a TL of 3 µg/ml.
Conclusion: The PRECISION study is the first prospective trial demonstrating a clinical benefit from personalized dosing in IBD patients. Dashboard guided dosing resulted in a significant higher proportion of patients who maintained clinical remission during 1 year of treatment compared to patients that continued treatment without proactive adjustments. In patients with perianal disease, de-escalating treatment to obtain an IFX TL of 3 µg/ml resulted in re-opening of their old fistula, suggesting that in these patients higher TLs are needed for disease control.

Faecal calprotectin is an early predictor of endoscopic response and histologic remission after the start of vedolizumab

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Background: Early prediction of the effect of vedolizumab (VDZ) In IBD patients is of paramount importance to guide clinical decisions. We aimed to assess the potential of serial faecal calprotectin (FC) levels after start of VDZ to predict endoscopic response and histological remission.
Methods: Patients who started VDZ with endoscopic inflammation and FC>100 µg/g were included. FC was tested at week 2, 4, 8 and 16. Endoscopy was scheduled at week 16. Endoscopic response was defined as a SES-CD reduction ≥50%, Rutgeerts score reduction or Mayo score reduction of ≥1. At week 16 endoscopy, ileum and segmental colon biopsies were collected. Histologic severity was scored accordingly on a 4-point scale. Median FC levels at the FU time points and the relative change in FC between baseline and week 16 were assessed with the Wilcoxon Rank Sum test. ROC statistics were used to determine a FC cut-off point with the best discriminatory performance and to assess the predictive value of FC levels at the FU time points.
Results: A total of 40 patients (24 CD, 14 UC and 2 IBD-U) (42% males, median age 40 (28-51) years (IQR)) were included. 33/40 patients (83%) were anti-TNF exposed, of whom 28/33 (85%) were refractory. In 26/40 patients (65%) VDZ was combined with steroid induction therapy and completely tapered at week 16 in 18/26 (69%) patients. Week 16 endoscopic response rates were 11/16 (69%) in UC and 12/24 (50%) in CD (p=0.33). Median FC levels (µg/g) are depicted in Figure 1, and were significantly lower as compared to FC in patients without endoscopic response. Patients with endoscopic response had a significant decrease in FC level at week 2 as compared to patients without endoscopic response (p=0.015). FC<250 µg/g at week 2 predicted endoscopic response (AUC=0.77): sensitivity 70%, specificity 93%, PPV 94% and NPV 67%. At week 8 (AUC=0.84): sensitivity 62%, specificity 100%, PPV 100% and NPV 55%. FC predicted histologic remission at week 8 (AUC=0.88): sensitivity 89%, specificity 89%, PPV 80% and NPV 94%.
Conclusion: Although delayed clinical effectiveness of VDZ has been reported previously, VDZ induces as early as week 2 a significant decrease of FC levels in IBD patients with an endoscopic response at week 16. At 8 weeks after the initiation of VDZ, FC<250 µg/g accurately predicts endoscopic response and histologic remission in this cohort.

Prediction model to safely cease anti-TNF therapy in Crohn's disease: individual patient data meta-analysis (IPD-MA)

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Background: Tools for patient stratification to safely cease anti-TNF therapy in Crohn's disease (CD) are urgently needed. This IPD-MA aims at development of a predictive diagnostic tool for a personalized approach towards anti-TNF cessation in CD.

Methods: A systematic literature search was conducted to identify studies investigating the risk of relapse and risk factors in CD patients after anti-TNF therapy cessation by using Medline Ovid, Embase, Cochrane, Web of Science and Google Scholar. Cohort studies with >50 CD patients in remission (clinical or biochemical or endoscopic/radiological) were selected. IPD from the original study databases were used for analysis. Inclusion criteria: luminal CD as indication for anti-TNF therapy, duration of treatment ≥6 months. We associated baseline demographic and clinical data (age, gender, smoking, disease duration, Montreal classification, history of surgical resection, type of anti-TNF, concomitant immunosuppressants, corticosteroids prior to cessation and previous anti-TNF therapy) with time to relapse using a Cox model. A prediction model was constructed, with backward selection and p>0.2 as criterion. To investigate the predictive performance internal-external validation was applied.

Results: A total of 10 cohort studies were identified, IPD were available from 6 studies. Anti-TNF was withdrawn in 1006 patients, who experienced 474 relapses after a median FU time of 14 months (IQR 8–28). At 1-year relapse rate was 36%, ranging from 24% to 44%. At 2-year the relapse rate was 54%. Risk factors for relapse were age (HR 0.98, CI 0.97–0.99), smoking at baseline (HR 1.19 (CI 0.96–1.48), disease duration (HR 1.06, CI 1.03–1.10), disease location (L2) (HR 1.04, 0.77–1.41), disease location (L3) (HR 1.25, CI 0.96-1.62), +L4 (HR 1.50, CI 1.00–2.27), type of anti-TNF therapy (adalimumab vs infliximab) (HR 1.18, CI 0.95-1.48), immunosuppressant use (HR 0.68, CI 0.54–0.85), steroids used 6-12 months prior to cessation (HR 1.24, CI 0.72-2.13), ≥1 anti-TNF therapy in medical history (HR 1.37, CI 1.04-1.80). The prediction model had a discriminative ability with a C-statistic of 0.62 (0.58 – 0.64). Biochemical parameters of remission (CRP, FC, hemoglobin, leucocytes), anti-TNF trough level and endoscopic data will be added to this preliminary prediction model.

Conclusion: The overall risk of relapse in CD patients in remission is 36% within 1 year after anti-TNF cessation. Despite associations between clinical parameters and relapse risk, individualized prediction solely based on clinical parameters remains challenging. Improvement of the discriminative ability of the prediction model may be anticipated after insertion of biochemical and endoscopic data.

The cytokine milieu in patients with Inflammatory Bowel Disease impacts the phenotype of mesenchymal stromal cells

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Background: Mesenchymal stromal cells (MSCs) have the capacity to promote healing of refractory perianal fistulas in Crohn's Disease (CD) and pre-treatment with cytokines may enhance therapeutic efficacy. Furthermore, locally applied MSCs are under clinical development for treatment of refractory proctitis in Ulcerative Colitis (UC). Despite these clinical advances, the mechanism of action of MSC therapy is largely unknown. We hypothesize that the proinflammatory environment in the patient promotes the immunomodulatory properties of MSCs. Therefore we analyzed cytokine levels in inflamed tissues obtained from CD and UC patients. Next, we assessed the expression of immunomodulatory molecules by MSCs upon exposure to these cytokines.
Methods: U-plex cytokine assay and ELISA were used to measure the levels of eleven cytokines, including interferon-γ, interleukin (IL)-17 and IL-1β, in perianal fistula scraping of patients with CD (n=20), colonic tissue samples (inflamed and non-inflamed) from patients with UC (n=18) and adjacent healthy tissue from patients with colorectal carcinoma (n=18). To determine the response of bone-marrow derived MSCs to different proinflammatory environments, MSCs were exposed to defined (sets of these) cytokines and the expression of immunomodulatory molecules was determined by flow cytometric and qPCR analyses.
Results: Scrapings of perianal fistulas obtained from CD patients contained high levels of cytokines, including IL-1β and IL-17 (IL-1β 0.102 pg/µg vs 0.012 pg/µg in normal colon tissue, $p=0.003$, and IL-17 0.206 pg/µg vs 0.009 pg/µg, $p<0.001$). In contrast, inflamed colon of UC patients only showed the presence of a selected set of cytokines of which some, like IL-1β, were already present in non-inflamed colons. Next, we evaluated the response of MSCs to exposure of the individual cytokines and 4 different cytokine mixtures which resemble the complex proinflammatory milieus in Inflammatory Bowel Disease. Interestingly, each cytokine mixture induced a unique expression pattern of intra –and extracellularly expressed immunomodulatory molecules in MSCs, including cyclo-oxygenase 2 and indoleamine 2,3-dioxygenase. Assays are ongoing to investigate the consequence of cytokine priming on the immunomodulatory function of MSCs.
Conclusion: The patient's proinflammatory milieu is strongly dependent on the underlying disease. We found *in vitro* evidence that infusion of MSCs into inflamed UC colonic tissue or CD fistulas induces upregulation of immunomodulatory molecules in MSCs that are unique for the patient's cytokine milieu and that play a role in the immunomodulatory properties of the cells. Differences in cytokine expression between patients may explain the different clinical efficacies that are observed following MSC therapy.

PNAd+ and MAdCAM+ High Endothelial Venules correlate with disease activity in ulcerative colitis

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Background: Tertiary lymphoid organs (TLOs) comprising peripheral node addressin positive (PNAd$^+$) and/or MAdCAM$^+$ high endothelial venules (HEVs) have been found to play an important role in local immunological dysregulation in chronic immune mediated disorders and malignancies. Their presence have a predictive value for disease course and response to therapy. Identification of these HEVs in the early phase of ulcerative colitis (UC) might help stratify patients to enable personalised medicine. We aimed to investigate the presence of these HEVs at UC diagnosis and their development during follow-up. Furthermore we studied their association with disease activity and response to therapy.
Methods: Retrospectively collected colonic biopsy specimens from 110 UC patients at first presentation and during follow-up were analysed by immunohistochemistry after determining the Geboes score. Immunostaining was performed using antibodies: MECA-79 (anti-PNAd), MECA-367(anti-MAdCAM), ERG(endothelial cells), CD3(T-cells) and CD20(B-cells). The expression of extrafollicular PNAd$^+$ on all vessels (ERG) was correlated to disease activity, disease course and response to therapy.
Results: 110 newly diagnosed UC patients were analyzed. Percentages of PNAd expressing ERG$^+$ vessels at baseline ranged from 0.0% to 29.8% (median 5.4; IQR 1.9-10.3). Higher numbers of extrafollicular PNAd$^+$HEVs were associated with higher numbers of colonic lymphoid follicles (r=+0.7 p=0.001). No extrafollicular PNAd$^+$ HEVs were detected in biopsies of patients in remission during follow-up (n=57 median 0.0: IQR 0.0-0.0). In active disease (n=53), PNAd expressing HEVs were not significant different from baseline numbers (median 4.2:IQR 1.6-7.6, p=0.178). Patients nonresponding to 5ASA induction therapy after initial diagnosis had significant higher baseline percentages of PNAd expressing ERG$^+$ vessels (p=0.046) in colonic biopsies compared to responding patients.
Median percentage of MAdCAM expressing ERG$^+$ vessels at baseline was 5.5% (IQR 2.6-10.1). During follow-up in both active disease and remission, significant elevation was demonstrated for MAdCAM expression on ERG$^+$ vessels (resp. 7.5%(IQR 3.3-12.5), p=0.028 and 8.8%(IQR 4.9-13.8), p=0.022).
Conclusion: Formation of extrafollicular PNAd$^+$HEVs was present in active disease while absent in remission. High numbers of PNAd$^+$HEVs were associated with no response to 5ASA induction therapy and with more colonic follicles, suggesting TLO formation. MAdCAM expression increased during disease course independent of disease activity.

Mucosal macrophages express elevated levels of HDAC9 in inflamed and uninflamed mucosa of Crohn's disease, but not ulcerative colitis

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Background: Histone deacetylases (HDACs) are a group of enzymes that control histone/-non-histone deacetylation and influence inflammatory gene transcription. Certain members of the HDAC family control the function of macrophages. We aimed to study the expression of HDACs in mucosal macrophages isolated from inflammatory bowel diseases (IBD) patients.
Methods: Both macroscopically inflamed and non-inflamed colon resection tissue were collected from 15 Crohn's disease (CD) and 9 ulcerative colitis (UC) patients operated on for therapy refractory disease. Of the CD patients, 53% had ileal and 47% ileocolonic disease. Of the UC patients, 44% had left-sided colitis and 56% pancolitis. Lamina propria was separated from the muscularis externa, and a targeted array for epigenetic enzymes was performed. To assess the relevance of HDAC9 gene expression in terms of protein level, immunofluorescence staining of HDAC9 protein was undertaken in tissue sections from inflamed and non-inflamed mucosa. CD68 was used as a pan-macrophage marker.
Results: From our array, expression of HDAC9 was significantly higher in the inflamed mucosa of CD patients compared to UC patients (p=0.005). Gene expression of HDAC9 in non-inflamed mucosa from CD was elevated compared to non-inflamed mucosa from UC. In addition, in CD, HDAC9 mRNA level was increased in inflamed tissue in comparison to non-inflamed tissue (p=0.046). In conjunction with the expression data, HDAC9 protein was found highly expressed in inflamed tissue. HDAC9 was predominantly localized in the cytoplasmic compartment of macrophages in non-inflamed tissue whilst HDAC9 localised to the nucleus of macrophages in inflamed tissue.
Conclusion: HDAC9 is member of class IIA HDAC superfamily that exerts pro-inflammatory properties. The inhibition of HDAC9 in experimental murine colitis clearly enhances regulatory T cell function, suggesting a critical role for HDAC9 in breaching immune homeostasis (de Zoeten EF et al, 2009). We suggest here, that HDAC9 can serve as an additional marker to distinguish CD from UC in tissue biopsies. Furthermore, we show for the first time that HDAC9 protein is expressed in muscosal macrophages of CD patients, indicating its potential in mediating macrophage inflammatory function in IBD. Further studies are currently being undertaken to elucidate the role of HDAC9 in CD pathogenesis.

Prognostic factors and survival in MEN1 patients with gastrinomas: results from the DutchMEN Study Group (DMSG)

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Background: Gastrinomas are the most prevalent functioning neuroendocrine tumors (NET) in multiple endocrine neoplasia type 1 (MEN1), leading to hypergastrinemia, hereby inducing gastric acid hypersecretion. Owing to presumed acceptable survival, guidelines suggest medical therapy in most patients. Nevertheless, surgery may be considered in a subgroup. Currently, prognostic factors to guide patient management are necessary. This population-based study aimed to determine prognostic factors of survival in MEN1 gastrinomas.
Methods: MEN1 patients with gastrinomas were identified in the Dutch MEN1 database from 1990-2014 based on fasting serum gastrin (FSG) levels and/or pathological reports. Survival probability estimates were obtained by Kaplan Meier curves. Predictors of overall survival were assessed using Cox proportional hazards regression.
Results: Sixty-three gastrinoma patients (16% of the MEN1 population) were identified with a mean age of 51 years. Five- and 10-year overall survival rates were 83% and 65%, respectively. Prognostic factors significantly associated with overall survival were initial FSG levels ≥20x upper limit of normal (ULN) (hazard ratio (HR) 6.2 (95% Confidence Interval 1.7 – 23.0)), pancreatic NET ≥2cm (HR 4.5 (1.5 – 13.1)), synchronous liver metastases (HR 8.9 (2.1 – 36.7)), gastroduodenoscopy suspicious for gastric NETs (HR 12.7 (1.4 – 115.6)) and multiple concurrent NETs (HR 5.9 (1.2 – 27.7)).
Conclusion: Life expectancy of MEN1 gastrinoma patients is reduced. FSG levels and pancreatic NETs ≥ 2 cm are prognostic factors. FSG levels might guide surveillance intensity, step-up to additional diagnostic procedures or provide arguments in selecting patients who might benefit from surgery.

Endoscopically removed colorectal NETs; a nationwide cohort study

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Background: Colorectal neuroendocrine tumors (NETs) often present as an incidental finding during colonoscopy. Complete endoscopic resection of low grade NETs up to 1cm during colonoscopy is considered safe. Whether this is also safe for larger NETs is unclear since the risk of recurrence is unknown. The ENETS guideline states that further evidence on this topic is needed. We performed a nationwide study to determine the risk of recurrence in endoscopically removed NETs.
Methods: All endoscopically removed colorectal NETs between 1990 and 2010 were identified using the national pathology database (PALGA) and the Dutch Cancer Registry. Each NET was stratified according to size, grade and resection margin. Follow up was until February 2016.
Results: Between 1990 and 2010 a total of 331 NETs were endoscopically removed of which 236 (95%) were smaller than 20mm. In 48% of NETs (n=160) no grade could be assessed from the pathology report, 4% were grade 2/3 (n=12), the remaining NETs were G1. The resection margins were positive in 36% of specimens. Median follow up was 9.6 years (IQR 6.4 – 15.2). During follow up 36 patients (11%) underwent surgical resection. Local recurrence was seen in 20/36 (55%) of surgical specimens, which all had a positive resection margin at endoscopic resection. Median time from endoscopic resection to surgery was 96 days (IQR 44-219). Metastatic recurrence was seen in 6 patients (2%) of whom 3 had previously undergone surgery. At endoscopic resection these 6 patients either had a NET larger than 20mm (n=3) or G2/3 grade (n=5). Mean time from endoscopic resection to diagnosis of metastases was 6.1 years (95% CI 2.9-9.2).
Conclusion: In our nationwide study no local or metastatic recurrence was seen in low grade (G1) NETs up to 20mm, provided they were resected completely. This adds evidence to the ENETS guideline that the cut off size for endoscopic resection of G1 NETs should be 20mm.

Effect of perioperative treatment on microsatellite instable gastric cancer in the CRITICS trial

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Background: Microsatellite instability (MSI) has been shown to be a positive prognostic factor for long term survival in resectable gastric cancer (GC) in several studies. However, the effect of perioperative treatment on MSI and microsatellite stable (MSS) tumors has not been conclusive. Here, we present the clinical outcome of patients with MSI and MSS tumors treated with chemotherapy or chemoradiotherapy after surgery and preoperative chemotherapy in the CRITICS trial

Methods: Formalin-fixed paraffin-embedded (FFPE) GC tissues were collected from patients in the CRITICS trial. Histological tumor type according to Lauren and pathological response to preoperative chemotherapy according to Mandard were assessed. MSI status was determined in biopsies by MSI-PCR with a five mononucleotide marker panel (Bat-25, Bat-26, MONO-27, NR-21, and NR-24). Tumors were considered MSI if at least two markers were instable. MSI status was correlated with survival using log-rank tests.

Results: Of 168 tumors analyzed so far, 13 (7.7%) were MSI. MSI occurred in 10 out of 85 (11.8%) patients treated with postoperative chemoradiotherapy, and in 3 out of 83 (3.6%) treated with postoperative chemotherapy. MSI was associated with distal location, intestinal subtype, and poor histological response to preoperative chemotherapy in resection specimens. Five-year overall survival was 69.2% for MSI and 40.8% for MSS (p=0.084). Five-year event-free survival was 61.5% for MSI and 36.1% for MSS (p=0.147).

Conclusion: GC patients with MSI tumors show a trend of favorable outcome compared to MSS tumors after perioperative treatment, despite poor histological response to preoperative chemotherapy. Results of an expanded dataset including multivariate analyses will be presented.

A comparison of elderly versus non-elderly patients in the CRITICS gastric cancer trial

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Background: The proportion of elderly patients in the gastric cancer population is high. About 60% of patients are above 65 years. Few randomized trials provide specific data on elderly patients. Here, we present a sub-analysis of the CRITICS trial comparing elderly with non-elderly patients.
Methods: Prior to D2 gastric cancer surgery, patients received 3 cycles of epirubicin + cisplatin/oxaliplatin + capecitabine (ECC/EOC). By upfront randomization, patients were allocated to postoperative chemotherapy (3x ECC/EOC) or chemoradiotherapy (45Gy + cisplatin + capecitabine). In the present analysis, treatment-related toxicity, relative dose intensity (RDI; interquartile range) and survival outcomes were compared between elderly (age ≥70 years) and non-elderly patients.
Results: Among the 788 patients, there were 172 elderly patients and 616 non-elderly patients. Preoperative chemotherapy started in 171 elderly patients and 610 non-elderly patients; 77% versus 62% experienced grade 3-5 toxicity (p<0.001). In elderly patients, the RDI was lower for epirubicin, cisplatin/oxaliplatin and capecitabine (all p<0.001). Potentially curative surgery was performed in 137 (80%) elderly patients versus 499 (81%) non-elderly patients (p=0.941), of whom 50% versus 46% had postoperative complications (p=0.441) and 4% versus 2% died in hospital (p=0.195), respectively.
Postoperative treatment started in 87 elderly patients (64% of patients who had curative surgery) and 391 non-elderly patients (78% of patients who had curative surgery) (p<0.001). Postoperative chemotherapy started in 41 elderly and in 192 non-elderly patients; 54% versus 59% experienced grade 3-5 toxicity (p=0.662). Elderly patients had lower RDIs for epirubicin (p=0.011), cisplatin/oxaliplatin (p<0.001) and capecitabine (p=0.002). Postoperative chemoradiotherapy started in 46 elderly patients and in 199 non-elderly patient; grade 3-5 toxicity was 48% versus 45% (p=0.828). There were no differences in RDIs of cisplatin and capecitabine, and of total radiotherapy administration. The 2-year overall survival was 59% (95%CI 52-67) for elderly patients and 61% (95%CI 57-65) for non-elderly patients.
Conclusion: In patients with resectable gastric cancer, advanced age was associated with higher chemotherapy-induced toxicity and higher chemotherapy dosage reduction during preoperative chemotherapy. Fewer elderly patients started postoperative treatment and elderly patients received reduced dosages in the chemotherapy arm, but there were no differences in treatment related toxicities. Surgical resection and postoperative complications, as well as overall survival were comparable between elderly and non-elderly patients.

Venous thromboembolism during preoperative chemotherapy in the CRITICS gastric cancer trial

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Background: Venous thromboembolism (VTE) is a common complication in patients with cancer. Gastric cancer has been associated with one of the highest risks of VTE. Risk factors for development of VTE have mainly been investigated in Asian populations and/or in metastasized setting and include: gender, age, body mass index (BMI), stage, primary tumor localization and chemotherapy, in particular cisplatin. The aim of this study was to identify risk factors for VTE during preoperative chemotherapy in resectable gastric cancer patients.
Methods: Patients with resectable gastric cancer were selected from the CRITICS trial and were preoperatively treated with 3 cycles of 3-weekly epirubicin, cisplatin/oxaliplatin and capecitabine (ECC/EOC). All patients who started preoperative therapy were studied. Preoperative period was defined as start date of last chemotherapy cycles plus 30 days or surgery, whatever came first. Venous thromboembolism was defined as any thrombus in the venous system, excluding superficial and/or device related VTE. Risk factors of interest were fitted in a multivariable regression model: age (<60years, 60-69 years, 70+years), gender, BMI (<25, 25-30, ≥30), ECC/EOC and tumor localization (distal, middle or proximal stomach, gastro-esophageal junction).
Results: A total of 781 patients were included in this analysis, of whom 78 (10%) developed a VTE during the preoperative period. In a multivariable analysis, only BMI ≥30 was significantly associated with VTE (reference BMI <25; OR 2.16; 95% CI 1.14-4.09; p=0.018). Seventy-four patients with VTE (95%) proceeded to surgery (both curative and palliative) compared to 666 (95%) patients without VTE (p=0.99).
Conclusion: High BMI (≥30) was the only independent risk factor for developing VTE in resectable gastric cancer, preoperatively treated with ECC/EOC. Cisplatin was, compared to oxaliplatin, not identified as a significant risk factor for VTE in this cohort. A diagnosis of VTE did not influence the clinical decision to proceed to surgery.

Factors associated with the progression of gastric intestinal metaplasia in a low risk population - A multicenter, prospective cohort study

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Background: Gastric cancer (GC) is preceded by several gastric precursor lesions (GPL) which makes it suitable for surveillance. For low risk areas the method and frequency of endoscopic surveillance is still under debate. This study aims to identify high and low risk subjects for progression of GPL to prevent unnecessary performed endoscopies. Patient characteristics and previously described discriminative serum markers (pepsinogens (PG) and gastrin-17) at baseline are assessed.
Methods: The PROREGAL study started in 2009 and is one of the largest prospective cohorts in the Netherlands and Norway. Inclusion: 1) >18 years of age, 2) previous diagnosis of PGL. Patients completed a questionnaire on lifestyle factors and underwent at least two endoscopies. Biopsies were obtained from visible lesions and 12 standardised stomach sites and assessed according to the operative link on gastric intestinal metaplasia (OLGIM) system. At baseline, PG and gastrin-17 samples were drawn. Progression of IM was defined as progression of OLGIM classification between follow-up (FU) endoscopy. A cox-regression was performed with a significance level of 0.05.
Results: 308 patients (median age 61 years, IQR17;male 48.4%) were included. Median FU time was 48 months (IQR 24). During FU 116 patients showed progression of OLGIM stage (37.7%) providing an incidence rate of 9 events/100 personyears (95%CI 8.8-9.2). Six patients (1.9%) developed GC (0.4 events/100 personyears (95%CI 0.002-0.01)). History of Hp-infection (HR1.2; 95%CI 0.7-2.0), smoking (HR1.3; 95%CI 0.8-2.3), alcohol use (HR0.9; 95%CI 0.5-1.4) and increased BMI (HR1.0; 95%CI 0.9-1.1) did not show significant associations. Also serum levels of PG I/II (HR1.0 95%CI 0.9-1.1), and gastrin-17 (HR1.0; 95%CI 0.9-1.1) were not significantly correlated with progression of IM.
Conclusion: This is the first study to assess RF for the progression of IM in low risk areas. Over 1/3 of the study cohort showed progression of IM, indicating surveillance remains of importance. Lifestyle factors were not correlated with progression of IM. Moreover, baseline serum markers are not predictive for future progression of IM during FU. Future studies should focus on the longitudinal assessment of these markers.

This research was funded by the UEG Research Prize awarded to EJK

Patient-reported burden of intensified surveillance and surgery in high-risk individuals under pancreatic cancer surveillance

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Background: Worrisome features detected in high-risk individuals participating in a pancreatic cancer surveillance program, warrant for intensified surveillance or, occasionally, surgery. We aimed to determine the psychological burden of intensified surveillance and/or surgery.
Methods: In the course of our pancreatic cancer surveillance program, participants completed questionnaires including the Hospital Anxiety and Depression Scale (HADS, subscales range 0-21) and the Cancer Worry Scale (CWS, ranges 8-32). For individuals who underwent intensified surveillance, questionnaires before, during, and ≥3 weeks after the decision to return to regular follow-up were analyzed. In addition, those who underwent intensified surveillance in the last 3 years, or surgery at any time, were invited for a semi-structured telephone interview.
Results: 34 individuals underwent intensified surveillance, 20 returned multiple questionnaires (response rate 59%) and 12 were invited for an interview, to which eight consented (response rate 67%). Of those who underwent surgery, 10 were interviewed (response rate 91%). The total cohort consisted of 31 individuals.
During intensified surveillance, cancer worries increased significantly (median CWS 14, IQR 7), as compared to before (median 12; IQR 9, P=0.007) or after (median 11, IQR 7, P=0.014), but eventually returned back to baseline (P=0.823). General anxiety and depression scores were low (both median 5, IQR 5) and not influenced by the event (P>0.100). The 8 interviewed participants regarded intensified surveillance as something positive (2), neutral (2), negative but necessary (3) or negative (1).
Of the 10 operated patients, 5 underwent a pancreatoduodenectomy and 5 a distal pancreatectomy. Pathology revealed one T1 pancreatic cancer, 7 low-grade premalignant lesions, and 2 cases of benign disease. Afterwards, 20% developed diabetes and 70% steatorrhea. Patients judged their recovery as good (20%), fair (50%), or poor (30%). Quality of life (median SF-12 PCS 56 and MCS 52) was not different from age-matched reference data from the general population. After surgery, patients' attitude towards surveillance was unchanged (60%) or more positive (40%), but never more negative. Knowing the pathological outcome, when asked if surgery had been justified, only 20% disagreed and all would again have chosen to undergo surgery.
Conclusion: In individuals at high risk for pancreatic cancer, intensified surveillance transiently increased cancer worries, without affecting general anxiety or depression. Although surgery led to substantial co-morbidity, quality of life was similar to the general population, and surgery did not negatively affect the attitude towards surveillance.

12 Years of prospective pancreatic cancer surveillance: results of the Dutch nation-wide program in high-risk individuals

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Background: Surveillance of individuals at high risk for pancreatic ductal adenocarcinoma (PDAC) may reduce pancreatic cancer-related mortality. We aimed to determine the yield of a nationwide pancreatic cancer surveillance program in the Netherlands during a 12-year follow-up.
Methods: From 2006 through 2018, asymptomatic individuals with an estimated more than 10-fold increased lifetime PDAC risk were enrolled. Surveillance commenced at the age of 50 or 10 years younger than cancer onset in the family, and ended at the age of 75. Surveillance was performed every 12 months with both MRI and EUS. For worrisome features the surveillance interval was shortened to 3 or 6 months or surgery was performed.
Results: 344 individuals from 229 families were enrolled (mean age 54 (SD 10.0) years, 44% male). 156 (45%) were germline mutation carriers and 188 (55%) familial pancreatic cancer kindred. They were followed for a median of 44 (IQR 74) months and a total of 1616 person-years. Cystic lesions were found in 185 (54%) participants, which were ≥1 cm in 43 (13%). 14 (4.1%) participants underwent surgery for a suspect lesion. Pathological results in these patients revealed PDAC in 4, low-grade precursor lesions in 7, a 5-mm neuroendocrine tumor in 1, autoimmune pancreatitis in 1, and no lesion in the specimen in 1 patient.
In total, 7 (2%) patients developed PDAC (median age 56 years, IQR 23). Two were diagnosed at baseline and underwent resection. Histology revealed a margin negative T2N1M0 and T1N0M0. Both patients died after 32 months. Another 5 individuals developed PDAC during follow-up, all of whom had prior abnormalities visible on both EUS and MRI (presumed side branch IPMN in 4, an indeterminate lesion in 2, a moderately dilated common bile duct in 1, and a main pancreatic duct stricture without visible mass in 1 case). Of the 5 PDACs detected at follow-up, 3 (60%) were irresectable (survival 1-4 months), two of which had presented as symptomatic interval carcinomas, of which one appeared to have arisen separately from the known side branch IPMN. One of the 5 underwent an irradical resection (T3N1M0, survival 18 months), and one was radically resected (T1N0M0, alive, 18 months after diagnosis). The overall median survival for the 6 deceased PDAC patients was 11 (IQR 30) months.
Conclusion: In this relatively young cohort of individuals at high risk for PDAC, timely identification of relevant resectable lesions proved challenging with surveillance with EUS and MRI. The quantitative effect on resectability rates and survival remain difficult to assess because of the limited number of cases and possible lead-time bias. Biomarkers may hold better promise to improve the outcome of surveillance.

Yield of malignant lymph node detection by EUS and FNA in restaging after neo-adjuvant chemoradiotherapy for esophageal cancer

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Background: Despite the known decreased accuracy, endoscopic ultrasonography (EUS) and fine-needle aspiration (FNA) are believed to be potential tools for detection of residual disease after neoadjuvant chemoradiotherapy (nCRT) for esophageal cancer. This study aimed to investigate the yield of EUS and FNA for detection of malignant lymph nodes after nCRT.
Methods: EUS and FNA were performed 12 weeks after completion of nCRT. Suspect lymph nodes were defined as round, hypo-echogenic, and with a size of ≥5 millimeters. Lymph nodes that were considered suspect but did not meet aforementioned criteria were recorded separately. To guide targeting of suspect lymph nodes, F18-FDG PET-CT was performed beforehand. Endoscopic nodal staging by EUS (uN) was compared to the histopathological examination of the resection specimen (ypN). Primary outcome of this study was the proportion of patients with malignant lymph nodes (ypN+) that was identified by EUS (uN+).
Results: 100 consecutive patients were included in this analysis. Tumor was passable in all patients. Twenty-one patients had ypN+ residual disease of which 11 were identified by EUS (sensitivity 52%). Subsequently, 62 of 79 ypN- patients were classified accordingly by EUS (specificity 78%). More than half of patients (n=6, 55%) in whom suspect lymph nodes did not meet predefined criteria had ypN+ residual disease. Missed malignant lymph nodes were located at the celiac trunk, the lesser curvature, and at the paraesophageal stations. Sensitivity and specificity of FNA were 75% (3/4) and 100% (11/11), respectively. FNA outcome was uncertain in 8 patients. A positive aspirate was collected in one FDG-avid lymph node that was deemed benign by EUS.
Conclusion: Only half of patients with ypN+ residual disease was identified by EUS after nCRT. For this reason and the absence of false-positive findings by FNA, all lymph nodes detected after nCRT should be sampled when aiming to detect residual disease.

Genomic biomarkers for cancer risk in Barrett's esophagus: an update on the longitudinal dutch barrett's esophagus cohort

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Background: Malignant degeneration to esophageal adenocarcinoma (EAC) of Barrett's esophagus (BE) patients with no dysplasia occurs infrequently. To reduce costs, periodic endoscopic surveillance intervals have been increased. Robust biomarkers that predict long term cancer risk are required to further improve the cost efficacy of surveillance. In previous cohort studies, we identified a set of genomic abnormalities and measures of clonal diversity as predictors for cancer development after a median follow up of 43 months. Here, we aimed at building prediction models using the same biomarkers and test their robustness to predict cancer risk over longer periods of time.

Methods: In this multi-center study, abnormalities for CEP7, CEP17, c-MYC, p16, p53, Her-2/neu and 20q earlier assessed by DNA FISH on brush cytology specimens and collected between 2002 and 2013, were used to determine marker scores and to perform clonal diversity measurements. These genetic biomarkers were combined with clinical variables and analyzed to obtain a cost-effective cancer prediction model. Hereto, Cox regression modeling, bootstrapping and leave-one-out analyses were applied.

Results: A total of 334 patients from 6 community hospitals (n=220) and one academic center (n=114) were included. Median age was 60 years (IQR= 16), 80.8% was male and average circumferential Barrett's length (CBL) was 2 cm (SD 4cm). The median prospective follow-up time was 87 months (IQR 40). All patients had no-dysplasia at inclusion, representative of a BE population undergoing routine endoscopic surveillance. The annual progression rate to EAC was 0.8% and to HGD or EAC 1.3%. A multivariate prediction model including the (borderline) significant variables age and CBL, and clonal diversity score over marker set CEP7, CEP17, 20q and c-MYC, resulted in an AUC 0.62. In the whole cohort, 17 out of 32 (53%) progressed to HGD/EAC within 5 years of follow-up and 15 (47%) progressed after 5 years. Only 1 patient progressed after 10 years of follow-up time. With a risk score cutoff at 1.357, the model had a sensitivity of 0.66 and a specificity of 0.67 to predict cancer risk over a median follow up time of >7 years. This model defines a high risk non-dysplastic BE population with an annual progression rate of 2.9%, versus 0.63% in the low risk group.

Conclusion: We propose that the implementation of the model can identify non-dysplastic BE patients that require more frequent surveillance or endoscopic treatment, while surveillance of patients with no dysplasia and a low score can be more relaxed.

Mutational signatures during the preneoplastic cascade towards cholangiocarcinoma in Primary Sclerosing Cholangitis

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Background: Primary sclerosing cholangitis (PSC) is associated with an increased risk of cholangiocarcinoma (CCA). Carcinogenesis and involved molecular processes are poorly understood. As PSC-related CCA (PSC-CCA) presumably follows the inflammation–dysplasia–carcinoma cascade, genetic aberrations might be detected at premalignant stage. We aimed to identify genetic alterations in PSC- related dysplasia and CCA by multiregional targeted sequencing.
Methods: A total of 19 PSC-patients with biliary dysplasia and/or CCA after surgical resection were included. Resection specimens of 18 patients contained CCA +/- dysplasia, and one only dysplasia. DNA was extracted from sections of formalin-fixed paraffin-embedded tissue blocks. Targeted next generation sequencing of a custom made cancer panel, consisting of 28 genes, was performed on 37 tumour and 6 dysplasia samples. Coverage of amplicons included in the gene panel was investigated in order to detect genomic imbalance of 13 genes of interest. In addition, copy number variations of *CDKN2A, EGFR, MCL1* and *MYC* were examined by fluorescence in situ hybridization (FISH).
Results: *TP53* mutations were the most common aberration observed in PSC-CCA (13 samples/ 8 patients), other mutations observed are in *KRAS* (7 samples), *GNAS* (3), *ERBB2* (2), *APC* (1) and *PIK3CA* (1). In addition, mutations in *TP53* (4) and *ERBB2* (3) were identified in four dysplasia samples. *CDKN2A* loss was seen in both tumour (7) and dysplasia (1), *SMAD4* and *TP53* loss only in tumour (10 and 1). Gain of *MYC, ERBB2, EGFR* and *PIK3CA* was found in 7/7/4/1 tumour and 3/2/1/1 dysplasia samples, respectively. Genomic imbalance assessment showed *MCL1*, *KRAS* and *FGFR3* amplification only in tumour samples (3/3/5). In one patient high level amplification of *EGFR* was found in dysplasia, while tumour did not show *EGFR* amplification. Strikingly, both loss and gain of *POLD1* were seen in tumour and dysplasia. The dysplasia samples demonstrating genetic alterations only concerned high grade dysplasia. In half of the samples that have demonstrated copy number variations in the genomic imbalance assessment, we were able to confirm *CDKN2A* loss and gain of *MCL1, MYC* and *EGFR* by using FISH. In the other half, one or both of the analyses were inconclusive.
Conclusion: PSC-CCA exhibits multiple genetic alterations, including mutations and chromosomal imbalance. *TP53* mutations and genomic instability of *CDKN2A, MYC, ERBB2*, *EGFR* and *PIK3CA* seem to occur early in the multistep process since these alterations were observed at premalignant stage. These genetic alterations seem promising for development of sequencing guided diagnostic strategies of PSC strictures.

Trends in incidence, treatment and survival of gallbladder cancer; a nation-wide cohort study

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Background: Gallbladder cancer (GBC) is rare tumour with a poor prognosis. Data from the Western world on the incidence, treatment, and survival is scarce. Population-based data is essential in order to identify prognostic factors, optimise treatment strategies and ultimately improve the prospects of GBC patients.
Methods: Data on all patients diagnosed from 2005 – 2016 with invasive GBC were derived from the Netherlands Cancer Registry. Trends in incidence, treatment strategies and overall survival (OS) were analysed using Chi-Square testing, Kaplan - Meier methods and Cox Regression analysis.
Results: Age-standardised incidence of GBC varied from 0.6 to 0.9 per 100.000 person years and did not change significantly during the study period. Between 2005 – 2009 and 2010 – 2016, more patients with early (T1/T2) GBC received radical as opposed to simple cholecystectomy (19% vs 33%, P<0.001) and more palliative chemotherapy was administered to metastatic patients (11% vs. 29%, P<0.001). OS across the entire cohort was 5.5 months and increased from 4.8 months to 6.1 months (P<0.017). OS in resected, non-resected non-metastatic and metastatic patients was 23.7, 3.6 and 2.9 months respectively. Radical surgery in early (T1/T2) GBC increased OS from 18.3 to 76.7 months (P<0.001). In non-resected and metastatic disease, palliative chemotherapy increased survival from 3.6 to 7.7 (P=0.011) and 2.1 to 7.3 (P<0.001) months respectively. Poor prognostic factors in resected GBC were increasing age, increasing T stage, poor differentiation, the presence of lymph node metastases and irradical resection.
Conclusion: The prognosis of GBC patients is poor and no clinically relevant improvement has been made in the past decade. Radical cholecystectomy in early GBC and palliative chemotherapy in non-resected and metastatic GBC appear to improve prognosis but were infrequently used.

A Functional Assay-Based Procedure to Classify Mismatch Repair Gene Variants in Lynch Syndrome. (MLDS-VOORDRACHT)

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Background: The inability to determine pathogenicity of the increasingly prevalent Variants of Uncertain Significance (VUS) in the DNA mismatch repair (MMR) genes, identified in individuals suspected of the cancer predisposition Lynch syndrome [1], precludes personalized healthcare. To enable classification of these VUS, we developed the *Cell-free In vitro MMR Activity (CIMRA)* assay that does not require any patient material and can be completed in a few weeks [2-4]. Here, we have calibrated and validated the assay and have integrated it with *in silico* prediction of pathogenicity.

Methods: Two sets of independently classified MLH1 and MSH2 variants were used to calibrate the CIMRA assay by regression analysis, followed by symmetric cross-validation and Bayesian integration with *in silico* analysis. CIMRA assay reproducibility was independently assessed in four laboratories worldwide.

Results: Bayesian integration of CIMRA assay results with *in silico* predictions of pathogenicity enabled the classification of 87% of all VUS, with a very low (<3%) error rate. Inter-laboratory results were highly reproducible [5].

Conclusion: This rapid and cost-effective diagnostic procedure will dramatically increase the rate of classification of VUS in the MMR genes, enabling personalized healthcare for carriers of pathogenic variants. Moreover, our strategy provides a template for the development of the diagnostic assessment of VUS in proteins associated with other hereditary cancer predisposition syndromes and genetic disorders.

This work has been funded by the National Institutes of Health and the Dutch Digestive Foundation.

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Detection of Barrett's esophagus through exhaled breath using a non-invasive screening tool

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Background: The majority of patients with esophageal adenocarcinoma (EAC) present with advanced disease, resulting in poor survival rates. Timely detection of EAC and its precursor Barrett's esophagus (BE) could decrease both cancer mortality and incidence. Currently, an accurate, minimally-invasive screening method for BE for widespread use is not available. Our objective was to establish the accuracy with which an electronic nose for breath analysis could discriminate patients with BE from controls without BE.
Methods: In this multicenter, cross-sectional, proof-of-principle study, patients undergoing a clinically indicated upper endoscopy between August 2017 and October 2018 were invited to provide a 5-minute breath sample using an electronic nose immediately prior to the scheduled endoscopy. Patients were allocated in three subgroups: BE (defined as ≥1 cm of columnar mucosa with histopathologic confirmation of intestinal metaplasia), gastro-esophageal reflux disease (GERD) (defined as GerdQ-score ≥8 or the endoscopic presence of reflux esophagitis), and controls without BE or GERD.
The Aeonose™ is an olfactory system that analyses volatile organic compounds (VOC). Three metal-oxide sensors interact with VOCs in the breath sample to create a digital breath print specific to the VOCs. Data was analyzed by an artificial neural network to identify data classifiers to extract breath-print differences between patients with BE, GERD and controls. Optimal models were cross-validated using a leave-10%-out approach. Main outcomes were sensitivity and specificity for detecting BE compared with upper endoscopy as the reference standard.
Results: Breath samples were obtained from 153 individuals. Recruitment rates were 97%. Mean age of participants was 60.8 years and 61% were male. Sixty patients had a diagnosis of BE with a median (IQR) length of the BE segment of 4 (3–7) cm, 53 patients were diagnosed with GERD (38% reflux esophagitis), and 40 patients did not have any upper gastrointestinal abnormalities except for hiatal hernia. Diagnostic accuracy was high for discrimination of BE from GERD and controls (area under the curve [AUC] 0.91, sensitivity 90% [95%CI: 79%–96%], specificity 81% [95%CI: 71%–88%]). Similarly, breath prints of BE patients could be differentiated from GERD patients (AUC 0.85, sensitivity 72% [95%CI: 58%–82%], specificity 89% [95%CI: 76%–95%]).
Conclusion: This portable electronic nose is able to detect the presence or absence of BE in patients with and without GERD with high accuracy. Given the high tolerability, high acceptability and low costs, breath testing may be a promising approach to be used for non-invasive screening for BE in a primary care setting.

E-Patient Counseling trial (E-PACO): computer based patient education is non-

inferior to nurse counseling prior to colonoscopy, a multicenter randomized controlled trial

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Background: Optimal patient education prior to colonoscopy improves adherence to instructions for bowel preparation and leads to cleaner colons. Endoscopy units are obligated to obtain informed consent prior to procedures, combined with risk assessment for use of sedative drugs. Current practice in the Netherlands to achieve both goals is a nurse counseling (NC) visit. This visit is costly and has disadvantages in terms of content uniformity and time consumption for both patient and the hospital. We developed a computer based education (CBE) supported by video and 3D animations. We hypothesized that CBE may replace NC in most cases, without losing quality of bowel cleanliness during colonoscopy.
Methods: A prospective, multicenter, endoscopist blinded, non-inferiority randomized controlled trial was conducted. The primary outcome was the rate of successful bowel cleansing, evaluated using the Boston Bowel Preparation Scale (BBPS). Secondary outcome measures were sickness absence due to outpatients clinic visit, patient anxiety and satisfaction scores and information re-call. Data was gathered through questionnaires, for endoscopist and patient, and endoscopy reports. The study was performed in four endoscopy units of different levels (rural, urban, tertiary). Inclusion criteria were adult age and referral for complete colonoscopy.
Results: Out of 1035 eligible patients, we randomized 845 patients. After evaluation, 497 patients were included in our per-protocol analyses, 217 in the NC group and 280 in the CBE group. Baseline characteristics were similarly distributed among groups. Overall response rates for the three patient questionnaires were 100%, 55.6% and 47.3%. The endoscopist questionnaire was completed in 42%, however BBPS scores were retrieved in 95%.
Successful bowel cleansing was achieved in 93.2 % (261/280) of the CBE group, which was non-inferior to the NC group (94%, 204/217), with a difference of -0.8% [95% confidence interval (CI) -5.1 – 3.5]. BBPS scores were 7.8 (SD 1.62) and 8.0 (SD 1.69), respectively.
Sickness absence was significantly more frequent in the NC group (28.0% vs 4.83%). In the CBE group, 21.8% of patients needed additional information, resulting in 4.8% extra outpatient clinic visits. Other secondary outcomes showed no significant difference in both groups.
Conclusion: As modality for patient education, CBE is non-inferior to NC in terms of bowel cleanliness during colonoscopy, with lower patient sickness leave. CBE therefore is practical and efficient for patient education prior to colonoscopy and is recommended for daily practice.

EndoRotor ablation of Barrett's esophagus; a safety and feasibility study

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Background: Several techniques exist for the ablation of Barrett's esophagus (BE); however, all have limitations in terms of successful conversion to squamous epithelium, as well as a complication profile. The EndoRotor is a new device that has, thus far, shown promising results for the ablation of BE. The EndoRotor is a non-thermal device, suctioning Barrett's epithelium into a small orifice, where a rotating knife resects the mucosa, automatically collecting tissue for pathological review. The aim of this study was to assess the safety and efficacy of the EndoRotor for the ablation of BE.
Methods: Between January 2017 and September 2018, 30 patients with BE were included from 2 tertiary referral centers in The Netherlands. Inclusion criteria: BE length 2-5cm, with low-grade dysplasia (LGD), high-grade dysplasia (HGD) or residual BE after endoscopic resection (ER) of a lesion containing HGD or early esophageal adenocarcinoma (EAC). Exclusion criteria: previous ER of >50% circumference, or previous ablation therapy. During the procedure, we aimed to ablate at least 50-100% of the BE. Follow-up (FU) endoscopy was performed 3 months after treatment. Primary outcomes: percentage of endoscopically visible surface regression of BE at 3 months FU, and complications. Secondary outcome: procedure time.
Results: Thirty patients (25 male, median age 66 yrs (IQR 59-73), median BE C0 (IQR 0-1) M3 (IQR 3-3.3)) were included. Eighteen patients had undergone ER prior to ablation. The median % BE ablated during the procedure was 100% (IQR 94-100) with a median circumferential extent of 95% (IQR 50-100). Median procedure time was 42 minutes (IQR 33-60) and median ablation time was 28 minutes (IQR 20-45). Median BE surface regression at 3-months FU was 90% (IQR 80-99). Multiple residual Barrett's islands were commonly seen. Serious complications occurred in 2/30 patients (7%): 1 perforation and 1 post-procedural bleed, both requiring intervention and hospitalization. 8/30 patients (27%) complained of dysphagia; 4 patients had a stricture requiring intervention. During FU endoscopy, non-circumferential scarring was seen in 10/27 patients (37%). 18/30 patients (60%) had post-procedural pain or odynophagia, during a median of 5 days (IQR 3-10).
Conclusion: For ablation of Barrett's esophagus, the EndoRotor seems non-inferior to established ablative techniques. However, complication rates seem higher and procedure time longer. Additionally, the difficulty level in operating the device is high, with a high potential for complications in inexperienced hands. For patients with therapy-naive BE, we advise against the use of the EndoRotor.

Predictors of adequate sampling in EUS guided TA of solid pancreatic lesions in a large prospective cohort of Dutch community hospitals

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Background: Endoscopic ultrasound (EUS) guided tissue acquisition (TA) is the method of choice to establish a pathological diagnosis of solid pancreatic lesions. EUS guided TA is a complex multistep procedure involving efforts of both endosonographers (ESGs) and cytopathologists. Reported outcomes on the quality and yield of EUS guided TA are skewed towards high-volume academic institutions. For community hospitals, in which the majority of these procedures are performed, these data are unknown. Rate of adequate sample(RAS) (the proportion of tissue samples sufficient for cytopathological evaluation) is the only quality indicator solely reflecting the work of the endosonography team. Study aims are therefore: 1. to determine and improve the RAS of EUS guided TA in a group of community hospitals and 2. to identify determinants of RAS
Methods: From January 2015 until October 2018 five community hospitals in the Rotterdam region in the Netherlands, prospectively included procedures. The primary outcome variable was RAS. Univariate and multivariate analyses were performed to identify determinants of yield such as type and size of needle used, application of suction, presence of rapid on site cytopathological evaluation (ROSE) and the number of procedures performed by the ESG.
Results: Seventeen ESGs, with individual EUS experience ranging from 1-12 years, performed 344 procedures over a period of 46 consecutive months. Overall RAS was 91.9% (ASGE ref standard: >85%) (1.). In a multivariate analysis the use of suction and number of procedures performed by ESGs were statistically significantly and positively associated with RAS (p=<0,01) and (p=<0,01) respectively. No significant interaction was found between number of procedures and use of suction. Nine ESGs performed 15 procedures or less (median 5 (1-15)) accounting for 53 procedures in total. Within this subgroup RAS was 79%. The remaining 8 ESGs performed 285 procedures (median 29 (16-62)) yielding a RAS of 94%. Differences in RAS between “low-volume” and “high-volume” ESGs were statistically significant p<0,01.
Conclusion: Both use of suction and higher number of procedures performed by ESGs are associated with better outcome of EUS guided TA in this prospective cohort in community hospitals. Therefore, fewer endosonographers doing more EUS procedures and routine use of suction seem obvious implementations to improve the yield of EUS guided TA of solid pancreatic lesions in community hospitals.

Guidance for setting alternative competence criteria for optical diagnosis of diminutive colorectal polyps which are easier to implement in daily practice - a simulation study

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Background: To safely implement the cost-saving optical diagnosis (OD) strategy for diminutive polyps, the PIVI (Preservation and Incorporation of Valuable Endoscopic Innovation) initiative of the ASGE proposed performance thresholds for endoscopists; (1) ≥90% surveillance agreement and (2) ≥90% negative predictive value (NPV) for neoplastic polyps in the rectosigmoid with histology as reference. A Dutch study showed that PIVI can be met after training. However, these criteria have drawbacks in daily practice; estimation of the NPV is hampered as hyperplastic polyps (HPs) in the rectosigmoid are already left-in and surveillance interval is mostly dependent on larger polyps found during colonoscopy. To provide guidance for setting criteria for OD competence that are easier to implement in daily practice, we aimed to assess the relation between an endoscopist's ability to correctly diagnose diminutive polyps, and his/her compliance with the PIVI criteria.
Methods: Data was used from a cohort of 3.144 Dutch faecal immunochemical test positive individuals who underwent colonoscopy. Proportion of high-confidence predictions was 79%, 42% and 65% for diminutive adenomas, SSLS, and HPs. The data were used to assess compliance with the PIVI for a hypothetical endoscopist in the cohort, under different assumptions for the proportion of correctly diagnosed diminutive polyps. Latter values were varied as follows: sensitivity for adenomas range 0.50-1.00, interval 0.01; SSLs and HPs range 0.00-1.00, interval 0.05. For each combination of sensitivities, we determined whether the PIVI were met with respect to the surveillance agreement (Dutch, ESGE) and NPV, using bootstrap-like methodology.
Results: Sensitivities of diminutive adenomas had to be considerably higher to reach the NPV criterion (≥92% (95% CI 90-94)) than for reaching the surveillance agreement criterion ((≥71% (95% CI 70-74) Dutch, ≥20% (95% CI 16-24) ESGE), under the assumption that all diminutive HPs and SSLs were correctly diagnosed. The NPV and surveillance agreement decreased by only 1% when diminutive SSLs were all incorrectly diagnosed instead. Both PIVI criteria *could* be met when ≥77% of all diminutive polyps were correctly diagnosed but were *always* met when ≥93% were correctly diagnosed.
Conclusion: This study suggests that when endoscopists reach the ≥90% NPV PIVI criteria, they also meet the surveillance agreement. Endoscopists in this study *always* comply with PIVI when ≥93% diminutive polyps are predicted correctly. This mainly depends on the OD of adenomas and HPs. These results provide guidance for developing criteria for OD competence which are easier to implement in daily practice.

Single-step treatment with endoscopic resection and cryoballoon ablation is feasible and safe in an esophageal porcine model

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Background: Treatment of early Barrett's neoplasia currently consists of two steps: endoscopic resection (ER) of visible lesions with subsequent ablation of the remaining Barrett segment at a 3-month interval. However, extensive resection might hamper subsequent ablation due to stenosis. Combining both treatment modalities in one session (single-step) offers the potential advantages of preventing ablation in a strictured esophagus and reducing the number of treatment sessions. Studies on single-step treatment with ER and radiofrequency ablation (RFA) showed this strategy to be feasible, but unsafe. Cryoballoon ablation (CBA) differs from RFA in that it preserves the extracellular matrix which might protect the esophagus even if the ablation effect reaches deep into the esophageal wall. Therefore, single-step treatment with ER and CBA might result in a more favorable outcome. The aim of this study is to evaluate the feasibility, safety and histopathological effects of single-step treatment with CBA and ER in either order.
Methods: Two single-step treatment regimens were evaluated in 3 pigs per regimen: 1) CRYO-ER: four adjacent cryoballoon ablations of 10 seconds duration followed by ER in the treated area; 2) ER-CRYO: ER followed by a 10-second ablation targeted on the ER wound. Primary outcomes were feasibility (technical success), and safety (acute/delayed perforations and clinically relevant strictures). Secondly, histopathological evaluation of the treatment effects was performed for the CRYO-ER specimens and all esophageal resection specimens.
Results: In total, 6 female pigs were treated with 5 treatment zones each resulting in 15 areas per treatment regimen. All ERs were technically successful. All pigs survived the aimed follow-up period of 28 days. No perforations (acute/delayed) or clinically relevant stenosis occurred. Histopathological evaluation was feasible for all ER specimens in the CRYO-ER group. Ablation effects were present throughout all layers of these ER specimens, while the architecture requisite for appropriate histopathological analysis remained intact. After 28 days of follow-up, the esophageal resection specimens were also evaluated for histopathological treatment effects. For ER-CRYO, the submucosa was the deepest layer with presence of post-treatment fibrosis. CRYO-ER resulted in deeper effects, including complete (87%, 13/15) and superficial (13%, 2/15) fibrosis of the muscularis propria.
Conclusion: Single-step treatment with limited endoscopic resection and cryoballoon ablation is feasible and safe in a porcine model and vindicates further evaluation in a clinical trial.

Clinical outcome of endoscopic treatment of symptomatic sterile walled-off necrosis

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Background: The majority of patients with sterile walled-off necrosis (WON) can and should be treated conservatively. Endoscopic drainage may be considered in patients suffering from persisting symptoms, but frequently results in complications. To date, no study has been published that solely focusses on the management of symptomatic sterile WON. Therefore, we aimed to evaluate clinical outcome of patients who underwent endoscopic drainage of symptomatic sterile WON.
Methods: This is a retrospective analysis of patients with symptomatic sterile WON who underwent endoscopic drainage between 2001 and 2018 in two Dutch tertiary referral hospitals. Patients were identified by searching local endoscopic report databases. Primary outcome was the number of interventions needed to achieve clinical success within 1-year follow-up. Secondary outcome parameters included clinical success, complications and total hospital stay.
Results: Sixty-two patients (56% male, mean age 53 years, SD 13) were identified. Indications for intervention were abdominal pain (66%), gastric outlet obstruction (45%), jaundice (19%) and failure to thrive (18%). Median time to intervention was 196 days (IQR 111-342) after onset of pancreatitis. Forty-seven patients (76%) underwent at least one additional intervention because of secondary iatrogenic infection: endoscopic necrosectomy (74%), multiple gateway drainage (5%), percutaneous drainage (11%) and surgical necrosectomy (2%). A median of 3 interventions (IQR 2 – 5) were needed to achieve clinical success. Patients were discharged after a median of 6 days (IQR 2 – 12) after initial drainage. More than half of patients (53%) were re-admitted. Total pancreatitis related hospital stay was 11 days (IQR 6 – 17). Post- and periprocedural complications included perforation (3%), bleeding (2%), stent migration (11%) and aspiration (2%). One patient died within 30 days after endoscopic drainage due to secondary iatrogenic infection. Follow-up data regarding clinical outcome was available for 52 patients, with a median follow-up of 14 months (IQR 6 – 38 months). Symptom resolution was reported in 46 patients (88%). Eleven patients (18%) suffered from residual fluid collections, for which endoscopic drainage (45%), transpapillary drainage (18%) and percutaneous drainage (27%) was performed.
Conclusion: This is the first study that focusses on clinical outcome of endoscopic drainage of symptomatic sterile WON. Clinical success was achieved in the majority of patients, but at the costs of multiple invasive procedures. Treatment of symptomatic sterile WON should therefore only be performed in patients in whom conservative management is no longer expected to result in symptom relief.

Feasibility, safety, tolerability and dose-related efficacy of a novel CryoBalloon Swipe Ablation (CbSAS90) device in dysplastic Barrett's esophagus

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Background: Cryotherapy offers potential advantages (better tolerability, less strictures) to heat-based ablation. Cryoballoon ablation(CBA) is a new technique comprising a through-the-scope catheter with a conformable balloon that is inflated and cooled using nitrous oxide. Thus far, focal CBA has been promising for short BE. The novel 90°-swipe CBA(CbSAS^{90}) ablates 90° of the esophageal circumference over 3cm in a single step. The controller software allows for dose adjustment (rate at which the diffuser traverses the 3cm long catheter axis while emitting cryogen). CbSAS^{90} has been feasible and safe in animal and pre-esophagectomy studies. This is the first clinical study to assess feasibility, safety and efficacy of CbSAS^{90} for dysplastic BE.
Methods: Patients with flat BE(≤3cm) and low or high-grade dysplasia (LGD/HGD) or residual BE after endoscopic resection (ER), were enrolled at 5 centers. The first study phase was for dose-finding: *semi-circumferential* treatment was performed with the start dose (0.8mm/sec), which was escalated with 0.1mm/sec (N=6 per dose) until the effective dose (ED) was found. ED was defined as the lowest dose resulting in BE regression ≥80% in absence of dose-related serious adverse events (DR-SAEs). Secondly, we confirmed the ED with *circumferential* treatment in 12 new pts. DR-SAEs included severe pain for ≥7 days or severe stenosis. Pain(VAS 0-10) and dysphagia(0-4) were evaluated at days 0,1,7&30. Outcomes were technical success, DR-SAEs and efficacy (BE regression at 8 weeks follow-up(FU) endoscopy assessed by 2 independent endoscopists).
Results: A total of 25 pts were included (median Prague score C0M3, 20% prior ER, 76% LGD, 12% HGD, 12% cancer). The procedure was technically successful in 23 pts (92%). Device malfunction occurred in 2 other pts (8%) and was resolved with device replacement. In the dose-finding phase, BE regression at FU was 78% (IQR 68-86) for 0.8mm/sec (dose 1) and 85% (IQR 75-95) for 0.7mm/sec (dose 2). No DR-SAEs were reported. Dose 2 was defined as ED and circumferential treatment in the second phase resulted in 94% (IQR 89-97) BE regression. However, 2 pts(17%) developed a stenosis requiring 1 and 3 dilations. Median pain scores after treatment were 3(IQR 1-5), 1(0-2), 0(0-0) and 0(0-0) at days 0,1,7&30 respectively. Median dysphagia scores were 0(IQR 0-0) at all FU time points.
Conclusion: CbSAS^{90} is feasible and a promising tool for ablating larger areas of dysplastic BE. However, because of concerns with respect to strictures, the optimal dose that leads to maximum efficacy with a low risk of stenosis needs to be further assessed in larger clinical studies with direct circumferential treatment.

Deep learning algorithm for characterization of Barrett's neoplasia demonstrates high accuracy on NBI-zoom images

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Background: The endoscopic diagnosis of early neoplasia in Barrett Esophagus (BE) is generally a two-step process of primary detection in overview, followed by targeted inspection of lesions. This targeted inspection is often performed using Narrow Band Imaging (NBI) for its improved visualization of mucosal and vascular patterns. General endoscopists, however, struggle in evaluating NBI-zoom images for characterization of BE neoplasia. Computer aided diagnosis (CAD) might improve the interpretation of NBI-zoom images.
Aim: To investigate the feasibility of a novel deep-learning CAD system for the interpretation of NBI-zoom images of BE.
Methods: We used a customized convolutional neural network (ResNet-UNet hybrid architecture), which was trained on 3 different datasets. First, this CAD system was pre-trained on a unique dataset of 494,364 labelled endoscopic images named *GastroNet*. Subsequently, the CAD system was further trained and enhanced by a dataset consisting of 690 white light endoscopy overview images of BE neoplasia and 557 non-dysplastic (ND)BE images. Finally, via both transfer and ensemble learning techniques, the CAD system was trained and tested with a third dataset using NBI-zoom images. This dataset consisted of NBI-zoom images with corresponding histology of 50 NDBE patients and 50 neoplastic BE patients. In total, 71 NDBE images and 112 neoplastic images were used for training and testing of the CAD system. Performance was evaluated using ten-fold repeated 80-20 train-validation holdout, to increase reproducibility of the results. The primary outcome was reported as diagnostic accuracy of the CAD system for characterization of neoplastic BE in magnified NBI images.
Results: The deep learning CAD system resulted in an average AUC of 91% (CI, 86% - 94%) an accuracy of 84% (CI, 81% - 88%), with a corresponding sensitivity of 88% (CI, 86% - 94%) and specificity of 78% (CI, 72% - 84%) for the correct differentiation between NDBE and BE neoplasia. A maximum AUC of 0.95 was reached by the best performing algorithm for this specific NBI-zoom dataset.
Conclusion: We report the first results of a unique CAD system for the characterization of NBI-zoom images of BE, based on a state-of-the-art deep-learning algorithm. These results are promising and show the feasibility of CAD for identification of early neoplasia in BE. Future work will focus on improving the current algorithm by increasing our current dataset, and validation of the CAD system on separate prospective validation sets and endoscopic videos.

Measuring KRAS mutations in pancreatic cyst fluid by droplet digital PCR and Next-Generation Sequencing

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Background: DNA-based testing of pancreatic cyst fluid, obtained with endoscopic ultrasound-fine needle aspiration (EUS-FNA), may be useful in the evaluation of pancreatic cystic neoplasms (PCN). Mutations in KRAS/GNAS are highly specific for mucinous pancreatic cystic neoplasm (i.e. IPMN, MCN) and can be detected by next generation sequencing (NGS; multiple genes simultaneously) or by droplet digital PCR (ddPCR; one gene at a time, but presumed higher sensitivity). The aim of this pilot study was to evaluate and compare NGS and ddPCR for measuring KRAS mutations in cyst fluid.
Methods: In this pilot study, pancreatic cyst fluid from patients who underwent EUS-FNA were included. KRAS mutation analysis was performed using ddPCR (Bio-Rad) and next-generation sequencing (Ion Torrent PGM). The detection of mutant alleles in cyst fluid by the different techniques was compared and correlated with histopathology.
Results: In this pilot study, 24 EUS-FNA obtained cyst fluid specimens of patients who subsequently underwent surgery were included for analysis (2007-2014). Surgical pathology showed 13 IPMNs, 7 MCNs, 3 SCNs and 1 cNET. Among these cases, 14 specimens were satisfactory for molecular testing by NGS (6 IPMN, 5 MCN, 1 cNET, 2 SCN), whereas 17 specimens by ddPCR (9 IPMN, 6 MCN, 1 cNET, 1 SCN). Mutations in KRAS were detected in 3/6 and 9/9 IPMNs by NGS and ddPCR, respectively. In addition, KRAS mutations were identified in 0/5 and 2/6 MCNs by NGS and ddPCR. One mutation was identified in cNET by ddPCR. No mutations were identified in SCN.
Conclusion: In this pilot study, ddPCR was superior to NGS for the detection of mutations in cyst fluid in concordance with surgical pathology. Although the sensitivity of both ddPCR and NGS assays is often limited by the amount of DNA that can be evaluated, less DNA is required for mutation analysis by ddPCR. The lower limits of detection of ddPCR should still be determined.

Treatment of disconnected and disrupted pancreatic duct in necrotizing pancreatitis: a systematic review and meta-analysis

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Background: Necrotizing pancreatitis may lead to loss of integrity of the pancreatic duct, resulting in leakage of pancreatic fluid. This pancreatic duct disconnection or disruption is associated with a prolonged disease course and additional complications. Since a standard treatment for this condition is currently lacking, we performed a systematic review to compare outcomes of different treatment strategies.
Methods: A systematic review was performed according to the PRISMA guidelines in the PubMed and EMBASE databases. Included were articles considering the treatment of patients with disconnected or disconnected pancreatic duct, as a result of acute necrotizing pancreatitis.
Results: Overall, 21 studies, including 1 prospective study, were included with 583 relevant patients,. The most frequently used treatment strategies included endoscopic transpapillary, endoscopic transluminal, surgical or combined procedures. Pooled analysis showed a success rates of 81% (95%-CI: 60-92%) for transpapillary and 92% (95%-CI: 77-98%) for transluminal drainage, 80% [95%-CI: 67-89%] for distal pancreatectomy and 84% [95%-CI: 73-91%] for Roux-and-Y internal drainage. Success rates did not differ between surgical procedures (cyst-jejunostomy or distal pancreatectomy [risk ratio = 1.06, p=0.26]) but distal pancreatectomy was associated with a higher incidence of endocrine pancreatic insufficiency (risk ratio = 3.06, p=0.01). Studies reporting on consecutive cohorts, the overall number of patients with disconnected/disrupted duct and conservative treatment are lacking.
Conclusion: Several different treatment strategies for pancreatic duct disruption and duct disconnection after necrotizing pancreatitis show high success rates. Prospective, high-quality studies are needed and should include all patients with disconnected/disrupted duct to establish the most effective treatment in specific subgroups of patients, including timing and long-term follow-up.

Is decompressing stoma a better alternative than stent as bridge to surgery for left-sided obstructive colon cancer? A nationwide, propensity score matched analysis

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Background: Bridge to elective surgery (BTS) with colonic stent placement is still a debated alternative to emergency resection of left-sided obstructive colon cancer (LSOCC) because of oncological concerns. Another BTS strategy is decompressing stoma formation. However, studies comparing stoma and stent are scarce. If we could directly compare these two methods, we may improve treatment and consequently health-related outcomes such as mortality and morbidity in patients with LSOCC. Therefore, the aim of the current study was to compare DS and SEMS as BTS for LSOCC in a large national cohort using propensity-score matched analyses.
Methods: All patients with curable LSOCC treated between 2009 and 2016 were included from the Dutch ColoRectal Audit, a prospective, (mandatory) national registry providing short-term outcomes. Additional long-term data were retrospectively collected by surgical residents under supervision of a consultant surgeon through a secured web application. Patients with an extracolonic malignancy or signs of bowel perforation on CT were excluded. Stoma and stent were compared after propensity score matching. Our main outcomes were three-year locoregional recurrence, disease free and overall survival, as well as temporary stoma rate, permanent stoma rate, and total hospital stay.
Results: In total, 75 out of 77 Dutch hospitals participated, leading to an inclusion of 574 BTS patients (345 stoma and 229 stent). Stoma patients were younger than stent patients (67 versus 71 years), had more pT4 tumors (34% versus 23%), and had more often undergone prior abdominal surgery (37% versus 24%) (MSD > 10%). Propensity score matching led to two well-balanced groups of 142 patients each (MSD < 10%). Median follow-up was 37 (18-60) months for the stoma group and 35 (15-63) months for the stent group (p=0.740). Decompressing stoma showed more temporary stomas (68% vs. 23%, p<0.001), permanent stomas (28% vs. 16%, p=0.022), and a longer total hospital stay (21 vs. 14 days, p=0.006). Three-year locoregional recurrence rate was 14% and 18% (HR 1.46, 95% CI 0.76-2.76, p=0.260), disease free survival was 59% and 65% (HR 0.86, 95% CI 0.59-1.25, p=0.430), and overall survival was 75% and 77% (HR 0.93, 95% CI 0.59-1.46, p=0.750) after DS and SEMS, respectively.
Conclusion: This nationwide, propensity score matched analysis revealed less stomas and a shorter total hospital stay after stenting, while oncological outcomes were not compromised. Therefore, if the lesion is amenable for stenting and sufficient experience is available, endoscopic stent placement seems to be the preferred BTS technique for LSOCC.

Changes in management of left-sided obstructive colon cancer: national practice and guideline implementation

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Background: The revised national and European guidelines (2014) recommended bridge to surgery (BTS) with either stoma or stent as an alternative to emergency resection (ER) in elderly and frail patients with left-sided obstructive colon cancer (LSOCC). Implementation and effects of these guidelines have not yet been evaluated. Therefore, the aim of the current study was to provide an in-depth update of national practice concerning curative treatment of LSOCC, including an evaluation of guideline implementation.
Methods: All patients with LSOCC who were treated with curative intent between 2009 and 2016 were included from the Dutch ColoRectal Audit, a prospective, (mandatory) national registry. Additional data were retrospectively collected by surgical residents under supervision of a consultant surgeon through a secured web application. Our main outcomes were primary anastomosis construction, surgical approach, and 90-day mortality and morbidity.
Results: In total, 75 of out 77 Dutch hospitals participated, leading to an inclusion of 2587 patients with a median age of 71 years (i.q.r. 62-79), of whom 2013 underwent ER, 345 stoma as BTS, and 229 stent as BTS. After 2014, a trend reversal in the application of ER (decrease: 86.2% to 69.6%) and stent (increase: 1.3% to 7.8%) was observed, with an ongoing increase in stoma formation (5.2% in 2009 to 22.7% in 2016). Stoma as BTS after 2014 resulted in more laparoscopic resections (66.0% vs. 35.5%, p<0.001) and more 2-stage procedures (41.5% vs. 28.6%, p=0.012). Overall, more laparoscopic resections (25.4% vs. 13.2%, p<0.001), fewer conversions (19.0% vs. 31.9% to, p=0.005), and a shorter total hospital stay (14 vs. 15 days, p<0.001) were observed since 2014. However, patients treated after 2014 showed a similar primary anastomosis rate (48.7% vs. 48.6%, p=0.961), 90-day complication rate (40.4% vs. 37.9%, p=0.254), and 90-day mortality rate (6.5% vs. 7.0%, p=0.635).
Conclusion: Guideline revision resulted in notable substitution from ER to BTS strategies for LSOCC. This was accompanied by more laparoscopic resections, fewer conversions, and a shorter total hospital stay, but overall 90-day complication and mortality rates remained relatively high.

Early detection of colorectal cancer and advanced adenomas based on faecal volatile organic compounds

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Background: Colorectal cancer (CRC) generally originates from adenomatous polyps (advanced adenomas (AA)) of which early detection and removal has been found to decrease incidence and mortality. In population based screening, individuals with a positive faecal immunochemical test (FIT) are referred for endoscopic assessment which is the gold standard for the detection and follow-up of CRC and AA. The FIT test has a low specificity for CRC and has suboptimal accuracy for the detection of AA. Faecal volatile organic compound (VOC) analysis is a new technique in the field of biomarker exploration. The aim of this study was to evaluate the potential of faecal VOCs for the detection and follow-up of CRC and AA.

Methods: Patients with a scheduled colonoscopy were asked to collect a faecal sample prior to bowel cleansing. Patients were included when CRC, AA or non-advanced polyps were observed during colonoscopy and confirmed in histology. Patients without colonic abnormalities were included as healthy controls (HC). In addition, patients undergoing a polypectomy were matched to HC on age, BMI and smoking status, and all were asked to collect a second faecal sample after 3 months. Faecal samples were measured using gas chromatography-ion mobility spectrometry (G.A.S. Flavourspec). The data were split into three sets, 70% for training and validation and 30% as test set. A Wilcoxon rank-sum test was used to find the 100 most discriminatory features and Random Forest classification was used to provide statistical results.

Results: A total 16 CRC, 64 AA, 68 large non-advanced polyps (0.5-1.0cm), 126 small non-advanced polyps (0.1-0.5cm) and 227 HC were included in this study. For the secondary analyses, 32 patients with AA undergoing a polypectomy and 32 HC were included. CRC, AA and polyps were discriminated from HC with high diagnostic accuracies (AUC (95%), p-values: CRC vs HC 0.99(0.89-1), $p<0.001$; AA vs HC 0.96(0.93-1), $p<0.001$; large polyp vs HC 0.96(0.92-0.99), $p<0.001$; small polyp vs HC 0.96(0.94-0.99), $p<0.001$). There were no significant differences between any of the CRC, AA and polyp groups. Faecal VOCs could discriminate between subgroups of patients with AA and HC prior to polypectomy, but not after polypectomy (AUC(95%), p-values: AA vs HC T0 0.98(0.95-1), $p<0.001$; AA vs HC T1 0.55(0.40-0.69), $p=0.26$.

Conclusion: Faecal VOCs can discriminate CRC, AA and non-advanced polyps from HC. There is no difference in VOC profiles of CRC, AA and non-advanced polyps. In addition, there is no difference in the faecal VOC pattern of patients with AA after polypectomy and HC. These findings underline the potential of faecal VOCs as biomarker for the detection and follow-up of colonic neoplasia.

Interval cancers after a negative faecal immunochemical test in the first screening round in the Netherlands for two cut-off levels

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Background: This study evaluated the interval cancer incidence after the first screening round in the national organised colorectal cancer (CRC) screening programme in the Netherlands using a faecal immunochemical test (FIT) in relation to FIT cut-off.
Methods: Screening participants with a negative FIT result in the first screening round in 2014 were included in the study. Main outcome measures were cumulative incidence of interval cancer after negative FIT and CRC sensitivity of FIT at a low (15 µg Hb/g faeces) and higher (47 µg Hb/g faeces) cut-off.
Results: Among the 485,112 participants with a negative FIT in 2014, 544 interval cancers were detected: 126 interval cancers among 111,800 FIT negatives at the low cut-off and 418 interval cancers among 373,312 FIT negatives at the higher cut-off. The age-adjusted two year cumulative incidence of an interval cancer after negative FIT did not differ significantly for the two cut-offs. The age-adjusted two year cumulative incidence of an interval cancer after negative FIT with a higher cut-off (13.8 per 10,000 persons) did not differ significantly from the lower cut-off (9.5 per 10,000 persons) (rate ratio of 0.68; 95%CI: 0.42-1.12). Age-adjusted CRC sensitivity of FIT was 90.5% at the low cut-off and 82.9% at the high cut-off, with no significant difference (rate ratio of 1.09, 95%CI: 0.91-1.30). The sensitivity of 87.4% among men was significantly higher than the sensitivity of 82.6% among women (p <0.001). There was no difference in the proportion of interval CRCs detected in an early stage (stage I and II) between the low cut-off (37.0%) and the high cut-off (37.3%)(rate ratio after age-adjustment of 0.98, 95%CI: 0.41-2.30). More than half (52.5%) of the interval CRC were located in the right side of the colon: 57.1% were detected right-sided at the low cut-off versus 50.6% at the higher cut-off (Figure 4). These percentages were not significantly different after age-adjustment with a rate ratio of 0.91 (95%CI: 0.41-2.01).
Conclusion: The incidence of interval CRC after a negative FIT is low. This supports the high sensitivity of FIT for CRC, also when using a relatively high FIT cut-off. The small but non-significant difference between the cut-offs is reassuring for all organised CRC screening programmes using higher FIT cut-offs aiming for an optimal balance between true and false positives or reduced colonoscopy demand.

Post-colonoscopy mortality in a FIT-based colorectal cancer screening program

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Background: Most population-based colorectal cancer (CRC) screening programs use a non-invasive stool test, followed-up by colonoscopy. As screening involves a healthy population, harms should be closely monitored. This study aims to evaluate the post-colonoscopy mortality in a fecal immunochemical test (FIT) based CRC screening program.
Methods: All participants of the Dutch CRC screening program with colonoscopy after positive FIT or with a negative FIT between Oct. 2013 and Dec. 2017 were included. Data on their FIT, colonoscopy (complications) and vital status were collected from the national screening database ScreenIT and the Dutch Registration of Complications in Endoscopy (DRCE). Fatal complication rate was determined by the registered fatal complications within 30 days after colonoscopy. Due to concerns about incomplete registration, two additional analyses were performed, despite their presumable overestimation. First, the 30-day post-colonoscopy excess mortality rate was estimated by comparing the 30-day mortality rate of FIT positive participants with colonoscopy (without CRC detected) versus FIT negative participants. Second, potentially colonoscopy-related deaths among FIT positive participants within 90 days after their colonoscopy were obtained using the reported underlying cause of death acquired from the Netherlands Statistics.
Results: A total of 172,834 FIT positive participants with colonoscopy (158,797 without CRC detected) and 3,532,132 FIT negative participants were included. Four fatal complications were registered by the complication registries, resulting in a fatal complication rate of 0.23 (95%CI: 0.090 – 0.60) per 10,000 participants. The 30-day mortality was 3.65 per 10,000 participants among FIT positive participants with colonoscopy (without CRC detected) and 2.30 per 10,000 participants among FIT negative participants. After age-adjustment, comparing both 30-day mortalities resulted in a 30-day post-colonoscopy mortality excess of 1.07 per 10.000 participants. Reported causes of death from the Netherlands Statistics were available until Dec. 2016. In 112,634 participants that underwent colonoscopy in this period, 240 deaths occurred within 90 days and 13 (1.15 per 10,000 participants, 95%CI: 0.67 – 1.97) were potentially colonoscopy-related: eight died from cardiovascular disease or infection within 7 days and five by an (endoscopic) intervention (two within 30 and three within 90 days).
Conclusion: The post-colonoscopy mortality after a positive FIT differed per analysis, ranging between 0.23 per 10,000 participants based on the reported fatal complication rate to 1.15 per 10,000 participants based on cause-of-death statistics potentially related to colonoscopy.

Joint surgical and gastroenterological assessment to decide on the optimal treatment of early colorectal neoplasia.

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Background: Benign or early malignant rectal lesions can be removed by the gastro-enterologist (Endoscopic Mucosal Resection (EMR), Endoscopic Submucosal Dissection (ESD)), or surgeon (Transanal Minimally Invasive Surgery (TAMIS)). Treatment choice is influenced by the recipient specialist. A joint assessment (JA) by both specialists could potentially lead to a more appropriate treatment.
Methods: Patients who were referred to either the surgeon or gastroenterologist were scheduled on a combined outpatient visit, including history, physical (rectal) examination, sigmoidoscopy and endoscopic ultrasound. We evaluated our first experience with this joint assessment.
Results: Since January 2018, twenty-two patients have been assessed. 17 patients were male (77%), average age was 71 years (56-88 years). Average lesion size was 27 mm (15-50mm), in 12 patients (55%) endoscopic ultrasound was used. Six patients were initially referred to the surgeon for TAMIS. After JA, three patients went on with the proposed TAMIS; one had an oncological resection and two ESD for benign lesions. Pathology confirmed correct decision in 5 patients; one patient had a TAMIS for a benign lesion which could have been treated with ESD. Sixteen patients were referred to the gastroenterologist. Five for a general decision on local treatment; JA resulted in one ESD, two TAMIS and two oncological resections. All decisions were pathology confirmed correct. Two EMR referrals remained unchanged after JA, which was the appropriate treatment seen the benign pathology. Nine patients were referred for ESD: two were downscaled to EMR; three remained unchanged; one was upscaled to TAMIS; and three went for oncological resection. All oncological resections and TAMIS were justified by pathology. Two out of three ESD's turned out to be benign lesion. Taken together, one TAMIS could have been done by ESD; and two ESD could have been done by EMR. All decisions were oncological correct.
Conclusion: Our first experience with joint assessment led to correct downsizing of local treatment modality in 18% of cases; upscale in local treatment modality occurred in 5%; upscale to oncological resection in 27%. In all cases salvage resections due to insufficient local treatment were avoided by JA which is a major advantage. The net effect on the number of TAMIS procedures was neglectable, they were only better allocated.

Discovery and selection of HBV-derived T cell targets for global immunotherapy based on HLA binding, conservation and viral indispensability

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Background: Immunotherapy represents an attractive treatment option for chronic Hepatitis B. Especially targeting viral proteins polymerase (pol) and X (HBx) is of interest as these are essential for viral replication, but likely least subject to immune exhaustion driven by antigen overexposure. Thus far, multiple HBV-antigen derived T cell epitopes have been reported which could act as targets in a therapeutic vaccination strategy. However, the vast majority of these is restricted to HLA-A*02, which is prevalent in only ~40% of the population. Thus, current epitopes are falling short in the development of a global immunotherapeutic approach. Moreover, established epitopes might not all be equally effective as they could be subject to different levels of immune escape. We therefore aimed to 1) assess which reported epitopes cover those parts of HBV proteins indispensable for viral replication or persistence and to 2) identify novel T cell targets for each of the most prevalent HLA types in the infected population.
Methods: Here, we applied a rational and stringent selection procedure based on viral indispensability of epitope-containing amino acids and their conservation across genotypes, to identify the most potent Pol- and HBx- derived epitopes described to date. In addition, we predicted novel HLA-binding peptides for the six HLA-supertypes most prevalent in the infected population. Potential epitopes expected to be least prone to immune escape were then subjected to a state-of-the-art *in vitro* assay to verify HLA- binding capacity.
Results: Our approach yielded 7 HBx-derived and 26 Pol-derived reported epitopes with functional association and high conservation that can now be rationally prioritized in immunotherapeutic usage. In addition, our prediction and subsequent validation of HLA-binding capacity identified 13 novel HLA-binders derived from HBx and 30 novel binders from Pol across the HLA-supertypes. Importantly, some described epitopes were identified as novel binders for other HLA-supertypes implicating a broad population coverage.
Conclusion: The resulting overview of T cell targets with high potential to drive viral eradication now provides a clear rationale for the development of globally effective HBV-antigen specific immunotherapies.

Mass spectrometry analysis of HLA class I peptides presented on human hepatocytes and hepatocellular carcinoma to guide antigen-based immunotherapy

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Background: Antigen specific immunotherapy is a promising treatment option for chronic hepatitis B (HBV) and hepatocellular carcinoma (HCC). Treatment effect requires induction of antigen specific T cells and presentation of the T cell-cognate peptide by HLA molecules of the target cells. T cell induction is studied extensively, yet it is unexplored which antigens are presented by target cells.
Methods: To investigate HLA-presentation by patient-derived hepatocytes, we developed a method to isolate hepatocytes from small liver samples of patients infected with HBV and/or suffering from HCC. Subsequently, mass spectrometry (MS) was applied on patient-derived hepatocytes and *in vitro* human (HBV infected) hepatocyte cell models. Downstream analysis of peptide length and HLA-binding were performed to determine the hepatic HLA-I peptidome and to allow identification of HBV-derived and tumor-associated T cell targets for immunotherapy.
Results: Our novel method of hepatocyte isolation yielded up to $535x10^6$ pure (>90%) hepatocytes per gram of tissue across etiologies including severe cirrhosis. MS on primary (HBV infected) malignant and non-malignant hepatocytes yielded hundreds of HLA-binding peptides including HBV antigens and tumor associated antigens that were found exclusively in the tumor. Furthermore, peptides could be linked to hepatic function and most 9-mers were predicted to bind HLA-alleles expressed on the source material, collectively validating that these peptides originated from hepatic peptide-HLA complexes.
Conclusion: Identified peptides now lay the basis for HBV-antigen and tumor antigen directed immunotherapy.

Combined TRC105/PD1 therapy synergistically inhibits tumor growth by targeting immune suppressing cells and activation cytotoxic responses

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Background: Colorectal Cancer (CRC) is one of the most common cancers in the western world. Although tumors arise from mutations in epithelial cells, the tumor microenvironment (TME) plays an important role in CRC pathogenesis . Several cell types in the TME, including cancer-associated fibroblast (CAFs) and endothelial cells, express the Transforming Growth Factor (TGF)-β co-receptor endoglin. TRC105 is an endoglin neutralizing antibody, which is currently under clinical development. Since the effects of TRC105 are CD8 T-cell dependent, we have investigated the combination of TRC105 with a PD-1 immune checkpoint inhibitor and showed synergistic inhibition of tumor growth in four CRC mouse models. In the current study we investigated the underlying mechanism.
Methods: To investigate the composition and number of infiltrating immune cells upon therapy, we induced subcutaneous tumors and analyzed tumor and blood 9 days after start of therapy by flow cytometry. To study the involvement of antibody dependent cellular cytotoxic (ADCC) responses we performed tumor studies in a FC-y receptor knockout mouse. Finally, we depleted the CD8 T-cells to gain more knowledge about the underlining mechanism.
Results: The combination of TRC105 and anti-PD1 therapy showed synergistic inhibition of tumor growth. To investigate whether the antibody requires directly interaction with the FC-y receptor to induce ADCC, we injected MC38 cells in a FC-y receptor knockout mouse. We found a complete abrogation of the therapeutic effects of the TRC105 mono- and combination therapy. Similar effects were observed when all the CD8+ T-cells were depleted, suggesting that the combination therapy strongly depends on both ADCC and CD8 T-cell responses. To investigate the local immune infiltrate, we performed a short-term MC38 tumor challenge. Increased CD8 cells were observed in the tumor upon TRC105 and TRC105/PD1 therapy. Surprisingly, we found a decrease in the number of T-regulatory cells (Tregs) in the tumor upon TRC105 monotherapy. This decrease was however not observed in the peripheral blood, suggesting that this might be a local TME effect. To investigate if Tregs could be directly targeted by TRC105, we checked their endoglin expression. We found higher levels of endoglin on Tregs in the tumor, compared to cells in the peripheral blood, indicating that the decrease might thus be a direct targeting of the Tregs by TRC105.
Conclusion: Taken together we have shown TRC105, although initially designed to target blood vessels might in fact have additional inhibitory effects on tumor promoting cell types. These therapeutic effects are strongly increased when TRC105 is combined with anti-PD1.

VCAM/Endoglin positive subpopulations of Mesenchymal Stromal (stem) Cells

reverse fibrogenesis in experimental liver fibrosis

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Background: Liver fibrogenesis starts with apoptotic hepatocytes that induce stellate cell proliferation and their differentiation into myofibroblasts. Myofibroblasts are a main source of extracellular matrix in fibrosis. Mesenchymal Stromal (stem) Cells (MSCs) are known to possess pro-regenerative and anti-inflammatory properties, but regarding their contribution in mediating fibrogenesis opposing findings have been reported. We hypothesised that these differences might be explained by the use of different subpopulations of MSCs. In the present study we compared the pro-regenerative and antifibrotic effects of four different subpopulations of MSCs, selected based on their expression of Endoglin and/or vascular cell adhesion molecule (VCAM).
Methods: Proliferation, wound healing and trans-well migration experiments were performed to study migratory and pro-regenerative effects of the MSC subpopulations. Basal expression levels of migratory (SDF1, CXCR4) and antifibrotic (TGFβ, VEGF, HGF and IGF) genes were measured by qPCR analysis. Furthermore, the ability of the different subpopulations to reverse fibrogenesis was tested in a mouse model for liver fibrosis. The severity of fibrosis was assessed by collagen deposition visualised by Sirius red staining.
Results: Proliferation and migration experiments with damaged HepG2 cells showed that VCAM positive MSC subpopulations have more pro-regenerative capacities compared to the VCAM negative subpopulations. VCAM/Endoglin positive subpopulations of MSCs also have more migratory and antifibrotic gene expression profiles. Furthermore, VCAM/Endoglin positive MSC subpopulations showed the highest potential to reverse fibrogenesis in a mouse model for liver fibrosis (85 vs 70% reduction of collagen deposition, $P<0.05$).
Conclusion: VCAM/Endoglin positive subpopulations of MSCs are superior compared to VCAM negative subpopulations in relation to their antifibrotic and pro-regenerative properties in liver fibrosis. These observations indicate that differences in subpopulations of MSCs may have a functional impact that should be considered in their functional assessment.

Pasteurized whey protein improves maturation of the immature intestine of preterm and near-term piglets

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Background: Intestinal immaturity predisposes preterm infants to necrotizing enterocolitis (NEC). Feeding preterm infants with infant milk formulas (IMF) is associated with an increased risk to develop NEC compared to human milk. Heat treatments are part of the IMF production process and heating is linked to whey protein denaturation and bioactivity loss, which might impact gut maturation. Aim of this study was to determine if pasteurized whey protein concentrate (P-WPC) has beneficial effects over extensively heated WPC (EH-WPC) on intestinal maturation in preterm/near-term piglets as model for preterm infants.
Methods: In total 34 preterm piglets (90% gestation, 2 litters) and 18 near-term piglets (96% gestation, 1 litter) were delivered by cesarean section. Piglets of each litter were block-randomized based on birth weight in 2 groups: 1) P-WPC group received formula based on pasteurized WPC (73°C, 30 sec) and 2) EH-WPC group received formula with WPC that was pasteurized and extensively heated (73°C, 30 sec + 80°C, 6 min). WPC was prepared from raw cow's milk by a process that did not involve heating. Piglets received minimal enteral nutrition for 5 days with parenteral nutrition support. Clinical symptoms were monitored daily. On day 5, a lactulose/mannitol test was performed to evaluate gut permeability. At sacrifice, the intestine was macroscopically scored for NEC and tissue was collected for histology, enzyme activity, RNA and protein analysis.
Results: Within all 3 litters, NEC incidence was lower in piglets fed P-WPC compared to EH-WPC. Gut permeability was decreased in near-term piglets fed P-WPC compared to EH-WPC. Histological scoring based on integrity of the epithelium, presence of edema, and erythrocyte and immune infiltration showed less damage in the colon of piglets fed P-WPC in comparison with EH-WPC. Reduced damage was associated with less epithelial hyperproliferation as measured by Ki67+ cells and crypt depth. Colonic IL1β, IL8, TNFα and TLR4 expression levels were reduced in the P-WPC group indicating less inflammation. Intestinal alkaline phosphatase (iALP), expressed by colonocytes and marker for intestinal maturation, showed increased expression and activity in the colon of piglets fed P-WPC compared to EH-WPC.
Conclusion: Compared to EH-WPC, P-WPC decreased NEC incidence and resulted in less histological damage and inflammation in piglets with an immature intestine. Increased iALP in P-WPC fed piglets might dampen colonic inflammation and improve the gut barrier. Together, the data show that P-WPC has beneficial effects on gut maturation in preterm/near-term piglets and might therefore also support gut maturation in preterm infants.

Autophagy regulates Rac1GTP and RhoAGTP activity in dendritic cells and epithelial cell lines

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Background: The SNP (T300A) in the ATG16L1 gene reduces autophagy and is one of the few highly prevalent risk factors associated with Crohn's disease. We have previously shown that reduced autophagy results in enhanced dendritic cell (DC) - T cell contact time and T cell hyperactivation. Furthermore, we have shown that autophagy^{low} DCs have altered cytoskeletal morphology and exhibit a reduced capacity to migrate. RhoGTPase Rac1^{GTP} activity was enhanced in autophagy^{low} DC, and morphology and migratory capacity were restored upon Rac1^{GTP} inhibition. Rac1^{GTP} inhibition was both obtained with a specific inhibitor as with 6TG, a commonly used drug in Crohn's Disease. Here we further investigated the role of autophagy and its effect on RhoGTPase modulation in DCs, and as the T300A SNP is a body wide phenomenon, in two intestinal epithelial cell lines.
Methods: Autophagy^{low} DCs and cell lines (Caco-2 and HT29) were generated using siRNA and lentiviral shRNA respectively. ATG16L1 protein knockdown was confirmed on Western Blot. Rac1^{GTP} and RhoA^{GTP} activity was measured using G-Lisa. Migration capacity of Caco-2 and HT29 cell lines was determined using a scratch assay. Proliferation was analyzed using EdU incorporation.
Results: In contrast to the increase of Rac1^{GTP} activity, RhoA^{GTP} activity was decreased in autophagy^{low} DCs (n=10 individual donors). Similarly, in both Caco-2 and HT29 autophagy^{low} cell lines Rac1^{GTP} activity was increased and RhoA^{GTP} was decreased compared to the respective control cell lines. Whole protein levels of Rac1 and RhoA however, were not altered, suggesting the regulation is not translational. In scratch assays, the autophagy^{low} Caco-2 and HT29 cell lines had reduced capacity to close the wound compared to the control cell lines, thus implicating reduced migratory capacity, similar to that found in DCs. This was not due to a decrease in proliferation in the autophagy^{low} cell lines. As seen in the moDCs migration capacity, 6TG indeed rescued the migrational capacity of the autophagy^{low} epithelial cell lines to the level of the control cell line.
Conclusion: Reduced autophagy in both DCs and epithelial cell lines causes an increase in Rac1^{GTP} activity and decrease in RhoA^{GTP} activity. These results suggest that a defect in the autophagosomal regulation of Rac1^{GTP} and RhoA^{GTP} underlies the association between ATG16L1 T300A SNP and Crohn's disease, which impacts both immune and epithelial wound healing responses.

Whole-exome sequencing in early-onset primary sclerosing cholangitis: first results of the WHELP-study

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Background: Primary sclerosing cholangitis (PSC) is a severe liver disease leading to fibrotic destruction of the bile ducts and ultimately to the need for liver transplantation. In children the connection with Inflammatory Bowel Disease (IBD) is close to 100%. Genome-wide association studies (GWAS) in adults have identified many risk loci for both IBD and PSC, but a large part of the heritability remains unexplained. We hypothesize that we can identify rare, but disease-causing variants in patients with an extreme PSC phenotype, such as children with early-onset PSC.

Methods: In this multicentre parent-offspring study,we collected DNA from 31 children who were diagnosed with PSC before the age of 13, and their biological parents. Whole exome sequencing (WES) was performed on all 93 DNA samples. We first performed parents-child trio analyses and prioritized rare coding and splice variants matching recessive (homozygous and compound heterozygous variants) and dominant (*de novo*) inheritance in the children. Pathogenicity of the variants was predicted with an in-house developed algorithm (GAVIN). Secondly, we performed a cohort analysis in which we prioritized genes that carried a rare pathogenic variant in 3 or more cases, but were not found in population controls.

Results: We identified compound heterozygous variants in three trios in genes *ABCB6, DACT1 and JMJDC1*, and in 13 other trios we identified a total of 16 *de novo* variants in 16 genes with predicted pathogenic effects on protein functions. The same *de novo CNOT2*variant was shared between two families, as well as the *de novo TNRC18* variant. Most identified genes have roles in bile salt transport and the immune system.

Conclusion: So far,19 candidate disease-causing variants withlarge effects on protein function were found in children with early-onset PSC involving immunological or bile salt pathways. Network analysis is currently being performed to assess the relation between these genes and signalling pathways associated with PSC and or IBD.

Loss of intestinal Indian Hedgehog enhances Apc-driven tumorigenesis

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Background: The most frequent initiating mutation in colorectal cancer (CRC) occurs in the *Apc* gene leading to hyperactivated Wnt signaling and the development of adenomatous tissue in the intestine. A role for Indian Hedgehog (Ihh) has been proposed in the development of CRC, but its exact function has been debated. Intestinal epithelium-derived Ihh signals to fibroblasts positioned within the underlying stromal compartment. In turn, a subset of hedgehog responsive stromal cells restricts proliferation of epithelial stem cells. Here we investigated the role of Ihh in the context of *Apc*-driven intestinal neoplasia.
Methods: Mice that lack Ihh expression in the intestinal epithelium were crossed with *Apc* double mutant mice which develop hyperproliferation of the epithelium in a course of 3-5 days (*VillinCreERT2-ZsGreen-Apcfl/fl-Ihhfl/fl* mice). Intestinal tissues were analyzed by immunohistochemistry, in situ hybridization (RNAscope), and quantitative reverse-transcription polymerase chain reaction. Gp38+ fibroblast subsets were isolated by FACS sorting and gene expression profiles were examined by microarray analysis. Perimeter and proliferation rate of stimulated *Apc* double mutant organoids were measured.
Results: Loss of Ihh from the intestinal epithelium of *Apc* double mutant mice resulted in a remarkable aggravation of the hyperproliferative phenotype of the intestine. Stem cell proliferation was increased and multiple Wnt target genes (*Lgr5, axin2, ascl2, CD44*) were upregulated. Gene profiling of gp38+ fibroblasts showed upregulation of inflammation-related genes (*Ifit44, Stat1*) upon deletion of Ihh. Strikingly, we also observed upregulation of epidermal growth factor receptor (EGFR) pathway components (*EREG, BTC and NRG1*). Mechanistically, stimulation of *Apc* double mutant intestinal organoids by recombinant EREG and BTC significantly increased organoid size and proliferation.
Conclusion: We conclude that epithelium-derived Indian Hedgehog acts as a tumor suppressor in the intestine. Loss of Ihh enhances *Apc*-driven intestinal proliferation via upregulation of the EGFR signaling pathway.

Loss of the Bone Morphogenetic Protein signalling in myofibroblasts initiates polyp formation in the mouse intestine

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Background: The bone morphogenetic protein (BMP) pathway is a crucial signalling pathway in the maintenance of intestinal tissue homeostasis. Several *in vivo* studies have showed that abrogating BMP signalling, as a results of BMP receptors or ligands, can lead to polyp formation as is observed in hereditary Juvenile Polyposis syndrome (JPS) patients. Interestingly, a cell specific knockout of BMPR1a in epithelial cells did not result in polyposis. In this study we aimed to decipher which intestinal cell types (epithelial, endothelial cells or fibroblasts), contribute to the polyp formation upon conditional knockout (cKO) of BMPR1a. Furthermore, we set out to investigate the mechanism underlying the polyposis in the hope to better understand how the polyps in JPS patients arise.
Methods: The Cre/LoxP system was utilized for generating four different knockout mouse models in which BMPR1a could be conditionally and specifically be knocked out using specific promotor driven CRE expression in epithelial cells (Cyp1a1-cre), endothelial cells (VE-cadh-cre), all fibroblast (Col1a2-cre) and myofibroblast together with smooth muscle cells (SM22-cre). Six and twelve months after induction, mice were sacrificed and intestines were collected for (immune)histochemical and mRNA analysis. For the *in vitro* experiments, intestinal fibroblasts were isolated from BMPR1a$^{fl/fl}$ mice and induced *in vitro* via the lentiviral transduction with a Cre-expressing vector.
Results: Conditional KO of BMPR1a in myofibroblasts using the SM22;BMPR1a$^{fl/fl}$ mice led to the formation of polyps with a serrated phenotype. These are thought to be the precursor lesions from which the CMS4 subtype CRC arise from. *In vitro* induction of the BMPR1a KO in myofibroblasts showed a 25-fold upregulation Gremlin mRNA, a BMP antagonist. Subsequent immunohistochemical stainings of the intestines from the SM22;BMPR1a KO showed an accumulation of Gremlin specific in the polyp regions where also an increase of Ki67 positive epithelial cells was observed. An immunohistochemical stainings for vimentin showed an expansion of the mesenchymal compartment in in the intestines of the SM22;BMPR1a KO, an increase that was even higher in the polyps.
Conclusion: Our data suggest that BMP-signalling in myofibroblasts contributes to intestinal homeostasis and a disturbance of fibroblastic BMP-signalling may lead to polyposis, potentially via Gremlin dysregulation. Gremlin could prevent the proliferating cells from losing their stemness by inhibiting BMP signalling in the proliferating epithelial cells. Further coculture experiments with normal colonic organoids and autologous fibroblasts should further elucidate if these processes are similar in a human setting.

Inhibition of BMP2 and BMP4 eradicates Barrett's esophagus and enhances the regeneration of squamous epithelium

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Background: Barrett's esophagus is a metaplastic condition in which the esophageal normal squamous mucosa is replaced by metaplastic columnar type of epithelium, which is a the result of chronic duodeno-gastric reflux, which causes an inflammatory response. One way to divert the risk of malignant progression of Barrett's esophagus would be by re-establishing squamous epithelium through inhibiting Barrett cells. In earlier studies the SHH-BMP4 pathway has been identified as one of the critical pathways involved in the generation of columnar metaplasia. BMPs are secreted stromal factors for instance involved in development and homeostasis of columnar epithelia. Therefore targeting BMPs to modulate signaling and inhibit columnar cell growth and proliferation could be an attractive approach for diverting cancer risk of metaplastic columnar epithelia such as Barrett's esophagus.
Methods: We first set out to study BMP signaling through analysis of RNA sequencing to identify which BMPs are involved in Barrett's esophagus and in three different models we investigated the effects of specific BMP inhibition and neo-squamous regeration. We finally investigated the origin of the neo-squamous cells by lineage tracing in one of our models.
Results: The activity of BMP2 and BMP4 signaling was high in Barrett's biopsies, whereas BMP7 and TGF-β pathways were higher in the esophageal squamous mucosa. Selective inhibition of BMP2 and BMP4 within an in vivo organoid model of Barrett's esophagus, favored the development of squamous cells, rather than the columnar Barrett cells. In a mouse model, conditional knockout of *Noggin*, a natural antagonist of BMP2, BMP4 and BMP7, induced expansion of Barrett's like neo-columnar epithelium from multi-lineage glands. Conversely, inhibition of BMP2 and BMP4 led to the development of a neo-squamous lineage. Similarly, in wild type mice, inhibition of BMP2 and BMP4 resulted in the regeneration of neo-squamous epithelium after the cryo-ablation of columnar epithelium at the squamo-columnar junction. Through lineage tracing it was evident that the neo-squamous mucosa originated from K5+ progenitor squamous cells.
Conclusion: Together, this work demonstrates that specific inhibition of BMP2 and BMP4 inhibits columnar metaplasia, providing a novel potential strategy for the treatment of Barrett's esophagus and prevention of progression to esophageal adenocarcinoma.

A chemoradiotherapy treatment response mRNA signature as predictor for esophageal adenocarcinoma treated according to the CROSS regimen

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Background: Despite advances in intervention strategies, esophageal adenocarcinoma (EAC) remains a highly aggressive malignancy with poor prognosis. To improve patient outcome, it is imperative to improve treatment stratification and upfront patient selection. In the current study, the relation of mRNA expression profiles to pathological treatment response to preoperative chemoradiotherapy was investigated.

Methods: In this prospective observational study, patients treated with chemoradiotherapy according to the CROSS regimen (carboplatin and paclitaxel) followed by surgery were included. A discovery cohort was set up, containing RNA sequencing profiles of endoscopic tumor biopsies obtained before treatment. The cohort consisted of 44 EAC patients treated between 2012 and 2017.

Patients were stratified in subgroups according to pathological response to the CROSS regimen as classified by the Mandard score and pathological T-stage (pT) as observed in the resection specimen. Mandard 1 and pT0 depict a complete response to CROSS, whereas higher Mandard scores and pT-stages are associated with incomplete response.

Results: Differential expression analysis of the RNA profiles was performed to investigate the differences between the complete (n=6) and incomplete (n=38) responders. This resulted in 144 genes that were significantly differentially expressed between these two groups. These genes, collectively referred to as “complete response signature”, are important in pathways involved in the immune system, including the regulation of cytokines and presence of T helper cells, macrophages and dendritic cells.

Using the 35 most statistically significant genes from the “complete response gene signature”, we trained a random forest model for prediction of response to CROSS therapy. This model has a sensitivity of 100% and a specificity of 89% for predicting complete response. Currently, an independent cohort of CROSS treated EAC patients is being assembled, to validate the performance of our 35 gene prediction set.

Conclusion: In conclusion, a signature defined by 144 differentially expressed genes separates patients with complete response from patients with incomplete response to CROSS therapy. Most of these genes are involved in the regulation of the immune system. We were able to reduce the gene set to 35 genes that could accurately predict complete versus incomplete responders. Application of this relatively small gene set will be more translatable to clinic and could be employed to improve treatment stratification of EAC patients.

Genetic variants of innate immunity receptors are associated with mortality but not with bacterial infections in liver cirrhosis

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Background: Acute on chronic liver failure (ACLF) is characterized by the presence of acute decompensation of cirrhosis (AD), organ failure(s) and a high risk of short term mortality. Bacterial infections are among the most frequently observed precipitating events for development of ACLF. The lectin pathway of complement activation is crucial to the innate immune (IM) response to pathogens. Single-nucleotide polymorphisms (SNPs) in the lectin pathway genes determine their liver-derived protein level and/or functional activity. Multiple other components are also involved in IM signalling against pathogens, among which TLR2, TLR4, MYD88 and NOD2. The aim of the present study was to investigate whether SNPs in IM genes for pathogen recognition are associated with the occurrence of bacterial infections or mortality in patients with cirrhosis hospitalized for AD or ACLF.
Methods: All patients hospitalized for AD or ACLF from the CANONIC study of whom we had DNA available were included. Twenty-one IM genes variants with known functional implications on protein level and/or functionality were genotyped in 826 patients. Associations between baseline characteristics of the patients, the occurrence of bacterial infections and survival rate at 90 days of follow-up in relation to the IM gene variants were analysed.
Results: None of the analysed SNPs was significantly associated with the occurrence of acute bacterial infections in general or spontaneous bacterial peritonitis (SBP) alone. However, in both univariate and multivariate logistic regression analyses the NOD2-G908R gene risk variant (OR 2.25, 95% CI 1.30 – 3.91, P=0.004) was found to be a strong independent predictor of mortality along with age (OR 1.03, 95% CI 1.02– 1.05, P<0.001) and Model For End-stage Liver Disease (MELD) Score (OR 1.15, 1.12– 1.17, P<0.001). In a predefined subgroup analysis in patients with bacterial infections (n=331) the same association with mortality was observed for NOD2-G908R (OR 2.78, 95% CI 1.74 – 4.44, P<0.001).
Conclusion: In patients with AD or ACLF, single nucleotide polymorphisms in the lectin complement pathway and innate immune signalling components for pathogen recognition were not associated with increased risk of bacterial infection or SBP alone. NOD2-G908R gene risk variant is independently associated with increased risk of short-term mortality in patients with AD or ACLF, particularly those with bacterial infections.

The effects of citrus flavonoids on intestinal permeability and inflammation using an in vitro co-culture model

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Background: Hesperidin and naringin are citrus flavonoids with anti-oxidant and anti-inflammatory properties. As several gastrointestinal diseases have been associated with oxidative stress and inflammation, contributing amongst others to intestinal barrier disruption, these compounds might beneficially affect gut health. Evidence shows that hesperidin and naringin are metabolized by gut microbes into a range of phenolic metabolites. Therefore, we aimed to assess the effect of a citrus flavonoid extract containing hesperidin and naringin, as well as their main metabolites on intestinal epithelial barrier function and inflammatory markers using an *in vitro* model.
Methods: Caco-2 cells were cultured in transwell inserts until a monolayer was formed and placed in co-culture with THP-1-Blue™ NF-κB cells (THP1 cells stably transfected with an NF-κB-inducible secreted embryonic alkaline phosphatase (SEAP) reporter construct) for 30 hours. At baseline, the test compounds (citrus flavonoid extract, hesperidin, naringin, hesperitin, naringenin, hydrocaffeic acid, isoferulic acid, 4-hydroxyphenylacetic acid, hydroferulic acid, ferulic acid, phloretic acid, hydrocinnamic acid and phloroglucinol) were added apically, each at a concentration of 100 μM. After 24 hours, THP1-Blue cells were incubated with Lipopolysaccharide (LPS; 500 ng/ml) in the basolateral compartment for an additional 6 hours. Intestinal barrier function was assessed by measuring transepithelial electrical resistance (TEER) and FITC–dextran (4kDa) permeation. (Anti-)Inflammatory potential was assessed by measuring NF-κB activity (QUANTI-Blue™ colorimetric enzyme assay) and cytokine production (fluorescence activated cell sorting analysis) in cell supernatant.
Results: Incubation with citrus flavonoid compounds did not induce changes in TEER or FITC-dextran permeation for any of the compounds tested. However, LPS-induced NF-κB activity was significantly inhibited by 27-52% by most compounds ($p<0.01$), except for the citrus extract, phloretic acid and phloroglucinol. This effect was most pronounced for isoferulic acid, 4-hydroxyphenylacetic acid and hydroferulic acid, which are mainly formed in the proximal colon as a result of bacterial metabolization.
Conclusion: These results suggest that several citrus flavonoids may decrease intestinal inflammation via inhibition of NF-κB activity.

HNF4A is essential for intestinal epithelial regeneration upon radiation-induced injury

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Background: The intestinal epithelium is characterized by rapid reconstitution and high plasticity upon damage. However, in many gastrointestinal diseases the regenerative response is impaired. For a better understanding of the factors and mechanisms that can modulate intestinal epithelial regeneration, we utilized γ-irradiation of murine small intestinal organoids, which consist solely of epithelial cells.
Methods: The organoids were irradiated with various amounts of radiation, in order to determine the optimal dose. Microarray analysis was performed on small intestinal organoids irradiated with 6 Gy of ionizing radiation. Differentially expressed genes were extracted and ingenuity pathway analysis (IPA) was performed, to discover the regulators of regenerative response. Next, in order to confirm IPA predictions, *in vivo* irradiation was performed on VillinCreERT2-Hnf4a$^{fl/fl}$ mice. By means of immunohistochemistry, qPCR and microarray analyses, loss of Hepatocyte Nuclear Factor-4α (HNF4α) after irradiation was assessed.
Results: 6 Gy was identified as the optimal dose of γ-irradiation for small intestinal organoids, where after a phase of cell death, hyperproliferation and increase of stem cell markers is observed, mimicking the *in vivo* irradiation response. Analyses of differentially expressed genes in irradiated organoids with IPA, identified HNF4α as a critical upstream regulator during regeneration process. Intestinal epithelium specific Hnf4a knock-out mice showed impaired regeneration at 96 hours after whole body irradiation, as determined by a reduction in the amount of regenerating crypts and epithelial proliferation. Mechanistically, Hnf4a knock-out led to loss of intestinal stem cell marker Olfactomedin 4 and increase of differentiation into the secretory cell lineage.
Conclusion: By performing an irradiation protocol on intestinal organoids, we established and validated a novel *in vitro* intestinal damage–repair model and identified HNF4α as a crucial regulator of intestinal regeneration.

Luminal preservation of the human small bowel graft reduces mucosal damage during cold storage

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Background: Graft survival rates in intestinal transplantation (ITx) are the lowest among solid organ transplantation. Unique for ITx is the presence of a large volume of metabolically-active luminal content consisting of a complex mixture of microbes, dietary and waste products. Cold ischemia during storage (CS) decreases mucosal integrity during preservation and leads to bacterial translocation, predisposing for rejection of the graft. CS of the bowel is limited up to 10 hours, after which it is deemed unsuitable for transplantation. Luminal preservation (LP) with polyethylene glycol (PEG) has shown promising effects in improving graft-viability in experimental models. We started a project to analyse the effect of luminally-applied solutions on preservation injury of the human bowel. Here, we report our preliminary data.
Methods: So far, 8 bowels from brain-dead donors from our region were included. In all cases, standard vascular perfusion (VP) with ice-cold University of Wisconsin solution (UW) was performed. Five bowels served as a control group with no LP and standard CS in UW. Three bowels were filled with 1.5 litres of PEG prior to procurement and CS. Tissue samples were taken at procurement and after 7 and 14 hours of CS. Jejunal and ileal samples were analysed for Park/Chiu score. The project has been extended to a centre in Belgium to include Institut Georges Lopez-1 (IGL-1) for VP and first results still need to be analysed.
Results: Control samples show the natural decay of the graft's structure. Median Park/Chiu score for jejunum is 3 (maximum value=5), 4 (7) and 5 (5) in successive time points; for ileum 0 (2), 3 (4) & 4 (7) respectively. Median score with LP for jejunum is 1 (4), 3 (4) and 3.5 (4) in successive time points; for ileum 1 (2), 3 (3) & 3 (3), respectively. LP with PEG seems to maintain the epithelial lining, with increasing signs of oedema of the villi tips.
Conclusion: These promising preliminary data show that both jejunum and ileum with LP tend to maintain a low level of preservation injury. LP might thus improve graft viability and increase its preservation time-window. Further analyses will be performed to study bacterial location and protein and gene expression. Additional luminal solutions and their relationship with different VP solutions will also be studied.

A history of cholecystectomy is associated with higher rates of metabolic syndrome and nonalcoholic fatty liver disease: a population based study

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Background: Obesity is a risk factor for a number of phenotypes such as gallbladder disease, metabolic syndrome (MS) and nonalcoholic fatty liver disease (NAFLD). Cholecystectomy for gallbladder disease is a common procedure and we explored whether cholecystectomy may serve as an early marker of MS and NAFLD in a large population-based study.
Methods: The Rotterdam Study is an ongoing prospective population-based cohort. We included participants who underwent ultrasound and completed a questionnaire on surgical history, or of whom cholecystectomy was entered in the Dutch Public Pathology Database. Based on these data we distinguished groups based on history (cholecystectomy or no cholecystectomy) and timing of a cholecystectomy (<10 years ago or >10 years ago). MS was defined according to the Adult Treatment Panel III criteria and NAFLD was defined as presence of steatosis in absence of alcohol misuse, viral hepatitis and steatogenic drug use.
Results: We included 4631 participants with a mean age of 68 years (±9.9) of whom 42.4% were male. MS was present in 50.3% of the participants and NAFLD in 30.5%. Cholecystectomy was performed in 291 participants (6.3%), at a median age of 55 years (IQR 45.5-64.5). Median time interval between cholecystectomy and examination for presence of MS and NAFLD was 11.0 (IQR 1-21) years. MS prevalence was higher in participants with a history of cholecystectomy versus those without cholecystectomy; 62.9 % versus 49.4%, p<0.001. NAFLD was significantly more present after a cholecystectomy; 39.2% versus 30.0%, p<0.001.
The prevalence of MS was independent of timing of cholecystectomy. Participants with surgery <10 years ago (n=96) had a MS prevalence of 60.4% compared to 64.1% in those with a history of cholecystectomy >10 years ago (n=195). This contrasted with our finding that NAFLD prevalence was higher (43.1% versus 31.3% (p=0.05)) when cholecystectomy was performed >10 years ago.
Conclusion: In the general population, cholecystectomy was associated with MS and NAFLD, emphasizing the close link between cholecystectomy and metabolic health. The prevalence of NAFLD was higher in participants with cholecystectomy earlier in life.

Ethnicity and response to primary standard three-dose hepatitis B vaccination in employees in the Netherlands, 1983 through 2017

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Background: Hepatitis B virus (HBV) vaccination is recommended to all employees who have an occupational risk in the Netherlands. Our objective was to assess the determinants of immune response to primary standard 3-dose HBV vaccination (0, 1, 6 months), with the main focus on ethnicity.
Methods: For this retrospective study, we analyzed data from the VAXIN database of Ease Travel Clinic. Ease Travel Clinic is specialized in vaccination and covers the South Limburg region of the Netherlands with a population of 599,025. Employees and students, 16 years of age and older who received HBV vaccination between 27 April 1983 and 20 December 2017 were to be included in the study. Subjects with unknown country of birth, unknown gender and incomplete vaccination data were to be excluded. Weighted multiple logistic regression with Firth's bias adjustment was used to assess determinants of non-response (anti-HBs <10 mIU/mL) and low-response (anti-HBs 10-99 mIU/mL).
Results: Out of 76,239 adult individuals, 12,193 persons were identified according to in- and exclusion criteria. Of all identified subjects, 180 (1.6%) were HBV vaccine non-responders and 549 (4.8%) were low-responders. Baseline characteristics were as follows: mean age 27.5 years (95% CI 27.23-27.72), 23.6% male gender, 99.4% born in the Netherlands and 93.5% of Western European origin.
All non-responders were born in the Netherlands and country of birth was therefore not included in further analyses. Although no significant association was found between non-response and individuals of Western European origin (adjusted odds ratio (aOR)=1.20, 95%CI 0.66-2.44, *p* =.163), low-response to HBV vaccination was significantly associated with Western European origin (aOR=2.13, 95%CI 1.35-3.71, *p* =.002), amongst other factors. The most significant determinants for non-response were older age at vaccination (aOR=1.06, 95%CI 1.06-1.07, *p* < .001) and male gender (aOR=2.51, 95%CI 1.97-3.22, *p* < .001).
Conclusion: The non-response rate was low in our study population. Western European origin was associated with low-response to the primary 3-dose HBV vaccinations.

Serum lipidomics profiling as a diagnostic tool for NAFLD in children: a matched case-control pilot study

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Background: Concomitant with the rise in obesity, non-alcoholic fatty liver disease (NAFLD) has become the most prevalent liver disease in children and adults in industrialized countries. Disturbances in lipid metabolism play an important role in the pathogenesis of NAFLD. In lipidomics, analytical chemistry techniques are used to identify and quantify lipid species in biological samples such as liver tissue and blood plasma. Adult studies showed lipid profiles are associated with different stages of the NAFLD spectrum. Therefore, this technique could offer new non-invasive diagnostic biomarkers for NAFLD, that are urgently needed due to a lack of accurate screening tools for NAFLD. In children, no lipidomic studies related to NAFLD have been reported. The aim of this study was to identify plasma lipids that are correlated with the presence of steatosis in children with obesity using lipidomics.
Methods: The prevalence of lipidomic metabolites was analyzed in blood samples of 21 children with obesity in whom steatosis was detected using proton magnetic resonance spectroscopy (^{1}H-MRS) and were compared to matched samples of non-steatotic subjects based on age, gender and body mass index (BMI). NAFLD was defined as a liver fat percentage of > 1.8% measured by ^{1}H-MRS, which has been validated to correspond with > 5% fat containing hepatocytes on liver histology. High-performance liquid chromatography-mass spectrometry (HPLC-MS) was used to measure lipidomic metabolites.
Results: Twenty-one matched sample pairs were analyzed (55% male; median age 14 years). HOMA-IR, total cholesterol and degree of steatosis were significantly different between steatotic and non-steatotic subjects (p=0.003, p=0.010, p=0.000, respectively). In total, 750 different metabolites were identified. No significant difference was found in the prevalence of lipid classes or lipid species in children with NAFLD and controls.
Conclusion: In contrast to adult studies, we did not find a significant difference in the prevalence of lipid classes between obese children with NAFLD and obese children without NAFLD. In addition, there was no significant difference in lipid species. In all, these results do not support a diagnostic role for lipidomics in diagnosing NAFLD in children with obesity.

Risk factors for symptomatic gallstone disease after Roux-en-Y gastric bypass

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Background: Patients with morbid obesity are at risk for symptomatic gallstone disease after bariatric surgery. Up to 15% of patients will develop biliary symptoms within two years after surgery. Although bariatric surgery is performed widely nowadays, specific risk factors for gallstones have not been well defined. Therefore, we aimed to identify risk factors for symptomatic gallstone disease after laparoscopic Roux-en-Y gastric bypass (LRYGB).
Methods: We conducted a case-control study of patients who underwent a LRYGB between 2013 and 2015 in the MC Slotervaart (Amsterdam, The Netherlands). Primary endpoint was symptomatic gallstone disease defined as the need for cholecystectomy because of postoperative biliary symptoms within two years after surgery. We selected for each case two controls who consecutively underwent surgery after that specific case. Logistic regression analyses were used to identify risk factors for symptomatic gallstone disease.
Results: Between 2013 and 2015, 1780 LRYGBs were performed. We identified 233 (13.1%) cases who developed symptomatic gallstone disease after a median [IQR] of nine months [5-14], and 466 controls. Five factors were significantly associated with the development of symptomatic gallstones disease after LRYGB in all patients: age [OR (95% CI), 0.98 (0.96-0.99); p=0.005], female gender [OR 1.83 (1.06-3.17); p= 0.031], Caucasian ethnicity [OR 1.82 (1.10-3.02); p=0.019], percent total weight loss (%TWL) at 12 months [OR 1.06 (1.04-1.09); p<0.001] and preoperative pain syndrome [OR 2.72 (1.43-5.18); p=0.002]. Pre-operative statin use was also associated in a subgroup analysis of patients who developed symptoms within 9 months with an OR of 0.27 (0.09-0.78); p=0.016) and showed a dose-response relationship. Use of birth control pills, fertility and having children were not associated with biliary symptoms in the female population.
Conclusion: In our study %TWL and preoperative pain syndrome were associated with gallstone disease besides the traditional risk factors age, female gender and Caucasian ethnicity. These factors can be used to identify high-risk patients, who might benefit from preventive measures. Hypothetically, statins can protect patients after bariatric surgery from developing gallstones, possibly by diminishing hepatic cholesterol levels.

A multicentre randomized non-inferiority trial comparing usual care to restrictive strategy for use of cholecystectomy in patients with gallstones and abdominal pain (SECURE trial)

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Background: Cholecystectomy is the preferred treatment for symptomatic, uncomplicated gallstones. Usual care in patients with abdominal pain and gallstones is associated with practice variation and persistent abdominal pain in 10-41% of post-cholecystectomy patients. We scrutinized (in)efficient use of cholecystectomy by determining non-inferiority of a restrictive standardized strategy with stepwise selection compared to current usual care for patients with abdominal pain and gallstones.
Methods: We randomly assigned patients with ultrasound proven gallstones and abdominal symptoms to a restrictive strategy with a stepwise selection for cholecystectomy (530 patients) or usual care (537 patients). The primary endpoint was the proportion of patients being pain-free at 12 months' follow-up. A 5% non-inferiority margin was chosen according to clinical relevance estimation. Secondary endpoints included the rate of cholecystectomy, the proportion of patients with gallstone related and surgical complications, patients' satisfaction, health status, working disability and time to pain-free.
Results: During a three-year period 1067 patients were included in 24 hospitals. At 12 months' follow-up 298 of 530 patients (56.2%) were pain-free in the restrictive strategy, compared to 321 of 537 patients (59.8%) in the usual care arm, and non-inferiority was not demonstrated. The restrictive strategy resulted in a significantly lower cholecystectomy rate than usual care (67.0% versus 75.4%, p=0.005). Other secondary outcomes were comparable between groups: median time to pain-free (7.87 months versus 7.29 months, respectively, p=0.130), patient satisfaction with treatment outcome at 12 months' follow-up (p=0.976), and patients' health status over time (p=0.820).
Conclusion: Usual care as well as a restrictive strategy for use of cholecystectomy in patients with gallstones and abdominal pain is insufficient in terms of pain relief. However, for a restrictive strategy this result is associated with significantly less cholecystectomies.

Per-oral endoscopic pyloromyotomy for severe refractory gastroparesis: a feasibility and efficacy study in the Netherlands

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Background: Management of patients with refractory gastroparesis to medical treatment is challenging as these patients often require nutritional support. Gastric per-oral endoscopic pyloromyotomy (GPOEM) has been recently introduced as a minimally invasive therapeutic modality for gastroparesis patients with refractory symptoms. Aim of the present study is to assess the feasibility, safety and clinical efficacy of GPOEM in patients with severe refractory gastroparesis in a tertiary referral center.
Methods: Eighteen consecutive patients (15 women, men age 57.7 ± 3.7 yrs) with severe refractory gastroparesis (9 idiopathic, 7 post-surgical, 2 diabetes mellitus) were prospectively included in a single center study. Twelve out of 18 patients (66.7%) were dependent on enteral feeding. From September 2017 to November 2018 patients underwent GPOEM under propofol deep sedation. Primary outcome was technical success and safety. Secondary outcome was clinical success using the Gastroparesis Cardinal Symptom Index (GCSI) before and at 3 months (n=14) and 6 months (n=10) after the procedure. Clinical success was defined as a reduction in GCSI >1 point. Gastric emptying test was performed before and at 3 months after the procedure.
Results: Technical success rate was 100% (18/18). Mean duration of the procedure was 57 ± 6.3 minutes and mean length of hospital stay was 2.9 ± 0.3 days. Three adverse events were observed: 2 patients with pneumoperitoneum, both conservatively treated with endoclip during procedure and antibiotics, 1 patient with melena several days after the procedure and no signs of active bleeding at gastroscopy. Clinical success rate was 78.6% (11/14) at 3 months and 80% (8/10) at 6 months. Mean GCSI improved significantly at 3 months (n=14) (GCSI: 2.8 ± 0.6 vs. 5.3 ± 0.4, p=0.002) and at 6 months (n=10) after GPOEM (GCSI: 3.3 ± 0.8 vs. 5.3 ± 0.4, p=0.03). Gastric emptying improved in 54.5% (6/11) of patients at 3 months. Enteral feeding could be stopped in 70% (7/10) of patients short after the procedure.
Conclusion: Per-oral endoscopic pyloromyotomy is a technically feasible and effective therapeutic option for patients with severe refractory gastroparesis at short term follow-up. However, longer follow-up data are required to assess long term effectivity and to identify subgroups of patients that could benefit most from this novel technique.

Long-term follow-up of gut-directed hypnotherapy self-exercises at home using CD versus individual therapy by qualified therapists in children with irritable bowel syndrome or functional abdominal pain (syndrome)

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Background: We previously showed that home-based gut-directed hypnotherapy treatment with CD is non-inferior to individual hypnotherapy (iHT) by a therapist in the treatment of children with irritable bowel syndrome (IBS) or functional abdominal pain (syndrome) (FAP(S)). Aim of this follow-up study was to investigate the long-term effects of iHT and CD-hypnosis-exercises at home.
Methods: 150 out of 250 participants from our previous randomized controlled trial (RCT) were invited to complete: 1) an online standardized abdominal pain dairy, on which pain frequency and intensity were scored, and 2) an online questionnaire including adequate relief, quality of life (QoL), anxiety/depression scores, somatization, pain beliefs, school and/or work absenteeism and health care utilization.
Results: To date, 70 CD-patients and 74 iHT-patients have completed this study. After a mean duration of 5.8 years follow-up, 80.0% in the CD-group vs 83.8% in the iHT-group reported adequate relief of abdominal complaints. More than 50% reduction in pain intensity and pain frequency was seen in 67.2% in the CD-group vs 66.7% in the iHT-group, respectively. Also, anxiety/depression scores, somatization, pain beliefs, healthcare utilization and school/work absenteeism improved significantly in both study groups. No differences were found in QoL.
Conclusion: Both home-based CD-self-exercises and iHT given by a qualified therapist show persisting positive results in the treatment of children with IBS or FAP(S) after more than 5 years of follow-up. These results support the rationale for implementation of this easy to use, widely available and cost - effective home-treatment in daily practice.

Reduction in IBS symptom severity does not result in improved quality of life in patients with irritable bowel syndrome

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Background: Irritable Bowel Syndrome (IBS) is a chronic disorder of the brain-gut-axis. The natural course of IBS may vary between patients and is difficult to predict. Objective: this study aimed to evaluate symptom evolution over time after a five-year follow-up period and to identify baseline predictors for a higher symptom severity or more quality of life impairment at follow-up.
Methods: Patients enrolled in the Maastricht IBS Cohort completed questionnaires upon inclusion regarding: demographics and lifestyle, gastrointestinal (GI) symptoms, general anxiety and depression, and quality of life (QoL). The same questionnaires, in addition to others, were completed after five years. A trained medical professional checked the Rome criteria during telephonic interviews at follow-up.
Results: At a mean follow-up period of 4.7 years, 379 patients were approached of whom 203 (53.7%) responded. Of these, 161 were reached by telephone and included in the analysis; 49 (30.4%) didn't fulfill the Rome III criteria anymore and had significantly lower levels of GI symptoms and GI specific anxiety compared with Rome III-positive patients ($p < 0.001$). However, although Rome III-negative, they had equal levels of impaired quality of life and general life satisfaction, comorbid anxiety and depression, absence from work and impaired work productivity. No baseline predictors could be found for being Rome III-positive or -negative. Younger age and higher physical quality of life at baseline predicted higher physical quality of life at follow-up,B -0.15, 95%CI -3.27 – 51.49, $p<0.005$ and B 0.63, 95%CI 0.44 – 0.82, $p<0.01$ respectively. Higher mental quality of life at baseline predicted higher mental quality of life at follow-up B 0.45, 95%CI 0.41 – 0.75, $p=0.005$.
Conclusion: GI symptom improvement in Rome III-negative patients does not lead to improved quality of life or more life satisfaction, which are associated with anxiety and depression at follow-up rather than GI symptoms. Patients are therefore likely to benefit from a multidimensional treatment approach.

Day-to-day variability in fecal microbiota and its association with stool consistency: do we need repeated sample collection on the short-term?

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Background: Stool consistency has been associated with the fecal microbiota, suggesting stool consistency as a potential confounding factor in intestinal microbiota analyses. Since stool consistency can fluctuate over time, especially in several gastrointestinal (GI) diseases, this raises the question of whether day-to-day variability in microbial composition should be considered, by collecting multiple fecal samples. As irritable bowel syndrome (IBS) often presents with temporal instability in stool consistency, we aimed to evaluate within-subject (day-to-day) variability in fecal microbiota and its association with stool consistency in IBS and healthy subjects, over a 7-day course.
Methods: Twelve IBS subjects (IBS) and 12 age- and sex-matched healthy subjects (HC) collected fecal samples once daily during seven consecutive days, which were frozen directly after collection. The percentage of dry weight was determined for each sample as a measure of stool consistency. 16S rRNA gene sequencing was performed and both microbial richness (*i.e.* alpha diversity) and composition (*i.e.* beta diversity) were assessed.
Results: Linear mixed-effects models showed no significant association between the interaction term stool consistency*time and microbial richness, but significant positive associations were observed between stool consistency and microbial richness. However, regression coefficients were small for both Chao1 index (B:1.231, 95%-CI: 0.835;1.628) and observed species (B:1.066, 95%-CI: 0.725; 1.407). In addition, in both IBS and HC, microbial richness was highly correlated (inter-item correlations>0.8; ICCs>0.850) between subsequent samples, for both measures of alpha diversity, indicating low within-subject (day-to-day) variability in fecal microbial richness. Principal coordinates analyses on beta diversity indices showed high similarity between the microbial community structure of samples of one individual, also indicating low within-subject variability in microbial composition from day to day.
Conclusion: This study demonstrates that stool consistency is associated with the fecal microbiota, but this association is not different between consecutive fecal samples (*i.e.* over time). In addition, the low within-subject variability in both alpha and beta diversity indicates that the microbiota of one single fecal sample is representative for a period of seven days. Therefore, in this context, we consider collecting multiple fecal samples unnecessary.

Physiotherapy for children with functional constipation: a pragmatic randomized controlled trial in primary care

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Background: Children with functional constipation (FC) may experience long-term symptoms despite treatment. Given that physiotherapy has shown promising results in hospital, we investigated the benefits of adding it to conventional treatment (CT) in primary care.
Methods: This was an 8-month pragmatic randomized controlled trial in primary care of children with FC aged 4–17 years. CT comprised toilet training, nutritional advice, and laxative prescribing, whereas physiotherapy focused on resolving dyssynergic defecation. The primary outcome was treatment success over 8 months, defined as the absence of FC (Rome III criteria) without laxative use. Secondary outcomes included the absence of FC irrespective of laxative use and the global perceived treatment effect. Researchers were blinded to group allocation during assignment and data analyses, but participants were not. Results of longitudinal analyses in the intention-to-treat population are reported as adjusted relative risks (aRR) and 95% confidence intervals (95%CI).
Results: Children were allocated to CT plus physiotherapy or CT alone (67 per group). The treatment success percentage was not statistically improved by adding physiotherapy to CT (aRR 0.80, 95%CI 0.44–1.30). At 4 months, fewer children receiving physiotherapy had treatment success (17%) than children receiving CT alone (28%), but this had equalized by 8 months (42% and 41%, respectively). The percentage of children without FC, irrespective of continued laxative use, was not statistically different between groups (aRR 1.12, 95%CI 0.82–1.34). After 4 and 8 months, the percentage of children without FC was respectively 40/59 (68%) and 38/52 (83%) in the physiotherapy group, and 34/53 (64%) and 30/49 (61%) in the CT group. Notably, parents reported significantly more global symptom improvement after physiotherapy than after CT (aRR 1.40; 95%CI 1.00–1.73).
Conclusion: We find no evidence to recommend physiotherapy for all children with FC in primary care. More research is needed to evaluate whether physiotherapy in primary care is effective for children with symptoms of longer duration.

Opioid usage is significantly associated with rectal hyposensitivity and functional evacuation disorders in patients with chronic constipation

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Background: Opioid usage has reached epidemic proportions, with 17.4% of the US population receiving ≥1 opioid prescription in 2017. Opioid-related adverse events are frequently reported, with opioid-induced constipation being most common (41% of patients with chronic non-cancer pain). In contrast to their known effect on colonic transit, the impact of opioids on rectal sensorimotor function is almost unstudied (current aim).
Methods: Consecutive patients referred to the Royal London Hospital GI Physiology Unit, UK (2004-16), who met core ROME IV criteria for functional constipation were included, as well as details of current opioid usage. All patients underwent diagnostic testing, which included assessment of both rectal sensation to balloon distension and evacuatory function using defecography. Rectal hyposensitivity (RH) was diagnosed when ≥2 sensory thresholds were above normal limits. A functional rectal evacuation disorder (fED) was diagnosed by impaired evacuation in the presence of poor opening of the anorectal angle, poor relaxation of the anal canal or poor expulsive effort generated.Radio-opaque marker whole-gut transit studies were performed in patients with a history of infrequent defecation. Symptom severity, and presence of RH and/or a fED were compared between patients taking or not taking opioids.
Results: A total of 3,019 patients (2,603 F [86.2%]; median age 51) were included. Opioid users had more severe symptoms compared to non-opioid users (CCCS 17 vs 15; $p<0.0001$). *RH* was the strongest single variable associated with opioid usage (opioids 17% vs non opioids 12%; OR 1.49 [1.14 – 1.95]; $p=0.004$), though both a fED and delayed whole gut transit were also significantly associated (opioids 30% vs non opioids 24%; OR 1.31 [1.05 – 1.65], $p=0.02$ and opioids 47% vs non opioids 38%; OR 1.43 [1.08 – 1.89], $p=0.01$, respectively). When patients with coexistent RH and fED were compared to those without, the association with opioid usage increased (opioids 10% vs non opioids 6%; OR 1.69 [1.10 – 2.60]; $p=0.02$).
Conclusion: A significant association has been found between opioid usage, rectal hyposensitivity and a functional evacuation disorder, which is numerically stronger than the association with delayed transit. Whether this is a causal effect cannot be determined with the current study design but merits further investigation.

A prospective evaluation of gastrointestinal symptoms and dysmotility in subjects with and without Hypermobility Spectrum Disorders

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Background: Hypermobility Spectrum Disorders (HSD) are a continuum of connective tissue disorders characterized by joint hypermobility (JH). Recent studies demonstrated that HSD are often associated with gastrointestinal (GI) symptoms. A higher prevalence of HSD has been demonstrated in patients with functional compared to organic GI disorders, pointing towards neuromuscular dysfunction of the GI tract as a possible underlying mechanism. We prospectively evaluated whether subjects with (undiagnosed) HSD present with different symptom patterns and GI motility compared to non-HSD subjects, in an unselected tertiary GI patient population in whom organic pathology had previously been excluded.
Methods: Sixty-two subjects (53 female; mean age: 40), referred for comprehensive GI motility assessment using gastric emptying test, esophageal, antroduodenal, and/or colonic manometry study, were consecutively included. Brighton criteria were used to diagnose HSD, and JH was assessed using the Beighton score. GI and psychological symptom scores, and quality of life were assessed using the Gastrointestinal Symptom Rating Scale, Hospital Anxiety and Depression Scale, and Rand Health Survey Short Form-36.
Results: Eighteen subjects (29.0%) met criteria for HSD. No significant differences between HSD and non-HSD subjects were found for age, BMI, GI symptom severity, depression/-anxiety, and mental as well as physical quality of life. Esophageal, gastric, antroduodenal, and/or colonic dysmotility was not significantly more prevalent in the HSD group vs. the non-HSD group (72.2% vs. 43.2%, p=0.091). However, subjects with clinically significant JH (*i.e.*Beighton score$\geq$6) more often showed abnormal GI motility compared to subjects with Beighton<6 (83.3% vs. 46.8%, p=0.028). The odds of having any form of GI dysmotility were 5.7 times higher (95%-CI: 1.121; 28.788) in cases with Beighton$\geq$6 than Beighton<6.
Conclusion: In patients with functional GI disorders referred for extensive GI motility analysis, HSD patients did not present with gastric, esophageal, antroduodenal, and/or colonic dysmotility significantly more often than non-HSD patients. However, the clinical phenotype of JH was a significant predictor for GI dysmotility. Therefore, the present study supports a possible role for neuromuscular dysfunction as a pathophysiological mechanism underlying GI symptoms in HSD.

Diagnostic value of inflammatory parameters in the work-up of functional abdominal pain

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Background: In the diagnostic work-up of chronic abdominal pain, a set of laboratory markers including inflammatory parameters (erythrocyte sedimentation rate (ESR), hemoglobin (Hb), C-reactive protein (CRP)), anti-tissue transglutaminase (anti-tTg), fecal calprotectin (FC) and Giardia lamblia (G. lamblia) is recommended. The aim of this study was to investigate the additional diagnostic yield of inflammatory parameters to anti-tTg, FC and G. lamblia when discriminating functional abdominal pain from organic disease.
Methods: This retrospective cohort study included pediatric patients (4-18 years) with chronic abdominal pain for >2 months in whom FC was determined between January 2012-July 2017. Data on Hb, CRP, ESR, anti-tTg, FC and functional or organic diagnosis were collected. FC values of >250 µg/g were considered abnormal.
Results: In total, 870 patients were identified, of whom 103 (11.8%) had an organic disorder. In 81 (78.6%) of these children, diagnosis was based on abnormal FC (>250 µg/g) and/or positive anti-tTg. Eight (7.8%) children had a positive G. lamblia stool test. Of the remaining 14 children, 3 had elevated ESR levels due to extra-intestinal infections. In the other 11 (10.7%) children, inflammatory parameters were not aberrant. These children were diagnosed with Helicobacter pylori (n = 5), food allergy (n = 2), acnes (n = 1), gastritis (n = 1), polycystic ovary syndrome (n = 1) and side effects due to medication (n = 1). Sensitivity and specificity of this group of diagnostic markers for organic disease was 0.89 (95% CI: 0.82-0.94) and 0.86 (95% CI: 0.84-0.89), respectively and changed to 0.86 (95% CI: 0.78-0.92) and 0.86 (95% CI: 0.84-0.89), respectively, when ESR was excluded from the diagnostic markers set. This difference was non-significant.
Conclusion: To distinguish between functional abdominal pain and organic disease, inflammatory parameters might be left out from the diagnostic work-up as they might have no additional diagnostic yield. However, caution should be taken not to miss extra-intestinal infections (3%).

The socioeconomic burden of IBS in a Dutch population

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Background: Irritable Bowel Syndrome (IBS) is a prevalent disorder that carries a substantial socioeconomic burden due to increased healthcare utilization and productivity losses. Data on this topic for the Dutch situation is lacking.
Objective: 1) to determine the socioeconomic cost of IBS and 2) to identify sociodemographic and clinical characteristics associated with costs.
Methods: Baseline data from the PERSUADE trial (peppermint oil versus placebo) was used. IBS patients (ROME IV), aged 18-75, were included via primary and secondary/tertiary care recruitment or self-referral and completed questionnaires regarding demographics and life style, symptom severity, quality of life, and mental health. Direct and indirect health costs were measured using the iMTA Medical Cost Questionnaire and Productivity Cost Questionnaire respectively. Costs were calculated by multiplying resource use by the cost price per resource unit, adopting reference prices derived from the Dutch guidelines for cost calculations. The friction cost method was applied to determine long term absenteeism and extrapolation to determine short term absenteeism costs.
Results: 111 patients (86% female, mean age 33) were included. Data were highly skewed. Mean total direct costs for a period of 3 months were +/- €573 (median €285; IQR €74-689). Visits to mental health care providers and outpatient visits contributed most to these direct costs (22% and 18% respectively), followed by physiotherapist consultations (14%). Depression scores were associated with direct costs (B €108, P<0.00; 95% CI 51-165). Mean total indirect costs for 3 months were +/- €459, but were caused entirely by a subgroup of 31 patients. In this subgroup (87% female, mean age 34), mean indirect costs were €1642, (median €729; IQR €286-1924). Indirect costs were primarily related to absenteeism.
Conclusion: Both direct and indirect costs lead to a socioeconomic burden in a Dutch IBS population. Absenteeism, mental health care, and outpatient consultations are important driving factors of costs.

Prevalence of child abuse in children with functional constipation

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Background: An association between functional constipation (FC) and child abuse has been described. However, data in pediatric patients are limited and the diagnosis of child abuse remains challenging. Our objective was to determine the prevalence of child abuse and neglect (CAN) in children with FC as compared to their healthy peers.
Methods: A case-control study was carried out in children aged 3-10 years old, including children with FC according to the Rome III criteria recruited at a single center (cases) and healthy children without gastrointestinal complaints recruited at schools (controls). Parents of children were questioned about their child's history of CAN and asked to fill out the Child Sexual Behavior Inventory (CSBI). Children were interviewed using the Sexual Knowledge Picture Instrument (SKPI) and the Life Events Checklist (LEC). Children with FC underwent a physical examination. A suspicion of CAN was determined according either a positive history of child abuse, a positive CSBI-Total scale, a positive SKPI and/or a positive report on the LEC questionnaire. Children with a suspicion of CAN were referred to a specialized therapist for further diagnostics.
Results: An interim analysis was performed including 224 children with FC and 128 controls. Both groups were age and gender comparable (50% females, median age 6 years (NS)). Significantly more parents of children in the control group had a high level of education as compared to parents of children with FC (80.0% vs. 51.4% of mothers and 76.0% vs. 48.6% of fathers, both p=0.000).
No significant differences in the prevalence of a suspicion of sexual abuse (12.1% vs. 18%, NS), physical abuse (7.1% vs. 11.7%, NS) and neglect (7.6% vs. 7.8%, NS) were found between children with FC and healthy controls separately. However, significantly more children in the control group had a total suspicion of CAN (either sexual abuse, physical abuse or neglect) as compared to the children with FC (32.0% vs. 22.3%, p=0.045). In 22/50 (44.0%) children with FC, the physician described (behavioral or physical) abnormalities suspect of CAN during physical examination. Results of the specialized therapist have yet to be analyzed.
Conclusion: Our preliminary results show no differences in the prevalence of sexual abuse, physical abuse and neglect between children with FC as compared to healthy controls. However, the prevalence of CAN in children with FC was higher in comparison with the available literature of CAN in the normative population. Physicians should therefore be alert of signs of CAN in the management of children with FC.

A smartphone application for symptom assessment and data collection in medical trials: example from an IBS drug intervention trial

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Background: Patient reported outcome measures (PROMS) are crucial to assess the efficacy of therapeutic interventions, especially for disorders such as Irritable Bowel Syndrome (IBS), without a well-defined organic substrate and lack of validated biomarkers. The reliability of paper diaries is often affected by recall bias and fake compliance. To acquire more valid data, electronic diaries have been developed and implemented in recent years. However, little has been reported on the compliance rates of these diaries so far, and when available, the rates vary widely between studies. Our aims were 1) to determine the compliance rate to a smartphone application in a randomised placebo-controlled trial (RCT) and 2) to identify sociodemographic and clinical patient characteristics associated with compliance rate.
Methods: The PERSUADE (peppermint oil versus placebo) study uses a smartphone application for patients to register their daily symptoms. IBS patients (ROME IV) were instructed to fill out this digital diary during a 8-week treatment period. In addition, patients were asked to complete electronic questionnaires (via email, not smartphone), regarding demographics and life style, symptom severity (IBS-SSS), Quality of Life (IBS-QoL), and anxiety and depression (GAD-7, PHQ-9). Compliance rate was defined as the percentage of days completed in the diary.
Results: 154 (79.1% female, mean age 33.8) patients had been included so far. The mean compliance rate was high (86.6%, 10.5 SD). No association was found between age, gender, educational level, and compliance. Interestingly, the number of adverse events was positively associated with compliance (B 0.01, $p=0.04$), whereas anxiety was inversely associated with compliance (B -0.05, $p=0.01$). Moreover, overall compliance declined over time ($F(5.8, 886.4) = 6.07$, $p<0.00$).
Conclusion: This study demonstrates that compliance to this smartphone application is, on average, more than 80%. However, the compliance rate decreased over time, which might suggest that this method is less suitable to measure treatment efficacy over long periods of time.

Coexistence of fecal incontinence and constipation in adults is an underappreciated clinical problem

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Background: Coexistence of fecal incontinence (FI) and chronic constipation (CC) is well recognized in pediatric and geriatric populations. In adults, however, these conditions are often considered separate entities with regard to both diagnostic evaluation and treatment. The aim of the current study was to: (1) determine coexistence of these symptoms in adults referred to a tertiary center for anorectal physiological investigation; and (2) assess how frequently coexistence is reported by the referring clinician.
Methods: Consecutive patients (aged 18 – 80) referred to the Royal London Hospital GI Physiology Unit (study period 2004-16) for investigation of FI or CC were included. All patients self-filled a questionnaire incorporating validated scoring systems. The primary reason for referral stated in the clinicians' referral letter (FI, CC or both) was compared to patient-reported symptoms defined by ROME IV criteria. The St Marks incontinence score (SMIS) and Cleveland Clinic constipation score (CCCS) were also used to investigate symptom severity. Patients with incomplete questionnaires were excluded.
Results: A total of 4,034 patients (3,379 F [83.8%]; median age 52 [IQR 41 – 63]) were included. Of females, 84% were parous (median 2 vaginal deliveries [IQR 1 – 3]). Primary reason for referral was CC in isolation in 2,062 patients (51%), FI in isolation in 1,641 patients (41%) and both symptoms in 331 patients (8%). However, according to ROME IV, 1,575 (39%) patients fulfilled criteria for CC alone, 804 (20%) patients had FI alone, and 1,655 (41%) patients had both symptoms. Using cut-offs of ≥9 on CCCS and ≥6 on SMIS to define significant symptoms, marked coexistence was confirmed, encompassing clusters likely to represent distinct disease phenotypes.
Conclusion: Over 40% of adult patients referred to a tertiary center for investigation of their symptoms had coexistence of fecal incontinence and constipation, based on validated criteria. This overlap was not acknowledged by the referrer in 80%. Lack of recognition of symptom coexistence has major treatment implications. For example, 50% of patients referred as having FI in isolation also had significant constipation; accordingly, therapy may be better directed at the latter, with FI representing a secondary phenomenon.

Proposed method for adequate surgical gallbladder examination

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Background: The Dutch Surgical Society changed its national "gallbladder" guideline 2016, regarding routine histopathologic examination after cholecystectomy in absence of macroscopic abnormalities. Thus, shifting the macroscopic examination of the gallbladder from the department of Pathology to the operating room. The surgeon is now asked to perform a macroscopic examination of the gallbladder, and decide whether additional histopathologic assessment is warranted. Up to this date, there is no clear guideline or protocol to perform a proper surgical examination. Leaving surgeons extemporaneous in regard to selective histopathologic gallbladder examination.
Methods: The present study describes a surgical approach for adequate macroscopic inspection of the gallbladder. This procedure was introduced in 2011 and implemented in 2012 following an evaluation of the existing literature in collaboration with the department of Pathology.
Results: Since incorporation of the selective policy we have performed over 2500 surgical macroscopic examinations of the gallbladder. As a result, we observed a significant decrease in histopathologic examination of the gallbladder following cholecystectomy. Whereas we observed a stable trend of gallbladder carcinoma in the same period.
Conclusion: Here, an easy and reproducible method is described for future macroscopic analysis by the surgeon following a cholecystectomy. In addition, we depict several frequent macroscopic abnormalities in order to provide some cases of abnormal macroscopic gallbladders.

Selective histological examination after cholecystectomy; an analysis of current daily practice in the Netherlands

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Background: The 2016 Dutch national guidelines on handling of a removed gallbladder for cholelithiasis favors a selective histopathologic policy (Sel-HP) rather than routine policy (Rout-HP). The aim of this study was to determine the current implementation of the present guideline and the daily practice of Sel-HP.
Methods: Surgeons who were engaged in gallbladder surgery and were involved in local hospitals' gallbladder protocols completed a questionnaire study between December 2017 and May 2018. Data were analyzed using standard statistics.
Results: A 100% response rate was obtained (n=74). Approximately 64% of all gallbladders (n=22 500) are currently examined microscopically. Sixty-nine (93.2%) hospitals confirmed they were aware of the new guidelines, and 56 (75.7%) knew the guideline was adjusted in favor of Sel-HP. Half of the hospitals (n=35, 47.3%) has adopted a Sel-HP, and 39 (52.7%) a Rout-HP. Of the 39 hospitals who currently practiced a Rout-HP, 36 are open to a transition to a Sel–HP although some expressed the need for more evidence on safety or novel guidelines.
Conclusion: The current implementation of the 2016 Dutch guideline advising a selective microscopic analysis of removed gallbladders for gallstone disease is suboptimal. Evidence demonstrating safety and cost-effectiveness of an on demand histopathological examination will aid in the implementation process.

Nationwide outcome including long-term quality of life after total pancreatectomy (PANORAMA)

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Background: Total pancreatectomy is increasingly advised for main duct intraductal papillary mucinous neoplasm and other conditions albeit concerns about poor quality of life related to 'brittle' diabetes. Data on postoperative outcome, diabetes management, and long-term quality of life after total pancreatecotmy from large nationwide series are however lacking.
Methods: A nationwide cohort study among adults who underwent TP between 2006 and 2016 in 17 Dutch centers was performed. Postoperative outcomes were retrospectively analyzed. QoL was assessed cross-sectionally using generic and disease-specific questionnaires and compared with reference data from the Dutch general population and patients with type 1 diabetes.
Results: Overall, 148 patients after TP were included. The annual volume of total pancreatectomies increased from 5 in 2006 to 32 in 2015 ($P < 0.05$). The rate of 30-day mortality rate was 5% and major morbidity 32%. Patients with quality of life assessment had a median follow-up of 36 months and reported a slightly lower global (QLQ-C30; 73 vs 78, $P = 0.03$) and daily health status (EQ-5D-5L; 0.83 vs 0.87, $P < 0.01$) compared to the general population. QoL did not worsen during follow-up (<3, 3-5 or >5 years). Patients were satisfied with their diabetes therapy and experienced similar diabetes-related distress as patients with type 1 diabetes.
Conclusion: In this nationwide study, total pancreatectomy was associated with acceptable mortality and morbidity rates, a slightly lower but stable quality of life compared to the general population, and satisfactory diabetes therapy.

Textbook outcome as a novel quality measure in pancreatic surgery: a nationwide analysis

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Background: Quality assurance through auditing is becoming increasingly popular in surgery but requires objective assessment of surgical outcome. Textbook Outcome (TO) is a multidimensional measure, reflecting the 'ideal' surgical outcome but has never been used in pancreatic surgery.
Methods: Patients who underwent pancreatoduodenectomy (PD) or distal pancreatectomy (DP) for all indications between 2014-2017 were evaluated. Data were obtained from the Dutch Pancreatic Cancer Audit (DPCA), a mandatory nationwide registry. An international survey (24 experts, 10 countries, 4 continents) was conducted to reach consensus on the definition of TO in pancreatic surgery. Univariable and multivariable logistic regression was performed to identify predictors of TO. Between-hospital variation in TO rates were compared using observed-versus-expected rates, based on casemix-adjustment.
Results: Overall, 3341 patients were included, of whom 2633 (79%) underwent PD and 708 (21%) underwent DP. Based on the survey (92% response rate), TO was defined by the absence of postoperative pancreatic fistula, bile leak, postpancreatectomy hemorrhage (all ISGPS grade B/C), severe complications (Clavien-Dindo grade III or higher), readmission and in-hospital mortality. The overall proportion of patients that achieved TO was 60.3%; 58.3% for PD and 67.4% for DP. On multivariable analysis, only class ASA 3 and 4 predicted a worse TO rate after PD (OR 0.59 [0.44-0.80] and OR 0.19 [0.04-1.02]), whereas a dilated pancreatic duct (>3mm) was associated with an improved TO rate (OR 2.70 [2.05-3.57]). For DP, a benign/premalignant diagnosis and the absence of neoadjuvant therapy was associated with a better TO rate (OR 1.48 [1.02 – 2.14] and OR 2.17 [1.03 – 4.59], respectively). When comparing institutions, the observed-versus-expected rate for achieving TO varied from 0.70 to 1.50 per hospital after adjustment for casemix.
Conclusion: Textbook Outcome is a novel quality measure in pancreatic surgery. The rate of TO varied considerably between pancreatic centers in the Netherlands, demonstrating the potential for improvement using quality assurance programs.

Comparing the revised European, AGA and IAP guidelines on pancreatic cystic neoplasms: accuracy in identifying advanced neoplasia in IPMN

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Background: Accurate detection of advanced neoplasia (high grade dysplasia or invasive cancer) in pancreatic cystic neoplasms (PCN) will improve outcome while minimizing unnecessary surgery. The revised European, the American Gastroenterological Association (AGA), and the International Association of Pancreatology (IAP) guidelines provide recommendations on surveillance and surgical intervention for PCN based on symptoms and risk of malignancy. The aim of this study is to identify which guideline is the most accurate in predicting advanced neoplasia in intraductal papillary mucinous neoplasm (IPMN).
Methods: Patients who underwent surgery for PCN were extracted from our prospective database (2006-august 2018). We considered surgery in hindsight justified for advanced neoplasia, pseudopapillary and neuroendocrine tumors and when symptoms improved. Patients with IPMN were evaluated separately. The final histopathological diagnosis was compared with the initial indication for surgery stated by the different guidelines. Receiver operating characteristic (ROC) curves were calculated and compared to measure diagnostic value.
Results: Overall, 210 patients underwent pancreatic resection for a PCN. In hindsight, surgery was justified in 91 patients (43%), based on histopathological outcomes and symptom improvement. Finally, 115 patients with IPMN were included in the analysis to identify accuracy of different guidelines for predicting advanced neoplasia. Of the 46 patients with advanced neoplasia, 44 would have correctly been recommended for surgery according to the European and IAP guidelines, versus 17 according to AGA guideline. The AGA guideline would have missed 29/46 (63%) patients with advanced neoplasia, including 16 with cancer. Of those without advanced neoplasia, 51 (74%), 56 (81%) and 5 (7%) patients would have been incorrectly recommended for surgery by the European, IAP and AGA guidelines, respectively. The ROC comparison analysis showed that the European guideline was superior to the IAP guideline (p=0.021), whereas no difference was seen between the European and AGA guideline (p=0.392).
Conclusion: ROC comparison analysis showed that the European guideline was superior in identifying advanced neoplasia in IPMN compared to the IAP guideline, whereas no difference was seen between the European and AGA guideline. Although fewer patients undergo unnecessary surgery based on the AGA guideline, the risk of missing advanced neoplasia with this guideline is unacceptable high.

Risk factors for the development of vascular complications after liver transplantation

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Background: Vascular complications such as hepatic artery thrombosis (HAT) and portal vein thrombosis (PVT) after orthotopic liver transplantation (OLT) may cause increased morbidity, graft loss, and patient death. We aimed to identify potential risk factors for early postoperative thrombosis in patients who underwent OLT.
Methods: A hospital-based case-control study was performed including adult patients who underwent OLT between 1993-2017. Early postoperative thrombosis was defined as a vascular stenosis or occlusion of the portal vein and / or hepatic artery, diagnosed by duplex ultrasonography and confirmed with computed tomographic angiography. Information on donor characteristics were derived from the Euro t rans plant database. T rans plantation-related characteristics and recipient characteristics were Collected from the electronic patient files .Logistic regression was performed to calculate odds ratios (ORs) with 95% confidence intervals (CIs), which were used as estimates of relative risks.
Results: A total of 479 patients underwent 558 OLT procedures. Of these, 88 OLT cases were diagnosed with early postoperative thrombosis after day 0 to 72, mean 8.4 days, whereas 470 OLT controls were not. Early postoperative thrombosis included isolated hepatic artery thrombosis (HAT) in 27 patients (30.7%), isolated portal vein thrombosis (PVT) in 40 patients (45.5%), and other thrombotic complications in 21 patients (23.9%). Combined PVT and HAT occurred in 2 patients (2.3%).
Longer warm ischemia time [OR 1.031 (1.015-1.048), P<0.001] and longer operation time [OR 1.004 (1.001-1.008), P=0.017] were significantly associated with early postoperative thrombotic complications. When splitting outcome by kind of thrombotic complication, risk factors for HAT are low recipient age [OR 0.961 (0.935-0.987), P=0.004], longer cold ischemia time [OR 1.006 (1.002-1.009), P=0.002], and longer operation time [OR 1.010 (1.003-1.017), P=0.005]. Risk factors for PVT are male sex [OR 2.246 (1.038-4.861), P=0.040] and longer warm ischemia time [OR 1.030 (1.012-1.049), P=0.001].
A multivariate analysis identified longer operative time [OR 1.012 (1.002-1.022), p=0.019], cold ischemia time [OR 1.026 (1.001-1.051), p=0.045] and longer warm ischemia time [OR 1.034 (1.002-1.068), p=0.039] as risk factors for early postoperative HAT and PVT respectively. Warm ischemia time as an independent transplant related risk factor for post-transplant thrombosis with an OR of 1.043 (1.011-1.076, p=0.009).
Conclusion: In patients who underwent OLT, the risk of early postoperative thrombotic complications is mostly related to perioperative risk factors from such as cold and warm ischemia times. This further highlights the need to reduce graft ischemia times by using dynamic, oxygenated preservation strategies.

Palliative gastrectomy for advanced gastric cancer does not result in additional morbidity compared to curative gastrectomy

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Background: Palliative gastrectomy (PG) for gastric cancer can be considered in selected cases to relieve symptoms. The aim of this study was to evaluate postoperative morbidity and mortality in patients that underwent PG for gastric cancer and to compare these results with an intended curative gastrectomy (CG).
Methods: All patients who underwent both palliative and curative gastrectomy for gastric cancer between 2011-2016 in the Netherlands were included from the Dutch Upper GI Cancer Audit. In this population-based cohort study postoperative morbidity, mortality, readmissions and short-term oncological outcomes were appraised. Propensity score matching (PSM) was applied to create comparable groups of patients that underwent PG versus CG, using patient (such as gender, age, Body Mass Index, comorbidities) and tumor (such as cTNM-stage, neoadjuvant treatment) characteristics. Categorical parameters were compared using the Chi-square test (or Fisher's Exact test in case of expected counts less than 5), and for continuous variables the student's t-test was used. For variables with a non-parametric distribution logarithmic transformation was applied.
Results: Of the 2202 eligible patients, 115 patients underwent PG and 2087 CG. After PSM, 227 CG-patients were matched to 115 PG-patients. More conversions from laparoscopic to open surgery occurred during PG (11% vs. 3%, p=0.007). Although postoperative mortality was higher after PG in the original cohort (10% vs. 5%, p=0.026), after PSM there was no difference between groups (10% vs. 7%, p=0.415). Postoperative morbidity, re-interventions and readmission rates did not differ significantly between groups. Resection of additional organs (30% vs. 12%, p<0.001) and irradical resections (65% vs. 12%, p<0.001) occurred more frequently during PG, whereas less lymph nodes were resected (15 vs. 19 nodes, p<0.001).
Conclusion: Although postoperative mortality after PG was higher in the original cohort, PG does not lead to additional postoperative morbidity compared to CG in patients with similar patient and tumor characteristics (after PSM). This might suggest that PG could be considered more often in symptomatic patients deemed fit enough for surgery. However, randomized trials evaluating potential (survival) benefits of PG in selected patients should be awaited.

A national cohort study evaluating the association of short-term outcome indicators with long-term survival after esophageal and gastric cancer surgery

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Background: Short-term outcome indicators are often used to evaluate the quality of esophageal and gastric cancer surgery and compare performance between hospitals. In the Dutch Upper gastrointestinal Cancer Audit (DUCA) 'textbook outcome' is used as one of the indicators. 'Textbook outcome', is defined as a complete resection (pR0) with at least 15 retrieved lymph nodes, together with an uneventful postoperative course and no hospital readmission. The aim of this study was to investigate the association between the short-term outcome indicators and long-term survival in a national cohort of operated esophageal and gastric cancer patients.

Methods: For this national cohort study, data were retrieved from the DUCA database and a national database containing survival information. All patients who underwent curative surgery for esophageal or gastric cancer between 2011 and 2016 were included. Outcomes were overall survival and conditional survival (under the condition of surviving the first postoperative 30 days and hospital admission). Outcomes were compared between patients with a 'textbook outcome' versus no 'textbook outcome', for esophageal and gastric cancer separately. A Cox regression model was used to study the independent association between the short-term outcomes and survival adjusted for patient characteristics, tumor characteristics and surgical approach.

Results: In total, 4414 esophageal and 2943 gastric cancer patients were included in this study. The 1-, 2-, and 3-year overall survival was 76%, 62%, and 54% for esophageal cancer and 71%, 56%, and 49% for gastric cancer. 'Textbook outcome' was independently associated with longer overall survival (hazard ratio (HR): 0.68 [95% confidence interval (95%CI): 0.61-0.76] and 0.62 [95%CI: 0.54-0.71], respectively) and longer conditional survival (HR: 0.75 [95%CI: 0.68-0.84] and 0.69 [95%CI: 0.60-0.79], respectively).

Conclusion: This study showed that the short-term outcome indicator 'textbook outcome' was associated with long-term survival. Benchmarked feedback of indicators such as 'textbook outcome' in clinical auditing may help hospitals to improve outcomes.

Added value of MRI to endoscopic and endosonographic response assessment after neoadjuvant chemoradiotherapy in oesophageal cancer: a pilot study

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Background: In order to select oesophageal cancer patients after neoadjuvant chemo-radiation (nCRT) for organ-preserving treatment instead of surgery, complete response (CR) assessment must be accurate. As endoscopic and endosonographic assessment with biopsies of the primary tumour area and fine needle aspiration (FNA) of lymph nodes is known to result in a high number of false negatives, our aim is to determine the added value of MRI.
Methods: Twenty-two patients with locally advanced oesophageal cancer underwent MRI (1.5 Tesla, T2-weighted and diffusion-weighted MRI using b-values 0,200,800 s/mm^2), endoscopy with biopsies and endosonography with FNA after nCRT. One radiologist scored MRIs using a 5-point score (1=definitely CR, 2=probably CR, 3=inconclusive, 4=probably residual tumour, 5=definitely residual tumour). Histopathology of the resection specimen was the reference standard (Mandard tumour regression grade 1=pathological CR, 2-5=residual tumour). Sensitivity and specificity of residual tumour detection were calculated for endoscopy+endosonography, and for endoscopy+endosonography including MRI.
Results: Three (14%) of 22 patients achieved a pCR. Endoscopy with biopsies and endosonography with FNA found residual tumour in 9 of 19 patients with residual disease (sensitivity 47%). After adding MRI, 17 of 19 residual tumours were assessed correctly (sensitivity 89%). All complete responders had negative endoscopic biopsies (specificity 100%); one was incorrectly assessed as residual tumour on MRI (specificity 67%).
Conclusion: The addition of MRI to endoscopic and endosonographic response assessment improves detection of residual tumour after nCRT in oesophageal cancer patients.

Direct oral feeding following minimally invasive esophagectomy (NUTRIENT II trial): an international, multicenter, open-label randomized controlled trial.

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Background: Elements of enhanced recovery after surgery (ERAS) protocols have been successfully introduced in patients undergoing an esophagectomy. However, start of oral intake, an essential part of the ERAS protocols, remains a matter of debate. Patients undergoing an esophagectomy are mostly kept nil-by-mouth postoperatively out of fear for increasing pulmonary complications and anastomotic leakage. However, some studies in strictly selected patients indicate a potential benefit of early oral feeding. A feasibility trial from our group showed that direct start of oral intake was safe. The aim of this study is to investigate whether direct start of oral feeding following minimally invasive esophagectomy reduces time to functional recovery compared to standard of care.
Methods: Patients in this multicenter, international randomized controlled trial were preoperatively randomized to directly start oral feeding (intervention) after a minimally invasive esophagectomy with intrathoracic anastomosis (Ivor-Lewis) or to receive tube feeding and nil-by-mouth for five days postoperative (control group). Primary outcome was time to functional recovery. Secondary outcome parameters included anastomotic leakage rate, pneumonia rate and other surgical complications scored by predefined definitions.
Results: Baseline characteristics were similar in the intervention (n=65) and control (n=67) group. Functional recovery was seven days for patients receiving direct oral feeding compared to eight days in the control group (p-value 0.436). Anastomotic leakage rate did not differ in the intervention (18.5%) and control group (16.4%, p-value 0.757). Pneumonia rates were comparable between the intervention (24.6%) and control group (34.3%, p-value 0.221). Other morbidity rates were similar, except for chyle leakage which was more prevalent in the standard of care group (p-value 0.032).
Conclusion: Direct oral feeding after an esophagectomy does not affect functional recovery and did not increase incidence or severity of postoperative complications.

The preoperative fecal lipidome but not fecal microbial diversity predicts post-operative ileus in elective colorectal surgery

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Background: There is increasing evidence that microbial-host interactions modulate post-operative bowel function and therefore may have a role in postoperative ileus (POI). The analysis of the fecal metabolome provides a unique insight into host-microbial interactions which may allow mechanistic investigation and clinical risk stratification. The aim of this pilot study was to identify if the preoperative stool lipidome is predictive of POI and to explore possible causes of its variation.
Methods: This was a cross-sectional study of the preoperative fecal lipidome and microbiome of patients recruited to the multicentred RCT SANICS II (Peters et al., 2018) in Denmark and the Netherlands. Adult patients were included if they underwent elective colorectal resection and were excluded if they had previous surgery likely to disrupt the microbiome or had medication to modulate acetylcholine metabolism. Fresh preoperative fecal samples were biobanked and metabolites with a mass:charge ratio of 120-600Da were analysed by Laser-assisted Rapid Evaporative Ionization Mass Spectrometry (LA-REIMS) in positive and negative mode using a Xevo G2-XS QToF mass spectrometer (Waters Corporation). LA-REIMS represents a high throughput analytical platform with no requirement for sample preparation and it can be deployed at the point of care. Data were analysed using multivariate statistical methods including Orthogonal Partial Least Squares-Discriminant Analysis (OPLS-DA) in SIMCA v14.1 (Umetrics). 16S rRNA sequencing data were analysed using MicrobiomeAnalyst (www.microbiomeanalyst.ca).
Results: 42 patients (78% male, mean age 68) were included in the analysis with 90.5% of resections performed for malignancy. 114 spectra were generated across positive and negative modes, with 102 passing quality control. PCA demonstrates the preoperative fecal lipidome was not significantly influenced by age, gender, BMI, malignancy status, smoking status, ASA grade, diabetes mellitus or tumor stage. In positive mode, an OPLS-DA model predicted the 23 patients who developed post-operative ileus following leave-one-spectrum-out cross validation (R^2 0.24, Q^2 0.132, AUC 0.9). There was no significant difference between the ileus and non-ileus patients in the Shannon diversity index of the microbiome ($p = 0.09$). LA-REIMS in negative mode had no predictive power for POI.
Conclusion: The preoperative fecal lipidome can be detected using LA-REIMS and may predict the development of POI. The fecal microbiome does not appear to contribute significantly to this model, implying host-microbial co-metabolism rather than changes in fecal diversity contribute to the mechanisms of POI.

Adhesion-related hospital readmissions in patients with open or laparoscopic abdominal or pelvic surgery: A nationwide cohort study (SCAR update)

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Background: In 1999 Ellis published the original SCAR study, the first epidemiological study on a large scale to determine the effect of adhesions on hospital readmissions. Over 1 in 3 patients who are operated in the abdominal or pelvic cavity were readmitted a mean of 2.1 times during the 10-year follow-up for adhesion related causes. In the past few decades multiple strategies have been developed to reduce adhesion formation. One the most promising strategies is minimally invasive surgery, which has become the standard in many operating fields. The effect of minimally invasive surgery on adhesion related readmission remains unknown. This study aims to determine the effect of minimally invasive surgery on adhesion related readmissions.
Methods: Validated population data from the Scottish National Health Service were used to identify a cohort of patients who underwent open or laparoscopic surgery on the abdominal or pelvic cavity between December 2008 and June 2011, without a history of abdominal or pelvic surgery. Adhesion related readmissions were reviewed until December 2017, and subdivided by the degree of certainty of adhesion relation. The primary outcome measure was time to first adhesion related readmission.
Results: A total of 72 270 patients were included in the analysis, 29.8% underwent initial laparoscopic surgery. Patients in the laparoscopic cohort were readmitted less frequently for adhesion related causes, 24.7% vs 31.8%. In the overall cohort patients were readmitted a mean of 1.9 times during the study period. Directly related readmissions were responsible for over 10% of all readmissions, 62.5% of these readmissions were managed operatively. Laparoscopic approach to the abdominal cavity reduced adhesion related readmissions in uni- and multivariable analysis.
Conclusion: Laparoscopic surgery reduces the incidence of adhesion related readmissions. Despite the rise in laparoscopic surgery, the overall rate of adhesion related readmissions did not drop drastically.

IMAGINE: Ileus Management International

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Background: Ileus is common after elective colorectal surgery and is associated with increased adverse events and prolonged hospital stay. The aim of this study was to assess the role of non-steroidal anti-inflammatory drugs (NSAIDs) when used as postoperative analgesia for expediting gastrointestinal recovery.
Methods: A prospective, multi-centre, student- and trainee-led cohort study was delivered across an international collaborative network. Adult patients undergoing elective colorectal resection between January - April 2018 were included. The primary outcome was time to gastrointestinal recovery, measured using a composite outcome of bowel function and oral tolerance (GI-2). The impact and safety of NSAIDs in expediting gastrointestinal recovery were explored using Kaplan Meier plots with Cox regression analyses.
Results: Of 4164 patients, 1061 (25.5%) received non-selective NSAIDs and 92 (2.2%) received COX-2-selective NSAIDs. There was no difference in the incidence of anastomotic leak (5.2%, 7.1%, 4.6%; *P*=0.488) or acute kidney injury (14%, 18.4%, 13.8%; *P*=0.508) between non-selective, COX-2-selective, and no NSAIDs groups respectively. The mean time to gastrointestinal recovery was 4.8 days in patients not receiving NSAIDs, compared to 4.6 in the two NSAID groups (p=0.128). This association remained non-significant after adjustment in multivariable regression models (*P*=0.557). Fewer patients receiving NSAIDs required strong opioid analgesia in the first three postoperative days (56.7%, 35.2%, 37.0%; *P*<0.001) respectively.
Conclusion: Whilst NSAIDs did not reduce the time for gastrointestinal recovery after colorectal surgery, they were used safely and reduced patients' post-operative opioid requirement.

Efficacy and safety of additional autologous Platelet Rich Stroma in transanal mucosal advancement flap repair of complex cryptoglandular anal fistulas

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Background: Treatment of complex cryptoglandular fistulas is challenging and associated with high recurrence rates. Flap repair fails in almost one of every three patients, probably due to chronic inflammation in the remnants of the fistulous tract. Mucosal advancement flap and platelet rich plasma (PRP) combined with progenitor cells from autologous Stromal Vascular Fraction (SVF), obtained from liposuction, could suppress chronic inflammation and therefore improve success rates. We aimed to assess the feasibility, safety and efficacy of additional injection of autologous SVF combined with PRP (Platelet Rich Stroma; PRS) in flap repair of complex cryptoglandular fistulas.
Methods: All patients with complex cryptoglandular fistulas who underwent transanal advancement flap repair between December 2017 and October 2018were included after informed consent. Inclusion criteria included complex fistulas with only one internal opening (or a second one very close by) and absence of pelvic sepsis. All patients underwent standardized transanal mucosal repair and standardized preparation of autologous PRS. A preoperative MRI and postoperative MRI following the diagnosis of 'clinical healing' (closure of the internal and external openings at physical examination) were performed.
Results: This pilot study includes 22 consecutive patients (12:10 male:female; median age 44.0 (IQR 33.6-55.0). Follow-up data of at least 4 months are available for 18 of these patients to date. All patients had one or more previous operations ranging from curating the fistula tract and leaving a seton in place to previous mucosal advancement (3/18) or ligation of the intersphincteric fistula tract (LIFT; 2/18). Clinical healing was reached in 16 out of 18 (89%) patients after a median postoperative follow-up of 6 months (IQR 5-7). Two of the 18 patients did not show clinical healing at their last consultation at 4 months follow-up. Of the available 14 MRIs to date (4 are pending), 13 showed complete closure of the fistula tract**.**Some patients experienced transient severe postoperative pain. One patient developed a hematoma due to liposuction. One patient experienced postoperative hemorrhage underneath the mucosal flap.
Conclusion: In 18 patients with cryptoglandular fistula treated with the addition of autologous SVF and PRP during transanal advancement flap repair, 93% (13/14) indeed showed a complete fibrosed fistula tract at MRI. The addition of autologous PRS appears to be feasible, safe, cheap and highly promising. Further research could focus on the effects of PRS on Crohn's fistula.

Decline in unnecessary surgery for locally advanced rectal cancer due to adequate multidisciplinary response evaluation following chemo-radiotherapy

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Background: Standard therapy for locally advanced rectal cancer is neoadjuvant chemo-radiation therapy (nCRT) to downstage the tumor followed by total mesorectal excision (TME). Pathologic Complete Response (pCR) after nCRT was found in 25% of these carcinomas. Therefore, a so called wait and see (W&S) strategy has been introduced as an alternative therapy. Selected patients with clinical Complete Response (cCR) during restaging with endoscopy and MRI might benefit from organ sparing therapy. Aim of our study was to compare the proportion of patients with pCR since the introduction of the multidisciplinary response evaluation in our hospital with the period before structural response evaluation.

Methods: In this retrospective cohort study, patient with locally advanced rectal cancer (tumor stage T3 or T4 with threatened or involved Mesorectal fascia (MRF) and/or more than three suspected locoregional lymphnodes) who underwent nCRT between 1 January 2009 and 31 May 2018 were included. Patients without multidisciplinary response evaluation were categorized in cohort A. Patient who underwent structural multidisciplinary response evaluation, introduced in 2015, with endoscopy and diffusion weighted (DWI) MRI were categorized in cohort B. Patients with cCR during restaging were offered a W&S strategy. pCR was defined as ypT0N0.

Results: A total of 263 patients were included in the study, 128 in cohort A and 135 in cohort B. In cohort A, 114 patients (89%) underwent TME after a median interval of 10 [5-29] weeks from completing nCRT. pCR in this cohort was found in 21 patients (16.4%).

In cohort B, 83 patients (61%) underwent primary TME after a median interval between end of nCRT and TME of 15 [10-44] weeks. Forty patients (30%) underwent W&S strategy. Local regrowth during W&S was found in 10 patients (25%) after a median of 14 [7-24] months. Nine of these 10 patients underwent curative salvage TME (n=7) or TEM (n=2). The other patient has developed distant metastasis and underwent palliative therapy. pCR was found in 8 patients (5.9%) in cohort B, which was significant lower than in cohort A (p=0.007).

Conclusion: Multidisciplinary response evaluation after nCRT has led to a significant decrease in unnecessary surgery in patients with locally advanced rectal cancer.

Randomised clinical trial of selective decontamination of the digestive tract in elective colorectal cancer surgery (the SELECT trial).

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Background: Infectious complications and anastomotic leakage affect approximately 30% of patients after colorectal cancer surgery. The aim of this multicenter randomized trial was to investigate whether selective decontamination of the digestive tract (SDD) reduces these complications of elective colorectal cancer surgery.
Methods: The effectiveness of SDD was evaluated in a multicenter, open-label, randomized clinical trial in 6 centers in The Netherlands. Patients with colorectal cancer scheduled for elective curative surgery with a primary anastomosis were eligible. Oral colistin, tobramycin, and amphotericin B were administered to the SDD group to decontaminate the digestive tract. Both groups received intravenous cefazoline and metronidazole for peri-operative prophylaxis. Mechanical bowel preparation was given for left sided colectomies, sigmoid and anterior resections. Anastomotic leakage was the primary outcome while infectious complications and mortality were secondary outcomes. This trial was registered with ClinicalTrials.gov number NCT01740947.
Results: In total, 228 patients were randomized to the SDD group and 227 to the control group until the trial was stopped after interim-analysis demonstrated that superiority was no longer attainable. Effective SDD was confirmed by interspace DNA profiling analysis of rectal swabs. Anastomotic leakage was observed in 14 patients (6.1%) in the SDD group and in 22 patients (9.6%) in the control group (odds ratio) (OR 0.61 (0.30-1.22)). In the SDD group, fewer patients had one or more infectious complications than in the control group (14.9% (n=34) versus 26.9% (n=61), (OR 0.48 (0.30-0.76)). On multivariable analysis, SDD reduced infectious complications OR 0.472 (0.294-0.755).
Conclusion: SDD reduces infectious complications after colorectal cancer resection but did not significantly reduce anastomotic leakage in this trial.