DIGESTIVE DISEASE DAYS

2021

PROGRAMMA

17 en 18 maart

DDD Online

NVGE
NEDERLANDSE VERENIGING
VOOR GASTRO-ENTEROLOGIE

DIGESTIVE DISEASE DAYS - DDD

Het programma van de DDD Online werd samengesteld met inbreng van de volgende verenigingen en secties:

Nederlandse Vereniging voor Gastro-enterologie
Nederlandse Vereniging voor Gastrointestinale Chirurgie
Nederlandse Vereniging voor Hepatologie
Nederlandse Vereniging van Maag-Darm-Leverartsen

Secties:
Sectie Gastrointestinale Endoscopie
Sectie Neurogastroenterologie en Motiliteit
Sectie Gastrointestinale Oncologie
Sectie Inflammatoire Darmziekten IBD
Sectie Kinder-MDL
Verpleegkundigen & Verzorgenden Nederland – MDL

INHOUDSOPGAVE **pag.**

Woensdag 17 maart 2021

De nummers achter de abstracttitels verwijzen naar het paginanummer waar het abstract te vinden

Tijdstippen diverse ledenvergaderingen (leden ontvangen separaat een link)

NVMDL i.o.	woensdag 17 maart	12.30 uur
Nederlandse Vereniging voor Hepatologie*	donderdag 18 maart	18.15 uur
Nederlandse Vereniging van Maag-Darm-Leverartsen*	maandag 22 maart	19.30 uur
Nederlandse Vereniging voor Gastroenterologie*	woensdag 31 maart	19.30 uur

**leden ontvangen automatisch een agenda link naar zoom meeting*

INHOUDSOPGAVE **pag.**

De nummers achter de abstracttitels verwijzen naar het paginanummer waar het abstract te vinden

Woensdag 17 maart 2021

Symposium – NVMDL i.o.

Voorzitters: *W.P. Brouwer en D.S.J. Wintjens*

The future is now

08.30 Gebruik van big data en machine learning in de dagelijks praktijk
Dr. M. de Nerée tot Babberich, product Owner, Pacmed, Amsterdam

08.50 Virtual reality en artificial intelligence binnen de endoscopie
Prof. dr. E.J. Schoon, MDL-arts, Catharina Ziekenhuis, Eindhoven

09.10 Duurzaamheid bij de MDL, wat is onze rol?
Dr. M. Duijvestein, MDL-arts, Amsterdam UMC, loc. VUmc

09.30 Einde van dit programma onderdeel

Symposium – Sectie Gastrointestinale Oncologie

Voorzitters: *L. Brouwer-Hol en E.A.R. Gielisse*

Voeding bij kanker

10.00 Voeding en kanker
Dr. F.J.B. van Duijnhoven, Universitair Docent Voeding, genen en dikkedarmkanker, WUR

10.15 Voeding bij pancreascarcinoom
Dr. M. van Driel, Radboudumc, Nijmegen

10.30 Endoscopische gastrojejunostomie
Prof. dr. F.P. Vleggaar, MDL-arts, UMCU, Utrecht

10.45 Discussie
Alle sprekers

11.00 Einde van dit programma onderdeel

Woensdag 17 maart 2021

Best of Dutch Gastroenterology 2020

Voorzitters: *L.P.S. Stassen en W.H. de Vos tot Nederveen Cappel*

State of the art lectures

11.30 A celiac mucosal barrier on-chip model to investigate its role in initiation of celiac disease
Dr. S. Withoff, associate professor, Universitair Medisch Centrum Groningen

11.50 Best of Dutch Endoscopy 2020
Prof. E.J. Schoon, MDL-arts, Catharina Ziekenhuis, Eindhoven

12.10 Best of Dutch Gastric Cancer 2020
Dr. J.W. van Sandick, chirurg, NKI Antoni van Leeuwenhoek, Amsterdam

12.30 Einde van dit programma onderdeel

Symposium – Nederlandse Vereniging voor Gastrointestinale Chirurgie

Voorzitters: *J.F.M. Lange*

14.00 Kock's Pouch
Dr. M. Gerhards, chirurg, OLVG, Amsterdam

14.20 Rol van mesenterium in IBD
Dr. C.J. Buskens, chirurg, Amsterdam UMC, loc. AMC

14.40 Sonde-voeding als work-up voor ileocoecaalresectie
Dr. A.C. de Vries, MDL-arts, Erasmus MC, Rotterdam

15.00 Afsluiting programma onderdeel

Symposium – Sectie Inflammatoire Darmziekten

Voorzitters: *J.J.L. Haans en S. Popal*

IBD@Home

15.30 Thuistherapie en thuismonitoring
Dr. M.C. Visschedijk, MDL-arts, Universitair Medisch Centrum Groningen

15.45 eHealth in de IBD praktijk
Dr. M.J.L. Romberg-Camps, MDL-arts, Zuyderland, Sittard-Geleen

16.00 Waardegedreven zorg
P. de Bey, Directeur Santeon, Utrecht

16.15 Discussie met alle sprekers tot 16.30 uur.

President Select

Voorzitters: *C.J. van der Woude en A.E. van der Meulen*

17.00 Insufficient evidence that polygenetic risk scores can be used to predict response to anti-TNFα therapy in inflammatory bowel disease (p. 38)

N. Karmi[1], A. Bangma[1], L.M. Spekhorst[1], H.M. Van Dullemen[1], M.C. Visschedijk[1], G. Dijkstra[1], R.K. Weersma[1], M.D. Voskuil[1], E.A.M. Festen[1] [1]Dept. of Gastroenterology and Hepatology, UMCG, Groningen, The Netherlands.

17.10 Dietary inflammatory index and diet quality in inflammatory bowel disease and irritable bowel syndrome patients (p. 39)

M.C.G. de Graaf[1], C.E.G.M. Spooren[1], E.J. den Brok[1], E.J.M. Feskens[2], D. Keszthelyi[1], M.J. Pierik[1], D.M.A.E. Jonkers[1] [1]Dept. of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, The Netherlands, [2]Dept. of Human Nutrition and Health, Wageningen University & Research, Wageningen, The Netherlands.

17.20 A randomized trial of aggressive fluid hydration to prevent post-ERCP pancreatitis (FLUYT) (p. 40)

C.J. Sperna Weiland[1], X.J.N.M. Smeets[1], W. Kievit[1], R.C. Verdonk[2], A.C. Poen[3], A. Bhalla[4], N.G. Venneman[5], B.J.M. Witteman[6], D.W. Da Costa[7], B.C. Van Eijck[8], M.P. Schwartz[9], T.E.H. Römkens[10], J.M. Vrolijk[11], M. Hadithi[12], A.M.C.J. Voorburg[13], L.C. Baak[14], W.J. Thijs[15], R.L. Van Wanrooij[16], A.C.I.T.L Tan[17], T.C.J. Seerden[18], Y.C.A. Keulemans[19], T.R. De Wijkerslooth[20], W. Van de Vrie[21], P. Van der Schaar[2], S.M. Van Dijk[22], N.D.L. Hallensleben[23], R.L. Sperna Weiland[24], H.C. Timmerhuis[2], D.S. Umans[2], J.E. Van Hooft[25], H. Van Goor[26], H.C. Van Santvoort[27], M.G. Besselink[22], M.J. Bruno[28], P. Fockens[16], J.P.H. Drenth[1], E.J.M. Van Geenen[1] [1]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, Nederland, [2]Dept. of Gastroenterology and Hepatology, St. Antonius ziekenhuis, Nieuwegein, Nederland, [3]Dept. of Gastroenterology and Hepatology, Isala ziekenhuis, Zwolle, Nederland, [4]Dept. of Gastroenterology and Hepatology, Haga ziekenhuis, Den Haag, Nederland, [5]Dept. of Gastroenterology and Hepatology, Medisch Spectrum Twente, Enschede, Nederland, [6]Dept. of Gastroenterology and Hepatology, Ziekenhuis Gelderse Vallei, Ede, Nederland, [7]Dept. of Radiology, St. Antonius ziekenhuis, Nieuwegein, Nederland, [8]Dept. of Gastroenterology and Hepatology, Spaarne gasthuis, Hoofddorp, Nederland, [9]Dept. of Gastroenterology and Hepatology, Meander MC, Amersfoort, Nederland, [10]Dept. of Gastroenterology and Hepatology, Jeroen Bosch ziekenhuis, Den Bosch, Nederland, [11]Dept. of Gastroenterology and Hepatology, Rijnstate ziekenhuis, Arnhem, Nederland, [12]Dept. of Gastroenterology and Hepatology, Maastad ziekenhuis, Rotterdam, Nederland, [13]Dept. of Gastroenterology and Hepatology, Diakonessenhuis, Utrecht, Nederland, [14]Dept. of Gastroenterology and Hepatology, OLVG, Amsterdam, Nederland, [15]Dept. of Gastroenterology and Hepatology, Martini ziekenhuis, Groningen, Nederland, [16]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, Nederland, [17]Dept. of Gastroenterology and Hepatology, Canisius Wilhelmina ziekenhuis, Nijmegen, Nederland, [18]Dept. of Gastroenterology and Hepatology, Amphia ziekenhuis, Breda, Nederland, [19]Dept. of Gastroenterology and Hepatology, Zuyderland ziekenhuis, Heerlen, Nederland, [20]Dept. of Gastroenterology and Hepatology, Antoni van Leeuwenhoekziekenhuis, Amsterdam, Nederland, [21]Dept. of Gastroenterology and Hepatology, Albert Schweitzer ziekenhuis, Dordrecht, Nederland, [22]Dept. of Surgery, Amsterdam UMC, Amsterdam, Nederland, [23]Dept. of Anesthesiology, Erasmus MC, Rotterdam, Nederland, [24]Dept. of Gastroenterology and Hepatology, University of Amsterdam, Amsterdam, Nederland, [25]Dept. of Gastroenterology and Hepatology, Leids Universitair Medisch Centrum, Leiden, Nederland, [26]Dept. of Surgery, Radboudumc, Nijmegen, Nederland, [27]Dept. of Surgery, St. Antonius ziekenhuis, Nieuwegein, Nederland, [28]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, Nederland.

Invited speakers

17.30 Checkpoint inhibitor-induced colitis: prevalentie, diagnostiek en behandeling
Dr. J.M. van Dieren, MDL-arts, NKI Antoni van Leeuwenhoek, Amsterdam, en
Dr. K.P.M. Suijkerbuijk, internist-oncoloog, UMC Utrecht

18.00 Afsluiting programma onderdeel

Abstractsessie Sectie Inflammatoire Darmziekten

Voorzitters: *M. Lutgens en F. Van Schaik*

08.30 Locally injected allogeneic bone marrow-derived mesenchymal stromal cells for the treatment of refractory proctitis: clinical results of a phase IIa trial. (p. 41)
L.F. Ouboter[1-3], M.C. Barnhoorn[1], L.J.A.C. Hawinkels[1], M. van Pel[2-3], J.J. de Zwaginga [3], F. de Koning[4], H.W. Verspaget[1], A.E. van der Meulen - de Jong [1] [1]Dept. of Gastroenterology and Hepatology, Leids Universitair Medisch Centrum, Leiden, Nederland, [2]Dept. of Immunohematology and Blood Transfusion, Netherlands Center for the Clinical Advancement of Stem Cell & Gene Therapies, Leiden, The Netherlands, [3]Dept. of Immunology, Leids Universitair Medisch Centrum, Leiden, Nederland, [4]Dept. of Immunopathology, Leids Universitair Medisch Centrum, Leiden, Nederland.

08.36 Histopathological features at Crohn's disease diagnosis as predictors for long-term disease course: results from the population-based IBD South-Limburg cohort (p. 42)
A. Rezazadeh Ardabili[1], D. Goudkade[2], D.S.J. Wintjens[1], M.J.L. Romberg-Camps[3], B. Winkens[4], H.I. Grabsch[5], M.J. Pierik[1], D.M.A.E. Jonkers[1] [1]Dept. of Gastroenterology and Hepatology, Maastricht University Medical Center+, Maastricht, The Netherlands, [2]Dept. of Pathology, Zuyderland Medical Center, Sittard-Geleen, The Netherlands, [3]Dept. of Gastroenterology and Hepatology, Zuyderland Medical Center, Sittard-Geleen, The Netherlands, [4]Dept. of Epidemiology, Maastricht University, Maastricht, The Netherlands, [5]Dept. of Pathology, Maastricht University Medical Center+, Maastricht, The Netherlands.

08.42 Healthy cotwins share gut microbiome signatures with their inflammatory bowel disease twins and unrelated patients (p. 43)
M.A.Y. Klaassen[1], E.C. Brand[2], R. Gacesa[1], A. Vich Vila[1], H. Ghosh[1], M.R. de Zoete[3], D.I. Boomsma[4], F. Hoentjen[5], C.S. Horjus Talabur Horje[6], P.C. van de Meeberg[7], A.H.M. Willemsen[4], J. Fu[8], C. Wijmenga[9], F. van Wijk[10], A. Zhernakova[9], B. Oldenburg[2], R.K. Weersma[1] [1]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, Nederland, [2]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, Nederland, [3]Dept. of Medical Microbiology, University Medical Center Utrecht, Utrecht, Nederland, [4]Dept. of Scientific Research, Vrije Universiteit Medical Center, Amsterdam, Nederland, [5]Dept. of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, Nederland, [6]Dept. of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, Nederland, [7]Dept. of Gastroenterology and Hepatology, Slingeland Hospital, Doetinchem, Nederland, [8]Dept. of Pediatric Gastroenterology Hepatology and Nutrition, University Medical Center Groningen, Groningen, Nederland, [9]Dept. of Clinical Genetics, University Medical Center Groningen, Groningen, Nederland, [10]Centre for Translational Immunology, University Medical Center Utrecht, Utrecht, Nederland.

08.48 Western and carnivorous dietary patterns are associated with greater likelihood of IBD occurrence in a large prospective population-based cohort (p. 44)
V. Peters[1], L.A. Bolte[1], E.M. Schuttert[1], S. Andreu-Sánchez[1], G. Dijkstra[1], R.K. Weersma[1], M.J.E. Campmans-Kuijpers[1] [1]Dept. of Gastroenterology and Hepatology, UMCG, Groningen, The Netherlands.

08.54 Host-genetics, dysbiosis, and clinical history explains fecal metabolic alterations in patients with inflammatory bowel disease (p. 45)
A. Vich Vila[1], S. Hu[1], S. Andreu-Sánchez[2], L.. Bolte[1], V. Collij[1], B.H. Jansen[1], R.A.A.A. Ruigrok[1], G. Abu-Ali[3], C. Giallourakis[3], J. Schneider[3], J. Parkinson[3], A. Al Garawi[3], A. Kurilshikov[2], R. Gacesa[1], A. Zhernakova[2], J. Fu[2], R.K. Weersma[1] [1]Dept. of Gastroenterology and Hepatology, Universitair Medisch Centrum Groningen, Groningen, Nederland, [2]Dept. of Clinical Genetics, Universitair Medisch Centrum Groningen, Groningen, Nederland, [3]Dept. of Gastroenterology, Takeda Pharmaceutical Company Limited, Cambridge, Verenigde Staten.

09.00 The effect of phenotype and genotype on the plasma proteome in patients with inflammatory bowel disease (p. 46)
A.R. Bourgonje[1], S. Hu[1], L.M. Spekhorst[1], D.V. Zhernakova[2], A. Vich Vila[1], Y. Li[1], M.D. Voskuil[1], L.A. van Berkel[3], B. Bley Folly[3], M. Charrout[4], A. Mahfouz[4], M.J.T. Reinders[4], M.C. Visschedijk[1], H.M. van Dullemen[1], K.N. Faber[1], J.N. Samsom[3], E.A.M. Festen[1], G. Dijkstra[1], R.K. Weersma[1] [1]Dept. of Gastroenterology and Hepatology, University of Groningen, University Medical Center Groningen, Groningen,[2]Dept. of Clinical Genetics, University of Groningen, University Medical Center Groningen, Groningen, [3]Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Erasmus University Medical Center, Rotterdam, Nederland, [4]Delft Bioinformatics Lab , Delft University of Technology, Delft, Nederland.

09.06 Inflammation status modulates the effect of host genetic variation on intestinal gene expression in inflammatory bowel disease (p. 47)
S.H. Hu[2],WUV T. Uniken Venema[2], H.W. Westra[3], A.V. Vich Vila[2], R.B. Barbieri[2], M.V.D. Voskuil[2], T.B. Blokzijl[2], B.J. Jansen[2], L.Y. Yanni[2], M.D. Daly[4], R.X. Xavier[5], G.D. Dijkstra[2], E.F. Festen[2], R.K. Weersma[2],[1]Dept. of Gastroenterology and Hepatology, University of Groningen and University Medical Center Groningen, Department of G, Groningen, Nederland, [2]Dept. of Gastroenterology and Hepatology, University of Groningen and University Medical Center Groningen, Groningen, Nederland, [3]Dept. of Clinical Genetics, University of Groningen and University Medical Center Groningen, Groningen, Nederland, [4]Dept. of Medicine, University of Helsinki, Helsinki, Finland, [5]Dept. of Microbiology and Systems Biology, Massachusetts Institute of Technology, Cambridge, Verenigde Staten.

09.12 Point-of-Care Intestinal Ultrasound provides additional information about disease activity in pediatric Crohn's Disease patients visiting the outpatient department (p. 48)
E.A. van Wassenaer[1], J.E. van Limbergen[1], G.R. D'Haens[2], M.A. Benninga[1], B.G.P Koot[1] [1]Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Emma Kinderziekenhuis, Amsterdam UMC, Universiteit van Amsterdam, Amsterdam,, [2]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Universiteit van Amsterdam, Amsterdam.

09.18 Decrease in bowel wall thickness at intestinal ultrasound accurately detects early endoscopic remission and treatment response in ulcerative colitis patients on tofacitinib: a longitudinal prospective cohort study (p. 49)
F.A.E. De Voogd[1], E.A. Van Wassenaer[2], A. Mookhoek[3], S. Bots[1], S. Van Gennep[1], M. Duijvestein[1], C. Ponsioen[1], M. Löwenberg[1], G. D'Haens[1], K. Gecse[1] [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam,, [2]Dept. of Pediatrics, Amsterdam UMC, Amsterdam, Nederland, [3]Dept. of Pathology, Amsterdam UMC, Amsterdam, Nederland.

09.30 Einde van dit programma onderdeel

Abstractsessie Sectie Neurogastroenterologie en Motiliteit

Voorzitters: *A.B. Beckers en D. Keszthelyi*

10.00 Appropriateness of Proton Pump Inhibitor Prescriptions in Clinical Practice (p. 50)
L.M. Koggel[1], M.A. Lantinga[1],F.L. Büchner[2], M.E. Numans[2], M. Heringa[3], J.P.H. Drenth[1], P.D. Siersema[1], [1]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, [2]Dept. of Public Health, Leids Universitair Medisch Centrum, Leiden, [3]Dept. of Clinical Pharmacy, SIR Institute for Pharmacy Practice and Policy, Leiden, The Netherlands.

10.06 A trial-based economic evaluation of peppermint oil for the treatment of Irritable Bowel Syndrome (p. 51)
Z.Z.R.M. Weerts[1], B.A.B. Essers[2], DMAE Jonkers[1], J.I.A. Willems[1], D.P.J.P.A. Janssen[1], B.J.M. Witteman[3], C.H.M. Clemens[4], A. Westendorp[5], A.A.M. Masclee[1], D. Keszthelyi[1], [1]Dept. of Gastroenterology and Hepatology, Maastrichtuniversity.nl, Maastricht, Nederland, [2]Dept. of Clinical Epidemiology and Medical Technology Assessment, Maastricht University, Maastricht, Nederland, [3]Dept. of Gastroenterology and Hepatology, Ziekenhuis Gelderse Vallei, Ede, Nederland, [4]Dept. of Gastroenterology, Alrijne Ziekenhuis, Leiden, Nederland, [5]Dept. of Gastroenterology and Hepatology, Leeuwarden Medisch Centrum, Leeuwarden, Nederland.

10.12 Factors affecting the placebo response rate in pharmacological trials in patients with irritable bowel syndrome – a systematic review and meta-analysis (p. 52)
M. Bosman[1], S. Elsenbruch[2], M. Corsetti[3], J. Tack[4], M. Simrén[5], B. Winkens[6], T. Boumans[1], A. Masclee[1], D. Keszthelyi[1] [1]Dept. of Gastroenterology and Hepatology, Maastricht UMC+, Maastricht, Nederland, [2]Dept. of Physiology, Ruhr University Bochum, Bochum, Duitsland, [3]Dept. of Research & Development, Nottingham University Hospitals NHS Trust, Nottingham, Verenigd Koninkrijk, [4]Dept. of Gastroenterology and Hepatology, University Hospitals Leuven, Leuven, België, [5]Dept. of Medicine, University of Gothenburg, Gothenburg, Zweden, [6]Dept. of Research & Development, Maastricht University, Maastricht, Nederland.

10.18 Do patients' and physicians' perspectives differ on preferences for IBS treatment? - a qualitative study to explore attributes for quantitative preference elicitation (p. 53)
R. Sturkenboom[1], B.A.B. Essers[2], A.A.M. Masclee[1], D. Keszthelyi[1] [1]Dept. of Gastroenterology and Hepatology, MUMC+, Maastricht, Nederland, [2]Dept. of Clinical Epidemiology and Medical Technology Assessment (KEMTA) , MUMC+, Maastricht, Nederland.

10.24 Examining the optimal cut-off values of HADS, PHQ-9 and GAD-7 as screening instruments for depression and anxiety in Irritable Bowel Syndrome (p. 54)
J.T.W. Snijkers[1], W. van den Oever[1], Z.Z.R.M. Weerts[1], L. Vork[1], Z. Mujagic[1], C. Leue[2], M.A.M. Hesselink[3], J.W. Kruimel[1], J.W.M. Muris[4], R.M.M. Bogie[1], A.A.M. Masclee[1], D.M.A.E. Jonkers[3], D. Keszthelyi[1] [1]Dept. of Gastroenterology and Hepatology, MUMC+ / Maastricht University, Maastricht, The Netherlands, [2]Dept. of Psychiatry, MUMC+ / Maastricht University, Maastricht, The Netherlands, [3]Dept. of Gastroenterology and Hepatology, Maastricht University, Maastricht, The Netherlands, [4]Dept. of Public Health, Maastricht University, Maastricht, The Netherlands.

10.30 The interplay between stress and fullness in functional dyspepsia and healthy controls: an exploratory experience sampling method study (p. 55)
T. Klaassen[1], L. Vork[1], F.G.M. Smeets[1], F.J. Troost[1], J.W. Kruimel[1], C. Leue[2], A.A.M. Masclee[1], D. Keszthelyi[1] [1]Dept. of Gastroenterology and Hepatology, Maastricht University Medical Center+, Maastricht, The Netherlands, [2]Dept. of Psychiatry, Maastricht University Medical Center+, Maastricht, The Netherlands.

10.36 The Dutch Microbiome Project defines factors that shape the healthy gut microbiome (p. 56)

R. Gacesa[1], A. Kurilshikov[2], A. Vich Vila[3], T. Sinha[2], M.A.Y. Klaasen[3], L.A. Bolte[3], S. Andreu-Sanchez[2], L. Chen[2], V. Collij[3], S. Hu[3], J.A.M. Dekens[2], V.C. Lenters[4], J. R. Bjork[3], J.C. Swarte[3], M. A. Swertz[2], B.H. Jansen[3], J. Gelderloos-Arends[2], M. Hofker[2], R.C.H. Vermeulen[4], S. Sanna[5], H. J. M. Harmsen[6], C.Wijmenga[2], J. Fu[7], A. Zhernakova[2], R.K. Weersma[3] [1]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen (UMCG), Groningen, The Netherlands, [2]Dept. of Clinical Genetics, University of Groningen and University Medical Center Groningen, Groningen, Nederland, [3]Dept. of Gastroenterology and Hepatology, University of Groningen and University Medical Center Groningen, Groningen, Nederland, [4]Dept. Julius Center for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, The Netherlands, [5]Dept. of Scientific Research, Institute for Genetic and Biomedical Research, Cagliari, Italië, [6]Dept. of Medical Microbiology, University of Groningen and University Medical Center Groningen, Groningen, Nederland, [7]Dept. of Pediatrics, University of Groningen and University Medical Center Groningen, Groningen, Nederland.

10.42 Growth and fat mass, but not fat-free mass, are compromised in infants with parenteral nutrition need after neonatal intestinal surgery (p. 57)

LE Vlug[1], EG Neelis[1], WLM Kastelijn[2], JF Olieman[2], MJ Vermeulen[3], JA Roelants[3], D Rizopoulos[4], JCK Wells[5], MS Fewtrell[6], RMH Wijnen[7], EHHM Rings[1], BAE de Koning[1], JM Hulst[8] [1]Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Erasmus MC University Medical Center-Sophia Children's Hospital, Rotterdam, The Netherlands, [2]Dept. of Dietetics, Erasmus MC University Medical Center-Sophia Children's Hospital, Rotterdam, The Netherlands, [3]Dept. of Pediatrics, Erasmus MC University Medical Center-Sophia Children's Hospital, Rotterdam, The Netherlands, [4]Dept. of Biostatistics, Erasmus MC University Medical Center, Rotterdam, The Netherlands, [5]Dept. of Human Nutrition and Health, UCL Great Ormond Street Institute of Child Health, London, Verenigd Koninkrijk, [6]Dept. of Public Health, UCL Great Ormond Street Institute of Child Health, London, Verenigd Koninkrijk, [7]Dept. of Surgery, Erasmus MC University Medical Center-Sophia Children's Hospital, Rotterdam, The Netherlands, [8]Dept. of Pediatric Gastroenterology Hepatology and Nutrition, The Hospital for Sick Children, Toronto, Canada.

10.48 Health-Related Quality of Life of Children on Home Parenteral Nutrition (p. 58)

SCJ Nagelkerke[1], HA van Oers[2], L Haverman[2], BAE de Koning[3], MA Benninga[1], MM Tabbers[1] [1]Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands, [2]Dept. of Pediatric Medical Psychology and Social Work, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands, [3]Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Sophia Children's Hospital, Erasmus University Medical Center, Rotterdam, The Netherlands.

11.00 Einde van dit programma onderdeel

Meet the expert sessie

11.30 uur – 12.30 uur

Thema: Coeliakie

Deze sessies – waarvoor tevoren moet worden ingeschreven - worden verzorgd door:
Prof. dr. L. Mearin, kinderarts-MDL, LUMC, Leiden
Dr. P.J. Wahab, MDL-arts, Rijnstate ziekenhuis, Arhnem

12.30 Einde van dit programma onderdeel, mogelijkheid tot volgen netwerksessie tot 14.00

Postersessie 1 **Discussietafel**

Voorzitter: *C.J. van der Woude*

12.30 Somatostatin analogues lead to an 82% reduction in red blood cell transfusions in patients with gastrointestinal bleeding due to angiodysplasias: an individual patient data meta-analysis. (p. 59)
L.C.M.J. Goltstein[1], K.V. Grooteman[1], A. Rocco[2], G. Holleran[3], S. Frago[4], P. Salgueiro[5], T. Aparicio[6], G. Scaglione[7], S. Chetcuti Zammit[8], R.P. Manzano[9], R. Benamouzig[10], D. McNamara[3], M. Benallaoua[10], D. Sauterau[11], S. Michopoulos[12], R. Sidhu[8], W. Kievit[13], J.P.H. Drenth[1], E.J.M. van Geenen[1] [1]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, Nederland. [2]Dept. of Gastroenterology, University of Parma, Parma, Italië. [3]Dept. of Gastroenterology, Trinity College Dublin, Dublin, Ierland. [4]Dept. of Digestive Diseases, Miguel Servet University Hospital, Zaragoza, Spanje. [5]Dept. of Gastroenterology, Centro Hospitalar Universitário do Porto, Porto, Portugal. [6]Dept. of Gastroenterology, Saint Louis Hospital, APHP, Parijs, Frankrijk. [7]Dept. of Gastroenterology, A.O.G. Rummo, Benevento, Italië. [8]Dept. of Gastroenterology, Royal Hallamshire Hospital, Sheffield, Verenigd Koninkrijk. [9]Dept. of Gastroenterology, Hospital San Pedro de Alcántara, Cáceres, Spanje. [10]Dept. of Gastroenterology, Avicenne Hospital, APHP, Parijs, Frankrijk. [11]Dept. of Gastroenterology, CHU Dupuytren, Limoges, Frankrijk. [12]Dept. of Gastroenterology, Alexandra Hospital, Athene, Griekenland. [13]Dept. of Health Evidence, Radboudumc, Nijmegen, Nederland.

12.34 Biofilm formation in duodenoscope working channels in a simulated ercp setting (p. 60)
J.A. Kwakman[1], M.J. Bruno[1], M.C. Vos[2][1]Dept. of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands. [2]Dept. of Medical Microbiology, Erasmus Medical Center, Rotterdam, The Netherlands.

12.38 Molecular profiling of primary sclerosing cholangitis-inflammatory bowel disease associated colorectal carcinomas (p. 61)
M. de Krijger[1], B. Carvalho[2], C. Rausch[2], A.S. Bolijn[2], P.M. Delis-van Diemen[2], M. Tijssen[2], M. van Engeland[3], N. Mostafavi[1], R.M.M. Bogie[4], E Dekker[1], A.A.M. Masclee[4], J Verheij[5], G.A. Meijer[2], C.Y. Ponsioen[11]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, The Netherlands. [2]Dept. of Pathology, The Netherlands Cancer Institute, Amsterdam, The Netherlands. [3]Dept. of Pathology, Maastricht University Medical Center, Maastricht, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, The Netherlands. [5]Dept. of Pathology, Amsterdam UMC, Amsterdam, The Netherlands.

12.42 Adverse drug reactions from real-world data in inflammatory bowel disease patients in the IBDREAM registry (p. 62)

E.L. Giraud[1], P.W.A. Thomas[2], J.A. van Lint[1], E.P. van Puijenbroek[1], T.E.H. Römkens[3], R.L. West[4], M.G.V.M. Russel[5], J.M. Jansen[6], N.T. Jessurun[7], F. Hoentjen[2]1Dept. of Pharmacovigilancy, Nederland bijwerkingencentrum LAREB, 's-Hertogenbosch, Nederland. [2]Dept. of Gastroenterology and Hepatology, Radboud Universitair Medisch Centrum, Nijmegen, Nederland. [3]Dept. of Gastroenterology and Hepatology, Jeroen Bosch Ziekenhuis, 's-Hertogenbosch, Nederland. [4]Dept. of Gastroenterology and Hepatology, Franciscus Gasthuis & Vlietland, Rotterdam, Nederland. [5]Dept. of Gastroenterology and Hepatology, Medisch Spectrum Twente, Enschede, Nederland. [6]Dept. of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam, Nederland. [7]Dept. of Pharmacovigilancy, Bijwerkingencentrum Lareb, 's-Hertogenbosch, Nederland.

12.46 Psychometric evaluation of an experience sampling method-Based Patient-Reported Outcome Measure in Functional Dyspepsia (p. 63)

T. Klaassen[1], F.G.M. Smeets[1], L. Vork[1], J. Tack[2], N.J. Talley[3], M. Simren[4], Q. Aziz[5], A.C. Ford[6], J.W. Kruimel[1], J.C. Conchillo[1], C. Leue[7], A.A.M. Masclee[1], D. Keszthelyi[1]1Dept. of Gastroenterology and Hepatology, Maastricht University Medical Center+, Maastricht, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, KU Leuven, Leuven, België. [3]Dept. of Gastroenterology and Hepatology, University of Newcastle, Callaghan, Australië. [4]Dept. of Gastroenterology and Hepatology, University of Gothenburg, Gothenburg, Zweden. [5]Dept. of Gastroenterology and Hepatology, Queen Mary University of London, London, Verenigd Koninkrijk. [6]Dept. of Gastroenterology and Hepatology, University of Leeds, Leeds, Verenigd Koninkrijk. [7]Dept. of Psychiatry, Maastricht University Medical Center+, Maastricht, The Netherlands.

12.50 A morphometric analysis of pathological alterations in haemorrhoidal disease versus normal controls: a controlled trial (p. 64)

S.Z. Kuiper[1], R.R. Van Tol[2], A. Lataster[3], J.P.M. Cleutjens [4], J. Melenhorst[5], P. Van Dijk[3], S.M.J. Van Kuijk[6], S.O. Breukink [5]1Dept. of Surgery, Universiteit Maastricht, Maastricht, Nederland. [2]Dept. of Surgery, Diakonessenhuis, Utrecht, Nederland. [3]Dept. of Anatomy and Embryology, Universiteit Maastricht, Maastricht, Nederland. [4]Dept. of Pathology, Maastricht Universitair Medisch Centrum, Maastricht, Nederland. [5]Dept. of Surgery, Maastricht Universitair Medisch Centrum, Maastricht, Nederland. [6]Centre for Translational Immunology, Maastricht Universitair Medisch Centrum, Maastricht, Nederland.

12.54 Universal immunohistochemistry for Lynch Syndrome: a systematic review and meta-analysis of 58,580 colorectal carcinomas (p. 65)

E.L. Eikenboom[1], A.S. van der Werf - 't Lam[2], M. Rodriguez-Girondo[3], C.J. van Asperen[2], W.N.M. Dinjens[4], R.M.W. Hofstra[5], M.E. van Leerdam[6], H. Morreau[7], M.C.W. Spaander[8], A. Wagner[5], M. Nielsen[2]1Dept. of Clinical Genetics, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Clinical Genetics, Leiden University Medical Center, Leiden, The Netherlands. [3]Dept. of Biostatistics, Leiden University Medical Center, Leiden, The Netherlands. [4]Dept. of Pathology, Erasmus MC Cancer Institute, University Medical Center Rotterdam, Rotterdam, The Netherlands. [5]Dept. of Clinical Genetics, Erasmus MC Cancer Institute, University Medical Center Rotterdam, Rotterdam, The Netherlands. [6]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands. [7]Dept. of Pathology, Leiden University Medical Center, Leiden, The Netherlands. [8]Dept. of Gastroenterology and Hepatology, Erasmus MC Cancer Institute, University Medical Center Rotterdam, Rotterdam, The Netherlands.

Postersessie 2 **Discussietafel**

Voorzitter: *A.E. van der Meulen*

13.00 Case-mix adjustment to compare colonoscopy performance between endoscopy services: a nationwide cohort study (p. 66)

K.J. Nass[1], M. van der Vlugt[1], A.K.E. Elfrink[2], A. van der Beek[3], C.L. van den Brand[2], A.A.J. van Esch[4], T. Hummel[5], M. Ledeboer[6], M.E. van Leerdam[7], R.J.T. Ouwendijk[8], P.J. van der Schaar[9], M.C.W. Spaander[10], M.A.M.T. Verhagen[11], J. WIlschut[2], P. Fockens[1], E. Dekker[1], M. Wouters[21]Dept. of Gastroenterology and Hepatology, Amsterdam University Medical Centers, Amsterdam, The Netherlands. [2]Dept. of Research & Development, Dutch Institute for Clinical Auditing, Leiden, The Netherlands. [3]Dept. of Internal Medicine , Rivierenland hospital, Tiel, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, Gelre hospitals, Apeldoorn, The Netherlands. [5]Dept. of Pediatrics, MST, Enschede, The Netherlands. [6]Dept. of Gastroenterology and Hepatology, Deventer hospital, Deventer, The Netherlands. [7]Dept. of Gastroenterology and Hepatology, Netherlands Cancer Institute, Amsterdam, The Netherlands. [8]Dept. of Gastroenterology and Hepatology, Bravis hospital, Roosendaal, The Netherlands. [9]Dept. of Gastroenterology and Hepatology, St. Antonius Hospital, Nieuwegein, The Netherlands. [10]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands. [11]Dept. of Gastroenterology and Hepatology, Diakonessenhuis, Utrecht, The Netherlands.

13.04 Efficacy of ultra-low volume (≤1L) bowel preparation fluids - systematic review and meta-analysis (p. 67)

M.L.M. van Riswijk[1], K.E. van Keulen[1], P.D. Siersema[11]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, The Netherlands.

13.08 Disease activity in Inflammatory Bowel Disease patients is associated with increased liver fat content during follow-up (p. 68)

E. van Lingen[1], M.E. Tushuizen[1], M.E.J. Steenhuis[1], T. Van Deynen[1], J. Martens[1], D. Diaz-Infante Morales[1], A.E. van der Meulen-de Jong[1], I. Molendijk[1], S. van der Marel[2], P.W.J. Maljaars[1] [1]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Haaglanden Medisch Centrum, Den Haag, The Netherlands.

13.12 The composition and metabolic potential of the human small intestinal microbiota within the context of inflammatory bowel disease (p. 69)

R.A.A.A. Ruigrok[1], V. Collij[1], P. Sureda[1], M.A.Y. Klaassen[1], L.A. Bolte[1], B.H. Jansen[1], M.D. Voskuil[1], J. Fu[2], C. Wijmenga[2], A. Zhernakova[2], R.K. Weersma[1], A. Vich Vila[11]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [2]Dept. of Clinical Genetics, University Medical Center Groningen, Groningen, The Netherlands.

13.16 Distinct and Permanent Gut Microbial Alterations in Renal Transplant Recipients (p. 70)

J.C. Swarte[1], Y. Li[1], S. Hu[1], R. Gacesa[1], J.R. Björk[1], A.V. Vila[1], R.M. Douwes[1], V. Collij[1], A. Kurilshikov[2], A. Post[3], M.F. Eisenga[3], A.W. Gomes-Neto[3], D. Kremer[3], B.H. Jansen[1], S.P. Berger[3], J.S.F. Sanders[3], R. Heiner-Fokkema[3], V. de Meijer[4], C. Wijmenga[2], E.A.M. Festen[1], A. Zhernakova[2], J. Fu[2], H.J.M. Harmsen[5], H. Blokzijl[1], S.J.L. Bakker[3], R.K. Weersma[11]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, Nederland. [2]Dept. of Clinical Genetics, University Medical Center Groningen, Groningen, Nederland. [3]Dept. of Internal Medicine , University Medical Center

Groningen, Groningen, Nederland. [4]Dept. of Surgery, University Medical Center Groningen, Groningen, Nederland. [5]Dept. of Medical Microbiology, University Medical Center Groningen, Groningen, Nederland.

13.20 Evaluating nationwide application of minimally invasive surgery for small bowel neuroendocrine neoplasms and the impact on survival (p. 71)
E. Kaçmaz[1], H.J. Klümpen[2], W.A. Bemelman[1], E.J.M. Nieveen van Dijkum[1], A.F. Engelsman[3], P.J. Tanis[1]1Dept. of Surgery, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands. [2]Dept. of Medical Oncology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands. [3]Dept. of Surgery, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, Nederland.

13.24 Harnessing the Gut Microbiome to Predict Response to Cancer Immunotherapy (p. 72)
J.R.B. Björk[1], A.T. Thomas[2], K.L. Lee[3], L.B. Bolte[4], V.B. Bataille[3], N.R. Rossi[3], T.S. Spector[3], N.S. Segata[2], G.H. Hospers[5], R.W. Weersma[4] [1]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen (UMCG), Groningen, The Netherlands. [2]Dept. of Microbiology and Systems Biology, CIBIO-University of Trento, Trento, Italië. [3]Dept. of Medical Oncology, King's College London, London, Verenigd Koninkrijk. [4]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [5]Dept. of Medical Oncology, University Medical Center Groningen, Groningen, The Netherlands.

Postersessie 3 **Discussietafel**

Voorzitter: *P.P.J. van der Veek*

13.30 Identification of dysplasia in the Barrett's esophagus using an endocytoscopy classification system: preliminary results of a prospective comparison between clinicians and artificial intelligence. (p. 73)
J.J.H. van der Laan[1], J.A. van der Putten[2], X. Zhao[1], I. Schmidt[1], R.Y. Gabriëls[1], A. Karrenbeld[1], F.T.M. Peters[1], J. Westerhof[1], F. van der Sommen[2], W.B. Nagengast[1]1Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, Nederland. [2]Dept. of Electrical Engineering, Eindhoven University of Technology, Eindhoven, Nederland.

13.34 Predictors of Gastrointestinal Transit Times in Colon Capsule Endoscopy (p. 74)
S. Moen[1], F.E.R. Vuik[1], T Voortman[2], E.J. Kuipers[1], M.C.W. Spaander[1]1Dept. of Gastroenterology and Hepatology, Erasmus University Medical Centre, Rotterdam, Nederland. [2]Dept. of Epidemiology, Erasmus University Medical Centre, Rotterdam, The Netherlands.

13.38 Prevalence And Clinical Outcomes Of Severe COVID-19 Among Inflammatory Bowel Disease Patients: Observations From A Population-Based Setting (p. 75)
A. Rezazadeh Ardabili[1], R.H. Creemers[2], M.J.L. Romberg-Camps[2], J.J.L. Haans[1], D.M.A.E. Jonkers[1], M.J. Pierik[1], A.A.M. van Bodegraven[2]1Dept. of Gastroenterology and Hepatology, Maastricht University Medical Center+, Maastricht, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Zuyderland Medical Center, Sittard-Geleen, The Netherlands.

13.42 Prognostic factors for advanced colorectal neoplasia in inflammatory bowel disease: systematic review and meta-analysis (p. 76)
A.M. Wijnands[1], M.E. de Jong[2], M.W.M.D. Lutgens[3], F. Hoentjen[2], S.G. Elias[4], B. Oldenburg[1], [1]Dept. of Gastroenterology and Hepatology, UMC Utrecht, Utrecht, Nederland. [2]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, Nederland. [3]Dept. of

Gastroenterology and Hepatology, ETZ Tilburg, Tilburg, Nederland. [4]Dept. Julius Center for Health Sciences and Primary Care, Julius Center for Health Sciences and Primary Care, UMC Utrecht, UU, Utrecht, Nederland.

13.46 Long term follow-up of high risk T1 colorectal carcinoma, a single center retrospective study (p. 77)

J.A. Govaert[1], M. de Graaf[1], E.B. Wassenaar[1], F. Boersma[2], P. Duijvendijk [1], E.S. van de Zaag[11]Dept. of Surgery, Gelre Ziekenhuis, Apeldoorn, Nederland. [2]Dept. of Gastroenterology, Gelre Ziekenhuis, Apeldoorn, Nederland.

13.50 Hepatocellular adenoma in men: a nationwide assessment of pathology and correlation with clinical course (p. 78)

B.V. van Rosmalen[1], A. Furumaya[1], A.J. Klompenhouwer[2], M.E. Tushuizen[3], A.E. Braat[4], R.J. Reinten[5], M.A.P. Ligthart[6], M.P.D. Haring[7], V.E. de Meijer[7], T. van Voorthuizen[8], R.B. Takkenberg[9], C.H.C. Dejong[6], A.S.H. Gouw[10], R.A.de Man[2], J.N.M. IJzermans[11], M. Doukas[12], T.M. van Gulik[1], J. Verheij[51]Dept. of Surgery, Amsterdam UMC, University of Amsterdam, Cancer Center Amsterdam, Amsterdam, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, LUMC, Leiden University, Leiden, The Netherlands. [4]Dept. of Surgery, LUMC, Leiden University, Leiden, The Netherlands. [5]Dept. of Pathology, Amsterdam UMC, University of Amsterdam, Cancer Center Amsterdam, Amsterdam, The Netherlands. [6]Dept. of Surgery, Maastricht University Medical Center, School of Nutrition and Translational Rese, Maastricht, The Netherlands. [7]Dept. of Surgery, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands. [8]Dept. of Medical Oncology, Rijnstate hospital, Arnhem, The Netherlands. [9]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, University of Amsterdam, Cancer Center Amsterdam, Amsterdam, The Netherlands. [10]Dept. of Pathology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands. [11]Dept. of Surgery, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands. [12]Dept. of Pathology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands.

13.54 Unravelling neoantigen-specific T cell responses in mismatch-repair proficient colorectal cancers (p. 79)

J. Van den Bulk[1], M.E. Ijsselsteijn[1], N.L. De Vries[1], A.M. Van der Ploeg[1], D. Ruano[1], R. Van der Breggen[1], K.C.M.J. Peeters[2], A.D. Weinberg[3], T. Duhen[4], N.F. De Miranda[11]Dept. of Pathology, Leiden University Medical Centre, Leiden, Nederland. [2]Dept. of Surgery, Leiden University Medical Centre, Leiden, Nederland. [3]Dept. of Immunopathology, Earle A Chiles Institute, Portland, Verenigde Staten. [4]Dept. of Medical Oncology, Earle A Chiles Institute, Portland, Verenigde Staten.

Abstractsessie Sectie Gastrointestinale Oncologie

Voorzitters: C. le Clercq en L.G. van Vlerken

14.00 Screening for synchronous esophageal second primary tumors in patients with head and neck cancer (p. 80)

S.E.M. van de Ven[1], W. de Graaf[1], O. Bugter[2], M.C.W. Spaander[1], S. Nikkessen[1], P.J.F. de Jonge[1], J.A. Hardillo[2], A. Sewnaik[2], D.A. Monserez[2], H. Mast[2], S. Keereweer[2], M.J. Bruno[1], R.J. Baatenburg de Jong[2], A.D. Koch[1] [1]Dept. of Gastroenterology and Hepatology, Erasmus MC Cancer Institute, University Medical Center, Rotterdam, The Netherlands, [2]Dept. of Otorhinolaryngology and Head and Neck Surgery, Erasmus MC Cancer Institute, University Medical Center, Rotterdam, The Netherlands.

14.06 Neoplastic recurrence after successful treatment for early Barrett's neoplasia: development of a penalized prediction model. (p. 81)

S.N. van Munster[1], E.A. de Nieuwenhuis[1], B.L.A.M. Weusten[2], L. Alvarez Herrero[2], A. Bogte[3], A. Alkhalaf[4], B.E. Schenk[4], E. Schoon[5], W.L. Curvers[5], A.D. Koch[6], P.J. de Jonge[6], T. Tang[7], W.B. Nagengast[8], J. Westerhof[8], M.H.M.G. Houben[9], J.J.G.H.M Bergman[1], R.E. Pouw[1] [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, location VUmc, Amsterdam,, [2]Dept. of Gastroenterology and Hepatology, Sint Antonius Hospital Nieuwegein, Nieuwegein,, [3]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht,, [4]Dept. of Gastroenterology and Hepatology, Isala Clinics, Zwolle, [5]Dept. of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven, [6]Dept. of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam,, [7]Dept. of Gastroenterology and Hepatology, IJsselland Hospital, Capelle a/d IJssel, The Netherlands, [8]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands, [9]Dept. of Gastroenterology and Hepatology, Haga Teaching Hospital, Den Haag, The Netherlands.

14.12 Circulating TP53 mutations are predictive and prognostic biomarkers in pancreatic cancer patients treated with FOLFIRINOX chemotherapy (p. 82)

F. Van der Sijde[1], Z. Azmani[2], M.G. Besselink[3], B.A. Bonsing[4], J.W.B. De Groot[5], Groot Koerkamp[1], B.C.M. Haberkorn[6], M.Y.V .Homs[7], W.F.J. Van IJcken[2], QP. Janssen[1], L.J.M. Mekenkamp[8], S.A.C. Luelmo[9], D.A.M. Mustafa[10], R.H.N. Van Schaik[11], J.W. Wilmink[12], C.H.J. Van Eijck[1], E.E. Vietsch[1], [1]Dept. of Surgery, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Dept. of Cell and Chemical Biology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [3]Dept. of Surgery, Cancer Center Amsterdam, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands, [4]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands, [5]Dept. of Medical Oncology, Isala Hospital, Zwolle, The Netherlands, [6]Dept. of Medical Oncology, Maasstad Hospital, Rotterdam, The Netherlands, [7]Dept. of Medical Oncology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands,[8]Dept. of Medical Oncology, Medisch Spectrum Twente, Enschede, The Netherlands,[9]Dept. of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands,[10]Dept. of Pathology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [11]Dept. of Clinical Laboratory, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [12]Dept. of Medical Oncology, Cancer Center Amsterdam, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands.

14.18 Dietary intake influences the response to cancer immunotherapy (p. 83)

L.A. Bolte[1], K.A. Lee[2], J. Björk[1], A.M. Thomas[3],.E. Leeming[4], L Kist de Ruijter[5], V. Bataille[4],N Segata[3], T. Spector[4], R.S.N. Fehrmann[6], G.A.P. Hospers[6], R.K. Weersma[1], [1]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen (UMCG), Groningen, The Netherlands, [2]Dept. of Medical Oncology, Kings College London (KCL), Dept. of Twin Research & Genetic Epidemiology, Lodon, Verenigd Koninkrijk, [3]Dept. of Biomedical Data Sciences, University of Trento, Dept. of Cellular, Computational and Integrative Biology, Povo, Italië, [4]Dept. of Medical Oncology, Kings College London (KCL), Dept. of Twin Research & Genetic Epidemiology, London, Verenigd Koninkrijk,[5]Dept. of Medical Microbiology, University Medical Center Groningen (UMCG), Groningen, Nederland, [6]Dept. of Medical Oncology, University Medical Center Groningen (UMCG), Groningen, The Netherlands.

14.24 Increased Risk of Barrett's Esophagus and Esophageal Adenocarcinoma among Individuals with a Positive Family History (p. 84)

Y. Peters[1], L. Huibertse[1], R.W.M. Schrauwen[2], A.C Tan[3], R.S. Van der Post[4], P.D. Siersema[1] [1]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, Nederland, [2]Dept. of Gastroenterology and Hepatology, Bernhoven, Uden, Nederland, [3]Dept. of Gastroenterology and Hepatology, Canisius Wilhelmina Ziekenhuis, Nijmegen, Nederland, [4]Dept. of Pathology, Radboudumc, Nijmegen, Nederland.

14.30 Phase II study of cisplatin and everolimus in patients with metastatic extrapulmonary neuroendocrine carcinoma (NEC) (p. 85)

S. Levy[1], W.H.M. Verbeek[2], F.A.L.M. Eskens[3], D.J.A. de Groot[4], M.E. van Leerdam[2], M.E.T. Tesselaar[1,1]Dept. of Medical Oncology, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands, [2]Dept. of Gastrointestinal Oncology, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands, [3]Dept. of Medical Oncology, Erasmus MC Cancer Center, Rotterdam, The Netherlands, [4]Dept. of Medical Oncology, University Medical Center Groningen, Groningen, The Netherlands.

14.36 Deep submucosal invasion as independent risk factor for lymph node metastasis in T1 colorectal cancer: a systematic review and meta-analysis (p. 86)

L.W. Zwager[1], B.A.J. Bastiaansen[1], N. Mostafavi[2], R. Hompes[3], V. Barresi[4], K. Ichimasa[5], H. Kawachi[6], I. Machado[7], T. Masaki[8], W. Sheng[9], S. Tanaka[10], K. Togashi[11], P. Fockens[1], L.M.G. Moons[12], E. Dekker[11]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, The Netherlands, [2]Dept. of Biostatistics, Amsterdam UMC, Amsterdam, The Netherlands, [3]Dept. of Surgery, Amsterdam UMC, Amsterdam, The Netherlands, [4]Dept. of Public Health, University of Verona, Verona, Italië, [5]Dept. of Gastroenterology and Hepatology, Digestive Disease Center, Showa University Northern Yokohama Hospital, Tsuzuki, Japan, [6]Dept. of Pathology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan, [7]Dept. of Pathology, Instituto Valenciano de Oncología, Valencia, Spanje, [8]Dept. of Surgery, Kyorin University, Tokyo, Japan, [9]Dept. of Pathology, Fudan University Shanghai Cancer Center, Shanghai, China, [10]Dept. of Endoscopy, Hiroshima University Hospital, Hiroshima , Japan, [11]Dept. of Gastroenterology, Aizu Medical Center Fukushima Medical University , Aizuwakamatsu, Japan, [12]Dept. of Gastroenterology and Hepatology, Utrecht University Medical Center, Utrecht, Nederland.

14.42 Discovery of a Serum N-Glycan Panel for Early Detection of Pancreatic Cancer in a High-Risk Surveillance Cohort (p. 87)

D.C.F. Klatte[1], I.J.M. Levink[2], R.G.Hanna-Sawires[3], Y.E.M. de Van der Burgt[4], K.A. Overbeek[2], B.D.M. Koopmann[2], D.L. Cahen[2], G.M. Fuhler[2], F.P. Vleggaar[5], M. Wuhrer[4], R.A.E.M. Tollenaar[3], B.A. Bonsing[3], H.F.A. Vasen[1], M.E. Van Leerdam[1], M.J. Bruno[2], W.E. Mesker[3] [1]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands, [2]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands, [3]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands, [4]Center for Proteomics and Metabolomics, Leiden University Medical Center, Leiden, The Netherlands, [5]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands.

14.48 Impact of dose-escalated chemoradiotherapy on patient reported outcomes in patients with locally advanced rectal cancer: 2-year follow-up of the randomized RECTAL BOOST trial (p. 88)

S. Hoendervangers[1], M.E. Verweij[1], A.M. Couwenberg[2], J.P.M. Burbach[3], W.M.U. van Grevenstein[10], M.P.W. Intven[1], H.M. Verkooijen[1], M. Berbee[4], J. Buijsen[4], J. Roodhart[5], A. Pronk[6], E.C.J. Consten[7], A.B. Smits[8], J.T. Heikens[9] [1]Dept. of Radiotherapy, UMC Utrecht, Utrecht, Nederland, [2]Dept. of Radiotherapy, Dutch Cancer Institute, Amsterdam, Nederland, [3]Dept. of Surgery, Medical Centrle Leeuwarden, Leeuwarden, Nederland, [4]Dept. of Radiotherapy, MAASTRO, Maastricht, Nederland, [5]Dept. of Internal Medicine , UMC Utrecht, Utrecht, Nederland, [6]Dept. of Surgery, Diakonessenhuis, Utrecht, Nederland, [7]Dept. of Surgery, Meander MC, Amersfoort, Nederland, [8]Dept. of Scientific Research, Antonius hospital, Nieuwegein, Nederland, [9]Dept. of Surgery, Riverienland hospital, Tiel, Nederland, [10]Dept. of Surgery, UMC Utrecht, Utrecht, Nederland.

14.54 Fluorescence Molecular Endoscopy (FME) using bevacizumab-800CW for the detection of (pre)malignant lesions and evaluation of neoadjuvant chemoradiotherapy in esophageal cancer: the preliminary results (p. 89)

I. Schmidt[1], R.Y. Gabriels[1], W.T.R. Hooghiemstra[1], X. Zhao[1], G. Kats-Ugurlu[2], A.M. van der Waaij[1], R.Y. Gabriels[1], J.H. van der Laan[1], F.A. Dijkstra[3], J.W. Haveman[3], B. van Etten[3], D.J. Robinson[4], V. Ntziachristos[5], D. Gorpas[5], W.B. Nagengast[1] [1]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands, [2]Dept. of Pathology and Medical Biology, University Medical Center Groningen, Groningen, The Netherlands, [3]Dept. of Surgery, University Medical Center Groningen, Groningen, The Netherlands, [4]Dept. of Otorhinolaryngology & Head and Neck Surgery, Erasmus Medical Center, Rotterdam, The Netherlands, [5]Center for Translational Cancer Research (TranslaTUM), Technische Universität München, Munich, Germany.

15.00 Einde van dit programma onderdeel

Abstractsessie NVGIC

Voorzitters: *P. van Duijvendijk en D. Roos*

15.30 Incidence and predictive factors for surgical complications and bile duct injury (BDI) after cholecystectomy for uncomplicated gallstone disease. Results from three prospective multicentre cohort studies. (p. 91)
F.M. Thunnissen[1], D. Comes[1], P.R. De Reuver[1], C.S.S. Latenstein[1], J.P.H. Drenth[2], C.J.H.M. Van Laarhoven[1] [1]Dept. of Surgery, Radboudumc, Nijmegen, Nederland, [2]Dept. of Gastroenterology, Radboudumc, Nijmegen, Nederland.

15.33 The definition and outcomes of oligometastatic esophagogastric cancer: a systematic review and meta-analysis (p. 92)
T. E. Kroese[1], P.S.N. van Rossum[2], H.W.M. van Laarhoven[3], R van Hillegersberg[1] [1]Dept. of Surgery, UMC Utrecht, Utrecht, The Netherlands, [2]Dept. of Radiation Oncology, UMC Utrecht, Utrecht, The Netherlands, [3]Dept. of Medical Oncology, Amsterdam University Medical Centers, Amsterdam, The Netherlands.

15.36 Management of Pancreatic Fistula and Biliary Leakage after pancreatoduodenectomy through Percutaneous Transhepatic Biliary Drainage (p. 93)
A.C. Henry[1], F.J. Smits[1], K. van Lienden[2], D.A.F. van den Heuvel[2], O.R. Busch[3], O.M. van Delden[4], M. van Leersum[2], M.J.L. van Strijen[2], J.A. Vos[2], W.W. te Riele[1], I.Q. Molenaar[1], M.G. Besselink[3], H.C. van Santvoort[1] [1]Dept. of Gastrointestinal Surgery, Regional Academic Cancer Center Utrecht, Utrecht, [2]Dept. of Radiology, St. Antonius Hospital, Nieuwegein, [3]Dept. of Gastrointestinal Surgery, Amsterdam University Medical Center, Amsterdam, [4]Dept. of Radiology, Amsterdam University Medical Center, Amsterdam, Nederland.

15.39 Pancreas-sparing duodenectomy for advanced duodenal polyposis in patients with familial adenomatous polyposis: short and long-term outcomes (p. 94)
A.S. Aelvoet[1], B.A.J. Bastiaansen[1], O.R.C. Busch[2], E Dekker[1] [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, location AMC, Amsterdam, The Netherlands, [2]Dept. of Surgery, Amsterdam UMC, location AMC, Amsterdam, The Netherlands.

15.42 Delaying surgery to achieve a complete response after neoadjuvant chemoradiotherapy for rectal cancer: at what "cost"? A single institution analysis of hospital costs, surgical and oncological outcomes. (p. 95)
V.M. Meyer[1], R.R. Meuzelaar[1], Y. Schoenaker[1], J.W. de Groot[2], E. de Boer[3], O. Reerink[4], W.H. de Vos tot Nederveen Cappel[5], G.L. Beets[6], H.L. van Westreenen[1] [1]Dept. of Surgery, Isala klinieken, Zwolle, Nederland, [2]Dept. of Medical Oncology, Isala klinieken, Zwolle, Nederland, [3]Dept. of Radiology, Isala klinieken, Zwolle, Nederland, [4]Dept. of Radiotherapy, Isala klinieken, Zwolle, Nederland, [5]Dept. of Gastroenterology and Hepatology, Isala klinieken,

Zwolle, Nederland, [6]Dept. of Surgery, NKI, Antoni van Leeuwenhoek ziekenhuis, Amsterdam, Nederland.

15.45 Postponing surgery to optimise patients with acute right-sided obstructing colon cancer - a pilot study (p. 96)
J.R.E. Boeding[1], I.E.Cuperus[2], A.M. Rijken[2], R.M.P.H. Crolla[2], C. Verhoef[3], P.D. Gobardhan[2], J.M.J.Schreinemakers[2] [1]Dept. of Surgery, Amphia ziekenhuis , Breda, Nederland, [2]Dept. of Surgery, Amphia Hospital, Breda, Nederland, [3]Dept. of Surgery, Erasmus MC, Rotterdam, The Netherlands.

15.48 Delayed surgery after neoadjuvant treatment for rectal cancer does not lead to regret, impaired quality of life or worry for cancer. (p. 97)
V.M. Meyer[1], R.R. Meuzelaar[1], Y. Schoenaker[1], J.W. de Groot[2], E. de Boer[3], O. Reerink[4], W.H. de Vos tot Nederveen Cappel[5], G.L. Beets[6], H.L. van Westreenen[1] [1]Dept. of Surgery, Isala klinieken, Zwolle, Nederland, [2]Dept. of Medical Oncology, Isala klinieken, Zwolle, Nederland, [3]Dept. of Radiology, Isala klinieken, Zwolle, Nederland, [4]Dept. of Radiotherapy, Isala klinieken, Zwolle, Nederland, [5]Dept. of Gastroenterology and Hepatology, Isala klinieken, Zwolle, Nederland, [6]Dept. of Surgery, NKI, Antoni van Leeuwenhoek ziekenhuis, Amsterdam, Nederland.

15.51 Long-term Outcome of Radical Excision vs. Phenolisation of the Sinus Tract in Primary Sacrococcygeal Pilonidal Sinus Disease; A Randomized Controlled Trial (p. 98)
A.A. Pronk[1], M.J. Vissink[1], N. Smakman[2], E.J.B. Furnee[3], [1]Dept. of Surgery, Diakonessenhuis Utrecht, Utrecht, [2]Dept. of Surgery, Diakonessenhuis, Utrecht, [3]Dept. of Surgery, University Medical Centre Groningen, Groningen, The Netherlands.

15.54 Chest X-ray in the follow-up of colorectal carcinoma: added value? (p. 99)
E.G.M. Steenhuis[1], I.J.H. Schoenaker[1], R.M. Brohet[1], J.W.B. De Groot[2], H.L. Van Westreenen[3], W.H. Vos tot Nederveen Cappel[1] [1]Dept. of Gastroenterology and Hepatology, Isala, Zwolle, Nederland, [2]Dept. of Internal Medicine, Isala, Zwolle, Nederland, [3]Dept. of Gastrointestinal Oncology, Isala, Zwolle, Nederland.

15.57 Discussie
Alle sprekers

Invited speaker

16.15 No guts, some glory
Drs. S. Hofker, chirurg, Universitair Medisch Centrum Groningen

16.30 Einde van dit programma onderdeel

Symposium – Sectie Experimentele Gastroenterologie

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

08.30 Effect of host genetics on the gut microbiome in 7,738 participants of the Dutch Microbiome Project (p. 100)
S.H. Hu[2], E.A.L. Lopera-Maya[3], A.K. Kurilshikov[3], A.G. Van der Graaf[3], S.A. Andreu- Sánchez[3], L.C. Chen[4], A.V. Vich Vila[2], R.G. Gacesa[2], T.S. Sinha[3], V.C. Collij[2], M.A.Y.K. Klaassen[2], L.A.B. Bolte[2], M.F.B.G. Brandao Gois[3], P.B.T.N. Neerincx[3], M.A.S. Swertz[5], H.J.M.H. Harmsen[6], C.W. Wijmenga[3], J.F. Fu[4], A.Z. Zhernakova[3], S.S. Sanna[3], R.W. Weersma[2], [1]Dept. of Gastroenterology and Hepatology, University of Groningen and University Medical Center Groningen, Nederland, [2]Dept. of Gastroenterology and Hepatology, University of Groningen and University Medical Center Groningen, Groningen, Nederland, [3]Dept. of Clinical Genetics, University of Groningen and University Medical Center Groningen, Groningen, Nederland, [4]Dept. of Pediatrics, University of Groningen and University Medical Center Groningen, Groningen, Nederland, [5]Dept. of Clinical Genetics, University of Groningen and University Medical Center Groningen, Groningen, Nederland, [6]Dept. of Medical Microbiology, University of Groningen and University Medical Center Groningen, Groningen, Nederland.

08.35 Human intestinal (regulatory) T cells show profound adaptation to the microenvironment and alteration of phenotype during inflammation in Crohn's disease patients (p. 101)
L. Lutter[1], E. Brand[2], B. Roosenboom[3], D. Hoytema van Konijnenburg[4], M. Van der Wal[1], C. Horjus-Talabur Horje[3], B. Oldenburg[2], F. Van Wijk[1] [1]Centre for Translational Immunology, Universitair Medisch Centrum Utrecht, Utrecht, Nederland, [2]Dept. of Gastroenterology and Hepatology, Universitair Medisch Centrum Utrecht, Utrecht, Nederland,[3]Dept. of Gastroenterology and Hepatology, Rijnstate ziekenhuis, Arnhem, Nederland, [4]Dept. of Pediatrics, Harvard Medical School, Boston, Verenigde Staten.

08.40 Fecal water from Crohn's disease patients: high mucin degradation, but no epithelial barrier disruption in vitro (p. 102)
H.E.F. Becker[1], N. Kameli[2], A. Rustichelli[1], B.A.M. Heijnens[1], F. Stassen[2], J. Penders[2], D.M.A.E. Jonkers[1] [1]Dept. of Gastroenterology and Hepatology, Maastricht University, Maastricht, Nederland, [2]Dept. of Medical Microbiology, Maastricht University, Maastricht, Nederland.

Key note lecture

08.45 Cellular microbiology of the crypt ecosystem: deciphering microbe-stem cell interactions in health and disease
Prof. Philippe Sansonetti, Institut Pasteur, Paris

09.15 Cross-presentation by cancer-associated fibroblasts suppresses anti-tumor T cell immunity and is enhanced by upregulation of the lysosomal protease Cathepsin S in human colorectal cancer. (p. 103)
T.J. Harrijvan[1], L.J.A.C. Hawinkels[1], E.M.E. Verdegaal[2], J. Hardwick[1] [1]Dept. of Gastroenterology and Hepatology, LUMC, Leiden, The Netherlands, [2]Dept. of Medical Oncology, LUMC, Leiden, The Netherlands.

09.20 Targeting GITR enhances human tumour-infiltrating T cell functionality in mismatch repair proficient primary colorectal carcinoma and liver metastases (p. 104)
Y.S. Rakké[1], D. Sprengers[2], J. Kwekkeboom[2], L. Campos Carrascosa[2], A.A. van Beek[2], V. de Ruiter[2], M. Doukas[3], S. ter Borg[4], P.G. Doornebosch[5], M. Vermaas[5], E. van der Harst[6], P.P.L.O. Coene[6], D.J. Grünhage[1], C. Verhoef[1], J.N.M. IJzermans[1] [1]Dept. of Surgery, Erasmus MC - University Medical Center, Rotterdam, The Netherlands, [2]Dept. of Gastroenterology and

Hepatology, Erasmus MC - University Medical Center, Rotterdam, [3]Dept. of Pathology, Erasmus MC - University Medical Center, Rotterdam, [4]Dept. of Pathology, Pathan BV, Rotterdam, [5]Dept. of Surgery, IJsselland Hospital, Capelle aan den IJssel, The Netherlands, [6]Dept. of Surgery, Maasstad Hospital, Rotterdam, The Netherlands.

09.25 Prevalence and Clinical Characteristic of Autoimmune Gastritis in Patients with Intestinal Metaplasia (p. 105)
X.P. Guo[1], M.C. Mommersteed[1], M. Tokat[1], M. Scherurs[2], N. Erler[3], M. Peppelenbosch[1], M. Spaander[1], G. Fuhler[1] [1]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, [2]Dept. of Immunopathology, Erasmus University Medical Center, Rotterdam, [3]Dept. of Biostatistics, Erasmus University Medical Center, Rotterdam, Nederland.

09.30 Einde van dit programma onderdeel, mogelijkheid tot volgen netwerksessie tot 10.00

Symposium Nederlandse Vereniging voor Hepatologie

Voorzitters: J.P.H. Drenth en E.M.M. Kuiper

10.00 Behandeling van Hepatitis C anno 2021: de laatste inzichten
M. van Dijk, arts-onderzoeker, Radboudumc, Nijmegen en
Dr. H. van Soest, MDL-arts, Haaglanden Medisch Centrum, Den Haag

10.30 Ascites: de behandelopties
Dr. A.J.P. van der Meer, MDL-arts, Erasmus MC, Rotterdam en
Dr. R.B. Takkenberg, Amsterdam UMC, loc. AMC

11.00 Afsluiting programma onderdeel

Symposium NVMDL

Voorzitter: E. Dekker en V.M.C.W. Spaander

Symposium Coloscopie surveillance

11.30 Inleiding
Prof. dr. E. Dekker, MDL-arts, Amsterdam UMC, Amsterdam

11.35 Surveillance adenomen
Prof. dr. M.E. van Leerdam, MDL-arts, NKI/AvL en LUMC

11.50 Surveillance SSLs
Dr. Y. Hazewinkel, MDL-arts, Radboudumc, Nijmegen

12.05 Surveillance na CRC
Dr. A.M. van Berkel, MDL-arts, Noordwest Ziekenhuisgroep, Alkmaar

12.15 Start/stopcriteria surveillance (oa leeftijd) en andere discussiepunten
Dr. I. Lansdorp-Vogelaar, iMGZ, Erasmus MC, Rotterdam

12.30 Afsluiting programma onderdeel

Symposium – Sectie Gastrointestinale Endoscopie

Voorzitters: *L.M.G. Moons en M. van Schaik*

Symposium: Less is more

14.00 ”Less or More”: gastroscopieën; wat is doelmatig?
Prof. dr. J.P.H. Drenth, MDL-arts, Radboudumc, Nijmegen

14.20 “Less is More” in EUS/ERCP
Dr. J.W. Poley, MDL-arts, Erasmus MC, Rotterdam

14.40 “Less is More” in Endoscopy
Prof. dr. J.J.G.H.M. Bergman, MDL-arts, Amsterdam UMC, loc. AMC, Amsterdam

15.00 Einde van dit programma onderdeel

Symposium – Sectie Kinder-MDL

Voorzitters: *V.M. Wolters en F.D.M. van Schaik*

Symposium: Jong gekregen, oud gehouden

15.30 FAP: stap voor stap
Zorg voor adolescenten met familiaire adenomateuze polyposis
Dr. A. van den Berg, kinderarts-MDL, WKZ/UMCU, Utrecht
Dr. M.C.A. van Kouwen, MDL-arts, Radboudumc, Nijmegen

16.00 Primair Scleroserende Cholangitis zorg anno 2021: one size fits all ages?
Dr. B.G.P. Koot, kinderarts-MDL, Amsterdam UMC, Amsterdam
Prof. dr. C.Y. Ponsioen, MDL-arts, Amsterdam UMC, Amsterdam

16.30 Einde van dit programma onderdeel, mogelijkheid tot volgen netwerksessie tot 17.00

Uitreiking prijzen

Voorzitters: *C.J. van der Woude en R. van Hillegersberg*

17.00 Bekendmaking Gastrostartsubsidies voorjaar 2021

17.10 **Uitreiking NVGE Gastrointestinale Proefschriftprijs 2020 en 2021 gevolgd door voordrachten door de prijswinnaars**

Uitreiking proefschriftprijs 2020 gevolgd door voordracht
Uitreiking proefschriftprijs 2021 gevolgd door voordracht

17.30 Huidige inzichten van behandeling Barrett neoplasie
Dr. A.D. Koch, MDL-arts, Erasmus MC

18.00 Afsluiting programma onderdeel

Abstractsessie Nederlandse Vereniging voor Hepatologie

Voorzitters: *J.P.H. Drenth en E.M.M. Kuiper*

08.30 Ursodeoxycholic acid for the prevention of symptomatic gallstone disease after bariatric surgery: a multicenter, randomized, placebo-controlled, double-blind superiority trial (UPGRADE trial) (p. 106)

S. Haal[1], M.S.S. Guman[2], T.C.C. Boerlage[3], Y.I.Z. Acherman[4], L.M. De Brauw[4], S. Bruin[5], S.M.M. De Castro[6], J.E. van Hooft[7], A.W.J.M. van de Laar[4], D.E. Moes[8], M. Schouten[9], R. Schouten[9], E.J. Van Soest[10], R.N. Van Veen[6], C.E.E. De Vries[6], P. Fockens[1], M.G.W. Dijkgraaf[11], V.E.A. Gerdes[2], R.P. Voermans[1] [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC locatie AMC, Amsterdam, Nederland, [2]Dept. of Internal Medicine , Amsterdam UMC locatie AMC, Amsterdam, Nederland, [3]Dept. of Gastroenterology, Sint Antonius Ziekenhuis, Nieuwegein, Nederland, [4]Dept. of Surgery, Spaarne Gasthuis, Hoofddorp, Nederland, [5]Dept. of Surgery, Spaarne Gasthuis, Hoofdorp, Nederland, [6]Dept. of Surgery, OLVG, Amsterdam, Nederland, [7]Dept. of Gastroenterology and Hepatology, LUMC, Leiden, Nederland, [8]Dept. of Surgery, Dijklander ziekenhuis, Hoorn, Nederland, [9]Dept. of Surgery, Flevoziekenhuis, Almere, Nederland, [10]Dept. of Gastroenterology, Spaarne Gasthuis, Hoofddorp, Nederland, [11]Dept. of Epidemiology and Biostatistics, Amsterdam UMC locatie AMC, Amsterdam, Nederland.

08.36 Liver decompensation as late complication in HCC patients with long term responses following selective internal radiation therapy. (p. 107)

D.J. van Doorn[1], P. Hendriks[2], M.C. Burgmans[2], D.D.D. Rietbergen[3], M. Coenraad[4], O.M. van Delden[5], R.J. Bennink[5], T.A. Labeur[1], H.J. Klümpen[6], F.A.L.M. Eskens[7], A. Moelker[8], E. Vegt[9], D. Sprengers[10], N. Mostafavi1[1], J. Ijzermans[12], R.B. Takkenberg[1] [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Universiteit van Amsterdam, Amsterdam, Nederland, [2]Dept. of Radiology, LUMC, Leiden, Nederland, [3]Dept. of Radiology and Nuclear Medicine, LUMC, Leiden, Nederland, [4]Dept. of Gastroenterology and Hepatology, LUMC, Leiden, Nederland, [5]Dept. of Radiology and Nuclear Medicine, Amsterdam UMC, Universiteit van Amsterdam, Amsterdam, Nederland, [6]Dept. of Medical Oncology, Amsterdam UMC, Universiteit van Amsterdam, Amsterdam, Nederland, [7]Dept. of Medical Oncology, Erasmus Medical Center, Rotterdam, Nederland, [8]Dept. of Radiology, Erasmus Medical Center, Rotterdam, Nederland, [9]Dept. of Radiology and Nuclear Medicine, Erasmus Medical Center, Rotterdam, Nederland, [10]Dept. of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, Nederland, [11]Dept. of Biostatistics, Amsterdam UMC, Universiteit van Amsterdam, Amsterdam, Nederland, [12]Dept. of Surgery, Erasmus Medical Center, Rotterdam, Nederland.

08.42 The alteration of gut microbiome in liver transplantation: first results from the TransplantLines Biobank and Cohort study (p. 108)

Y. Li[1], S. Hu1, C. Swarte[1], G. Ranko [1], A. Vich Vila[1], R. Douwes[1], H. Harmsen[2], B. Jansen[1], V. De Meijer[3], J. Fu[4], E.A.M. Festen[1], S. Bakker[5], H. Blokzijl[1], R. Weersma[1] [1]Dept. of Gastroenterology and Hepatology, University Medical Center of Groningen, Groningen, Nederland, [2]Dept. of Medical Microbiology, University Medical Center of Groningen, Groningen, Nederland, [3]Dept. of Surgery, University Medical Center of Groningen, Groningen, Nederland, [4]Dept. of Pediatrics, University Medical Center of Groningen, Groningen, Nederland, [5]Dept. of Neurosurgery, University Medical Center of Groningen, Groningen, Nederland.

08.48 Hepatitis C Elimination in the Netherlands (CELINE): nationwide retrieval of lost to follow-up patients with chronic hepatitis C (p. 109)

C.J. Isfordink[1], M. van Dijk[2], S.M. Brakenhoff[3], J.E. Arends[4], R.J. de Knegt[3], M. van der Valk[5], J.P.H. Drenth[2] [1]Dept. of Gastroenterology and Hepatology, University Medical Centre Utrecht, Utrecht, The Netherlands, [2]Dept. of Gastroenterology and Hepatology, Radboud University Medical Centre, Nijmegen, The Netherlands, [3]Dept. of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands, [4]Dept. of Infectious Diseases, University

Medical Centre Utrecht, Utrecht, The Netherlands, [5]Dept. of Infectious Diseases, Amsterdam University Medical Centers, Amsterdam, The Netherlands.

08.54 End of treatment HBsAg, HBcrAg and HBV RNA levels predict risk of off-treatment ALT flares in patients with chronic hepatitis B (p. 110)
S.M. Brakenhoff[1], R.J. de Knegt[1], M.J.H. van Campenhout[1], A.A. van der Eijk[2], W.P. Brouwer[1], F. van Bömmel[3], A. Boonstra[1], B.E. Hansen[4], T. Berg[3], H.L.A. Janssen[4], R.A. De Man[1], M.J. Sonneveld[1] [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, University Medical Center, Rotterdam, Rotterdam, The Netherlands, [2]Dept. of Viroscience, Erasmus MC, University Medical Center, Rotterdam, Rotterdam, The Netherlands, [3]Dept. of Hepatology, Leipzig University Medical Center, Leipzig, Duitsland, [4]Toronto Center for Liver Disease, Toronto General Hospital, Toronto, Canada.

09.00 Autoimmune hepatitis – primary biliary cholangitis variant often treated outside Paris criteria with similar results (p. 111)
M. Biewenga[1], J.P.H. Drenth[2], X. Verhelst[3], A.J.P. van der Meer[4], Y.S. de Boer[5], G. Bouma[5], A.C. Poen[6], R.C. Verdonk[7], A.P. van der Berg[8], J.T. Brouwer[9], T. Vanwolleghem[10], W.J. Lammers[4], A. Farina Sarasqueta[11], J. Verheij[11], T. Roskams[12], B. van Hoek[1] [1]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, Nederland, [2]Dept. of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, Nederland, [3]Dept. of Gastroenterology and Hepatology, UZ Gent, Gent, België, [4]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, Nederland, [5]Dept. of Gastroenterology and Hepatology, Amsterdam UMC locatie VUmc, Amsterdam, Nederland, [6]Dept. of Gastroenterology and Hepatology, Isala clinics, Zwolle, Nederland, [7]Dept. of Gastroenterology and Hepatology, Sint Antonius Hospital, Nieuwegein, Nederland, [8]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, Nederland, [9]Dept. of Gastroenterology and Hepatology, Reinier de Graaf Gasthuis, Delft, Nederland, [10]Dept. of Gastroenterology and Hepatology, UZ Antwerpen, Antwerpen, België, [11]Dept. of Pathology, Amsterdam UMC locatie AMC, Amsterdam, Nederland, [12]Dept. of Pathology, UZ Leuven, Leuven, België.

09.06 Pearl studie
Dr. R.B. Takkenberg, Amsterdam UMC, loc. AMC

09.18 Camaro studie
R.J.A.L.M. Snijders, Radboudumc, Nijmegen

09.30 Einde van dit programma onderdeel, mogelijkheid tot volgen netwerksessie tot 10.00

Symposium – Sectie Experimentele Gastroenterologie

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

10.00 **Battle junior researcher award**

10.15 Mass cytometry reveals networks of tissue resident immune cell clusters associated with inflammation in IBD
Prof. dr. F. Koning, Hoogleraar Immunologie, Leids Universitair Medisch Centrum

10.45 Single cell RNA sequencing identifies distinct intestinal inflammation patterns in primary sclerosing cholangitis associated colitis compared to ulcerative colitis (p. 112)
A. Bangma[1], W.T.C. Uniken Venema[1], M.G.P. van der Wijst[2], G. Katz[3], A. Vich Villa[1], R.K. Weersma[4], E.A.M. Festen[1] [1]Dept. of Gastroenterology and Hepatology, Universitair Medisch Centrum Groningen, Rijksuniversiteit Groningen, Groningen, Nederland, [2]Dept. of Genetics, Universitair Medisch Centrum Groningen, Rijksuniversiteit Groningen, Groningen, Nederland, [3]Dept. of Pathology, Universitair Medisch Centrum Groningen, Groningen, Nederland, [4]Dept. of Gastroenterology and Hepatology, Universitair Medisch Centrum Groningen, Groningen, Nederland.

10.51 Homeostatic function and inflammatory activation of ileal CD8+ tissue-resident (CD69+CD103+) T-cells is dependent on mucosal location (p. 113)
L. Lutter[1], B. Roosenboom[2], E. Brand[3], J. Ter Linde[3], E. Van Lochem[4], B. Oldenburg[3], C. Horjus-Talabur Horje[2], F. Van Wijk[1] [1]Centre for Translational Immunology, Universitair Medisch Centrum Utrecht, Utrecht, Nederland, [2]Dept. of Gastroenterology and Hepatology, Rijnstate ziekenhuis, Arnhem, Nederland, [3]Dept. of Gastroenterology and Hepatology, Universitair Medisch Centrum Utrecht, Utrecht, Nederland, [4]Dept. of Microbiology and Immunology , Rijnstate ziekenhuis, Arnhem, Nederland.

10.57 Activated, cytotoxic CD27+PD1+ CD8-T cells in RCDII duodenum (p. 114)
T. Dieckman[1], M. Schreurs[2], A.M.E.T.A de Mahfouz[3], G. Bouma[4], F. de Koning[1] [1]Dept. of Immunology, LUMC, Leiden, Nederland, [2]Dept. of Immunohematology and Blood Transfusion, LUMC, Leiden, The Netherlands, [3]Dept. of Human Genetics, LUMC, Leiden, The Netherlands, [4]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, location VUmc, Amsterdam, The Netherlands.

Battle winner announcement

11.00 Einde van dit programma onderdeel

Meet the expert sessie

11.30 uur– 12.30 uur

Thema: IBS

Deze sessies – waarvoor tevoren moet worden ingeschreven - worden verzorgd door:
Prof. dr. A.A.M. Masclee, MDL-arts, MUMC, Maastricht
Dr. L.A. van der Waaij, MDL-arts, Martini ziekenhuis, Groningen

12.30 Einde van dit programma onderdeel, mogelijkheid tot volgen netwerksessie tot 14.00

Postersessie 4 **Discussietafel**

Voorzitter: *A.E. van der Meulen*

12.30 Addition of neutralizer to duodenoscope samples increases yield of cultures acquired after high level disinfection (p. 115)
J.A. Kwakman[1], M.J. Bruno[1], M.C. Vos[2][1]Dept. of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands. [2]Dept. of Medical Microbiology, Erasmus Medical Center, Rotterdam, The Netherlands.

12.36 Gut mucosa dissociation protocols influence cell type proportions and single-cell gene expression levels (p. 116)
W.T.C. Uniken Venema[1], A.D. Ramirez Sanchez[2], E.V. Bigaeva[1], S. Withoff[2], I. Jonkers[2], R. McIntyre[3], M. Ghouraba[3], R.K. Weersma[1], L. Franke[2], M.G.P. van der Wijst[4], E.A.M. Festen[1] [1]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [2]Dept. of Clinical Genetics, University Medical Center Groningen, Groningen, The Netherlands. [3]Moleculaire Celbiologie en Immunologie, Sanger Institute, Hinxton, Verenigd Koninkrijk. [4]Dept. of Genetics, University Medical Center Groningen, Groningen, The Netherlands.

12.42 Loss-of-response to anti-TNFα critically depends on treatment duration in patients with inflammatory bowel disease (p. 117)
P.D. Schultheiss[1],R. Mahmoud[1],H.H. Fidder[1],B. Oldenburg[1], J.M. Louwers[1], M. van der Kaaij[2], B.P. van Hellemondt[1], P. van Boeckel[3], N. Mahmmod[3], B. Jharap[4][1]Dept. of Gastroenterology, UMC Utrecht, Utrecht, The Netherlands. [2]Dept. of Medicine, St. Jansdal ziekenhuis, Harderwijk, The Netherlands. [3]Dept. of Gastroenterology, Antonius ziekenhuis, Nieuwegein, The Netherlands. [4]Dept. of Gastroenterology, Meander MC, Amersfoort, The Netherlands.

12.48 Comparison of linear versus circular-stapled gastroenterostomy in Roux-en-Y gastric bypass: a nationwide population-based cohort study (p. 118)
M.M. Romeijn[1], S. van Hoef[1], L. Janssen[1], K.G.H. van de Pas[1], F.M.H. van Dielen[1], K.W.A. Göttgens[1], J.W.M. Greve[2], W.K.G. Leclercq[1][1]Dept. of Surgery, Máxima Medical Center, Veldhoven, The Netherlands. [2]Dept. of Surgery, Zuyderland Medical Center, Heerlen, The Netherlands.

12.54 Update on Incidence, Prevalence Treatment and Survival of Patients with Small bowel Neuroendocrine Neoplasms in The Netherlands (p. 119)
E. Kaçmaz[1], A. Farina Sarasqueta[2], S. van Eeden[2], K.M.A. Dreijerink[3], H.J. Klümpen[4], E.J.M. Nieveen van Dijkum[1], P.J. Tanis[1], A.F. Engelsman[5][1]Dept. of Surgery, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands. [2]Dept. of Pathology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands. [3]Dept. of Gastroenterology, Hepatology and Endocrinoligy, Amsterdam UMC, Vrije Universiteit

Amsterdam, Amsterdam, Nederland. [4]Dept. of Medical Oncology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands. [5]Dept. of Surgery, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, Nederland.

Postersessie 5 **Discussietafel**

Voorzitter: *L.P.S. Stassen*

13.00 ATP tests after manual cleaning do not predict the presence of microorganisms on duodenoscopes and linear echoendoscopes after high level disinfection (p. 120)
J.A. Kwakman[1], A.W. Rauwers[2], M.C. Vos[3], M.J. Bruno[1] [1]Dept. of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands. [2]Dept. of Gastroenterology, Erasmus Medical Center, Rotterdam, The Netherlands. [3]Dept. of Medical Microbiology, Erasmus Medical Center, Rotterdam, The Netherlands.

13.04 Crohn's Disease fistula show skewed lymphoid/myeloid balance and altered myeloid cell profiles (p. 121)
M.A.J. Becker[1], M. de Krijger[1], W.A. Bemelman[2], W.J. de Jonge[1], C.J. Buskens[2], M.E. Wildenberg[1] [1]Dept. of Gastroenterology and Hepatology, Tytgat Institute, Amsterdam, Nederland. [2]Dept. of Surgery, Amsterdam UMC, Amsterdam, Nederland.

13.08 Perspectives on treatment of inflammatory bowel diseases in older patients; gut-feeling or evidence-based medicine? – a qualitative study in professionals and patients (p. 122)
V.E.R. Asscher[1], C.M. Verbiest[1], S.N. Waars[1], A.E. Van der Meulen-de Jong[1], S.P. Mooijaart[2], A.H. Pieterse[3], P.W.J. Maljaars[1] [1]Dept. of Gastroenterology and Hepatology, LUMC, Leiden, The Netherlands. [2]Dept. of Gerontology and Geriatrics, LUMC, Leiden, The Netherlands. [3]Dept. of Biomedical Data Sciences, LUMC, Leiden, The Netherlands.

13.12 Societal cost-of-illness of inflammatory bowel disease has rapidly increased over the years and differs between continents: a systematic review (p. 123)
R.C.A. van Linschoten[1], E. Visser[1], C.D. Niehot[2], C.J. van der Woude[3], J.A. Hazelzet[4], D. van Noord[1], R.L. West[1] [1]Dept. of Gastroenterology and Hepatology, Franciscus Gasthuis & Vlietland, Rotterdam, Nederland. [2]Medical Library, Erasmus MC, Rotterdam, Nederland. [3]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, Nederland. [4]Dept. of Public Health, Erasmus MC, Rotterdam, Nederland.

13.16 Incidence and predictive factors of biliary complications in patients presenting with uncomplicated gallstone disease. Results from three prospective multicentre cohort studies. (p. 124)
F.M. Thunnissen[1], D. Comes[1], P.R. De Reuver[1], C.S.S. Latenstein[1], J.P.H. Drenth[2], C.J.H.M. Van Laarhoven[1] [1]Dept. of Surgery, Radboudumc, Nijmegen, Nederland. [2]Dept. of Gastroenterology, Radboudumc, Nijmegen, Nederland.

13.20 Risk of Barrett's Esophagus and Esophageal Adenocarcinoma among Patients Diagnosed with Breast Cancer – a Nationwide Study (p. 125)
Y. Peters[1], J. Sijben[1], R.S. Van der Post[2], R.H.A. Verhoeven[3], P.D. Siersema[1] [1]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, Nederland. [2]Dept. of Pathology, Radboudumc, Nijmegen, Nederland. [3]Integraal Kankercentrum Nederland (IKNL), Integraal Kankercentrum Nederland (IKNL), Utrecht, Nederland.

13.24 Effect of Family History on the Risk of Barrett's Esophagus and Esophageal Adenocarcinoma: Systematic Review and Meta-analysis (p. 126)
Y. Peters[1], E. Van Grinsven[1], P.D. Siersema[1] [1]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, Nederland.

Postersessie 6 **Discussietafel**

Voorzitter: *W.H. de Vos tot Nederveen Cappel*

13.30 The Workgroup Serrated Polyps and Polyposis (WASP) classification for optical diagnosis of diminutive colorectal polyps using iScan (p. 127)
E. Soons[1], T.M. Bisseling[1], R.S. van der Post[2], I.D. Nagtegaal[2], Y. Hazewinkel[1], M.C.A. van Kouwen[1], P.D. Siersema[1] [1]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, Nederland. [2]Dept. of Pathology, Radboudumc, Nijmegen, Nederland.

13.35 The small bowel is protected by the presence of luminal preservation solution during cold storage in a brain-dead rat model (p. 128)
G. Trentadue[1], L. Vecchio Dezilio[2], G. Kats-Ugurlu[3], J.W. Haveman[4], K.N. Faber[1], M. Rumbo[2], H. Leuvenink[4], G. Dijkstra[1] [1]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, Nederland. [2]Dept. of Immunopathology, National University of La Plata, La Plata, Argentinië. [3]Dept. of Pathology, University Medical Center Groningen, Groningen, Nederland. [4]Dept. of Surgery, University Medical Center Groningen, Groningen, Nederland.

13.40 Adaptation and content validity of the Dutch Crohn's Life Impact Questionnaire (p. 129)
E.M. van Andel[1], D.P. van Asseldonk[1], N.K.H. de Boer[2], G. Bouma[2] [1]Dept. of Gastroenterology and Hepatology, Noordwest Ziekenhuisgroep, Alkmaar, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, location VUmc, Amsterdam, The Netherlands.

13.45 Self-reported Health-Related Quality of Life and Disease Control of Patients with Inflammatory Bowel Disease during the COVID-19 pandemic in The Netherlands (p. 130)
E. de Paulides[1], A. de Pasma[2], N.S. Erler[3], R.L.A. van Eijk[1], A.C. de Vries[4], C.J. van der Woude[1] [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, Nederland. [2]Dept. of Rheumatology, Erasmus MC, Rotterdam, The Netherlands. [3]Dept. of Biostatistics, Erasmus MC, Rotterdam, The Netherlands. [4]Dept. of Gastroenterology, Erasmus MC, Rotterdam, The Netherlands.

13.50 Efficacy of Permacol injection for perianal fistulas in a tertiary referral population: poor outcome in patients with complex fistulas (p. 131)
P.F. Vollebregt[1], G.J. Vander Mijnsbrugge[2], C.B.H. Molenaar[2], R.J.F. Felt-Bersma[3] [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands. [2]Dept. of Surgery, Proctos Kliniek , Bilthoven, The Netherlands. [3]Dept. of Gastroenterology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands.

13.55 The complexities of analysis for APC mosaicism (p. 132)
D. Terlouw[1], M. Suerink[2], A. Boot[3], A.M.J. Langers[4], D. Ruano[1], C.M. Tops[2], T. van Wezel[1], M. Nielsen[2], H. Morreau[1] [1]Dept. of Pathology, Leiden University Medical Center, Leiden, Nederland. [2]Dept. of Clinical Genetics, Leiden University Medical Center, Leiden, Nederland. [3]Dept. Of Molecular Cancer Research, Duke-NUS Medical School, Singapore, Singapore. [4]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, Nederland.

Abstractsessie – Sectie Inflammatoire Darmziekten

Voorzitters: *A.G.L. Bodelier en S.F.G. Jeuring*

14.00 Ustekinumab for Crohn's Disease: Two-Year Results of the Initiative on Crohn and Colitis (ICC) Registry, a Nationwide Prospective Observational Cohort Study (p. 133)
T.S. Straatmijer[1], V.B.C. Biemans[2], F. Hoentjen[3], P.W.J. Maljaars[4], B Oldenburg[2], J Haans[5], K.H.N. de Boer[6], C.I.J. Ponsioen[7], M.C. Visschedijk[8], J.M. Jansen[9], R.L. West[10], A.G.L. Bodelier[11], C.J. van der Woude[12], W.A. van Dop[3], A.C. de Vries[13], G Dijkstra[8], S van der Marel[14], M.J. Pierik[5], M. Duijvestein[7], A. E. van der Meulen[4] [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, The Netherlands, [2]Dept. of Gastroenterology and Hepatology, UMCU, Utrecht, The Netherlands, [3]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, The Netherlands, [4]Dept. of Gastroenterology and Hepatology, LUMC, Leiden, The Netherlands, [5]Dept. of Gastroenterology and Hepatology, MUMC, Maastricht, The Netherlands, [6]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, locatie VUmc, Amsterdam, The Netherlands, [7]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, locatie AMC, Amsterdam, The Netherlands, [8]Dept. of Gastroenterology and Hepatology, UMCG, Groningen, The Netherlands, [9]Dept. of Gastroenterology and Hepatology, OLVG, Amsterdam, The Netherlands, [10]Dept. of Gastroenterology and Hepatology, Franciscus Gasthuis & Vlietland, Rotterdam, The Netherlands, [11]Dept. of Gastroenterology and Hepatology, Amphia, Breda, The Netherlands, [12]Dept. of Gastroenterology, Eramus MC, Rotterdam, The Netherlands, [13]Dept. of Gastroenterology and Hepatology, Eramus MC, Rotterdam, The Netherlands, [14]Dept. of Gastroenterology and Hepatology, HMC, Den Haag, The Netherlands.

14.06 Acceptance and perceived control are independently associated with quality of life in inflammatory bowel disease: introduction of a new segmentation model (p. 134)
L.W. van Erp[1], J. van Gerven[2], S. de Bloem[3], M.J.M. Groenen[2], P.J. Wahab[4] [1]Dept. of Gastroenterology and Hepatology, Rijnstate ziekenhuis, Arnhem, Nederland, [2]Dept. of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, The Netherlands, [3]Center for Marketing & Supply Chain Management, Nyenrode Business University, Breukelen, The Netherlands, [4]Dept. of Gastroenterology and Hepatology, Nyenrode Business University, Breukelen, The Netherlands.

14.12 Exclusive enteral nutrition or prednisolone induction treatment: clinical and endoscopic evaluation of new-onset luminal paediatric Crohn's disease. (p. 135)
M.M.E. Jongsma[1], M.A. Cozijnsen[1], M. van Pieterson[1], T.G.J. de Meij[2], O.F Norbruis[3], M. Groeneweg[4], V.M. Wolters[5], H.M. van Wering[6], I. Hojsak[7], K.L. Kolho[8], M.P. van Wijk[1], S. Teklenburg-Roord[3], J.C. Escher[1], L. de Ridder[1] [1]Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Erasmus MC University Medical Center-Sophia Children’s Hospital, Rotterdam, Nederland, [2]Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Amsterdam UMC-Emma children's hospital , Amsterdam , Nederland, [3]Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Isala ziekenhuis, Zwolle, Nederland, [4]Dept. of Pediatrics, Maasstad ziekenhuis, Rotterdam, Nederland, [5]Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Utrecht UMC- Wilhelmina kindeziekenhuis, Utrecht, Nederland, [6]Dept. of Pediatrics, Amphia ziekenhuis, Breda, Nederland, [7]Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Zagreb children's hospital , Zagreb, Kroatië, [8]Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Tampere University Hospital, Helsinki, Finland.

14.18 De-escalation of biological therapy in inflammatory bowel disease patients following prior escalation (p. 136)
P.W.A. Thomas[1], L.J.T. Smits[1], M. Te Groen[1], R.L. West[2], M.G.V.M. Russel[3], J.M. Jansen [4],

T.E.H. Römkens[5], F. Hoentjen[1] [1]Dept. of Gastroenterology and Hepatology, Radboud Universitair Medisch Centrum, Nijmegen, Nederland, [2]Dept. of Gastroenterology and Hepatology, Franciscus Gasthuis & Vlietland, Rotterdam, Nederland, [3]Dept. of Gastroenterology and Hepatology, Medisch Spectrum Twente, Enschede, Nederland, [4]Dept. of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam, Nederland, [5]Dept. of

Gastroenterology and Hepatology, Jeroen Bosch Ziekenhuis, 's-Hertogenbosch, Nederland.

14.24 Safety and drug survival of methotrexate versus tioguanine after failure of conventional thiopurines in Crohn's disease (p. 137)
E.H.J. Savelkoul[1], M.H.J. Maas[1], M.G.V.M. Russel[2], T.E.H. Römkens[3], F. Hoentjen[1] [1]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, Nederland, [2]Dept. of Gastroenterology and Hepatology, Medisch Spectrum Twente, Enschede, Nederland, [3]Dept. of Gastroenterology and Hepatology, Jeroen Bosch Ziekenhuis, 's Hertogenbosch, Nederland.

14.30 Switching within or out of class are the most effective strategies in IBD patients with immunogenicity against anti-TNF antibodies (p. 138)
S.I. Anjie[1], J. Hanzel[1], K.B. Gecse[1], G.R.A.M. D'Haens[1], J.F. Brandse[1] [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, Nederland.

14.36 Long-term outcomes following a swith from originator Adalimumab to the biosimilar SB5 (IMRALDI) in a real-world IBD cohort (p. 139)
L.A.A.P. Derikx[1], N. Plevris[2], L. Lucaciu[2], H.W. Dolby[2], C.S. Rees[2], M. Lyons[2], SI Siakavellas[2], C Noble[2], C O'hara[2], L. Merchant[2], I.D. Arnott[2], GR Jones[2], C.W. Lees[2] [1]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, The Netherlands, [2]Dept. of Gastroenterology and Hepatology, Western General Hospital, Edinburgh, Verenigd Koninkrijk.

14.42 Gut microbiome and proteomic changes as biomarker of response to vedolizumab in patients with inflammatory bowel disease (p. 140)
V. Collij[1], M.A.Y. Klaassen[2], S. Hu[2], W.T.C. Uniken Venema[2], A. Bangma[2], J.B. Aardema[2], A.R. Bourgonje[2], B.H. Jansen[2], G. Dijkstra[2], E.A.M. Festen[2], M.C. Visschedijk[2], J.N. Samsom[3], R. Gacesa[2], A. Vich Vila[2], R.K. Weersma[2] [1]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands, [2]Dept. of Gastroenterology and Hepatology, Universitair Medisch Centrum Groningen, Groningen, The Netherlands, [3]Dept. of Pediatrics, Erasmus University Medical Center, Rotterdam, The Netherlands.

14.48 Pregnant women with perianal Crohn's disease: the current guideline on delivery method needs improvement (p. 141)
I.J. Schaafsma[1], F.J. Hoogenboom[2], G. Dijkstra[1], J.R. Prins[3], M.C. Visschedijk[1] [1]Dept. of Gastroenterology and Hepatology, University of Groningen, University Medical Center Groningen, Groningen, the Net, Groningen, The Netherlands, [2]Dept. of Surgery, University of Groningen, University Medical Center Groningen, Groningen, the Net, Groningen,The Netherlands, [3]Dept. of Gynaecologic Oncology, University of Groningen, University Medical Center Groningen, Groningen, the Net, Groningen, The Netherlands.

15.00 Einde van dit programma onderdeel

Abstractsessie – Sectie Gastrointestinale Endoscopie

Voorzitters: *A. Inderson en W.B. Nagengast*

15.30 Optimal timing of rectal diclofenac in preventing post-ERCP pancreatitis (p. 142)

C.J. Sperna Weiland[1], X.J.N.M. Smeets[1], R.C. Verdonk[2], A.C. Poen[3], A. Bhalla[4], N.G. Venneman[5], W. Kievit[1], H.C. Timmerhuis[2], D.S. Umans[2], J.E. Van Hooft[6], M.G. Besselink[7], H.C. Van Santvoort[8], P. Fockens[9], M.J. Bruno[10], J.P.H. Drenth[1], E.J.M. Van Geenen[1] [1]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, Nederland, [2]Dept. of Gastroenterology and Hepatology, St. Antonius ziekenhuis, Nieuwegein, Nederland, [3]Dept. of Gastroenterology and Hepatology, Isala ziekenhuis, Zwolle, Nederland, [4]Dept. of Gastroenterology and Hepatology, Haga ziekenhuis, Den Haag, Nederland, [5]Dept. of Gastroenterology and Hepatology, Medisch Spectrum Twente, Enschede, Nederland, [6]Dept. of Gastroenterology and Hepatology, Leids Universitair Medisch Centrum, Leiden, Nederland, [7]Dept. of Surgery, Amsterdam UMC, Amsterdam, Nederland, [8]Dept. of Surgery, St. Antonius ziekenhuis, Nieuwegein, Nederland, [9]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, Nederland, [10]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, Nederland.

15.33 Evaluation of Gastroscopy Referrals in Primary Care in the Netherlands (p. 143)

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15.36 Endoscopic Papillectomy; a Delphi consensus (p. 144)

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15.39 Discussie

15.48 Endoscopic expert revision of previous histological confirmed flat low-grade dysplasia in Barrett's esophagus (p. 145)

E.A. Nieuwenhuis[1], S.N. van Munster[1], B.L.A.M. Weusten[2], L. Alvarez Herrero[2], A. Bogte[3], A. Alkhalaf[4], B.E. Schenk[4], E. Schoon[5], W.L. Curvers[5], A.D. Koch[6], M.C.W. Spaander[6], T. Tang[7], W.B. Nagengast[8], J. Westerhof[8], M.H.M.G. Houben[9], J.J.G.H.M Bergman[1], R.E. Pouw[1] [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, location VUmc, Amsterdam, The Netherlands, [2]Dept. of Gastroenterology and Hepatology, Sint Antonius Hospital Nieuwegein, Nieuwegein, The Netherlands, [3]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands, [4]Dept. of Gastroenterology and Hepatology, Isala Clinics, Zwolle, The Netherlands, [5]Dept. of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven, The Netherlands, [6]Dept. of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands, [7]Dept. of Gastroenterology and Hepatology, Ijsselland Hospital, Capelle a/d Ijssel, The Netherlands, [8]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands, [9]Dept. of Gastroenterology and Hepatology, Haga Teaching Hospital, Den Haag, The Netherlands.

15.51 Poor healing and poor squamous regeneration after radiofrequency ablation therapy for early Barrett's neoplasia: incidence, risk factors, and outcomes (p. 146)

C.N. Frederiks[1-3],S.N. van Munster[2-3], L. Alvarez Herrero[3], A. Bogte[1], A. Alkhalaf[4], B.E. Schenk[4], E. Schoon[5], W. Curvers[5], A. Koch[6], S.E.M. van de Ven[6], P.J.F. de Jonge[6], T. Tang[7], W.B. Nagengast[8], F.T.M. Peters[8], J. Westerhof[8], M.H.M.G. Houben[9], J.J. Bergman[2], R.E. Pouw[2], B.L.A.M. Weusten[1-3] [1]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, Nederland, [2]Dept. of Gastroenterology and Hepatology, Amsterdam University Medical Centers, Amsterdam, Nederland, [3]Dept. of Gastroenterology and Hepatology, St. Antonius Hospital, Nieuwegein, Nederland, [4]Dept. of Gastroenterology and Hepatology, Isala Hospital, Zwolle, Nederland, [5]Dept. of Gastroenterology and Hepatology, Catharina Hospital Eindhoven, Eindhoven, Nederland, [6]Dept. of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, Nederland, [7]Dept. of Gastroenterology and Hepatology, IJsselland Hospital, Cappelle a/d IJssel, Nederland, [8]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, Nederland, [9]Dept. of Gastroenterology and Hepatology, Haga Hospital, Den Haag, Nederland.

15.54 Endoscopic submucosal dissection for Barrett's related neoplasia in the Netherlands: results of a nationwide cohort of 130 cases (p. 147)

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15.57 Disruption or disconnection of the pancreatic duct in patients with severe acute pancreatitis: a large prospective multi-center cohort (p. 148)

HC Timmerhuis[1], SM van Dijk[2], RA Hollemans[3], CJ Sperna Weiland[4], L Boxhoorn[5], BJ Witteman[6], R Quispel[7], MP Schwartz[8], J-W Poley[9], MJ Bruno[9], JE van Hooft[10], RP Voermans[11], MG Besselink[12], TL Bollen[13], RC Verdonk[14], HC van Santvoort[15] [1]Dept. of

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16.00 Lumen-apposing metal stents versus double-pigtail plastic stents in the endoscopic step-up approach for infected necrotizing pancreatitis (p. 149)

L. Boxhoorn[1], R.C. Verdonk[2], M.G.H. Besselink[3], M.A. Boermeester[3], T.L. Bollen[4], S.A. Bouwense[5], V.C. Cappendijk[6], W.L. Curvers[7], C.H. Dejong[5], S.M. van Dijk[3], H.M. van Dullemen[8], C.H.J. van Eijck[9], E.J.M. van Geenen[10], M. Hadithi[11], W.L. Hazen[12], P. Honkoop[13], J.E. Van Hooft[14], M.A.J.M. Jacobs[1], E. Kouw[15], S.D. Kuiken[16], M.Ledeboer[17], V.B. Nieuwenhuijs[18], L.E. Perk[19], J.W. Poley[20], R. Quispel[21], R. de Ridder[22], H.C. van Santvoort[23], M.W.J. Stommel[24], H.C. Timmerhuis[25], B.J. Witteman[26], D.S. Umans[1], N.G. Venneman[27], F.P. Vleggaar[28], R.L. van Wanrooij[1], C.J. Sperna Weiland[10], M.J. Bruno[20], P. Fockens[1], R.P. Voermans[1] [1]Dept. of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, The Netherlands, [2]Dept. of Gastroenterology and Hepatology, St. Antonius Hospital, Nieuwegein, The Netherlands, [3]Dept. of Surgery, Amsterdam UMC, Amsterdam, The Netherlands, [4]Dept. of Radiology, St. Antonius Hospital, Nieuwegein, The Netherlands, [5]Dept. of Surgery, Maastricht UMC+, Maastricht, The Netherlands, [6]Dept. of Radiology, Jeroen Bosch Hospital, Den Bosch, The Netherlands, [7]Dept. of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven, The Netherlands, [8]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands, [9]Dept. of Surgery, Erasmus MC University Medical Center, Rotterdam, The Netherlands, [10]Dept. of Gastroenterology and Hepatology, Radboudumc, Nijmegen, The Netherlands, [11]Dept. of Gastroenterology and Hepatology, Maasstad Hospital, Rotterdam, The Netherlands, [12]Dept. of Gastroenterology and Hepatology, Elisabeth-TweeSteden Hospital, Tilburg, The Netherlands, [13]Dept. of Gastroenterology and Hepatology, Albert Schweitzer Hospital, Dordrecht, The Netherlands, [14]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands,[15]Dept. of Gastroenterology and Hepatology, Gelre Hospital, Apeldoon, The Netherlands,[16]Dept. of Gastroenterology and Hepatology, OLVG, Amsterdam, The Netherlands,[17]Dept. of Gastroenterology and Hepatology, Deventer Hospital, Deventer, The Netherlands, [18]Dept. of Surgery, Isala Clinics, Zwolle, The Netherlands, [19]Dept. of Gastroenterology and Hepatology, Haaglanden Medical Center, The Hague, The Netherlands, [20]Dept. of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands, [21]Dept. of Gastroenterology and Hepatology, Reinier de Graaf Gasthuis, Delft, The Netherlands, [22]Dept. of Gastroenterology and Hepatology, Maastricht UMC+, Maastricht, The Netherlands, [23]Dept. of Surgery, University Medical Center Utrecht, Utrecht, The Netherlands, [24]Dept. of Surgery, Radboudumc, Nijmegen, The Netherlands, [25]Dept. of Surgery, St. Antonius Hospital, Nieuwegein, The Netherlands, [26]Dept. of Gastroenterology and Hepatology, Hospital Gelderse Vallei, Ede, The Netherlands, [27]Dept. of Gastroenterology and Hepatology, Medisch Spectrum Twente, Enschede, The Netherlands, [28]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands.

16.03 Postponed or immediate drainage of infected necrotizing pancreatitis (POINTER): a multicenter randomized trial (p. 150)

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16.06 Discussie

16.30 Einde van dit programma onderdeel

Symposium – V&VN MDL – Endoscopie

Voorzitters: *A.P.M. Boersen*

11.30 Anticoagulantia medicatie tijdens endoscopische ingrepen: een bloedstollende ingreep?
Dr. P.R. van der Valk, Internist-hematoloog, Van Creveldkliniek, Utrecht

11.50 Classificatie van poliepen
Dr. F.H.J. Wolfhagen, MDL-arts, Albert Schweitzer Ziekenhuis, Dordrecht

12.10 Endo-Echografie
Dr. L..M. Kager, MDL-arts, Noordwest Ziekenhuisgroep Alkmaar

12.30 Einde van dit programma onderdeel

Symposium – V&VN MDL – IBD

Voorzitters: *M.H. François-Verwey*

14.00 Microscopische colitis
Dr. H.H. Fidder, MDL-arts, Universitair Medisch Centrum Utrecht

14.20 Leefstijladviezen en IBD
R. Theeuwen, verpleegkundig specialist IBD, Leids Universitair Medisch Centrum

14.40 PSC en CU
Dr. A.C. de Vries, MDL-arts, Erasmus MC, Rotterdam

15.00 Einde van dit programma onderdeel

Abstractsessie – V&VN MDL

Voorzitters: *C.J.R. Verstraete en A.N. Reijm*

17.00 Factors influencing health related quality of life in patients with Barrett's Esophagus
M. van der Ende-van Loon, verpleegkundig specialist/ PhD kandidaat, Catharina Ziekenhuis, Eindhoven

17.15 De IBD-verpleegkundige als nieuwe functie in het UMC Utrecht
B. Muskens, verpleegkundig specialist i.o, Universitair Medisch Centrum Utrecht

17.30 Kwaliteitsverbeterplan over voorlichting bij oncologische patiënten, die in verband met passageklachten een stent geplaatst krijgen, in de hoge tractus digestivus.
W. Theunisse, MDL & Oncologieverpleegkundige, Albert Schweitzer Ziekenhuis, Dordrecht

17.45 Fecale incontinentie (FI) bij de oudere IBD patient
D. van den Berg, verpleegkundig specialist IBD, Leids Universitair Medisch Centrum

18.00 Afsluiting programma onderdeel

Insufficient evidence that polygenetic risk scores can be used to predict response to anti-TNFα therapy in inflammatory bowel disease

N. Karmi[1], A. Bangma[1], L.M. Spekhorst[1], H.M. Van Dullemen[1], M.C. Visschedijk[1], G. Dijkstra[1], R.K. Weersma[1], M.D. Voskuil[1], E.A.M. Festen[1] [1]Dept. of Gastroenterology and Hepatology, UMCG, Groningen, The Netherlands.

Background: Anti-tumour necrosis factor alpha (TNFα) therapy is widely used for inducing and maintaining remission in Crohn's disease (CD) and ulcerative colitis (UC). However, up to a third of patients do not respond to induction therapy and another third of patients lose response over time. Identifying predictors of response to anti-TNFα therapy would prevent patients from being needlessly exposed to expensive and ineffective drugs. To aid patient stratification, polygenetic risk scores have been identified as predictors of response to anti-TNFα therapy. This study aimed to replicate the association between polygenetic risk scores and response to anti-TNFα therapy in an independent cohort of IBD patients, to establish its clinical validity.
Methods: Primary non-response, primary response, durable response and loss of response to anti-TNFα therapy was retrospectively assessed for each patient using stringent definitions. Genome wide genotyping was performed and previously described polygenetic risk scores for primary non-response and durable response consisting of 50 genomic variants were calculated. We compared polygenetic risk scores between patients with primary response and primary non-response, and between patients with durable response and loss of response, for CD and UC separately.
Results: A total of 446 patients with IBD treated with anti-TNFα therapy (infliximab or adalimumab) were included in this study. Out of 334 patients with CD, 15 (4%) patients met criteria for primary non-response, 221 (66%) for primary response, 115 (34%) for durable response and 35 (10%) for loss of response. Out of 112 patients with UC, 12 (11%) met criteria for primary non-response, 68 (61%) for primary response, 19 (17%) for durable response and 20 (18%) for loss of response. No significant differences in polygenetic risk scores were found between primary non-responders and primary responders, and between durable responders and loss of responders.
Conclusion: This study failed to replicate the previously reported association between polygenetic risk scores and response to anti-TNFα therapy in an independent cohort of patients with CD or UC. Currently, there is insufficient evidence for clinical use of polygenetic risk scores to predict response to anti-TNFα therapy in patients with IBD.

Dietary inflammatory index and diet quality in inflammatory bowel disease and irritable bowel syndrome patients

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Background: Inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS) patients indicate that diet can exacerbate their symptoms. However, how diet quality relates to inflammation markers and symptom occurrence is not completely clear. We aimed to investigate the relationship of dietary indices with inflammatory markers and gastrointestinal symptoms in IBD and IBS patients.
Methods:A cross-sectional study was performed including 238 IBD patients, 261 IBS patients and 195 healthy controls (HC) of the region South Limburg. A validated 147-item food frequency questionnaire was used to calculate the inflammatory potential of the diet using the Adapted Dietary Inflammatory Index (ADII), and the diet quality using the Dutch Healthy Diet index 2015 (DHD15-index). Faecal calprotectin was used as marker of intestinal inflammation and symptom domains were assessed using the Gastrointestinal Symptom Rating Scale (GSRS). Analyses were performed using multivariable linear regression with covariates age, gender, BMI, age at diagnosis according to the Montreal classification (for IBD) and medication use.
Results: Age was comparable between IBD, IBS and HC. Significantly more women with IBS (74%) were included compared to IBD (52.9%, p<0.001) and HC (63.1%, p=0.007). BMI was significantly lower in HC (23.9±3.8kg/m^2) compared to IBD (25.5±4.2kg/m^2, p<0.001) and IBS (25.0±4.6kg/m^2, p=0.021). ADII scores did not differ between IBD, IBS and HC (0.052±2.41 vs. 0.055±2.47 vs. 0.054±2.33, resp., p>0.099). The DHD15-index was significantly lower in IBD (68.476±16.49) and IBS (71.176±16.57) compared to HC (76.861±17.48; IBD vs. HC: p<0.001; IBS vs. HC: p=0.001). Faecal calprotectin levels were not associated with the ADII in either of the subgroups, but were associated with the DHD15-index in IBD patients only (IBD: b=-3.717, p=0.007; IBS: p=0.700; HC: p=0.356). Additionally, in IBD, significant associations were found for the GSRS domains abdominal pain (b=0.162, p=0.008) and diarrhoea syndrome (b=0.244, p=0.015) with the ADII, and indigestion syndrome (b=-0.019, p=0.031) with the DHD15-index. In IBS, the DHD15-index was significantly associated with abdominal pain (b=-0.011, p=0.028) and reflux syndrome (b=-0.014, p=0.016). No associations were found with the ADII in IBS nor with any of the dietary indices in HC.
Conclusion: A more pro-inflammatory diet and a lower overall diet quality were associated with higher symptom scores in IBD and IBS, and a lower diet quality with more intestinal inflammation in IBD. Current findings support the need for further research on the role of diet on disease course and gastrointestinal symptoms in these patients.

A randomized trial of aggressive fluid hydration to prevent post-ERCP pancreatitis (FLUYT)

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Background: Pancreatitis is the most common complication of endoscopic retrograde cholangiopancreatography (ERCP). Rectal non-steroidal anti-inflammatory drugs (NSAID) reduce post-ERCP pancreatitis rates and are current standard-of-care as per European and American guidelines. A number of studies suggest that aggressive periprocedural hydration is effective and safe in reducing post-ERCP pancreatitis. However, patients in these studies did not receive rectal NSAID. It is therefore unclear whether periprocedural hydration affords additional protection against post-ERCP pancreatitis in a population treated with rectal NSAIDs. Thus, we performed a randomized trial to investigate whether periprocedural hydration with Lactated Ringer's solution can prevent post-ERCP pancreatitis in moderate- to high-risk patients undergoing ERCP who already receive prophylactic rectal NSAID.

Methods: In this multicenter, parallel-group open-label randomized controlled superiority trial, patients with moderate- to high-risk of post-ERCP pancreatitis were assessed for eligibility in 22 Dutch hospitals. Patients were randomly assigned (1:1) by a web-based module with varying block sizes to a combination of aggressive hydration and rectal NSAIDs (hydration group) or rectal NSAIDs monotherapy (control group). Aggressive hydration comprised 20mL/kg lactated Ringer's intravenously from the start of ERCP within 60 minutes, followed by 3mL/kg/h for 8 hours. The control group received normal saline with a maximum of 1.5mL/kg/h and 3L/24h. The primary endpoint was post-ERCP pancreatitis. Secondary endpoints included pancreatitis severity and ERCP- and hydration-related complications. ISRCTN registry, identifier ISRCTN13659155.

Results: A total of 826 patients were randomized. Patient baseline and ERCP characteristics were similar in both groups. Post-ERCP pancreatitis developed in 30 of 388 patients (8%) in the hydration group and in 39 of 425 patients (9%) in the control group (relative risk, 0.84; 95% confidence interval [0.53-1.33]; P=0.53). 21 patients (5%) in the hydration group and in 32 patients (8%) in the control group (P=0.39) developed a moderate-to-severe pancreatitis. ERCP- and hydration-related complications did not differ between both groups (P=0.6 and P=1.0, respectively). There were no differences in other secondary endpoints, including serious adverse events.

Conclusion: The combination of aggressive periprocedural hydration and rectal NSAIDs was not superior in reducing the incidence of post-ERCP pancreatitis, as compared to rectal NSAID monotherapy in patients with moderate- to high- risk of post-ERCP pancreatitis.

Locally injected allogeneic bone marrow-derived mesenchymal stromal cells for the treatment of refractory proctitis: clinical results of a phase IIa trial.

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Background: Ulcerative proctitis (UP) can be refractory to treatment, which calls for development of new (local) therapies. Local injection of mesenchymal stromal cells (MSCs) has shown beneficial effects in patients with fistulizing Crohn's disease and promising results have been obtained when MSCs were locally injected in the bowel of mice with experimental colitis . Therefore, our primary aim was to determine the safety, feasibility and tolerability of endoscopically injected allogeneic bone marrow-derived MSCs (bmMSCs) in UP patients.
Methods: UP patients with endoscopic MAYO score (EMS) 2 or 3, who failed on both rectal 5-ASA and corticosteroids for at least 4 weeks, were eligible for inclusion. Rectal therapies were stopped 2 weeks prior to baseline, but other medications were kept constant until at least 6 weeks after MSC administration. MSCs were locally injected in 4 places of the inflamed rectal submucosa if the inflammation was limited to 7 cm and if the length of inflammation was >7 cm MSCs were injected in 8 places. Patients in the 1st cohort (n=7) were treated with $5*10^6$ MSCs/spot and in the 2nd cohort (n=6) with $10*10^6$MSCs/spot. Adverse events, clinical Mayo score, biochemical parameters, EMS, and quality of life (QoL), sIBDQ, were assessed at baseline and at week 2, 6, 12 and 24, and evaluated by non-parametric paired statistical analyses.
Results: Of the thirteen patients included, the reported adverse events were minor, none required interventions and no feasibility issues were reported. Median[interquartile range (IQR)] clinical Mayo score was 11[9.5-12] at baseline, 9[8-11] at week 2 (p=0.005), 8[6-10] at week 6 (p=0.003) and 4[1.5-7] at week 24 (p=0.001). The Fecal Calprotectin (FCP) improved in 9/13 patients at week 2, in 6/13 patients at week 6 and in 11/13 patients at week 24 compared to baseline. The EMS at baseline was 3 (n=10 patients) and 2 (n=3 patients) and improved in 3 patients at week 2 (p=0.08, 1 point improvement) in 4 patients at week 6 (p=0.05, 1 point improvement) and in 10 patients at week 24 (p=0.004), of whom 7 improved with 2 points and 3 with 1 point. Median[IQR] sIBDQ showed improvement of QoL during follow-up; week 2 (45(37.5-52);p=0.12), 6 (47(42.50-55);p=0.02), 12 (59(39.50-62);p=0.004) and 24 (56(44.50-64.50);p=0.002) compared to baseline (41 (34-49,50)). No dose response effect was observed in our study when comparing cohort 1 and 2.
Conclusion: Local administration of allogeneic bmMSCs appears safe, tolerable and feasible for the treatment of refractory UP and shows encouraging signs of clinical efficacy. Further mechanistic and immunological analyses are anticipated.

Histopathological features at Crohn's disease diagnosis as predictors for long-term disease course: results from the population-based IBD South-Limburg cohort

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Background: Crohn's disease (CD) is characterized by a heterogeneous disease course and treatment response. Patient stratification using clinical markers is not sufficient for clinical decision making. Therefore, this study aimed to investigate the additive predictive value of histopathological features at diagnosis to discriminate between patients with a long-term mild and severe disease course.
Methods: Endoscopic biopsies, taken at time of CD diagnosis, from treatment-naïve patients with mild or severe disease courses, based on number of quarterly flares in the first 10 years after diagnosis, were examined retrospectively by two senior GI pathologists using a standardized form to score 15 histopathological features related to acute and chronic inflammation. Two multivariable logistic regression models were built. Model 1 included clinically relevant baseline characteristics alone (Montreal Classification, smoking status and gender). Next, histopathological features were added by applying two different model-building strategies (forward selection and purposeful selection algorithm)(Model 2). Predicted probabilities were calculated and used to compute receiver operating characteristics (ROC) curves. Prediction models were internally validated using bootstrapping to obtain optimism-corrected performance estimates.
Results: In total, 817 biopsies from 137 CD patients (64 mild disease course, 73 severe disease course) were included. Based on clinical baseline characteristics alone, disease course could only be moderately predicted (Model 1 Area under ROC (AUROC): 0.738 (optimism 0.018), 95%CI 0.65-0.83, sensitivity 83.6%, specificity 53.1%, PPV 67.0%, NPV 73.9%). When adding histopathological features, in colon biopsies a combination of (1) basal plasmacytosis, (2) severe lymphocyte and plasma cell infiltration in the lamina propria, (3) Paneth cell metaplasia and (4) absence of ulcers were identified and resulted in significantly better prediction of a severe course (Model 2 AUROC: 0.883 (optimism 0.033), 95%CI 0.82-0.94, *p* < 0.001, sensitivity 80.4%, specificity 84.2%, PPV 83.3%, NPV 81.4%). In contrast, no additive predictive value of histopathological features was found for ileal biopsies.
Conclusion: In this first study investigating the additive predictive value of histopathological features in biopsies from time of CD diagnosis, we found that certain features of chronic inflammation in colon biopsies contribute to prediction of a long-term severe disease course, thereby presenting a novel approach to improve patient stratification and facilitate clinical decision making.

Healthy cotwins share gut microbiome signatures with their inflammatory bowel disease twins and unrelated patients

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Background: It is currently unclear whether reported changes in the gut microbiome are *cause* or *consequence* of inflammatory bowel disease (IBD). Therefore, we studied the gut microbiome of IBD-discordant and -concordant twin pairs, which offers the unique opportunity to assess individuals at increased risk of developing IBD, namely healthy cotwins from IBD-discordant twin pairs.
Methods: Fecal samples were obtained from 99 twins (belonging to 51 twin pairs), 495 healthy age-, sex- and BMI-matched controls,and 99 unrelated IBD patients. Whole-genome metagenomic shotgun sequencing was performed. Taxonomic and functional (pathways) composition were compared between healthy-cotwins, IBD-twins, healthy controls, and unrelated IBD patients with multivariable, i.e. adjusted for potential confounding, generalized linear models.
Results: No significant differences were observed in the relative abundance of species and pathways between healthy cotwins and their IBD-twins (false discovery rate (FDR)<0.1). Compared to healthy controls, 13, 19, and 18 species, and 78, 105, and 153 pathways were found to be differentially abundant in healthy-cotwins, IBD-twins and unrelated IBD patients, respectively (FDR<0.1). Of these, 8/19 (42,1%) and 1/18 (5,6%) species, and 37/105 (35.2%) and 30/153 (19,6%) pathways overlapped between healthy cotwins and IBD-twins, and healthy cotwins and unrelated IBD patients respectively. Most of the shared species and pathways have previously been associated with IBD. The shared pathways include potentially inflammation-related pathways, for example: an increase in propionate degradation and L-arginine degradation pathways.
Conclusion: The gut microbiome of healthy cotwins from IBD-discordant twin pairs displays IBD-like signatures. These IBD-like microbiome signatures might precede the onset of IBD.

Western and carnivorous dietary patterns are associated with greater likelihood of IBD occurrence in a large prospective population-based cohort

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Background: Dietary modifications are often used as complementary strategies by patients with Crohn's Disease (CD) or Ulcerative Colitis (UC) and might also be effective as primary prevention in the general population. Here, we associated dietary patterns and scores with IBD-occurrence in a population-based cohort.
Methods: Participants prospectively answered health-related and dietary questionnaires (FFQ). Of 124,885 participants, 190 developed UC and 73 CD over a maximum 11-year follow-up period. Principal Component Analysis (PCA) was conducted to derive *a-posteriori* dietary patterns and several *a-priori* hypotheses-based dietary scores were calculated, including the Protein score, Healthy Eating Index, LifeLines Diet Score (LLDS) and alternate Mediterranean Diet Score. Logistic regression models were performed between dietary patterns, scores and IBD-occurrence.
Results: Five dietary patterns were identified using PCA. Adherence to a pattern characterized by high intakes of condiments, non-alcoholic beverages, prepared meals, and snacks and low intakes of vegetables and fruits, was associated with higher likelihood of CD occurrence (OR: 1.17, 95% CI: 1.02-1.32, p=0.017). A pattern comprising poultry, processed meat and red meat, was associated with increased likelihood of UC-occurrence (OR: 1.11, 95% CI: 1.01-1.22, p=0.024). A high diet quality score (LLDS) was associated with decreased risk of reporting UC (OR: 0.97, 95% CI: 0.95-1.00, p=0.03).
Conclusion: A Western dietary pattern was associated with higher likelihood of CD-occurrence and a carnivorous pattern with UC-occurrence, while relative high diet quality (LLDS), was negatively associated with UC-occurrence. Our study strengthens the importance of evaluating dietary patterns and scores to aid prevention of IBD in the general population.

Host-genetics, dysbiosis, and clinical history explains fecal metabolic alterations in patients with inflammatory bowel disease

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Background: Gastrointestinal dysbiosis has been suggested as a key factor in the pathogenesis of inflammatory bowel diseases. The mechanisms driving the alterations of the gut microbiota composition are, however, not fully understood. Bacteria establishes multiple relations with the host, being the metabolism of nutrients one of the most relevant ones. We hypothesize that the study of small molecules present in fecal samples can help us to understand the relations between the host and its gut microbiota, to characterize the metabolic changes in IBD, and, to reveal new biomarkers for the disease.
Methods: We explored the relationship between host genetics, gut microbiota and fecal metabolites composition of 500 patients with IBD and 255 population controls. In short, we used shotgun sequencing to profile the microbiota composition, and untargeted metabolomics platform (Metabolon INC, USA) was used to identify the levels of 1684 fecal metabolites and 8 short chain fatty-acids. Whole exome sequencing and GSA Illumina chip were used to characterize host's genetics. Linear regression models were used to integrate different omics layers and correct for potential confounders.
Results: Patients with IBD showed marked alterations in the fecal metabolite composition. The levels of 597 metabolites were altered in Crohn's disease and 209 in patients with ulcerative colitis as compared to the controls (FDR<0.05). Interestingly, metabolic profiles could discriminate IBD samples from non-IBD samples (Random Forest AUC= 0.81). Patients with surgeries in the ileum presented an altered bile-acid metabolism. Moreover, we could identify the use of medication and dietary patterns based on the presence of certain metabolites. Furthermore, 3 host genetic loci were associated with metabolites, including the association between *NAT2* gene and coffee metabolites. We observed a strong correlation between the overall gut microbiota composition and the metabolomic profile, suggesting a link between bacteria and fecal metabolites. In fact, gut microbiota composition could explain more than 30% of the variation in the levels of 250 metabolites. For example, *Faecalibacterium prausnitzii* was strongly correlated with the levels of butyrate, while *Ruminococcus gnavus* with tryptamine (FDR<0.05).
Conclusion: Gut dysbiosis is translated into the alteration of the fecal metabolic profile. Metabolite levels can be used to distinguish IBD from non-IBD individuals. Moreover, we observed a strong correlation between various metabolites and bacterial species which could lead to new therapeutic approaches

The effect of phenotype and genotype on the plasma proteome in patients with inflammatory bowel disease

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Background: Protein profiling in patients with inflammatory bowel diseases (IBD) for diagnostic and therapeutic purposes is underexplored. Assessment of interactions between genetics and the plasma proteome could lead to identification of novel disease-associated molecular pathways. In this study, we performed the largest gene-protein association analysis thus far in patients with IBD, taking into account relevant phenotypic covariates and integrating information from multiple biological data layers.
Methods: Ninety-two (92) inflammation-related proteins were quantified in plasma of 1,028 patients with IBD (567 Crohn's disease [CD]; 461 ulcerative colitis [UC]) to assess proteome-phenotype associations. Both whole-exome sequencing data and a genome-wide genotyping array (*Global Screening Array*) of 919 patients with IBD were included to study associations between over 8 million genetic variants and protein levels (*protein quantitative trait loci* [pQTL]). *Cis*-pQTLs were defined within ± 1 Mb of the region of each protein-coding gene center, whereas *trans*-pQTLs were outside of that region. After adjusting for phenotypic covariates, a step-wise conditional analysis was used to identify all independent pQTLs in CD and UC separately, followed by a meta-analysis. Intestinal mucosal RNA sequencing and fecal metagenomic data were used for complementary analyses.
Results: Seventy-two (72) proteins were significantly associated to 14 phenotypic factors, including age, sex, medication, and surgical history. Drug-protein association analyses revealed that FMS-like tyrosine kinase 3 ligand (Flt3L) levels were elevated in thiopurine users. Fibroblast growth factor-19 (FGF-19) levels were decreased in CD patients with ileal disease or a history of ileocecal resection. Thirteen (13) novel *cis*-pQTL variants were identified and 10 replicated from previous studies, together affecting 21 different plasma proteins. One *trans*-pQTL variant of the *FUT2* gene (rs602662) and two independent *cis*-pQTL variants of the *CCL25* gene significantly affected plasma C-C motif chemokine ligand 25 (CCL25) levels. Intestinal gene expression data revealed an overlapping *cis*-expression (e)QTL-variant (rs3745387) of the *CCL25* gene. The *FUT2* rs602662 *trans*-pQTL variant associated significantly with reduced abundances of multiple fecal butyrate-producing bacteria, including the genus *Blautia* and the species *Faecalibacterium prausnitzii*.
Conclusion: This study shows that both genotype and multiple disease phenotypes strongly associate with the plasma proteome in patients with IBD and identifies disease-associated pathways that may help to improve disease management in the future.

Inflammation status modulates the effect of host genetic variation on intestinal gene expression in inflammatory bowel disease

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Background: Although genetics is known to be associated with Inflammatory bowel disease (IBD), it is still poorly understood how it contributes to disease development. The effect of genetic variation on gene expression (expression quantitative trait loci— *cis*-eQTLs) has mostly been studied by combining GWAS and transcriptome data from peripheral blood. However, the importance of studying these eQTLs in the disease- tissue and in the right disease- context is increasingly being recognized. We set out to examine the effect of genetic variants on gene expression in intestinal mucosal biopsies of IBD patients, in both inflamed and non-inflamed conditions, to identify inflammation-dependent eQTLs.
Methods: We collected 299 snap-frozen intestinal biopsies from 171 IBD patients, 113 deriving from non-inflamed tissue and 186 from inflamed tissue. Mucosal transcription profiles were determined by RNA-sequencing and genotypes were obtained by Whole Exome Sequencing (WES) combined with Genome Wide Screening Array (GSA) data. In total, 28,746 genes and SNPs located in +/- 500kb genomic regions surrounding these genes were included for identifying *cis*-eQTLs. *cis*-eQTLs were identified using linear mixed models and by regressing out the effect of potential confounding variables. To explore the effect of genetic variants in the context of inflammation, we then assessed the *cis*-eQTLs in inflamed versus non-inflamed tissue.
Results: Overall, 419,858 *cis*-eQTLs were found to be significant in gut tissue (FDR<0.05), with replication rates > 90% compared with Genotype-Tissue Expression (GTEx) datasets, showing robustness of our method. The inflammation-interaction analysis revealed 8.881 inflammation-dependent *cis*-eQTLs in 190 unique genes (FDR<0.05). We identified inflammation-dependent *cis*-eQTLs involving known IBD-associated genes and immune-cell receptors and antibodies, *IL26*, *HLA-DQA1*, *HLA-DQA2* and *TREML4*. The inflammation-dependent *cis*-eQTL SNPs (eSNPs) mainly interact with prevalence of immune cell types.
Conclusion: Inflammation-dependent intestinal *cis*-eQTLs reveal genetic susceptibility under inflammatory conditions that can help identify the cell types involved in and the pathways underlying inflammation, knowledge that may guide future drug development and profile patients for precision medicine in IBD.

Point-of-Care Intestinal Ultrasound provides additional information about disease activity in pediatric Crohn's Disease patients visiting the outpatient department

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Background: Pediatric Crohn's Disease (CD) patients need to be monitored frequently in order to detect disease activity timely. Point of Care Intestinal Ultrasound (POCUS) may provide useful information in addition to other surrogate markers of disease activity, such as fecal calprotectin (FC). We aimed to assess how often POCUS leads to a different classification of disease activity than FC.
Methods: In this ongoing prospective cohort study, consecutive CD patients aged 3-17 years visiting the outpatient department undergo a POCUS examination, in addition to FC tests. POCUS is performed within two weeks of FC analysis without change in treatment. FC results are categorized in three categories: low (0-250 mg/kg), uncertain (250-500 mg/kg) and high (>500 mg/kg). An abnormal POCUS is defined as: increased bowel wall thickness (BWT) (>2.5 mm) combined with either hyperemia and/or mesenteric fat proliferation. In case of borderline BWT without other signs of inflammation, POCUS is defined as uncertain. Treating physicians are blinded to POCUS results, unless a stenosis/fistula/abscess is noted, or unless treating physicians need the result in order to choose the right (e.g. local vs. systemic) treatment.
Results: A total of 35 CD patients were included in this interim analysis (mean (SD) age: 16 (2) years, range 9-17, 18 (51%) male). FC levels were low, uncertain and high in 20 (57%), 4 (11%) and 11 (31%) patients respectively. Of the patients with low FC levels, nine (45%) had a normal POCUS, five (25%) an uncertain and six (30%) an abnormal POCUS. Of the patients with an uncertain FC level, one (25%) had a normal and three (75%) an abnormal POCUS. Of the patients with a high FC level, 10 (91%) had an abnormal- and one (9%) an uncertain POCUS. POCUS results were disclosed in 4 (17%) patients; one time because of a stenosis, and in the other cases the physician needed the POCUS results to choose the right treatment.
Conclusion: POCUS leads to a more severe classification of disease activity in one third of pediatric CD patients with a low FC level and demonstrates inflammation in the majority of patients with an uncertain FC level. These results suggest that regular POCUS provides useful additional information about disease activity in children with CD. More research on the clinical implications of discrepancy in classification of disease activity is needed.

Decrease in bowel wall thickness at intestinal ultrasound accurately detects early endoscopic remission and treatment response in ulcerative colitis patients on tofacitinib: a longitudinal prospective cohort study

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Background: Intestinal ultrasound (IUS) highly correlates with endoscopic outcomes when assessing disease activity. However, few studies evaluated treatment response in ulcerative colitis (UC) with IUS. In this study we evaluate IUS to determine treatment response in moderate-severe UC with blinded IUS, endoscopy and histology at multiple time points.
Methods: Patients with moderate-severe UC (endoscopic Mayo score (EMS)≥2) extending the rectum starting tofacitinib 10 mg bid were included. Disease activity was evaluated with clinical scores (SCCAI), fecal calprotectin (FCP), IUS and endoscopy with biopsies from the sigmoid (SC) and descending colon (DC) at baseline and at 8 weeks. Bowel wall thickness (BWT) and EMS were assessed per segment (SC and DC). Histology was scored with the Geboes score (GS). Endoscopy and histology were centrally read and IUS cine-loops were read by two readers and blinded to patient information. Endoscopic remission was defined as EMS=0, endoscopic improvement as EMS≤1, endoscopic response as a decrease of EMS≥1, clinical remission as SCCAI<5 and biochemical remission as FCP≤250mg/kg. A linear mixed model was used for statistical analysis. Correlation was analyzed with a Spearman's test. Area under the ROC was used to determine cut-off values. Inter-observer agreement was analyzed by intra-class correlation coefficient (ICC).
Results: 29 patients were included and started tofacitinib. 64% reached clinical, 39% biochemical, and 10% endoscopic remission after 8 weeks. EMS per-segment analysis showed 21% and 39% reaching remission and 41% and 65% having improvement in the SC and DC, respectively. BWT in SC and DC correlated highly with EMS (rho=0.68, rho=0.75,both p<0.0001) and GS (rho=0.55,p=0.003, rho=0.43,p=0.029). Patients with EMS≥2 had increased BWT (SC:mean:5.05±1.63 mm vs 2.04±0.85 mm,p<0.0001 and DC:mean:5.27±2.22 mm vs mean: 2.80±1.41 mm,p<0.0001) compared to patients with EMS≤1 in the similar segment. BWT decreased after 8 weeks when there was endoscopic response (SC: mean:-3.41±1.74 mm vs -0.78±1.67 mm,p=0.001 and DC: mean:-2.42±3.02 mm vs -0.50±1.23 mm,p=0.04). BWT cut-off values for segmental endoscopic remission were 2.87 mm and 2.80 mm for the SC and DC, respectively. Furthermore, agreement for BWT in the SC and DC was excellent (ICC:0.91) and moderate (ICC:0.71), respectively.
Conclusion: BWT reduction correlated with histology and early endoscopic response and remission after 8 weeks of tofacitinib treatment. Furthermore, accurate cut-off values for BWT in SC and DC were found for endoscopic remission and response. Therefore, this non-invasive and accurate modality should be incorporated in the standard follow-up and close monitoring of UC patients.

Appropriateness of Proton Pump Inhibitor Prescriptions in Clinical Practice

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Background: Proton pump inhibitors (PPIs) are commonly used in daily clinical practice. They are particularly indicated for treatment of gastroesophageal reflux disease and peptic ulcer disease, and for the prevention of gastroduodenal lesions due to risk medication (non-steroidal anti-inflammatory drugs (NSAIDs) and low-dose acetylsalicylic acids (LDASA)) use or previous peptic ulcer (gastroprotection). Nonetheless, PPIs are also frequently used for inappropriate indications. In this study, we aimed to evaluate the appropriateness of PPI prescriptions in general practice (GP) in the Netherlands.
Methods: Encoded data of the ELAN database containing GP patients in the region Leiden/Den Haag were used. We retrospectively identified all PPI prescriptions between 2016 and 2018. Demographics, clinical data and details on PPI use were collected. Appropriateness of PPI prescriptions was evaluated using the Dutch College of General Practitioners guideline 'Upper gastrointestinal symptoms' (version 2013). Chronic PPI use was defined as > 180 Defined Daily Doses/year.
Results: A total of 148,926 adult patients from 27 general practices were assessed. We identified 32,401 PPI usage periods in 23,601 patients (16% of total). Median age at prescription was 58 years (IQR 45-70) of whom 59% were female. About 30% fulfilled the criteria for chronic PPI use. In 18,228 (56%) of PPI usage periods, no valid indication was identified. Treatment of upper gastrointestinal symptoms (n=7,056, 22%) and/or gastroprotection (n=7,632, 24%) were the most common indications for the 14.173 (44%) appropriately prescribed PPI's. Dyspepsia was the leading upper gastrointestinal symptom for PPI prescriptions (n=5,144, 16%). NSAID and/or LDASA use were responsible for respectively 18% and 5% of PPI prescriptions. Despite cessation of risk medication, almost 18% of PPIs were continuously used for a period of more than three months.
Conclusion: More than half of PPIs are prescribed for an inappropriate indication in a GP population in the Netherlands. Interventions are needed to educate physicians to prescribe PPIs according to accepted indications and duration of use.

A trial-based economic evaluation of peppermint oil for the treatment of Irritable Bowel Syndrome

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Background: Irritable Bowel Syndrome (IBS) is a highly prevalent and incurable gastrointestinal disorder and imposes a substantial socioeconomic burden. Peppermint oil is among the most frequently used treatments for IBS, but evidence about cost-effectiveness is lacking. The objective of this trial-based economic evaluation was to assess the cost-effectiveness of peppermint oil versus placebo in patients with IBS. Two formulations were investigated; small-intestinal and ileocolonic release peppermint oil.
Methods: In a multicenter randomized placebo-controlled clinical trial, data on cost-effectiveness were evaluated from a societal perspective. The incremental cost-effectiveness ratios were expressed as 1) incremental costs per Quality Adjusted Life Years (QALY), and 2) incremental costs per successfully treated patient, *i.e.* per abdominal pain responder (according to FDA definitions), both after an eight-week treatment period. Cost-utility and uncertainty were estimated using the non-parametric bootstrapping method. Sensitivity analyses were performed to examine parameter uncertainty.
Results: The analysis comprised 189 patients (*N*=64 placebo, *N*=62 small-intestinal peppermint oil, *N*=63 ileocolonic peppermint oil). At a conservative willingness-to-pay threshold of €25.000 per QALY, small-intestinal peppermint oil was the most cost-effective treatment in 51% of bootstrap replications, versus 35% in ileocolonic peppermint oil, versus 14% in placebo. Small-intestinal peppermint oil was also most cost-effective per additional successfully treated patient according to FDA definitions, *i.e.* in 81% of replications. Cost-effectiveness planes and sensitivity analyses showed some uncertainty of the results.
Conclusion: In patients with IBS, small-intestinal release peppermint oil is a cheap and cost-effective treatment, when compared to placebo in an eight-week treatment.

Factors affecting the placebo response rate in pharmacological trials in patients with irritable bowel syndrome – a systematic review and meta-analysis

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Background: Clinical trials in irritable bowel syndrome (IBS) are associated with high placebo response rates. We aimed to identify the magnitude and the contributing factors to this placebo response rate in pharmacological trials in IBS.
Methods: We conducted a systematic review and meta-analysis with a medical search on MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials between 1959 and April 2020. We included all randomized controlled trials (RCTs) in adult patients with IBS that compare an active pharmacotherapeutic agent with placebo. We extracted information form published reports and pooled proportions through meta-analysis with random effects. The pooled response rate was examined for the following endpoints: global improvement responder, abdominal pain responder and the FDA endpoints. Several variables were examined to investigate the moderating effect on the placebo response. The study was registered with PROSPERO, CRD42020170908.
Results: Of the 6863 publications identified, 73 RCTs were included in this our analysis. The pooled placebo response rate was 27.3% (95% CI 24.3%-30.9%) using the global improvement-, 34.4% (95% CI 31.2%-37.8%) using the abdominal pain- and 17.9% (95% CI 15.2%-21%) using the composite FDA endpoint responder definition, all with substantial heterogeneity between the trials. Studies published prior to 2006, conducted in Europe, with a parallel design, a run-in period of ≤ two weeks, a dosage schedule of ≥ three times a day, and a smaller sample size of the control group were significantly associated with a higher pooled placebo response rate.
Conclusion: The pooled placebo response rate in pharmacological trials in IBS is 27.3% for the global improvement responder endpoint. Multiple moderators were associated with the pooled placebo response rate; we recommend future trials to apply a run-in period of at least two weeks without placebo and a daily dosage of one or two times a day.

Do patients' and physicians' perspectives differ on preferences for IBS treatment? - a qualitative study to explore attributes for quantitative preference elicitation

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Background: IBS is a highly prevalent disorder of the gut-brain interaction and poses a significant burden to patients and the health care system. Pharmacotherapy, diet and psychotherapy all have largely comparable clinical efficacy. Therefore, factors outside efficacy can have an important impact in determining preferences for a specific therapeutic entity. The aim of this study is to perform qualitative research to prepare quantitative preference elicitation in the management of Irritable bowel syndrome (IBS). Perspectives of both patients and physicians will be compared and attributes and levels will be selected for development of a discrete choice experiment (DCE).
Methods: Semi-structured interviews were performed among IBS patients (n=8) and surveys were sent to physicians involved in IBS care (n=15). To identify most relevant treatment aspects, the level of importance was ranked for each attribute. Final definitions and levels were set during an expert opinion meeting.
Results: The survey and interviews took place between June and September 2020. Nine potential attributes for use in DCE were revealed: effectiveness, time until response, cessation of response, side effects, location, waiting period, treatment burden, frequency of healthcare appointments and willingness to pay. Effectiveness, duration of response, side effects and treatment burden were all scored as important by patients and physicians. Time to response, location and waiting time were less important for patients compared to physicians.
Conclusion: This study assessed potential attributes and levels regarding preferences for IBS treatments by qualitative research. A future discrete choice experiment about this topic will help us find a more personalized treatment among this heterogenous category of patients.

Examining the optimal cut-off values of HADS, PHQ-9 and GAD-7 as screening instruments for depression and anxiety in Irritable Bowel Syndrome

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Background: Self-rating scales are frequently used to screen for anxiety and depression in patients with Irritable Bowel Syndrome (IBS). Different cut-off values are recommended in literature and guidelines have suggested the use of other screening instruments over time. The aim of this study was to assess the correlation between the most commonly used psychological screening instruments for anxiety and depression in IBS and to compare custom cut-off scores for these instruments.
Methods: IBS patients (n=192) completed several questionnaires including the Hospital Anxiety and Depression Scale (HADS, HADS-A and HADS-D subscale), Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7). Agreement at different cut-off points, for depressive and anxiety disorder, was assessed by use of the Gwet AC1 coefficient.
Results: HADS-D and PHQ-9 scores, and HADS-A and GAD-7 scores showed high correlations (r_s= 0.735 and r_s=0.805, respectively). For depressive disorder, a Gwet AC1 value of 0.829 was found when recommended cut-off points from literature were compared (PHQ-9 cut-off ≥10, HADS-D cut-off ≥8). For anxiety disorder, a Gwet AC1 value of 0.806 was found when recommended cut-off points from literature were compared (GAD-7 cut-off ≥10, HADS-A cut-off ≥8). Even higher agreements were found when higher HADS cut-off values were chosen, with impact on sensitivity and specificity. Conclusion: Custom cut-off values deem the HADS subscales (HADS-D and HADS-A) concordant to PHQ-9 and GAD-7 scores. The choice of a cut-off value has substantial impact on sensitivity/specificity and is dependent on patient population, setting, and the purpose of use.

The interplay between stress and fullness in functional dyspepsia and healthy controls: an exploratory experience sampling method study

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Background: Fullness is a cardinal symptom in functional dyspepsia (FD). The use of real-time symptom assessment might provide more insight in factors, such as stress, that can influence fullness. Currently, it is unknown whether real-time assessment of fullness is able to capture the construct early satiation. Therefore, this study aimed to use a real-time, repeated measurement method (Experience Sampling Method, ESM) to primarily assess the association between stress and fullness in FD patients and healthy controls (HC). Second, this study aimed to evaluate whether real-time assessment of fullness can capture the construct early satiation.
Methods: Thirty-five FD patients (25 female, mean age 44.7 years) and 34 healthy controls (HC, 24 female, mean age 44.1 years) completed ESM (a maximum of 10 random moments per day) for seven consecutive days. Stress, fullness, and the ability to finish meal scores were rated on an 11-point Numeric Rating Scale.
Results: FD patients scored 2.24 points higher on fullness (*p<0.001*), 1.37 points higher on stress (*p<0.01*), and 1.94 points lower on ability to finish meals (*p<0.001*) compared with HC. In FD, fullness scores increased with 0.14 for every 1-point increase in concurrent stress scores (*p=0.01*) and increased with 0.20 for every 1-point decrease in ability to finish meal (p<0.001). Fullness scores at t=0 increased with 0.09 for every 1-point increase in stress scores at t=-1 (*p=0.02)*. No associations between stress scores or ability to finish meals and fullness scores were found for HC.
Conclusion: Concurrent and preceding stress scores are associated with fullness scores in FD patients, but not in HC, indicating a difference in response to stress. Moreover, real-time assessment of the symptom fullness is able to capture the construct early satiation.

The Dutch Microbiome Project defines factors that shape the healthy gut microbiome

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Background: The gut microbiome is associated with numerous diseases, but the definition of a healthy and unhealthy microbiome remains elusive, and it is unclear how genetics, environment, lifestyle and diet shape the microbiome. The aims of this project are to establish microbiome patterns associated with health, to identify pathobionts in diseases, and to determine how genetics, host characteristics, and early life and current exposures shape the microbiome.
Methods: We collected stool samples and used metagenomic sequencing to characterize composition and function (biochemical pathways, virulence factors and antibiotic resistance) of gut microbiota of 8,208 Dutch individuals (age range 8-84, 57.4% female) from a three-generational cohort comprising 2,756 families. We then correlated these features to 241 host and environmental factors, including physical and mental health, medication use, diet, socioeconomics and childhood and current exposures. Unsupervised clustering and machine-learning were used to define healthy microbiome and pathobionts associated with individual diseases and shared across disease groups. Additionally, we quantified microbiome variance explained by phenotypes, and used family structures and co-housing data to quantify microbiome heritability using the variance components model of heritability.
Results: By identifying 2,856 significant associations (FDR < 0.05) between microbiome and health, we find that seemingly unrelated diseases share a common signature that is independent of comorbidities. Disease-associated microbiome is characterized by an increase in opportunistic pathogens of genera *Clostridium, Gordonibacter* and *Eggerthela,* a reduction in carbohydrate catabolism and synthesis of amino-acid and vitamins, and by an increase in antibiotic resistance and virulence. The healthy microbiome is associated with an increase of butyrate producers from genera *Alistipes, Roseburia, Faecalibacterium* and *Butyrivibrio.* The microbiome composition and function is significantly explained (FDR < 0.05) by host factors (such as age, sex, BMI), and current as well as early-life exposures (including diet, pets, smoking and rural environments). Genetics explains a minor part of the variance, with 26 microbial taxa significantly heritable (FDR < 0.1), none of which is an opportunistic pathogen.
Conclusion: We demonstrate that unrelated diseases share common gut microbiome patterns. The microbiome is primarily shaped by the environment and lifestyle, but the healthy microbiome has a heritable component. Microbiome alterations through improving diet, lifestyle and the environment, and use of probiotics are a promising strategy for improvement of general health.

Growth and fat mass, but not fat-free mass, are compromised in infants with parenteral nutrition need after neonatal intestinal surgery

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Background: Children with intestinal failure (IF) receiving long-term home parenteral nutrition (PN) have an altered body composition (BC), but early data on BC changes from the start of PN onwards are lacking. We aimed to assess growth and BC in infants after neonatal intestinal surgery necessitating PN, and to explore associations with clinical parameters.
Methods: In this prospective cohort study, infants were included after intestinal surgery. IF was defined as PN-dependency for >60 days. Standard deviation scores (SDS) for anthropometric parameters were calculated until 6 months corrected age (ca). In a subgroup, fat mass (FM) and fat-free mass (FFM) were measured with air-displacement plethysmography (ADP) at 2 and 6 months ca, and SDS for FM, FFM, FM index (=FM in kg / (length in m)^2) and FFM index were calculated. The association between the cumulative amount of PN (PNcum=area-under-the-curve of duration x energy percentage from PN) and anthropometric and BC parameters was evaluated with linear regression analyses correcting for sex and gestational age.
Results: Overall, 90 neonates were included (53% boys, 67% preterm, median birth weight -0.1 SDS) after surgery for gastroschisis (35%), necrotising enterocolitis (28%), intestinal atresia (20%) and for other pathology (17%)). IF was present in 36 infants (40%). Studied infants had compromised anthropometric parameters during follow-up. At 6 months ca, there was some catch-up growth, but infants still remained smaller (median weight-for-age SDS -0.9, p<0.001) and shorter (median length-for-age SDS -0.4, p=0.003) than the normal population. In 56 infants, 90 ADP measurements were performed. FM index SDS was significantly lower than the reference population at both 2 and 6 months ca (-0.8, p<0.001 and -0.7, p=0.001), but the FFM index SDS did not differ. PNcum was not associated with anthropometric or BC parameters.
Conclusion: The previously reported increased FM and decreased FFM in children with IF on long-term PN were not observed in this prospective cohort of infants with PN need after neonatal intestinal surgery, but compromised growth, decreased FM and adequate FFM were observed during the first 6 months after surgery. The cumulative amount of PN was not a predictor of anthropometric and BC outcomes. The need for continuing growth monitoring after 6 months of age seems obvious, but further research needs to explore the benefit of incorporating ongoing monitoring of BC during follow-up.

Health-Related Quality of Life of Children on Home Parenteral Nutrition

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Background: The aim of this study is to describe health related quality of life (HRQOL) over time in children with chronic intestinal failure (CIF) on home parenteral nutrition (HPN).
Methods: Prospective, observational study conducted over 7 years in patients suffering from CIF receiving HPN from two tertiary hospitals in The Netherlands. Every 3-6 months, parents (if child <8 years old) or patients (if child ≥8 years old) completed two questionnaires on the KLIK PROM portal (www.hetklikt.nu): the Pediatric Quality of Life Inventory 4.0 (PedsQL) Generic and Fatigue, prior to the outpatient consultation. Last completed answers were compared to a Dutch general population using Mann Whitney U for PedsQL and one sample t-test for PedsQL fatigue. Second, linear mixed models (LMMs) were constructed to investigate the course of HRQOL over time (duration of HPN treatment), the relationship of prematurity, underlying disease and the number of days per week receiving HPN.
Results: Of 65 patients suffering from CIF receiving HPN , 46 (71%) agreed to participate and were included (44% female). Twenty children had SBS, 15 a motility disorder, 4 a congenital enteropathy and 7 another disease leading to IF. At time of last KLIK contact, patients were 6.3 years of age (IQR; 3.7 – 10.4) and received HPN for a median of 4.3 years (IQR; 1.6 – 8.3). In total, 272 questionnaires were completed; 168 PedsQL Generic (58 for age 2-7, 110 for age 8-18) and 104 PedsQL Fatigue (53 for age 2-7, 51 for age 8-18).
PedsQL for ages 5-7 and 8-12 years was significantly lower than healthy controls (P< .01 for both age groups) with effect sizes of .77 and .80 respectively. PedsQL fatigue for age 5-7 years was also significantly lower than healthy controls (P= .01) with an effect size of .70. No difference was observed in other age groups.
LMMs for PedsQL 2-7 and 8-18 years showed no significant coefficient for duration of HPN; estimate -.20 (95% CI; -.44 – .05) and .09 (95% CI; -.02 – .19) respectively. Also, LMMs for PedsQL fatigue ages 2-7 and 8-18 years showed no significant coefficient for duration of HPN; estimate -.02 (95% CI; -.35 – .30) and .04 (95% CI; -.09 – .18) respectively.
In children aged 8-18 years, the model for PedsQL fatigue showed that children who were prematurely born scored significantly lower (estimated marginal mean (EMM) -1.83SD) than patients who were not prematurely born (EMM .04SD) P= .04, this was not seen in other age groups. No significant coefficient was observed for underlying disease or number of days per week of HPN in all age groups.
Conclusion: Children aged 5 to 12 years have highly impaired HRQOL. Surprisingly, HRQOL does not change during long term treatment with HPN in these children.

Somatostatin analogues lead to an 82% reduction in red blood cell transfusions in patients with gastrointestinal bleeding due to angiodysplasias: an individual patient data meta-analysis.

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Background: Several small cohort studies and one randomised controlled trial suggest that somatostatin analogues (SSA) may decrease rebleeding rates in patients with gastrointestinal angiodysplasias (GIADs). The true effect size of SSA therapy on clinical outcomes in bleeding GIADs is unknown. There is a lack of data on patient and treatment characteristics that inform treatment effectiveness. This individual patient data meta-analysis aimed to establish the efficacy of SSA therapy on red blood cell (RBC) transfusion requirement of patients with GIADs and to identify subgroups that benefit most.
Methods: We performed a systematic search up to February 2020 using MEDLINE, EMBASE and the Cochrane Library to identify articles on the SSA effect on GIADs. The primary outcome was the mean percentage and absolute decrease in RBC transfusions during SSA treatment. Patients were classified as good responders (≥ 50% reduction) or poor responders (< 50% reduction). The mean absolute increase in haemoglobin level, adverse events and treatment predictors were considered as secondary outcomes.
Results: We identified 11 studies and obtained individual patient data from 9 cohorts. Aggregated data were available from the 2 other studies. We analysed data from 212 patients and SSA reduced RBC transfusions by a mean of 81.8% (Incidence Rate Ratio [IRR] 0.18; 95% CI 0.14 – 0.24, *p* < 0.001). SSA led to a mean absolute decrease in RBC transfusions from 12.8 to 2.3 (-10.5; 95% CI -8.5 – -12.9) over a period of 12 months. A good response was seen in 177/212 patients (83.5%). Most good responders (109/177 patients: 61.6%) had a complete response. The mean absolute haemoglobin level increased from 7.1 (95% CI 6.9 – 7.3) to 10.4 (95% CI 10.1 – 10.7) g/dl during SSA therapy (*p* < 0.001). Adverse events occurred in 38/212 patients (17.9%; 95% CI 13.1% – 23.9%), mainly loose stools, cholelithiasis and erythema at the injection site. Only 10/212 patients (4.7%; 95% CI 2.4% – 8.8%) discontinued SSA therapy due to adverse events. Octreotide (Ratio 0.84, $p = 0.021$) was independently associated with better treatment response compared to lanreotide. Location of GIADs in the stomach (Ratio 0.87, $p = 0.016$) was associated with worse treatment response.
Conclusion: SSA therapy greatly reduces the need for RBC transfusions and increases the haemoglobin levels of patients with transfusion-dependent bleeding secondary to GIADs.
Patients treated with octreotide who have GIADs located in the small bowel or colon benefit the most.

Biofilm formation in duodenoscope working channels in a simulated ercp setting

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Background: Despite adjustments of the distal tip, with completely disposable caps and elevators, contamination of duodenoscopes still prevails. This might be due to biofilm formation inside the channels. In this study, biofilm formation inside working channels of duodenoscopes was researched in a simulated ERCP setting.
Methods: Three new duodenoscopes (DEC ED34-i10T2, Pentax) were used in a simulated ERCP setting where they were soiled with artificial test soil (ATS2015, Healthmark) containing an excessive amount of 10^8 CFU/mL of *Pseudomonas aeruginosa, Klebsiella pneumoniae, Escherichia coli* and *Enterococcus faecium*. Soiling was followed by manual cleaning, high level disinfection (HLD) and overnight storage in drying cabinets. After forty tests, only the *P. aeruginosa* strain (Pa-Type 1) was switched to a different *P. aeruginosa* strain (Pa-Type 2) for twenty subsequent tests. Cultures of the tip and working channel were acquired after HLD and overnight storage. Maldi-Tof MS was used to differentiate between the presence of the two different *P. aeruginosa* strains.
Results: One of the three duodenoscopes showed persistent growth of *P. aeruginosa* from the fifth test until the end of the study. Pa-Type 1 remained present in the cultures of this duodenoscope, despite the fact that soiling with that specific strain was discontinued, until the end of the study with just a few negative tests in between. Quickly after introduction, Pa-Type 2 became also present in conjunction to Pa-Type 1. Borescope inspections of all three duodenoscopes revealed no abnormalities. The other two duodenoscopes only showed incidental contamination.
Conclusion: The persistent contamination by Pa-Type1, even after replacing with Pa-Type2 and 55 times HLD, of one duodenoscope, suggests presence of a biofilm. No clear explanation was found for the formation of this biofilm, as no abnormalities of this duodenoscope were identified and the other two exact same duodenoscopes did not develop persistent positive cultures.

Molecular profiling of primary sclerosing cholangitis-inflammatory bowel disease associated colorectal carcinomas

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Background: Patients with primary sclerosing cholangitis (PSC) and inflammatory bowel disease (IBD) run a 10-fold increased risk of developing colorectal cancer (CRC) compared to patients with IBD only. The aim of this study was to perform an extensive screen of known carcinogenic genomic alterations in patients with PSC-IBD, and to investigate whether such changes occur already in non-dysplastic mucosa.
Methods: Archival cancer tissue and non-dysplastic mucosa from resection specimens of 19 patients with PSC-IBD-CRC were characterized, determining DNA copy-number variations, microsatellite instability (MSI), mutations in 48 cancer genes and CpG island methylator phenotype (CIMP). Genetic profiles were compared with two independent cohorts of IBD associated CRC (IBD-CRC, n=11) and sporadic CRC (s-CRC, n=100).
Results: Patterns of chromosomal aberrations in PSC-IBD-CRC were similar to those observed in IBD-CRC and s-CRC. MSI occurred in only one PSC-IBD-CRC. Mutation frequencies were comparable between the groups, except for mutations in the *KRAS* gene, which occurred less frequent in PSC-IBD-CRC (5%) versus IBD-CRC (38%) and s-CRC (31%) (p=0.034) and the *APC* gene, which occurred less frequent in PSC-IBD-CRC (5%) and IBD-CRC (0%) versus s-CRC (50%) (p<0.001). PSC-IBD-CRCs were frequently CIMP high (44%), similar to s-CRC (34%; p=0.574) but less frequent than IBD-CRC (90%; p=0.037). Similar copy number aberrations and mutations were present in matched cancer and adjacent mucosa in 5/15 and 7/11 patients, respectively.
Conclusion: Excess risk of CRC in PSC-IBD patients was not explained by copy number aberrations, mutations, MSI, nor CIMP status, in cancer tissue, nor adjacent mucosa. These findings set the stage for further genome-wide and epigenetic studies.

Adverse drug reactions from real-world data in inflammatory bowel disease patients in the IBDREAM registry

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Background: Inflammatory bowel disease (IBD) frequently requires chronic immunosuppressive treatment and active involvement from patients during treatment decision making. Information about the risk of developing adverse drug reactions (ADRs) to IBD therapies is required in this process. This study aimed to describe the ADRs reported in IBD patients from real-world data, using the Dutch nationwide IBDREAM registry, and compare the occurrence and cumulative incidences with the summary of product characteristics (SmPC) of the associated drugs.
Methods: In this retrospective multicentre study, ADRs related to IBD medication were assessed. Only reports associated with the use of one of the seven drugs with the absolute most reported ADRs were included. All ADRs were verified by HCPs and coded by trained pharmacovigilance assessors.
Results: In total, 2,927 ADRs were reported in 1,178 patients. 24 new drug-ADR associations related to the use of azathioprine, mercaptopurine, infliximab, oral mesalamine and thioguanine were reported in the IBDREAM registry that were not mentioned in the corresponding SmPCs. The most frequently reported new associations were pyrexia for azathioprine (3.1%) and mercaptopurine (4.9%). In addition, there were seven ADRs with a higher cumulative incidence in IBDREAM compared with the SmPC and included among others arthralgia during mercaptopurine use (2.5%), and diarrhoea (1.4%), alopecia (1.2%) and infections (1.6%) during azathioprine use.
Conclusion: Based on real-world data, ADR reporting demonstrated new ADRs and higher incidences of ADRs to IBD therapies. This information will contribute to drug safety by updating the SmPCs, allowing better risk assessment and communication towards patients.

Psychometric evaluation of an experience sampling method-Based Patient-Reported Outcome Measure in Functional Dyspepsia

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Background: Due to important biases, conventional end-of-day and end-of-week assessment methods of gastrointestinal symptoms in functional dyspepsia (FD) are considered suboptimal. Real-time symptom assessment based on the experience sampling method (ESM) could be a more accurate measurement method. The present study aimed to evaluate validity and reliability of an ESM-based patient-reported outcome measure (PROM) for symptom assessment in FD.
Methods: Thirty-five patients with FD (25 female, mean age 44.7 years) completed the ESM-based PROM (a maximum of 10 random moments per day) and an end-of-day symptom diary for 7 consecutive days. On day 7, end-of-week questionnaires were completed including the Nepean Dyspepsia Index (NDI) and Patient Assessment of Gastrointestinal Symptom Severity Index (PAGI-SYM).
Results: ESM- and corresponding end-of-day scores for gastrointestinal symptoms were significantly associated (ICCs ranging from 0.770-0.917). However, end-of-day scores were significantly higher (0.329-1.031) than mean ESM scores (p<0.05). Comparing ESM with NDI and PAGI-SYM scores, correlations were weaker (Pearson's r ranging from 0.467-0.846). Cronbach's coefficient was good for upper gastrointestinal symptoms (=0.842). First-half-week and second-half-week scores showed very good consistency (ICCs ranging from 0.913-0.975).
Conclusion: The present results demonstrate good validity and reliability of a novel ESM-based PROM for assessing gastrointestinal symptoms in patients with FD. Moreover, this novel PROM allows to evaluate individual symptom patterns and can evaluate interactions between symptoms and environmental/contextual factors. This will increase patients' disease insight, provide tools for self-management, and improve shared decision-making. Hence, this novel tool may aid in the transition towards personalised healthcare for patients with FD.

A morphometric analysis of pathological alterations in haemorrhoidal disease versus normal controls: a controlled trial

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Background: Until today, the true pathophysiology of haemorrhoidal disease (HD) has not yet been unravelled. More and more evidence guides us towards the hypothesis that reduced connective tissue stability is associated with a higher incidence of haemorrhoids.
This study aimed to compare the quantity and quality of collagen, and vessel morphometrics, in patients with symptomatic HD compared to normal controls.
Methods: This study was conducted at a single centre in the Netherlands.
Twenty-two samples of grade III and grade IV HD tissue from patients undergoing a haemorrhoidectomy between January 2004 and June 2015 were included in the study group. Samples of fifteen persons without HD who donated their body to science and died a natural death served as controls.
Quantity and quality of anal collagen, and anal vessel morphometrics were objectified. Quality of collagen was subdivided in young (immature) and old (mature) collagen, with old collagen being more cross-linked.
Results: Patients with HD had an increased percentage of total anal collagen (62.1 ± 13.8 vs.18.7 ± 14.5 %; $P = 0.0001$), a decreased percentage of young collagen (0.00009 ± 0.00008 vs. 0.0008 ± 0.0008 %; $P = 0.001$),and a smaller surface area of the anal vessels (795.1 ± 1215.9 micrometre^2 vs. 1219.0 ± 1976.1; $P = 0.003$) compared with controls. The percentage old collagen did not differ between the control group and the study group (0.588 ± 0.286 % vs. 0.389 ± 0.242 %; $P = 0.06$).
Conclusion: Patients having haemorrhoids had increased total collagen, decreased young collagen and smaller surface area of the anal vessels compared to the control group. These outcomes suggest that alterations in anal collagen composition may play a role in the formation of haemorrhoids.

Universal immunohistochemistry for Lynch Syndrome: a systematic review and meta-analysis of 58,580 colorectal carcinomas

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Background: Lynch Syndrome (LS) is a form of hereditary colorectal cancer (CRC), caused by germline variants in DNA mismatch repair (MMR) genes. Currently, many Western countries perform universal immunohistochemistry (IHC) testing on CRC to increase the identification of LS patients and their relatives. For a clear understanding of health benefits and costs, data on the total outcome, namely the proportions of LS, sporadic MMR-deficient (MMRd) cases, and unexplained MMRd cases, are required.
Methods: Ovid Medline, Embase and Cochrane CENTRAL were searched for studies reporting on universal MMR IHC, followed by MMR germline analysis, until March 20, 2020. Proportions were calculated, subgroup analyses were performed based on age and diagnostics used, and random effects meta-analyses were conducted. Quality was assessed using the QUADAS-2 tool.
Results: Of 2723 identified articles, 56 studies covering 58,580 CRCs were included. In 6% (95% CI 5%-8%; I^2=96%) MMR deficient protein staining was identified. An MMR germline variant was present in 2.0% (95% CI 2%-2%, I^2=92%), ranging from 1.8% to 7.3% based on completeness of diagnostics and age restriction. IHC outcomes were missing in 13%, germline testing was performed in 76% of eligible patients. In seven studies, including 6848 CRCs completing all diagnostic stages, germline variants and biallelic somatic MMR inactivation were found in 3.0% and 1.7%, respectively; 0.6% remained unexplained MMRd.
Conclusion: The percentage of germline and sporadic MMR variants and unexplained cases is highly dependent on age, completeness and type of diagnostics used: complete diagnostics explained MMRd in almost all CRCs. These findings are relevant in application of guidelines for testing and surveillance in MMRd CRCs.

Case-mix adjustment to compare colonoscopy performance between endoscopy services: a nationwide cohort study

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Background: Case-mix factors for colonoscopy are defined as non-modifiable patient and endoscopy characteristics, which might influence colonoscopy performance. Differences in case-mix factors are likely to exist between endoscopy services. This study aims to examine the importance of case-mix adjustment when comparing colonoscopy performance between endoscopy services.
Methods: Prospectively collected data recorded in the Dutch Gastrointestinal Endoscopy Audit (DGEA) between 01-01-2016 and 31-12-2019 were analyzed. The DGEA is the national colonoscopy registry of endoscopy services in the Netherlands. Academic, non-academic and private endoscopy services are participating in the DGEA. Performance on cecal intubation rate (CIR) and rate of adequate bowel preparation (ABPR) were studied in the total study population per endoscopy service. The polyp detection rate (PDR) was studied in FIT-positive screening colonoscopies. Variation in case-mix factors between endoscopy services and expected outcomes for the CIR, ABPR and PDR were calculated, based on the case-mix factors of all patients per endoscopy service, using a multivariable logistic regression model.
Results: During the 4-year study period, 363,840 colonoscopies were recorded from 51 endoscopy services in the DGEA. Significant differences in the mean percentage per endoscopy service were observed for several case-mix factors; age higher than 65 years (range (r): 33.4 - 53.6%, *p* < 0.001), male patients (r: 46.2 - 58.2%, *p* < 0.001), ASA 3 or higher (r: 0.2 - 24.9%, *p* < 0.001) and diagnostic colonoscopies (r: 18.5 - 85.8%, *p* < 0.001). In the FIT-positive population (n = 77.536), the mean percentages per endoscopy service were significantly different for: age higher than 65 years (r: 36.0 - 62.7%, *p* < 0.001), male patients (r: 51.8 - 67.3%, *p* = 0.001) and ASA 3 or higher (r: 0.3 - 30.8%, *p* < 0.001). For CIR and ABPR, age, sex, ASA classification and indication for colonoscopy were confirmed as significant case-mix factors. Age, sex and ASA classification were significantly associated with PDR in the FIT-positive population. The expected CIR, ABPR and PDR per endoscopy service ranged from 95.0% to 96.9%, from 93.5% to 96.4% and from 75.7% to 79.0%, respectively.
Conclusion: Variation in case-mix factors between endoscopy services results in variation in expected outcomes for colonoscopy between these endoscopy services. Our findings emphasize that for comparison of colonoscopy performance measures between endoscopy services, adjustment for case-mix factors should be considered.

Abbreviations: ABPR, adequate bowel preparation rate; CIR, cecal intubation rate; DGEA, Dutch Gastrointestinal Endoscopy Audit; PDR, polyp detection rate; r, range

Efficacy of ultra-low volume (≤1L) bowel preparation fluids - systematic review and meta-analysis

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Background: High-quality bowel preparation is important for the diagnostic accuracy and safety of colonoscopy. However, it is often difficult for patients to adhere to high-volume laxatives, which may contribute to poor bowel preparation. This review aims to assess the efficacy of bowel preparation fluids of 1L or less.
Methods: We performed a systematic review including all relevant randomized controlled trials on ultra-low volume (≤1L) bowel preparation fluids for colonoscopy published since 2015. The primary endpoint was the percentage of adequately prepared patients. Secondary endpoints included adenoma detection rate (ADR) and safety. We used a random-effects model to calculate the pooled proportions of adequately prepared patients, using the restricted maximum likelihood method with Freeman-Tukey double arcsine transformation. Using subgroup analysis, we assessed the additional effect of additives (e.g., bisacodyl) and dosing protocol (split-dose, same day, or day before).
Results: Our systematic search yielded 3029 records, of which 43 were included in our analysis. Bowel preparation with sodium picosulfate/magnesium citrate (SPMC) (19 trials, n=10,287), 1L-polyethylene glycol with ascorbate (PEGA) (10 trials, n=1,717), sodium phosphate (NaP) (2 trials, n=621), and oral sulfate solution (OSS) (3 trials, n=597) was adequate in 75.2%, 82.9%, 81.9%, and 92.1%, respectively, of patients; however, heterogeneity between studies was considerable (I^2 range: 86%-98%). A negative trend for bowel cleansing efficacy was seen when taken the day before colonoscopy instead of split-dosing. Ultra-low volume preparation fluids combined with additives performed significantly better than without additives (p<0.01). Pooled ADRs with SPMC were 31.1%, with 1L-PEGA 32.3%, with NaP 30.4%, and with OSS 40.9%. Temporary electrolyte changes were seen with all ultra-low volume bowel preparation fluid solutions; however, with no clinically significant long-term effects.
Conclusion: Bowel preparation fluids of 1L or less frequently do not meet the 90% quality standard for adequate bowel preparation as defined by the European Society of Gastrointestinal Endoscopy guidelines. Nonetheless, ultra-low volume preparation fluids can be considered in patients intolerant for higher-volume laxatives and without risk factors for inadequate bowel preparation or dehydration-related complications.

Disease activity in Inflammatory Bowel Disease patients is associated with increased liver fat content during follow-up

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Background: Current data suggest an increase in the prevalence of non-alcoholic fatty liver disease (NAFLD) in patients with inflammatory bowel diseases (IBD) compared to the general population, which varies from 8-59% depending on the diagnostic criteria used. Different factors are believed to contribute to this co-occurrence, including both metabolic and IBD-associated risk factors. Furthermore, survival in patients with NAFLD is associated with the level of fibrosis. The aim of our study was to evaluate the prevalence of liver steatosis (LS) and fibrosis (LF) in IBD patients at enrollment, and to evaluate prospectively which factors influence changes in steatosis and fibrosis during follow-up.
Methods: From June 2017 to February 2018, consecutive adult IBD patients were enrolled. Demographic and biochemical data were collected at baseline and after 6 to 12 months. The degrees of LS and LF was assessed by transient elastography (Fibroscan). LS was defined as a Controlled Attenuation Parameter (CAP) ≥248, LF as a liver stiffness value (Emed) ≥7.3 kPa and IBD disease activity as C-reactive protein (CRP) ≥10 mg/l and/or fecal calprotectin (FCP) ≥150 μg/g. Changes in LS and LF were studied using ΔCAP and ΔEmed (follow-up minus baseline). An independent sample T-test was used to analyze the mean change in ΔCAP and ΔEmed. Univariate and multivariate linear regression analysis were performed, a P-value of ≤0.05 was considered significant.
Results: A total of 117 IBD-patients were enrolled, of which 54% were male with a mean age of 44 (12.1) years. 56% of the patients suffered from Chron's disease. The mean Body Mass Index (BMI) was 25.35 (4.6) kg/m^2 and 34 patients (29.1%) had an active episode of IBD at enrollment. The prevalence of LS at baseline was 41.0%, the prevalence of LF at baseline 12.0%. The mean change in ΔCAP was 22.44 (75.7) in patients with active disease at baseline and -34.12 (67.4) in patients in remission at baseline (p=0.001). Using a multivariate analysis, disease activity at baseline (B=37, 95%CI 6.38-67.61, P=0.018) and LS at baseline (B=-0.4, 95%CI -0.64 - -0.23, P=0.000) were associated with an increase in LS during follow-up. The mean change in ΔEmed was 0.39 (1.9) in patients with active disease at baseline and -0.53 (2.7) in patients in remission at baseline (p=0.075). In univariate analyses, no factors associated with LF during follow-up were found.
Conclusion: Our study reveals a high prevalence of liver steatosis and liver fibrosis in IBD patients. Active IBD at baseline was associated with an increase in liver steatosis during follow up, but not with an increase in liver fibrosis.

The composition and metabolic potential of the human small intestinal microbiota within the context of inflammatory bowel disease

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Background: The human gastrointestinal tract harbours distinct microbial communities, collectively known as the gut microbiota, which are essential for health. Alteration to the composition of these communities has been described for several disorders, including inflammatory bowel disease (IBD) however, this is mostly specific to the colonic content due to the wide use of faecal samples. Little is known about small intestinal microbes, which may be at least as important for human health given the fundamental role of the small intestine in nutritional energy absorption and host-microbe immune homeostasis. Moreover, translocation of typically oral bacteria to the colon has been implicated in several microbiome-associated diseases. Considering the proximity of the small intestine to the colon, one may expect that small intestinal bacteria are also likely to enter the colon and induce a disease phenotype.
Methods: Using faecal samples collected from 57 individuals with an ileostomy or ileoanal pouch due to IBD and 1656 from the general population and patients with IBD, we aimed to study the small intestinal microbiota in comparison with the faecal microbiota. IBD samples were further stratified into patients without and with segmental intestinal resections. The bacterial composition and microbial metabolic pathway profiles were compared between all groups using multivariate linear regressions.
Results: Microbial diversity in ileostomy and ileoanal pouch derived samples, representing the small intestinal content, was significantly lower compared with the faecal microbiome of the general population and patients with IBD. 89 species were differentially abundant in small intestinal samples compared with general population samples. 82 & 49 species were differentially abundant in small intestinal samples compared with IBD samples without and with resections, respectively. *Veillonella atypica*, *Streptococcus salivarius* and *Actinomyces graeventzii* were among the species enriched in small intestinal samples. Predicted metabolic pathways enriched in the small intestine are primarilyinvolved in simple carbohydrate and energy metabolism and also suggest a higher proinflammatory potential.
Conclusion: The IBD faecal microbiota, particularly in patients with resections, deviated from the 'healthy' faecal microbiome and showed resemblance to that of the small intestine. Many species found enriched in the small intestine have also beenpreviously associated with IBD. The distinct composition and functional roles of the small intestinal microbiota can, therefore, also be relevant in IBD. These results highlight the importance of studying the small intestinal microbiota to gain new insight into disease pathogenesis.

Distinct and Permanent Gut Microbial Alterations in Renal Transplant Recipients

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Background: Renal transplantation is life-changing in many aspects and is currently the only curative treatment for end-stage renal disease. All renal transplant recipients (RTR) use immunosuppressive medication and are frequently exposed to antibiotics which can change the gut microbiome. However, little is known about the gut microbiome of RTR and the effect of immunosuppressive medication on the gut microbiome. Therefore, we used metagenomic sequencing data from 2154 fecal samples to characterize the gut microbiome of RTR.
Methods: We aimed to define the gut microbiome of end stage renal disease and to study the post-transplantation gut microbiome longitudinally. We collected 1,340 fecal samples from a total of 678 RTR from the Groningen TransplantLines study, including 369 longitudinal fecal samples of 76 RTR (pre-transplantation and at 3, 6, 12 months post-transplantation) and >1 year post transplantation samples of 602 RTR. We also collected 1183 fecal samples from matched HC from the Dutch Microbiome Project. Shotgun metagenomic sequencing was performed to analyze gut microbial diversity, metabolic pathways, virulence factors and antibiotic resistance genes.
Results: We first analyzed gut microbiome diversity longitudinally and found that microbial diversity significantly decreased post-transplantation compared to pre-transplantation (P<0.001). Furthermore, RTR had a significantly lower gut microbial diversity and increased richness of virulence factors and antibiotic resistance genes compared to HC (P<0.001). Strikingly, case-control analysis including RTR >1 year post-transplantation and HC revealed 229 taxa, 289 pathways, 89 virulence factors and 116 antibiotic resistance genes that were significantly different (P_{FDR}<0.10). A large shift in compositionality of RTR was observed compared to HC. The use of immunosuppressive medication significantly explained 3.5% of variance within the gut microbiome and was associated to multiple metabolic pathways (P_{FDR}<0.10).
Conclusion: In this study, we characterized the gut microbiome of RTR using shotgun metagenomic sequencing data of 971 RTR and 1183 HC fecal samples and conclude that RTR suffer from dysbiosis. The gut microbiome of RTR is very different from HC and is characterized by a lower microbial diversity and increased richness of virulence factors and antibiotic resistance genes. Immunosuppressive medication changes the composition of the gut microbiome and it leaves a signature in the metabolic pathways of gut microbes in RTR. We show that the gut microbiome of RTR is permanently different from healthy controls and this could have far reaching implications for the outcome of renal transplantation.

Evaluating nationwide application of minimally invasive surgery for small bowel neuroendocrine neoplasms and the impact on survival

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Background: Open surgery for small bowel neuroendocrine neoplasms (SB-NEN) is still considered standard of care, mainly because of frequently encountered multifocality and central mesenteric masses. The aim of this study was to evaluate surgical approach for SB-NEN at a national level and to determine predictors for overall survival.
Methods: Patients with SB-NEN who underwent surgery between 2010-2015 were included from the Netherlands Cancer Registry. Patient and tumour characteristics were compared between laparoscopic and open approach. Overall survival was assessed by Kaplan-Meier and compared with the Log-rank test. Independent predictors were determined by Cox proportional hazards model.
Results: In total, 482 patients were included, of whom 342 (71%) underwent open and 140 (29%) laparoscopic surgery. Patients in the open surgery group had significantly more multifocal tumours resected (24% vs. 14%), pN2 lymph nodes (15% vs. 6%) and stage IV disease (33% vs. 20%). Overall survival after open surgery was significantly shorter compared to laparoscopic surgery (3-year: 81% vs. 89%, 5-year: 71% vs. 84%, P=0.004). In multivariable analysis, age above 60 years (60-75, HR 3.38 (1.84-6.23); >75 (HR 7.63 (3.86-15.07)), stage IV disease (HR 1.86 (1.18-2.94)) and a laparoscopic approach (HR 0.51 (0.28-0.94)) were independently associated with overall survival, whereas sex, multifocal primary tumour, grade and resection margin status were not.
Conclusion: Laparoscopy was the approach in 29% of SB-NEN at a national level with selection of the more favorable patients. Laparoscopy remained independently associated with better overall survival besides age and stage, but residual confounding cannot be excluded.

Harnessing the Gut Microbiome to Predict Response to Cancer Immunotherapy

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Background: Microbiome increasingly being recognized to modulate health and disease, including immune homeostasis. Checkpoint inhibitor treatment (ICI) revolutionized anticancer therapy, specifically for stage 4 melanoma. Recent evidence from mouse models and small human cohorts have revealed a link between the gut microbiome (GM) and responsiveness to ICI. In this study, we performed the largest prospective study using metagenomic sequencing to increase our understanding of the GM's role in cancer immunotherapy.
Methods: We prospectively collected 490 faecal samples from 195 subjects with advanced melanoma who received ICI. These patients were treated across a number of cancer centres and received their first cycle of ICI between 2015 and 2020. We further added 4 publicly available cohorts to our analysis. To identify species and metabolic functions associated to ICI response, we conducted both baseline and longitudinal analyses of metagenomic sequencing data using machine learning together with robust statistical methods accounting for confounders.
Results: We found strong batch effects and a poor segregation of responders (R) and non-responders (NR) based on the overall microbial community, with improvements using microbial functions over species abundances. We found response to ICI to be partially predictive of the GM with 2 cohorts exhibiting an AUC > 0.7, 3 cohorts with AUCs between 0.6-0.7 and 4 cohorts with AUCs between 0.55-0.6. However, reproducibility of these predictions on unrelated cohorts was poor. We identified species such as *Enorma massiliensis* to be associated with NR and *Roseburia CAG 471* to be associated with R, but overall significance was assigned by only some statistical methods. Our longitudinal analysis of 34 patients with 4 follow-up visits showed that *E. massiliensis*, *Klebsiella pneumoniae* and *Firmucutes bacterium CAG 83* could be ascribed to NR even after controlling for factors such as time since ICI, PPI, toxicity, bmi and age. This analysis also showed that species such *Akkermansia muciniphila* or *Bifidobacterium* which previous studies linked to ICI response were in fact associated to PPI use. Instead, our analysis instead found that species such as *Faecalibacterium prausnitzii*, *Anaerostipes hadrus* and *Eubacterium hallii* were significantly associated with ICI response.
Conclusion: While our results indicate that the strength of the association between the GM with response to immunotherapy is largely cohort specific, it also shows that biomarker species can be identified, especially with rich prospective data. This highlights the exciting possibility for therapeutic interventions to optimise GM composition to improve anticancer therapy.

Identification of dysplasia in the Barrett's esophagus using an endocytoscopy classification system: preliminary results of a prospective comparison between clinicians and artificial intelligence.

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Background: Endocytoscopy (EC) is an ultra-magnification endoscopy technique (factor x520) that could enable the practice of 'optical biopsy'. In conjuction with artificial intelligence (AI), a more targeted approach of tissue sampling of the Barrett's esophagus (BE) could be enabled.
We aimed to investigate the feasibility of EC in differentiating dysplastic from non-dysplastic tissue in the BE in vivo, performance of clinicians and a computer-aided diagnosis (CADx) algorithm were assessed and compared with each other. Ultimately, the potential of the implementation of CADx will be determined during a test in which clinicians can use the help of the CADx.
Methods: EC was prospectively performedin BE patients; areas of interest were videotaped using EC and included for analysis if frames were classifiable and could be correlated to histology of targeted biopsies. An EC classification system for the BE was developed that differentiated BE metaplasia from BE neoplasia. Online training and examination modules were designed for clinicians (5 BE experts, 5 gastroenterologists and 5 residents) and scored. Finally, a convolutional neural network was trained on the collected frames and tested on a separate test set.
Results: We performed EC in 52 BE patients. A selection of 728 metaplastic and 824 dysplastic images from 20 patients was made for training of CADx. Accuracy, sensitivity and specificity of clinicians before training (n = 14) were 62.6%, 56.2% and 70.6% and after training (n = 14) were 78.6% (P < 0.05), 86.2% (P < 0.05) and 69.5% (P > 0.05) respectively. After an interval of at least two weeks, their (n = 9) accuracy and sensitivity significantly decreased to 73.0% and 75.6%. The average accuracy, specificity and sensitivity of the algorithm on image basis over 5 runs were 79.6%, 74.0%, and 85.3%, respectively.
Conclusion: EC allows in vivo discrimination of metaplastic and dysplastic BE tissue. Interpretation is however not straightforward for clinicians and requires training and maintenance. AI shows promising performance in analyzing EC images and can enable highly accurate diagnosis. This could help facilitate generalization of EC in clinical practice.

Predictors of Gastrointestinal Transit Times in Colon Capsule Endoscopy

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Background: In order for Colon Capsule Endoscopy (CCE) to obtain images of the entire gastrointestinal tract, the optimal transit time has to be fast enough to achieve completion within the battery time but not so fast that lesions may be missed. We aimed to identify predictors for CCE transit times in a prospective population-based cohort.
Methods: Participants received CCE with corresponding bowel preparation (5mg bisacodyl, 2L polyethylene glycol (PEG) and 2L water, both split-dose) and booster regimen (10mg metoclopramide (if capsule remained in stomach > 1 hour) and 0.5L oral sulfate solution split dose). Possible transit time predictors were obtained through questionnaires and included age, gender, body mass index (BMI), smoking status, coffee intake, fiber intake, diet quality, physical activity, dyspeptic complaints, changed stool pattern, history of abdominal surgery, medication use and CCE findings. Multivariable logistic and linear regressions with backward elimination were performed to predict CCE completion rate and stomach-, small bowel (SB)-, colonic- and total transit times.
Results: 451 CCE procedures were analyzed. Completion rate was 51.9%. Median CCE transit time was 55 minutes (IQR 39-93) for the stomach, 47 minutes (IQR 29-78) for SB and 391 minutes (IQR 191-528) for the colon. Predictors for a slower stomach transit were lower BMI (β=0.104, p=0.014) and higher physical activity (β=0.101, p=0.017). Predictors for a slower SB transit were lower BMI (β=0.137, p=0.001), lower physical activity (β=0.135, p=0.002), unchanged stool pattern (β=0.084, p=0.049) and no need to use the prescribed metoclopramide (β=0.140, p=0.001). Participants with a higher fiber intake had a slower colonic transit (β=0.111, p=0.025) and those with a lower BMI (β=0.120, p=0.013) had a slower total transit time. Overall completion rate was higher among older participants (OR 1.539, 95% CI 1.040-2.278, p=0.031) and among those with changes in stool pattern (OR 2.273, 95% CI 1.202-4.297, p=0.012), while those with a history of abdominal surgery (OR 0.536, 95% CI 0.358-0.804, p=0.003) had a lower completion rate.
Conclusion: Lower BMI, unchanged stool pattern, higher fiber intake, younger age and history of abdominal surgery were significant predictors for slower CCE transit times or lower completion rate. In future practice these factors can be used to anticipate a longer capsule transit time and possibly intensify the preparation protocol. The faster SB transit in participants who took metoclopramide due to a long stomach transit, suggests that it might be beneficial to use metoclopramide in all CCE procedures.

Prevalence And Clinical Outcomes Of Severe COVID-19 Among Inflammatory Bowel Disease Patients: Observations From A Population-Based Setting

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Background: True estimates on the prevalence and outcomes for a severe course of COVID-19 among Inflammatory Bowel Disease (IBD) patients remain unclear as population-based data are lacking. Therefore we sought to determine these measures in a population-based setting.
Methods: We retrospectively identified all IBD patients who presented at the emergency department (ED) of one of the three hospitals in the South-Limburg region with COVID-19 associated symptoms. Confirmed COVID-19 diagnosis was based on a clinical presentation with COVID-19 associated symptoms combined with either a positive SARS-CoV-2 PCR, a CT-CORADS score (≥4) or both. The primary outcome of interest, the prevalence of severe COVID-19, was defined as a composite outcome of requiring hospitalization, ICU admission, and/or death. Baseline characteristics and data on COVID-19 course for all severe COVID-19 cases were collected. Currently, the total IBD population in South-Limburg is estimated at 4980 patients.
Results: Between February 1, 2020 and November 1, 2020, a total of 61 IBD patients (1.22%) presented at the ED of the three regional South-Limburg hospitals with COVID-19 associated symptoms. Of these, 18 IBD patients (0.36%; 11 UC, 7 CD) had a confirmed COVID-19 diagnosis and fulfilled the criteria for a severe course of COVID-19. Based on the physician global assessment, 12/18 patients (66.7%) were in remission at time of presentation. Furthermore, 12/18 patients were using medication for their IBD (combination therapy in 5/18 patients). Mean age at time of admission was 64.5 years (SD: 10.8) and mean time of complaints till admission was 9.0 days (SD: 4.0). All hospitalized patients had at least one comorbidity (with more than 1 comorbidity in 13/18 patients (72.2%)), cardiovascular being most prevalent (12/18), and mean BMI at time of admission was 27.3 (SD: 4.2). Thirteen patients (72.2%) required oxygen support and 3 patients (16.7%) required ICU admission, of which 2 patients needed mechanical ventilation. No IBD patients died as result of severe COVID-19. On statistical testing no significant differences were observed for all variables between UC and CD patients.
Conclusion: The prevalence of severe COVID-19 among IBD patients in a population-based setting in a heavily impacted area was 0.36% (3.6/1000 patients). Severe COVID-19 appears to impact older IBD patients with at least one comorbidity. In addition, clinical outcomes of severe COVID-19 in the IBD population are favourable. Further studies should determine risk factor-adjusted standardized incidence rates for the same region to assess if risk of severe COVID-19 is higher among IBD patients in comparison to the general population.

Prognostic factors for advanced colorectal neoplasia in inflammatory bowel disease: systematic review and meta-analysis

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Background: Patients with inflammatory bowel disease (IBD) have an increased risk of colorectal cancer (CRC). We performed a systematic review and meta-analysis to identify all prognostic factors for advanced colorectal neoplasia (aCRN, high-grade dysplasia or CRC) in patients with IBD.
Methods: A systematic literature search was conducted according to the MOOSE guidelines. Risk of bias was assessed using the Quality in Prognostic Studies tool. Random-effects models were created separately for odds and hazard ratios, different study designs, and univariable or multivariable data. The evidence for all prognostic factors was categorized as 'weak', 'moderate', or 'strong', based on estimate of effect sizes, heterogeneity, and risk of bias.
Results: A total of 164 studies were included allowing pooled analysis of 31 potential prognostic factors. In the univariable analysis, the evidence for extensive disease was classified as strong while evidence for low-grade dysplasia, strictures, primary sclerosing cholangitis, post-inflammatory polyps, family history of CRC, and ulcerative colitis versus Crohn's disease was considered moderate. Evidence for any dysplasia, colon segment resection, aneuploidy, male sex and age was classified as weak. In addition, histologic inflammation was identified as a risk factor in multivariable analysis (weak evidence). The evidence for the protective factors colonoscopic surveillance, 5-ASA, thiopurines, and smoking was moderate in univariable analysis. Multivariable analysis provided weak evidence for statin use.
Conclusion: In this systematic review and meta-analysis we identified 13 risk factors and 5 protective factors for aCRN in IBD patients, based on univariable and/or multivariable pooled analyses. These findings might lay the groundwork for an improved CRC risk stratification-based surveillance in IBD.

Long term follow-up of high risk T1 colorectal carcinoma, a single center retrospective study

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Background: Adequate counseling of T1 CRC patients for surgery is hampered by a lack of evidence regarding long-term outcomes. This is in particular the case when scheduling frail patients and those with prior local tumor resection for (additional) surgery. The aim of this study was to analyze long-term outcomes of high-risk T1 colorectal carcinoma (CRC) patients undergoing surgical resection.
Methods: Data was retrieved from a prospective database from the department of surgery of the Gelre Hopsitals. Clinical outcomes of all T1 CRC surgical resections between 1st January 2010 and 1st January 2020 were retrospectively analyzed. Follow-up was till January 1st 2020. Disease-free survival and overall survival were analyzed.Disease related mortality was defined as any death within 90 days after surgery or death due to recurrence and/or metastasis during follow-up.
Results: From a total of 1249 CRC surgical procedures, 119 patients were eligible for analysis (46 patients had a prior local resection, 73 patients had a prior tumor biopsy). Median follow-up was 42 months. Disease related mortality was 3.3% (n=4): two patients died due to recurrence of disease, two patients died as a result of postoperative complications. A total of 13 patients died due to another cause then CRC. Mean overall survival was 107 months. CRC recurrence rate was 4.2% (n=5): two patients had local recurrence, two patients had metachrone metastasis and one patient had both. Mean disease-free survival was 96 months. In patients undergoing additional surgical resection after prior local resection, positive lymph nodes and/or residual tumor rate was 13% (n=6).
Conclusion: Disease related mortality after surgical resection of high-risk T1 CRC during a median follow-up of 42 months was low (3.4%). However, an additional surgical resection must be balanced against a low overall survival in this frail group of patients. Moreover, patients with prior local tumor resection should be careful counseled for additional surgery given risk of over-treatment.

Hepatocellular adenoma in men: a nationwide assessment of pathology and correlation with clinical course

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Background: Hepatocellular adenomas (HCA) rarely occur in males, and if so, are frequently associated with malignant transformation. Guidelines are based on a small number of patients and advise resection of HCA in male patients, irrespective of size or subtype. The aim of the current study was to correlate histopathological and molecular findings with the clinical course of HCA in the Dutch male population.
Methods: Tissue samples of Dutch male patients with a (differential) diagnosis of HCA between 2000 and 2017 were identified with the aid of Dutch Pathology Registry (PALGA). Histopathology and relevant immunohistochemistry according to international guidelines were revised by two expert hepatopathologists. Next generation sequencing (NGS) was performed to confirm hepatocellular carcinoma (HCC) and/or subtype HCA. Definitive diagnosis and HCA subtype were correlated with recurrence, metastasis and death.
Results: A total of 66 male patients from 26 centers with a mean (±SD) age of 45.0 ±21.6 years were included. After expert revision and NGS, the diagnosis was revised in 33 of the 66 patients (50%). Final diagnoses included 20 HCA (30%), 26 borderline HCA/HCC (39%), and 20 HCC (30%). Median follow-up was 9.6 (interquartile range [IQR]; 4.3-13.6) years. Clinical data were limitedly available. Tumor related mortality of patients with accessible clinical data was 1/18 (5.6%), 5/14 (35.7%) and 4/9 (44.4%), in the HCA, borderline HCA/HCC and HCC group respectively (p=0.031). There were no recurrences in the HCA group.
Conclusion: Establishing the pathological diagnosis of HCA in male patients is difficult, but expert pathology revision may help. NGS may be more important than indicated in current guidelines, especially to identify β-catenin activated HCA.

Unravelling neoantigen-specific T cell responses in mismatch-repair proficient colorectal cancers

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Background: Innovative treatment options are required for patients diagnosed with advanced colorectal cancer. In tumours with low mutation burden, such as mismatch repair proficient (MMR-p) colorectal cancers, the scarcity of mutated antigens (neoantigens) is most likely responsible for their insensitivity to T cell checkpoint blockade therapies. Nevertheless, we and others have identified the presence of neoantigen-specific T cells infiltrating MMR-p colorectal cancers. This observation raises the question as to why these cells are not able to mediate therapeutic responses to checkpoint blockade but also whether they can be exploited by specific therapeutic approaches.
Methods: We investigated the phenotypes of tumour-infiltrating immune cells in colorectal cancers using single-cell and imaging CyTOF analysis to identify markers associated with tumour-reactive T cells. In order to determine an association between neoantigen-specificity and the expression of these markers on T cells, we sorted tumour-infiltrating $CD8^+$ T lymphocytes of ten MMR-p colorectal cancers based on the absence or presence of these markers on the cell surface. Each T cell subset was expanded independently and was interrogated for its potential to evoke an immune response upon co-culture with peptides corresponding to neoantigens predicted by exome and transcriptomic sequencing of the tumours.
Results: The presence of T cells expressing CD103 and CD39, markers associated with tumour-reactive T cells, in both MMR-proficient and -deficient tumours was demonstrated by single cell and imaging CyTOF analysis. As hypothesized, we were able to validate neoantigen-directed immune reactivity for MMR-p colorectal cancer patients only in the $CD39^+CD103^+$ CD8 T cell subset, while the subsets that lacked expression of CD39 and/or CD103 were not able to evoke such responses.
Conclusion: These observations highlight the possibility of undertaking immunotherapeutic strategies in MMR-p colorectal cancer patients, for instance, through the enrichment of neoantigen-specific T cells for the development of therapeutic T cell products.

Screening for synchronous esophageal second primary tumors in patients with head and neck cancer

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Background: Patients with head and neck squamous cell carcinoma (HNSCC) have an increased risk of developing esophageal second primary tumors (SPTs). We aimed to determine the incidence, stage and outcome of synchronous esophageal SPTs in patients with HNSCC in a Western population.
Methods: We performed a prospective, observational, cohort study. Patients diagnosed with HNSCC in the oropharynx, hypopharynx, any other sub-location in combination with alcohol abuse, or patients with two synchronous HNSCCs, between February 2019 and February 2020, were included. Screening esophagogastroduodenoscopy (EGD) was performed in all patients during the work-up for HNSCC. In general, EGD was performed with white light high resolution endoscopy, narrow-band imaging and Lugol chromoendoscopy by an experienced interventional endoscopist within two weeks after HNSCC diagnosis. A lesion was considered a possible esophageal SPT if it was suspect on at least one of the three detection techniques and had a diameter of at least 5mm. Esophageal SPT was defined as presence of esophageal squamous cell carcinoma (ESCC) or high grade dysplasia (HGD).
Results: Eighty-five patients were included. The majority of HNSCC were located in the hypopharynx (33%) or oropharynx (29%). A lesion suspected for esophageal SPT was detected in 14 of 85 patients, which was pathologically confirmed in 5 patients (1 ESCC, 4 HGD). The radiotherapy field was extended to the esophagus in 2 of 5 patients, HGD was treated with endoscopic resection in 3 of 5 patients. None of the esophageal SPTs were detected on MRI and/or CT-scan prior to EGD. Of the remaining 9 patients, 3 had low grade dysplasia on histology whereas the other 6 patients had benign lesions.
Conclusion: Incidence of synchronous esophageal SPT was 5.9% in our cohort of HNSCC patients. All SPTs were diagnosed at an early stage and treated with curative intent. We believe that screening for synchronous esophageal SPTs in patients with HNSCC is promising and should be first considered in high-risk patients.

Neoplastic recurrence after successful treatment for early Barrett's neoplasia: development of a penalized prediction model.

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Background: The combination of endoscopic resection (ER) and radiofrequency ablation (RFA) is the treatment of choice for Barrett's esophagus (BE) with early neoplasia. Since long-term outcomes are limited, patients still undergo regular follow-up endoscopies after successful treatment (i.e., complete eradication of BE containing early neoplasia, CE-BE). We aimed to develop a prediction model for recurrence, which can be used for personalized follow-up.
Methods: We collected data from the Dutch Barrett Expert Center Registry, a nationwide registry that captures outcomes from all BE patients that underwent endoscopic treatment for early BE neoplasia in expert centers. Recurrence was defined as a histologic finding of low-grade dysplasia (LGD), high-grade dysplasia (HGD) or esophageal adenocarcinoma (EAC) during endoscopic follow-up after achievement of CE-BE. We built a prognostic survival model taking account of competing risks (i.e. Fine and Gray) with LASSO penalization. We assessed: age, gender, baseline pathology, BE-length, new visible lesion(s) (VL) during ablation, poor healing, persisting esophagitis, number of ablation endoscopies, number of endoscopic resection endoscopies, persisting IM in cardia.
Results: A total of 1,154 patients was included with a mean endoscopic follow-up of 4 years (±2) per patient. Overall, 38 patients developed recurrence during FU (0.8%/person year [95%CI 0.6-1.1]). Recurrence histology was LGD in 14 patients (37%), HGD in 7 patients (18%), and EAC in 17 patients (45%). Recurrence occurred median 30 months (22-40) after CE-BE was established. The following characteristics were independently associated with recurrence (strongest to weakest): new VLs during ablation, higher number of ER endoscopies, increasing BE-length, HGD/EAC at baseline, younger age, male gender. The internally validated C-statistic was 0,76 [95%-CI 0,73; 0,79]. For example, a 50 year old male with 10cm BE with EAC and 3 endoscopic resection sessions including 1 for a new VL during RFA, had a cumulative risk for recurrence of 48% during 7 years. In contrast, a 70y female with 3cm BE with flat LGD, had 3% risk.
Conclusion: We built the first prediction model for recurrence after successful treatment of early neoplastic BE in a centralized setting, with good discrimination. If external validation confirms its predictive power, this model can help clinicians and patients to manage expectations and determine a personalized follow-up strategy.

Circulating TP53 mutations are predictive and prognostic biomarkers in pancreatic cancer patients treated with FOLFIRINOX chemotherapy

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Background: The standard first-line treatment for locally advanced pancreatic cancer (LAPC) and metastatic pancreatic cancer (PDAC) is FOLFIRINOX chemotherapy. Moreover, several clinical trials are investigating the benefit of neoadjuvant FOLFIRINOX followed by surgical resection in resectable patients. Despite increased survival in patient groups treated with FOLFIRINOX, only a minority of patients will show complete or partial response of the tumor after FOLFIRINOX chemotherapy and approximately 70-80% will show disease control. Unfortunately, 60-70% of patients will experience severe toxicity from FOLFIRINOX. Biomarkers are needed to stratify patients for available therapies, especially those that can be easily measured in the circulation as opposed to tumor tissue. Being able to select only patients that will benefit from FOLFIRINOX chemotherapy could prevent non-responding patients from unnecessary severe FOLFIRINOX-induced toxicity. The aim of this study was to identify circulating tumor DNA (ctDNA) signatures with predictive value for tumor progression and prognosis in FOLFIRINOX-treated PDAC patients.
Methods: Circulating cell-free DNA was sequenced with a 57 gene next-generation sequencing panel using plasma samples of 48 patients of all disease stages. Blood samples were collected before start and after one cycle of FOLFIRINOX chemotherapy. Chemotherapy response in patients was determined with CT scans as disease control (n=30) or progressive disease (n=18) according to the RECIST 1.1 criteria.
Results: Detection of a *TP53* ctDNA mutation before start of chemotherapy (OR 7.00, *P*=0.028) and the presence of a homozygous *TP53* Pro72Arg germline variant (OR 5.00, *P*=0.028) were both significant predictors of tumor progression during FOLFIRINOX in multivariable binary logistic regression. The combination of both *TP53* mutations showed a sensitivity of 27.8% and specificity of 100% to predict tumor progression during FOLFIRINOX. Detection of a *TP53* ctDNA mutation before start of chemotherapy was significantly associated with shorter progression-free survival (PFS) (HR 4.35, *P*=0.025) in multivariable Cox regression analysis. Kaplan-Meier curves showed that the combination of both *TP53* mutations was associated with shorter median PFS and overall survival (OS) (PFS 1.6 months and OS 4.4 months) compared to patients without any *TP53* mutations (PFS 8.5 months, *P*<0.001 and OS 13.0 months, *P*<0.001).
Conclusion: The combination of a *TP53* ctDNA mutation detected before start of chemotherapy and a homozygous *TP53* Pro72Arg variant is a highly specific predictor of tumor progression during FOLFIRINOX chemotherapy and is associated with poor prognosis.

Dietary intake influences the response to cancer immunotherapy

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Background: Immune checkpoint inhibitors (ICIs) have prolonged the survival of patients across several tumor types at the advanced stage. While clinical trials have shown a significant impact in melanoma, immunotherapy is becoming increasingly established in cancers of the upper and lower gastrointestinal tract. However, there is a large variability in efficacy and adverse events. New insights into factors that shape response are needed to help more patients benefit. Nutrition, through its interaction with immunity and gut microbiota, recently gained interest as a modulator of the immune response. While evidence from animal models is promising, little is known about the role of diet for clinical outcomes during ICI-therapy.
Methods: Here, we investigated the link between dietary habits and response to ICI's in 93 metastatic melanoma patients in a multi-center cohort study. RECIST 1.1 and CTC 5.0 were used to grade response and toxicity. Dietary intake was assessed through Food Frequency questionnaires (Dutch Healthy Diet-FFQ, EPIC-Norfolk FFQ). Food items were mapped to create one dataset. We performed dietary pattern analyses, using predefined scoring systems as well as unsupervised clustering. Adherence to dietary patterns was compared between responders and non-responders, and patients with severe (grade≥3) and mild (grade<2) toxicity, performing a Wilcoxon–Mann–Whitney test (WMW-test). *P*<.05 was considered as statistical significance cut-off.
Results: Patients who discontinued treatment due to toxicity consumed significantly more refined grains, high sugar foods and beverages (u-PDI-score, p=0.015) and showed lower adherence to Mediterranean diet (a-MED-score, p=0.004) compared to patients with mild or no toxicity. Vegetable intake was significantly lower in patients who developed colitis (p=0.019). Responders (defined by RECIST) were more likely to consume a Mediterranean diet than non-responders, albeit not significant (p=0.068). Clinical progression however was significantly linked to low adherence to Mediterranean diet (p=0.023, WMW-test).
Conclusion: High intake of sugar and refined grains and low vegetable consumption are linked to immunotherapy-discontinuation due to toxicity, including colitis. Patients who clinically progressed during treatment, poorly adhered to Mediterranean diet, which is a widely reported model of healthy eating. Our study underlines the importance of dietary assessment in patients starting immunotherapy and supports a role for dietary strategies to improve treatment outcomes. Clinical trials of immunotherapy are being expanded to various tumor types, including GI-cancers, implying that the findings will be relevant for a large group of cancer patients.

Increased Risk of Barrett's Esophagus and Esophageal Adenocarcinoma among Individuals with a Positive Family History

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Background: Considering the poor prognosis of esophageal adenocarcinoma (EAC), efforts should be made to identify individuals at high risk for EAC who may benefit from early detection and prevention strategies. Although familial clustering of EAC and its precursor Barrett's esophagus (BE) has been reported, current guidelines differ in screening recommendations for individuals with a first-degree relative with BE or EAC. We aimed to determine whether individuals with a positive family history (FH) of BE and EAC are indeed at an increased risk of developing esophageal neoplasia.
Methods: We conducted a multi-center case-control study of BE patients with or without related neoplasia and randomly selected controls from the population. Eligible individuals received a questionnaire to collect detailed information on FH and other risk factors for BE and EAC. Positive FH was defined as having at least one first-degree relative with BE or EAC whose diagnosis was histologically confirmed in the Dutch nationwide histopathology database. Multivariate logistic regression modeling was used to estimate odds ratios (ORs) and corresponding 95% confidence intervals (CIs).
Results: Our final analysis included 480 patients with BE and 420 controls without BE who had 6393 first-degree relatives. A pathologically confirmed positive FH was significantly higher among BE patients compared with controls (6.5% vs 0.9; p<0.001). A positive FH was independently associated with an increased risk of BE (OR 5.04; 95% CI 1.45–17.58; p=0.01) after adjusting for known risk factors (such as GERD, smoking, and BMI) and family size. No differences in the presence of lifestyle risk factors were found between familial and non-familial cases. GERD symptoms were more common in first-degree relatives of familial BE patients than in relatives of sporadic patients (30% vs 12%; p<0.001).
Conclusion: This study shows that familial clustering was seen in 6.5% of BE patients. Subjects with at least one first-degree relative with BE or EAC have a 5-fold increased risk of BE and EAC. These findings should be reflected in the development of individualized screening and prevention strategies and emphasize the importance of obtaining a detailed FH. Physicians should consider FH in determining which patients may benefit from upper endoscopy to prevent unnecessary death from EAC.

Phase II study of cisplatin and everolimus in patients with metastatic extrapulmonary neuroendocrine carcinoma (NEC)

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Background: Extrapulmonary NEC (EP-NEC) are an aggressive subgroup of neuroendocrine neoplasms (NEN). Advanced EP-NEC are generally treated with platinum-based cytotoxic regimens. Although highly responsive to cytotoxic therapies, recurrence occurs frequently and rapidly, with a poor prognosis and lack of further treatment options. Genetic alterations in the mTOR pathway have been identified in NEN, providing a rationale for treatment with the mTOR inhibitor everolimus. In this study, we investigated efficacy and safety of cisplatin in combination with everolimus in patients with advanced EP-NEC.
Methods: In this prospective, phase II, open-label, national multicenter study, chemotherapy naïve patients with metastatic EP-NEC received cisplatin 75mg/m2 every 3 weeks in combination with daily everolimus 7.5 mg for a maximum of 6 cycles, followed by maintenance everolimus until progression. Response evaluation was performed at 9-weekly intervals and documented according to RECIST 1.1. Toxicity was evaluated according to CTCAE version 5.0.
Results: Thirty-nine patients, with median age 64 years (range 28-74), of whom 20 (51%) were male, were enrolled in 3 Dutch ENETS centers. Primary tumor location was colorectal in 11 (28.2%) patients, pancreas in 6 (15.4%), esophagus in 4 (10.3%), cervix in 4 (10.3%), gastric in 3 (7.7%), merkel cell carinoma in 3 (7.7%), ovarium in 1 (2.6%) and appendix in 1 (2.6%) patient, and of unknown primary location in 6 (15.4%) of patients. Disease control rate was 82% (95% confidence interval [CI] 66.4-92.4), overall response rate was 59% (CI 42.1-74.4). Median duration of response (DOR) was 6.4 (CI 5.8-7.0) months and median progression free survival was 6.0 (CI 4.3-7.8) months. One patient had ongoing response at end of study, with a DOR of 12.5 months. Median overall survival was 8.7 (CI 7.9-9.5) months. Most common grade 3/4 toxicities were hematological (36%) and renal (21%).
Conclusion: Cisplatin in combination with everolimus is an effective and tolerable first-line treatment for advanced EP-NEC.

Deep submucosal invasion as independent risk factor for lymph node metastasis in T1 colorectal cancer: a systematic review and meta-analysis

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Background: Accurate risk estimation for lymph node metastasis (LNM) in T1 colorectal cancer (CRC) is critical to optimize further treatment. Currently, deep submucosal invasion (DSI) is considered a strong indicator for radical surgery. However, multiple studies suggest that DSI in absence of other histologic high-risk features might not be a strong predictor for LNM. We conducted a systematic review and meta-analysis to determine whether DSI is an independent risk factor for LNM in T1 CRC.
Methods: A systematic search in MEDLINE, EMBASE and Cochrane Library was performed from inception to July 2020 (PROSPERO: CRD42020145938). To establish the risk of DSI for LNM in univariate analysis, all suitable studies were included in meta-analysis. To determine whether DSI (≥1000µm or sm2-3) was an independent risk factor in relation to other accepted histological risk factors such as poor differentiation (PD), lymphovascular invasion (LVI) and/or high-grade tumor budding (TB), studies were eligible if 1) DSI was described as the only present high-risk factor or 2) the above-mentioned four main histological risk factors were simultaneously included in a multivariate analysis. Authors were contacted to provide multivariate analysis or raw patient data when required. Meta-analysis was performed using a random-effects model and reported as pooled odds ratio (OR) with 95% confidence interval (CI).
Results: 59 studies were included comprising in total 19,793 patients. Overall, LNM was present in 11.2%. The number of cases with LNM in univariate analysis, analyzed in all included studies, was significantly higher in the group with DSI (1,903/12,432; 15.3%) compared to the group with superficial invasion (228/4,343; 5.2%) (OR 2.73; 95%CI 2.19-3.41). Seven studies (3303 patients) described presence of DSI in absence of all other high-risk factors. The overall rate for LNM was 2.7% (n=26/977) resulting in a pooled incidence rate of 0.03 (95%CI 0.02-0.05). Seven studies (3515 patients) included DSI in a multivariate analysis in relation to the other three risk factors. DSI was the weakest predictor for LNM with an OR of 1.94 (95%CI 1.05 – 3.57), compared to PD (OR 2.71; 95%CI 1.70 – 4.32), TB (OR 2.59; 95%CI 1.85 – 3.62) and LVI (OR 3.52; 95%CI 2.01 – 6.17).
Conclusion: Our meta-analysis demonstrates that DSI is an independent, but weak predictor for LNM. In DSI cancers, the rate of LNM is low (2.7%) in the absence of other risk factors. In light of the expanding spectrum of endoscopic resection methods and overtreatment by surgery for many patients with T1 CRC, DSI should be reconsidered as strong indicator for oncologic surgery.

Discovery of a Serum N-Glycan Panel for Early Detection of Pancreatic Cancer in a High-Risk Surveillance Cohort

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Background: For imaging-based pancreas surveillance programs of high-risk individuals, detection of curable pancreatic cancer (PC) has proven challenging. Therefore, discovery of novel biomarkers is crucial. Previous research has shown that mass spectrometry (MS)-based analysis of protein glycosylation is able to distinguish (sporadic) PC cases from healthy controls. We aimed to identify serum glycosylation markers for early detection of asymptomatic PC in high-risk individuals undergoing surveillance.
Methods: From a prospective study in asymptomatic high-risk individuals with an estimated > 10-fold increased risk of developing PC undergoing yearly surveillance, serum samples were stored (-80°C) in three academic hospitals between 2006 and 2018. Individuals were included in case of ≥ 2 collected serum samples during ≥ 5 months of follow-up. The cohort was divided in a case (development of PC) and control group. N-glycans were enzymatically released from serum glycoproteins, chemically derivatized, purified, MS-analyzed, identified and quantified. To focus on promising biomarkers, we selected the first quartile (Q1) of significant N-glycans, as published by Vreeker et al (Cancer Medicine 2020). Subsequently, a delta-analysis was performed: (last sample [prior to surgery for cases] – 2nd last sample)/#months between samples. Significant markers were selected after comparison of this delta for cases and controls (Mann-Whitney U).
Results: 166 individuals were included (median age 52 years [IQR 46-59], 40% male). 99 (60%) were germline mutation carriers (79 *CDKN2A*, 14 *BRCA2*, 1 *BRCA1*, 5 *STK11* or *LKB1*) and 67 (40%) were familial pancreatic cancer kindreds. Median number of 3 serum samples (IQR 2-5) were collected during a median follow-up of 38 months (IQR 40). The case group consisted of 11 patients (7%; 4 stage I, 6 stage II, 1 stage III) and the control group of 155 individuals. Delta-analysis showed a significant difference between cases and controls for 6 of 13 N-glycans from Q1 (P≤0.05; Fig. 1; A3F, A3LF, A4FE, A3FE, A3F0E, A3F0L). Evaluation of these markers over time reveals that values of PC cases were already different at baseline (x=0; P≤0.05; Fig. 2), years before developing PC.
Conclusion: This prospective surveillance study identified 6 promising candidate N-glycan markers that may indicate early progression to PC in a high-risk surveillance cohort. A prospective study with a larger sample size is required to validate these findings.

Impact of dose-escalated chemoradiotherapy on patient reported outcomes in patients with locally advanced rectal cancer: 2-year follow-up of the randomized RECTAL BOOST trial

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Background: Dose–escalated chemoradiation (CRT) for locally advanced rectal cancer (LARC) aims to increase patients' eligibility for rectum-preserving approaches. This study compared patient reported outcomes (PROs), overall survival (OS) and disease free survival (DFS) between patients that received dose-escalated CRT (boost group) or standard CRT (control group) within the randomized RECTAL BOOST trial (Clinicaltrials.gov NCT01951521).
Methods: Patients with LARC (n=128), participating in the RECTAL BOOST trial, filled out EORTC QLQ-C30 and CR29 questionnaires on quality of life (QoL) and symptoms at baseline, and at 3, 6, 12, 18 and 24 months following start of treatment. A linear mixed-effect model was applied to compare differences in functional QoL domains. Differences were quantified using the effect size (ES), calculated as the mean difference devided by the pooled standard deviation at baseline. Symptoms were compared using Chi-square test or Fisher's exact test. PROs were compared in per protocol analysis. OS and DFS were compared with Kaplan-Meier method in intention-to-treat analysis.
Results: The boost group (n=51) experienced a significantly larger deterioration in global health at 3 and 6 months (ES -0,4 resp. -0,4), role functioning at 3 and 6 months (ES -0,7 resp. -0,5) physical functioning at 6 months (ES -0,7) and social functioning at 6 months (ES -0,6) than the control group (n=64). Cognitive and emotional functioning were comparable between groups. There were no differences in functional QoL after 6 months following start of treatment. Patients in the boost group reported significantly more pain at 3 and 6 months (31% vs. 9% resp. 42% vs. 16%), less urinary incontinence at 12 months (0% vs. 10%) and more blood or mucus in stool at 12 months (14% vs. 0%). OS and DFS at 2 years were comparable.
Conclusion: In patients with LARC, dose-escalated radiotherapy is associated with a transient deterioration in most of the functional QoL domains and more pain up to 6 months following start of treatment. At two years follow up, there was no difference in QoL, OS or DFS between groups.

Fluorescence Molecular Endoscopy (FME) using bevacizumab-800CW for the detection of (pre)malignant lesions and evaluation of neoadjuvant chemoradiotherapy in esophageal cancer: the preliminary results

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Bovenstaand abstract is gebaseerd op de combinatie van de twee volgende abstracts:

Near-infrared fluorescence molecular endoscopy shows promising results in detecting dysplastic esophageal lesions using topically administered bevacizumab-800CW: the preliminary results of a phase 2 study.

Background: Esophageal cancer (EC) is affecting more than 450,000 people worldwide and is the 6th leading cause of cancer-related deaths. The poor EC survival is attributed to the insufficient methods for premalignant lesion detection and therefore there is a great need for new endoscopic techniques that can visualize early-stage lesions. In 2017 our group published promising results using near infrared fluorescent molecular endoscopy (NIR-FME) against vascular endothelial growth factor A (VEGF-A) to improve early (pre)malignant lesion detection. In this phase II study we aim to evaluate the sensitivity and specificity of the tracer bevacizumab-800CW in combination with NIRFME for detecting (pre)malignant lesions in patients with Barrett's esophagus (BE).
Methods: The tracer, Bevacizumab-800CW, was topically administered to the patients and after 5 minutes of incubation NIR-FME was performed. To quantify the intrinsic fluorescent signal, we used multidiameter single fiber spectroscopy / single fiber fluorescence (MDSFR/SFF) spectroscopy measurements both in vivo and ex vivo. In case of additional fluorescent lesions biopsies were taken to analyze if dysplasia was present. The day after the endoscopic procedure the endoscopic mucosal resection (EMR) specimen was analyzed with widefield back-table imaging.
Results: In our preliminary results, 38 patients were included and topical-based NIR-FME detected all dysplastic lesions. Visible lesions presented with a median TBR of 2.33 ± 1.07. Additionally, in 12 patients, this novel endoscopic technique identified in total 14 additional lesions which was not visualized by high-definition white light endoscopy (HD-WLE) and narrow band imaging (NBI) inspection. In three patients, no fluorescence was visible and histology results of random biopsies showed no dysplasia (n=2) or low-grade dysplasia (n=1). Within a subset of 23 patients spectroscopy results were analyzed. Both visible lesions and additional lesions showed in all individual 23 patients a significantly ($P < 0.001$) higher mean intrinsic fluorescence compared to Barrett's tissue, 0.073 ± 0.015, 0.064 ± 0.017, 0.018 ± 0.005 respectively. In our cohort no (serious) adverse events related to the tracer were observed.
Conclusion: Based on the preliminary results combined with the results of the Phase I study we can conclude that VEGF-A guided NIR-FME is able to reliably detect (pre)malignant dysplastic lesions in patients with BE and seems to improves early lesion detection compared with HD-WL/NBI endoscopy. Moreover, the topically administered tracer Bevacizumab-800CW is safe and well tolerated.

Fluorescence Molecular Endoscopy (FME) using bevacizumab800CW to evaluate response to neoadjuvant chemoradiotherapy in esophageal cancer: preliminary results.

Background: Currently, patients diagnosed with locally advanced esophageal adenocarcinoma receive neoadjuvant chemoradiotherapy (nCRT) followed by esophagectomy independent of the patients' response to nCRT. Roughly 16-43% of esophageal cancer patients will achieve a pathological complete response (pCR) after nCRT. Current imaging devices cannot adequately distinguish pCR from pathological partial response (pPR) before esophagectomy. There is a need for a reliable pre-operative method which can precisely distinguish pCR from pPR and prevent (possibly) unnecessary surgery.
Methods: This study aims to determine the safety and feasibility of fluorescence molecular endoscopy (FME) using bevacizumab-800CW for identification of pCR after nCRT in patients with esophageal adenocarcinoma. Patients were intravenously injected with either 4.5, 10 or 25 mg bevacizumab800CW 3 days prior to the endoscopy. FME was performed to monitor the effect of the nCRT and biopsies were taken from normal and (residual) tumor area. Multi-diameter single fiber spectroscopy/single fiber fluorescence (MDSFR/SFF) spectroscopy was used to quantify the intrinsic fluorescence intensity, both in-vivo and ex vivo.
Results: In this ongoing trial, patients diagnosed with locally advanced esophageal adenocarcinoma scheduled for neoadjuvant chemoradiotherapy followed by surgery were enrolled between November 2018 and November 2020. No tracer related (serious) adverse events were observed. The preliminary results show a significant difference between normal esophageal tissue and residual area in all three dose groups based on quantitative MDSFR/SFF spectroscopy measurements. When considering the signal-to-background ratio (SBR), it shows a value of 1.36±0.08, 1.83±0.46 and 1.97±0.97 for 4.5, 10 and 25 mg respectively. This could be the results of the variation in TNM stage and Mandard score within these dose groups.
Conclusion: Preliminary results show that Bevacizumab-800CW is safe for administration in patients with locally advanced esophageal adenocarcinoma. The current dose escalation study will be extended to find the optimal dose for treatment monitoring.

Incidence and predictive factors for surgical complications and bile duct injury (BDI) after cholecystectomy for uncomplicated gallstone disease. Results from three prospective multicentre cohort studies.

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Background: Post-operative morbidity and BDI after cholecystectomy are generally associated with acute surgery for complicated gallstone disease. However, surgical complications and BDI are poorly researched in patients who present with uncomplicated cholecystolithiasis eligible for cholecystectomy.
Methods: A prospective multicentre cohort study was performed with data from the SECURE-, SUCCESS-, and PERFECT-trial. Patients with abdominal pain and gallstones, without a history of complicated gallstone disease, eligible for cholecystectomy were included. The primary outcome was the incidence of surgical complications and BDI. Surgical complications were classified according to Clavien-Dindo (CDC) and BDI according to the Strassberg classification. Complications were defined as minor (CDC<3) or major (CDC≥3). The influence of patient characteristics, symptomatology or biliary events (eg. cholecystitis, choledocholithiasis, or biliary pancreatitis) on surgical complications were evaluated.
Logistic regression analyses were performed to analyze variables associated with outcome. A p-value < 0.05 was considered statistically significant. Analyses were performed using SPSS statistics version 25.0 (IBM).
Results: Between February 2014 and June 2019 a total of 1956 patients were eligible for inclusion in 29 Dutch hospitals. Cholecystectomy was performed in 1417 patients (72.4%). A biliary event occurred in 79 of 1417 patients (5.6%) prior to surgery. Surgical complications occurred in 13.1% (185/1417) and were classified as minor in 11.0% (156/1417) and major in 2.0% of patients (29/1417). BDI occurred in 14 patients (1.0%). Biliary events after first consultation were associated with occurrence of major surgical complications (OR 3.7, 95%CI 1.37-9.97, p = 0.01). No other associations with major complications were found. The only factor associated with BDI was the development of a biliary event after first consultation (OR 4.8, 95%CI 1.30-17.43, p = 0.02). Fewer days to surgery (OR 0.99, 95%CI 0.98-1.00, p = 0.059) and increased patient age (OR 1.04, 95%CI 0.99-1.08, p = 0.054) showed a trend towards an association with BDI. Other patient characteristics or symptomatology were not associated with BDI.
Conclusion: Although most surgical complications were minor, the 1% risk of BDI in patients who present with initially uncomplicated cholecystolithiasis is not negligible. Biliary events occur in 5.6% and are associated with major surgical complications and BDI. Cholecystectomy for patients initially presenting with uncomplicated gallstone disease is associated with a 1% risk of BDI and 13.1% risk of surgical complications.

The definition and outcomes of oligometastatic esophagogastric cancer: a systematic review and meta-analysis

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Background: Growing evidence suggests improved overall survival (OS) can be reached in patients with limited (oligo)metastatic esophagogastric cancer treated with local metastasis directed-therapy (MDT) with curative intent. However, a uniform definition of oligometastatic disease in this setting is lacking.The primary aim was to summarize a definition of oligometastatic esophagogastric cancer. A secondary aim was to compare the OS after local MDT with patients who underwent systemic therapy alone.
Methods: Studies or trial protocols reporting on a definition of oligometastatic esophagogastric cancer were included as well as interventional studies including ≥7 patients with oligometastatic esophagogastric cancer who underwent local MDT (i.e. metastasectomy or stereotactic body radiation therapy). The primary outcome measure was the maximum number of organs and lesions to be considered oligometastatic ('general oligometastatic') and the maximum number of lesions per organ to be considered oligometastatic ('organ-specific oligometastatic'). Agreements between ≥2 studies of <50%, 50%-75%, and ≥75% were considered poor, fair and consensus, respectively. The secondary outcome measure was the hazard ratio (HR) of OS after local MDT as compared with systemic therapy alone. Pooling of HRs was performed using a random-effects model. Quality assessment was performed with the ROBINS tool.
Results: A total of 80 studies of which 3 trial protocols provided a definition of general or organ-specific oligometastatic esophagogastric cancer were included. Metastatic disease limited to 1 organ (fair agreement) and 3 lesions was considered 'general' oligometastatic. Liver metastasis limited to both lobes (bilobar; consensus) and 3 lesions, lung metastasis limited to 1 lung (unilateral; fair agreement) and 3 lesions, extra-regional lymph node metastasis limited to 1 lymph node station (fair agreement) and 4-5 lesions and brain metastasis limited to 2 lesions, was considered 'organ-specific' oligometastatic. The pooled HR after local MDT was for general oligometastatic disease 0.42 (95% CI: 0.21-0.83) among 4 non-randomized studies with serious risk of bias and after local MDT for liver oligometastasis 0.33 (95% CI 0.19-0.57) among 2 non-randomized studies with serious risk of bias both as compared with systemic therapy alone.
Conclusion: Current literature considers metastatic esophagogastric cancer limited to 1 organ with a maximum of 3 lesions, oligometastatic. Non-randomized studies with serious risk of bias suggest that local MDT with curative intent was associated with improved OS as compared with systemic therapy alone in patients with general oligometastatic disease and liver oligometastasis.

Management of Pancreatic Fistula and Biliary Leakage after pancreatoduodenectomy through Percutaneous Transhepatic Biliary Drainage

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Background: Biliary and biliopancreatic leakage through a hepaticojejunostomy or pancreaticojejunostomy after pancreatoduodenectomy are difficult to treat and associated with high morbidity and mortality. The aim of this study was to assess the technical and clinical success rates of percutaneous transhepatic biliary drainage (PTBD) in these patients.
Methods: We performed a retrospective cohort study in two high-volume centers including all patients undergoing PTBD for hepaticojejunostomy or pancreaticojejunostomy leakage after pancreatoduodenectomy (January 2014 to December 2019). Technical success was defined as placement of an intrajejunal PTB drain. Clinical success was defined as hospital discharge with a resolved leak without the need for additional interventions other than intra-abdominal percutaneous catheter drainage.
Results: Out of 822 pancreatoduodenectomies, 67 patients (8%) underwent PTBD. Indications were leakage of the pancreaticojejunostomy (n=23; 34%), hepaticojejunostomy (n=15; 22%) and of both anastomoses (n=22; 33%). PTBD was performed on median postoperative day 12 (IQR 9–17) and technically successful in 99% (n=66). Revision of the PTB drain was performed in 41 patients (63%) due to obstruction (n=21) or dislodgement (n=29). The clinical success rate was 94% (n=63). Leakage was resolved on median day 33 (IQR 21 – 59) since PTBD. PTBD related complications (n=23; 34%) included bleeding (n=12; 3 requiring embolization), cholangitis (n=8) and bacteremia (n=5). In hospital mortality was 6% (n=4) and PTBD related mortality was 1% (n=1), due to respiratory failure after pleural perforation.
Conclusion: PBTD is effective in the treatment of biliopancreatic leakage after pancreatoduodenectomy. Revisions of the PTB drain are often needed and complications are not infrequent.

Pancreas-sparing duodenectomy for advanced duodenal polyposis in patients with familial adenomatous polyposis: short and long-term outcomes

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Background: Nearly all patients with familial adenomatous polyposis (FAP) develop duodenal adenomas and 4-10% duodenal cancer, warranting endoscopic surveillance. Extensive duodenal polyposis not amenable to endoscopic intervention may demand a surgical resection. In our center, a prophylactic pancreas-sparing duodenectomy (PSD) is offered for diffuse premalignant duodenal polyposis. We evaluated our 20-year experience with PSD.
Methods: We performed a cohort study including FAP patients who underwent PSD between 2000 and 2020. Reconstruction with Billroth II anastomosis and short blind ending jejunal loop to the neo-papilla was performed to facilitate endoscopic surveillance, guided by the "neo-Spigelman" stage but not exceeding a 3 years interval. Data on short and long-term surgical outcomes and findings at surveillance endoscopies were evaluated.
Results: In total, 29 patients underwent PSD (15 men, median age 54). They had Spigelman stage III (n=6) or IV (n=23). No invasive cancers were found. Postoperative, 15 (52%) patients experienced a severe complication defined as Clavien-Dindo grade III or IV. Clinical relevant pancreatic fistula (grade B/C) occurred in 11 (38%) patients, gastro/duodeno-jejunostomy leakage in 4 (14%), delayed gastric emptying in 5 (17%) and 1 (3%) patient had severe acute pancreatitis. Median hospital stay was 14 days (IQR 9-29). No deaths occurred.
At long-term follow-up, 4 (14%) patients developed acute pancreatitis, 1 (3%) a new onset diabetes mellitus and 3 (10%) exocrine pancreatic insufficiency.
For surveillance, a total of 176 endoscopies were performed in 27 patients during a median follow-up of 119 months (IQR 55-148). Visualization of the end of the blind ending jejunal loop and neo-ampulla was documented in 25 (93%) and 22 (81%) of patients, respectively. In 22 (81%), one or more adenomas were detected in the jejunum. An advanced jejunal adenoma (defined as adenoma ≥10mm and/or HGD) was detected in 11 (41%) patients after a median of 44 months (IQR 14-19). Progression of jejunal polyposis resulted in neo-Spigelman stage IV in 7 (26%) patients after a median of 91 months (IQR 59-119). For 4 (15%) patients a surgical re-resection of the proximal jejunum was required for jejunal polyposis after a median of 109 months (IQR 98-123). No patients developed jejunal cancer.
Conclusion: PSD effectively prevents duodenal cancer in FAP patients with advanced duodenal polyposis. However, perioperative morbidity is substantial and most patients will have jejunal adenomas sometime at follow-up. With regular endoscopic surveillance, jejunal cancer can be prevented.

Delaying surgery to achieve a complete response after neoadjuvant chemoradiotherapy for rectal cancer: at what "cost"? A single institution analysis of hospital costs, surgical and oncological outcomes.

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Background: A Watch & Wait strategy for patients with rectal cancer with a clinical complete response (cCR) after neoadjuvant chemoradiotherapy (NCR) is a valuable alternative for rectal resection. Even a near complete response can evolve in a cCR and therefore further delaying response assessment is accepted. However, there are still patients who will have residual tumor or regrowth during watch & wait. These patients will still require TME surgery, albeit it being delayed. Although the overall oncological results of the watch and wait cohorts are highly promising, data on patients requiring salvage or delayed surgery is limited. Also, there is concern that the longer interval between radiotherapy and surgery allows for more pronounced post-radiation fibrosis which could lead to a higher complication rate. Finally, it is unclear what the economical cost is of the stringent follow-up and eventual perioperative costs in this specific group.
We aimed to address the shortage of evidence regarding safety and costs for patients who underwent delayed TME surgery after NCR in order to achieve a cCR.
Methods: Patients who received NCR for locally advanced adenocarcinoma of the rectum followed by TME surgery within Jan 2015- May 2020 were included. Exclusion criteria were delayed surgery for other reasons than achieving clinical response, synchronous metastases, palliative treatment and other malignancy.
Patients without a complete clinical response received (direct) TME surgery, whereas patients with a near complete response or a subsequent regrowth received delayed TME surgery. Data regarding (re)admission and complications were collected until 30 days postoperatively. Primary endpoints were were morbidity, hospital costs and three year overall survival and disease-free survival.
Results: Ninety-four patients (29 delayed surgery vs 65 direct surgery) were included in the final analysis.There was no difference in re-admission rate (p = 0,10), surgical re-intervention (p = 0,10) and anastomosis rate (p = 0,62) between direct and delayed surgery groups. Hospital costs were higher in the delayed group (€15611 vs €17116). 3-year overall survival (92% vs 100%, p = 0,47) and disease-free survival (76% vs 87%, p = 0,61) rates were similar. Stoma-free survival was 52,6% (30/57) in the direct surgery group vs 33,3% (10/30) in the delayed surgery group (p = 0,09).
Conclusion: Delayed TME surgery has similar morbidity compared to patients who underwent direct surgery without a substantial rise in costs. In our series, there was no difference in overall- and disease free survival. Therefore, repeated response assessment after NCR to look for a cCR will not harm outcome for patients who turned out to have no cCR.

Postponing surgery to optimise patients with acute right-sided obstructing colon cancer - a pilot study

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Background: Right-sided obstructing colon cancer (OCC) is usually treated with acute resection. Recent studies on right-sided obstructing colon cancer report high mortality and morbidity compared to patients without obstruction. The aims of this study are to retrospectively analyse whether it is possible to optimise the medical condition of patients with acute right-sided OCC prior to surgery and whether this is improves postoperative outcomes.
Methods: All consecutive patients with high suspicion or histological proof of right-sided colon cancer that were treated with curative intent between March 2013 and December 2019 were analysed. Patients were divided into two groups: optimisation and no optimisation. Preoperative optimisation included nutritional interventions (total parenteral nutrition or tube feeding), physiotherapy, and bowel decompression if needed.
Results: In total 54 patients were analysed in this study. Twenty-four patients received optimisation before elective surgery and thirty patients received emergency surgery without optimisation. Elective surgery was performed after a median of eight days (IQR 7-12). Postoperative complications were found in 50% (n=12) and 77% (n=23) of the patients, respectively for patients with and without optimisation (p=0.051). Major complications were diagnosed in three (13%) patients with optimisation compared to ten (33%) patients without optimisation (p=0.111). Postoperative in-hospital stay, 30-day mortality, and primary anastomosis were comparable between both groups.
Conclusion: This pilot study shows that optimisation in patients with acute right-sided OCC is possible and might lead to fewer complications compared to patients without optimisation before surgery. To compare preoperative optimisation in patients with OCC with current treatment options, a prospective study has started (NL8266).

Delayed surgery after neoadjuvant treatment for rectal cancer does not lead to regret, impaired quality of life or worry for cancer.

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Background: Non operative management of complete clinical responders after neoadjuvant treatment for rectal cancer has promising oncological results. Even a near complete response can evolve in a cCR and therefore further delaying response assessment is accepted. However, up to 40% of patients will develop a regrowth and require delayed surgery after all. To date, it is unknown if and to what extent quality of life of these patients is affected.
Methods: Between January 2015-May 2020, 200 patients were treated with neoadjuvant therapy of which 94 received TME surgery. Fifty-one (59%) of 87 alive patients returned the questionnaires: 33 patients who underwent direct and 17 patients who underwent delayed surgery. Quality of life was measured through the QLQ-C30, QLQ-CR29 and Cancer Worry Scale questionnaires. Possible decision regret was measured through the Decision Regret Scale. Exploratory factor analysis (EFA) and known groups comparison was performed to assess questionnaire validity in this sample.
Results: Higher mean physical function scores (89.2 vs 77.6, p = 0,03) were observed in the direct surgery group, which lost significance after correction for operation type (p = 0,25). Arousal for men was higher in the delayed surgery group (20.0 vs 57.1, p = 0,02). There were no differences between surgical groups for the other questionnaire items. Worry for cancer was lower in the delayed surgery group (10.8 vs 14.0, p = 0,21). Patients who received delayed surgery still reported a very positive attitude towards the watch and wait treatment option. EFA reproduced most subscales with good internal consistency.
Conclusion: Quality of life or worry for cancer is not impaired in patients undergoing delayed surgery after neoadjuvant treatment for rectal cancer. Patients who received delayed surgery showed no regret towards the watch and wait treatment decision. Therefore, this study supports a repeated response assessment strategy after CRTx for rectal carcinoma to identify all complete responders from a quality of life perspective.

Long-term Outcome of Radical Excision vs. Phenolisation of the Sinus Tract in Primary Sacrococcygeal Pilonidal Sinus Disease; A Randomized Controlled Trial

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Background: The optimal treatment of pilonidal sinus disease is still a widely discussed topic. Phenolisation of the sinus tract(s) is a minimal invasive treatment option for pilonidal sinus disease and has shown to have advantages over radical excision with regard to short-term outcome, including less pain and surgical site infections, faster wound healing and sooner return to normal daily activities. However, long-term outcomes with regard to the phenolisation technique are essentially lacking. The aim of this randomized trial was to compare the long-term outcome between phenolisation of the sinus tracts vs. radical excision with primary wound closure as treatment for sacrococcygeal pilonidal sinus disease (SPSD).
Methods: Between 2013 and 2017, 100 patients with primary SPSD were randomized and eventually, 50 patients underwent phenolisation and 46 radical excision. After a follow-up of at least two years, all patients were contacted to participate in this long-term follow-up. Long-term outcome was obtained by an online questionnaire, including quality of life (Short-Form-36), recurrence of SPSD, SPSD-related complaints (pain, fluid discharge and itch) and patient's satisfaction. Patients were scored as no recurrence if they never had a recurrence objectified by a physician or a second procedure for recurrent SPSD, and in addition, if they denied the impression of recurrent SPSD in the questionnaire.
Results: A total of 74 patients (77.1%) completed the questionnaire; 36 patients after phenolisation and 38 after excision. Mean (±standard deviation) time to follow-up was 48.4 (±12.8) and 47.8 (±13.5) months, respectively. There was no significant difference between both groups with regard to quality of life and SPSD-related symptoms at the natal cleft. In the phenolisation group, two patients (5.6%) developed a recurrence and one patient (2.6%) in the excision group (P=0.604). The impact of the whole treatment was significantly less after phenolisation (P=0.010). In addition, 30 patients (83.3%) in the phenolisation group and 22 (57.9%) in the excision group would undergo the same treatment again (P=0.024).
Conclusion: No significant difference in recurrence rate and quality of life between phenolisation of the sinus tracts and radical excision with primary wound closure for primary SPSD was found after a follow-up of four years. However, the impact of the whole treatment was significantly less after phenolisation compared to radical excision. Therefore, due to the previously shown favorable short-term results and comparable long-term recurrence rate and quality of life, phenolisation of the sinus tracts should be considered primary treatment option in patients with pilonidal sinus disease.

Chest X-ray in the follow-up of colorectal carcinoma: added value?

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Background: Colorectal carcinoma (CRC) has a high incidence worldwide, with a large share in cancer-related mortality. The risk of recurrence is 30-50% with metastases frequently localised in the lungs. Treatment of pulmonary metastases with stereotactic ablative radiotherapy (SABR) or pulmonary metastasectomy increases survival. The best modality for thoracic screening in the follow-up however remains topic of discussion. We studied the benefit of CXR in the follow-up of CRC.
Methods: In this retrospective study, patients whom participated in the follow-up after CRC between 01-01-2013 and 01-01-2017 were included. Follow-up consisted of routinely CXR, serum Carcino-Embryonic Antigen (CEA) and ultrasound of the liver. We searched for patients with pulmonary metastases of CRC, found only through an aberrant chest X-ray. These patients had normal serum CEA levels. Furthermore, we noted treatment of these patients to identify influence on survival.
Results: We included 633 patients, of whom 34 (5.4%) with pulmonary secondary tumours. Of the patients with pulmonary metastases, 17 (50%) had aberrancies on chest X-ray whilst having normal CEA levels. Eleven (33%) of these patients were treated with curative intent. Therefore, 273 CXRs had to be made, to treat one patient with curative intent.
Conclusion: Half of the patients with lung metastases on CXR in the follow up would not have been detected with CEA-levels only. Therefore CXR seems to have additional value within the follow-up of colorectal carcinoma although not all patients found can be treated with curative intent.

Effect of host genetics on the gut microbiome in 7,738 participants of the Dutch Microbiome Project

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Background: Host genetics are known to influence the gut microbiota, yet their role remains understudied. Previous findings of genome-wide association studies (GWAS) between host genetics and gut microbiota are suffering from poor reproducibility due to relatively limited sample sizes. Here we present the largest GWAS of the gut microbial composition and function to robustly characterize the host – microbiota interactions, taking into account both intrinsic and extrinsic factors.
Methods: We used shotgun metagenomic sequencing on feces from 7,738 individuals of the Dutch Microbiome Project and matched their imputed genotypes from genome-wide genotyping array. A linear mixed model was used to associate over five million variants with 207 taxa and 205 pathways to identify microbial quantitative trait loci (mbQTL), with age, sex and the genetic relationship matrix as covariates. Effect from diet and blood type was assessed using interaction models. We further performed a bi-directional Mendelian randomization analysis to infer the potential causality between the gut microbiota and diet, biomarkers and diseases. Finally, we carried out a power calculation to estimate the ability to detect mbQTLs in terms of high inter-individual variation of microbiota.
Results: We observed two robust, study-wide significant (p<1.89x10^{-10}) mbQTLs. The T allele of variant rs182549, near the lactase intolerance related gene *LCT*, was associated with decreased abundance of genus *Bifidobacterium* and species *Bifidobacterium adolescentis*. This effect was also modulated by lactose intake of the participants. The other locus rs550057 was close to gene *ABO*, coding a histo-blood group ABO system transferase, associated with species *Bifidobacterium bifidum*, *Collinsella aerofaciens* and pathways of lactose and galactose degradation, which also interacted with participant secretor status determined by *FUT2* genotype. 18 novel loci involved in metabolic diseases showed genome-wide associations (p<5x10^{-8}) with microbial taxa and pathways. A higher abundance of family Rikenellaceae was causally linked to lower consumption of salt (FDR<0.1). However, the current sample size is still underpowered to detect genetic effects on taxa present <80% of our samples.
Conclusion: This study confirmed previously reported host-microbiota interactions and identified multiple novel genomic loci influencing the abundance of bacterial taxa and pathways, hereby supporting the role of diet and secretor status of *FUT2* modulating genetic effects. We also demonstrated that even larger sample sizes than ours are needed to elucidate the host genetic effects on the gut microbiota with low-present rates.

Human intestinal (regulatory) T cells show profound adaptation to the microenvironment and alteration of phenotype during inflammation in Crohn's disease patients

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Background: CD4 resident T-cells (Trms) have been implicated in the relapsing-remitting course of Crohn's disease (CD). It is hypothesized that Trms can lose their tissue adaptation, focused on immunosurveillance, gaining an inflammatory profile.
Methods: We performed protein and transcriptomic (bulk/single-cell) profiling of human CD4 (CD4 non-Treg, Tregs) intraepithelial and lamina propria (LP) small intestinal (SI) and colonic T-cell populations of CD patients, including CD-discordant twins, and healthy controls (HCs).
Results: Our data indicate the microenvironment as main driver of CD4 T-cell signatures in CD. First, epithelial CD4 T-cells showed an "activated-yet-resting" phenotype compared to the LP, confirmed by flow-cytometry. Secondly, in the colon all LP but not epithelial CD4 T-cell subsets shared NFκB- and TLR-signaling, whereas no dominant pathways were shared among SI CD4 T-cells. On single-cell level CD4 T-cell populations in CD formed a continuum instead of clear clusters. Additionally, CD4 Trms ($CD69^{high}$) did not differ between HCs and CD patients in remission, both in the LP and epithelium. However, LP Tregs and $CD4CD69^{low}$ T-cells showed upregulation of KLRB1, NKG7, IFNG and CCL5 in inactive CD compared to HCs, indicative for pro-inflammatory signaling. In CD patients with active disease only epithelial Tregs showed significant changes in transcriptional profile, with increased expression of amongst others FOXP3, TIGIT, CXCR3, and LAG3, and upregulation of cytokine/TCR-signaling and oxidative phosphorylation.
Conclusion: Together our data show profound local adaptation on protein and transcriptomic level of CD4 T-cells to the human intestinal mucosal microenvironment. During inflammation epithelial Tregs demonstrate the largest transcriptional profile changes indicating induction of strong regulatory activity.

Fecal water from Crohn's disease patients: high mucin degradation, but no epithelial barrier disruption in vitro

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Background: Crohn's disease (CD) is a chronic inflammatory gastro-intestinal condition with a variable disease course. Both, impaired intestinal integrity and microbial dysbiosis are associated with disease onset and the occurrence of exacerbations. We hypothesized that a perturbed microbial activity in CD patients may contribute to the impaired barrier function. Therefore, this study aimed to examine the impact of bacterial products derived from fecal samples of either active CD patients, CD patients in remission or healthy controls on mucin degradation and intestinal epithelial barrier function *in vitro*.
Methods: Six healthy subjects and twelve CD patients were included. Disease activity was determined by endoscopic evaluation (SES-CD). Fresh fecal samples were collected within one week prior to endoscopy and processed to obtain fecal water (FW) within six hours. Bacterial membrane vesicles (MVs) were isolated from frozen samples using an ultrafiltration and size exclusion chromatography-based protocol. FW and MVs were applied on mucin agar plates to determine mucin degradation. Further, FW and MVs were applied on differentiated Caco-2 cell monolayers. The difference in transepithelial electrical resistance (TEER) and fluorescein-isothiocyanate dextran 4 kDa (FITC-d4) flux was determined to detect paracellular junction disruption. Relative abundances of fecal bacterial genera were evaluated using metagenomic 16S sequencing.
Results: FW-induced mucin degradation was more pronounced in CD samples as compared to healthy subjects (p<0.01), but was not linked to bacterial relative abundances. MVs did not induce detectable mucin degradation. FW resulted in 78-87% decrease of TEER in three of the remissive (p<0.001) but not the active CD samples. MVs did not induce changes in TEER or FITC-d4 permeation.
Conclusion: The higher ability of CD patient-derived FW to degrade mucin might indicate contributions of microbial products to CD pathophysiology and warrants further investigation. Moreover, the altered epithelial resistance in some individuals appears to be rather due to altered ion fluxes or nutrient exposure than paracellular alterations.

Cross-presentation by cancer-associated fibroblasts suppresses anti-tumor T cell immunity and is enhanced by upregulation of the lysosomal protease Cathepsin S in human colorectal cancer.

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Background: Cross-presentation is the process of presenting exogenous antigens in human leukocyte antigen (HLA)-class I and is essential to initiate an adaptive immune response. Professional antigen presenting cells are best known for their ability to cross-present but recent murine studies show that cancer-associated fibroblasts (CAFs) can also acquire this capacity and thereby suppress T cell function in the murine tumor microenvironment. However, it is currently unknown whether human CAFs are able to cross-present, which molecular pathways are involved and how this influences T-cell function.
Methods: In this study we investigated the ability of human colorectal cancer (CRC)-derived CAFs to cross-present neoantigen-derived synthetic long peptides (SLPs), corresponding to tumor-derived mutant peptides, and how this affects tumor-specific T-cell function. Processing of the SLP was studied by targeting components of the cross-presentation machinery through CRISPR/Cas9 and siRNA-mediated genetic ablation to identify the key molecules involved in fibroblast-mediated cross-presentation. T cell assays (cytokine production and T cell activation markers) and killing assays were performed to study the effect of fibroblast cross-presentation on T cell function. Finally, our findings were validated in primary, CRC-derived fibroblasts and human CRC tissues.
Results: Our results indicate that human CRC derived CAFs display enhanced cross-presentation capacity compared to matched, normal fibroblasts. Mass spectrometry analysis revealed presence of the short peptide epitope in HLA class-I molecules on the fibroblast surface, indicating processing of the SLP by fibroblasts. The CAF phenotype can be mimicked by exposing normal fibroblasts to colorectal cancer cell-conditioned medium. Mechanistically cross-presentation can occur via a partially transporter associated with antigen processing (TAP)-independent pathway. Zooming in on this pathway, our data show that cross-presentation of a neoantigen-derived SLP was dependent on the lysosomal protease Cathepsin S. Cathepsin S expression was detected in CAFs in human CRC tissues and in primary, CRC derived CAFs. Exposure of quiescent fibroblasts to CRC-conditioned medium induced Cathepsin S expression and subsequently enhanced cross-presentation. Finally, we studied the role of fibroblast-mediated SLP cross-presentation on the function of tumor-specific T cells and preliminary data show that this diminishes anti-tumor killing capacity of T cells.
Conclusion: In conclusion, our data show the potential role of CAFs in directly inhibiting an anti-tumor T cell response in an antigen-dependent fashion which would have implications for T-cell based immunotherapy of CRC.

Targeting GITR enhances human tumour-infiltrating T cell functionality in mismatch repair proficient primary colorectal carcinoma and liver metastases

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Background: Immune checkpoint blockade (ICB; e.g. anti-PD-1/-CTLA-4) has been proven to be clinically effective in mismatch repair deficient (dMMR) colorectal carcinoma (CRC). Yet, the majority of patients caries mismatch repair proficient (pMMR) CRC, especially those with liver metastasis, and does not respond to ICB. Here, we studied the effect of immune checkpoint stimulation via GITR targeting on human tumour-infiltrating lymphocyte (TIL) functionality in primary CRC and liver metastases (CRLM).
Methods: Human TIL were isolated from freshly resected pMMR tumours of patients with primary CRC (stage 1-3) or liver metastases. GITR expression on TIL was determined using flow cytometry and compared to leukocytes isolated from blood (PBMC) and tumour-free surrounding tissues (tumour-free colon/liver, resp. TFC and TFL). Ex vivo functional assays were used to assess TIL expansion, activation and cytokine/cytotoxic mediator secretion upon CD3/CD28 bead activation and co-stimulation using an antibody-crosslinked recombinant trimeric GITR ligand (GITRL).
Results: GITR was overexpressed on TIL when compared to other stimulatory immune checkpoints (4-1BB, OX40). GITR was predominantly expressed on $CD4^+$ and $CD8^+$ TIL compared to PBMC and TFC or TFL compartments in both primary CRC and CRLM. Among $CD4^+$ TIL, GITR was increasingly expressed on $CD45RA^{+/-}$ $FoxP3^-$ helper T (Th), $CD45RA^-$ $FoxP3^{int}$ activated helper T (aTh), and $CD45RA^-$ $FoxP3^{hi}$ activated regulatory T cells (aTreg), respectively. Within $CD8^+$ TIL, GITR expression was higher on TOX^+ $PD1^{Hi}$ and putative tumour-reactive $CD103^+$ $CD39^+$ TIL. Impaired effector cytokine production upon ex vivo PMA/ionomycin stimulation was observed in $CD4^+$ and $CD8^+$ GITR-expressing TIL, hinting on functional exhaustion of the target population. However, recombinant GITRL reinvigorated ex vivo TIL responses by significantly enhancing $CD4^+$ and $CD8^+$ TIL numbers and proinflammatory cytokine secretion in a dose-dependent manner. Treg depletion did not fully abrogate the stimulatory effect of GITR ligation on CD4 and CD8 T cell expansion. Importantly, GITR-ligation also enhanced expansion of purified $CD8^+CD39^+$ TIL. Dual treatment with GITR ligand and nivolumab (anti-PD-1) further enhanced $CD8^+$ TIL responses compared to GITR ligand monotherapy, whereas nivolumab alone did not show any effect.
Conclusion: Agonistic targeting of GITR enhances ex vivo human TIL functionality in CRC and might therefore be a promising approach for novel mono- or combinatorial immunotherapies in primary CRC and CRLM.

Prevalence and Clinical Characteristic of Autoimmune Gastritis in Patients with Intestinal Metaplasia

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Background: Endoscopic surveillance of precancerous gastric lesions (PGL) is recommended to decrease the risk of developing gastric cancer. The MAPS 2019 guideline for PGL surveillance recommends that patients with autoimmune gastritis (AIG) may benefit from endoscopic surveillance as this leads to focal atrophy of oxyntic mucosa or intestinal metaplasia (IM). Accurate diagnosis of AIG in patients with gastric atrophy is critical to decide surveillance strategies. We studied AIG prevalence in patients with atrophy or IM and aimed to identify functional biomarkers to optimize AIG detection in IM patients.
Methods: 257 patients were included from the PROREGAL study, a multicenter, prospective cohort study comprising patients gastric atrophy and IM. Controls were 89 individuals undergoing urea breath test for suspected *H. pylori*infection. GastroPanel (PGI, PGII, G-17 and *H pylori*IgG) was used. Anti-parietal cells antibodies (APCA) were determined by indirect immunofluorescence staining and EliA immunoassay. Histological features were assessed according to the OLGIM system. Binary logistic regression was used to evaluate the relationship between AIG and IM. Differences in proportions for the presence of autoantibody and IM were calculated using chi-square test.Receiver operating characteristic (ROC) curve were used to assess the diagnostic efficiency of PGI, PGII, PGI / PGII and G-17, separately. Logistic regression model was used for combines models.
Results: Significantly more patients in the PROREGAL cohort showed APCA positivity compared to controls (17.5% vs. 5.6%, p = 0.006). In the PROREGAL cohort, patients with positive APCA more often showed corpus-limited IM (39% vs. 11%, p <0.001). Median serum level of PGI and PGII were significantly decreased in patients with APCA compared to those without APCA (PGI, 15.2 µg / l vs. 138 µg / l, p <0.001; PGII, 17.26 µg / l vs. 22.4 µg / l, p = 0.03, ratio PGI / GPII 0.86 vs. 6.21, p <0.001). The median serum level of G-17 was increased significantly in patients with positive APCA scores (107.28 pg / l vs. 5.35 pg / l, p <0.001). The area under the ROC (95% confidence interval [CI]) was 0.845 (95% CI = 0.766 to 0.925) for PGI, 0.849 (95% CI = 0.765 to 0.932) for PGI / PGII and 0.86 (95% CI = 0.798 to 0.922) for G-17. A combination of PGI, PGII and G17 was able to predict APCA positivity with an AUC of 87.7%, a sensitivity of 84.4% and specificity of 89.9%.
Conclusion: The prevalence of autoimmune gastritis is significantly increased in IM populations and most of them may go underdiagnosed. Patients with corpus-limited IM should be suspected for the AIG. GastroPanel test may aid in the diagnosis of AIG-associated intestinal metaplasia.

Ursodeoxycholic acid for the prevention of symptomatic gallstone disease after bariatric surgery: a multicenter, randomized, placebo-controlled, double-blind superiority trial (UPGRADE trial)

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Background: Approximately 8% to 15% of patients develop symptomatic gallstone disease within 24 months after bariatric surgery. We conducted the UPGRADE trial to provide evidence on the use of ursodeoxycholic acid (UDCA) prophylaxis in preventing symptomatic gallstone disease.
Methods: For this multicenter, randomized, placebo-controlled, double-blind superiority trial with end-point adjudication (Dutch Trial Registry NL5954), patients with an intact gallbladder and morbid obesity scheduled for Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy in three high-volume bariatric centers in the Netherlands were assessed for eligibility. Patients were randomly assigned (1:1) to either UDCA 900mg daily for 6 months or placebo treatment. Randomization was stratified for the presence of gallbladder stones at preoperative ultrasonography and for type of surgery. The primary end-point was symptomatic gallstone disease within 24 months, defined as admission or hospital visit for symptomatic gallstone disease. The reported analysis was based on modified intention-to-treat. Supervised backward logistic regression was used to account for stratification and adjust for baseline differences (health utility and presence of type 2 diabetes), for statin use at baseline, therapy compliance and postoperative weight loss.
Results: Between January 2017 and October 2018, 985 patients were randomly assigned to UDCA (n=492) or placebo treatment (n=493). Twenty six patients were excluded for not meeting the inclusion criteria, for withdrawing informed consent prior to treatment administration or for missing endpoint assessment. Most patients (889 [91.9%]) received a RYGB, and asymptomatic gallstones were present at baseline in 189 patients (19.5%). The primary end-point occurred in 31 of 475 patients (6.5%) in the UDCA-arm and in 47 of 484 patients (9.7%) in the placebo-arm (odds ratio (OR) 0.65; 95% confidence interval [CI], 0.41 to 1.04; P=0.073; relative risk (RR) 0.67). The adjusted OR for UDCA treatment was 0.44 (95% CI, 0.24 to 0.80; P=0.008) with a significant interaction between UDCA treatment and asymptomatic gallstones at baseline (OR 2.88; 95% CI, 1.03 to 8.02; P=0.043). In the gallstone negative group at baseline, the primary end-point occurred in 16 of 381 patients in the UDCA-arm (4.1%) and in 35 of 392 patients (8.9%) in the placebo-arm (OR 0.45; 95% CI, 0.24 to 0.82; RR 0.47. The OR for statin use at baseline was 0.38 (95% CI, 0.16 to 0.88; P=0.025).
Conclusion: In bariatric patients without asymptomatic gallstones at baseline, UDCA prophylaxis for 6 months after surgery reduces symptomatic gallstone disease within 24 months.

Liver decompensation as late complication in HCC patients with long term responses following selective internal radiation therapy.

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Background: Selective internal radiation therapy (SIRT) is used for the treatment of intermediate and advanced stage hepatocellular carcinoma (HCC). The aim of this study was to assess the long-term liver-related complications of SIRT in patients with HCC who had not developed Radioembolization Induced Liver Disease (REILD).
Methods: In this multicenter retrospective study, patients who had undergone SIRT between 2011 and 2019 were included. A predefined subgroup consisting of patients who had not developed REILD was specifically explored. Biochemical, radiological and performance status data were analyzed. Primary outcomes were clinical and/or biochemical signs of liver decompensation 6 months or later after SIRT, defined as a Child Pugh (CP) score ≥B7. Secondary outcomes were overall survival (OS), tumor response and time to progression (TTP). Data were compared with a matched cohort of patients treated with sorafenib.
Results: Eighty-five (total cohort) patients were included in this analysis, of whom 16 (14%) developed REILD. Of the remaining 69 patients, 38 (55%) developed liver decompensation CP>B7, that were compensated CP A at baseline. Thirty patients (43%) developed clinically relevant ascites during follow-up. Median OS of all patients analyzed was 18 months (95% CI 14-22). In the group of patients without REILD, median OS in patients with CP>B7 was significantly shorter than that of patients without CP>B7; 16 (95% CI 11-21) vs 31 months (95% CI 19-43); p=0.001. In a case-matched analysis between this total study cohort and patients treated with sorafenib, median OS was significantly longer in patients treated with SIRT; 17 (95% CI 12-21) vs 11 months (95% CI 8-14); p=0.027. Liver decompensation occurred significantly more often in the SIRT cohort as compared to the matched patients with sorafenib (40% difference, p<0.001). ALBI-score was an independent predictor for liver decompensation (OR 0.07; 95% CI 0.01-0.48; p=0.006) and OS (HR 2.82; 95% CI 1.43-5.60; p=0.003).
Conclusion: Liver decompensation often develops as late complication of SIRT in HCC patients who have not developed REILD after SIRT and significantly impacts OS. The ALBI score was predictive for the development of liver decompensation and OS and may be a valuable marker for patient selection for SIRT.

The alteration of gut microbiome in liver transplantation: first results from the TransplantLines Biobank and Cohort study

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Background: While the role of the gut microbiome in liver disease is increasingly being understood, little is known in the setting of liver transplantation (LT) and its outcomes. The dynamics of gut microbiota during LT and the relationship with mortality after LT remain unknown. A better understanding of the gut microbiome in the setting of end-stage liver disease and LT would enable the development of gut microbiome directed therapies to improve long-term outcomes of LT patients.
Methods: Shotgun metagenomic sequencing was performed on 425 fresh frozen fecal samples from 375 patients during screening period (pre-LT), short-term (3, 6, 12 months), 1-5 years, 5-10 years and long-term post- LT (> 10 years) derived from the TransplantLines Biobank. Clinical characteristics of underlying disease, disease severity, surgical parameters, immunosuppressive regime, comorbidities and patient survival were extracted from hospital records. Microbial diversity and community description were compared using Wilcoxon test between the groups by calculating Shannon diversity and Bray-Curtis dissimilarities. Multivariable general linear mixed model analyzes, which corrected for identified confounderswere performed to compare microbial taxa, pathways, antibiotic resistant genes and virulence factors. The association between microbiota and patient mortality was calculated using Cox proportional-hazards analysis.
Results: Compared to healthy controls, patients with end-stage liver disease had a significantly lower gut microbial diversity (p<0.001). In addition, patients with severe liver disease (MELD> 18 and Child-pugh C) showed the lowest microbial diversity. Interestingly, the diversity was significantly decreased in peri-operative LT (within 3 months) and increased long-term post-LT (>1-year post-LT), compared to pre-LT samples (p<0.001). The microbiome of Pre-LT patients was characterized by a loss of short chain fatty acid producing bacteria including *Subogranulum spp.* and *Akkermansia spp.* (PFDR<0.20). The use of immunosuppressive medication was associated with an increasein the abundance of microbial pathways involved in biosynthesis of cyclosporine and mycophenolic acid (PFDR<0.20). Strikingly, the high microbial diversity was associated with a lower patient mortality post-LT (adjusted p-value = 0.043, hazard ratio 0.34, 95% CI 0.12 to 0.97).
Conclusion: This study is the largest survey on the role of microbiome in the context of liver transplantation to date. We found several significant gut microbial signatures pre- and post-LT that could have important clinical implications. Moreover, microbial diversity was associated with survival post-LT, revealing a new potential biomarker or therapeutic target.

Hepatitis C Elimination in the Netherlands (CELINE): nationwide retrieval of lost to follow-up patients with chronic hepatitis C

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Background: Hepatitis C virus (HCV) prevalence in the Netherlands is estimated at 0.16%. Presumably, up to 30% of the diagnosed population has been lost to follow-up (LTFU) before being successfully treated. Retrieval of LTFU patients has the potential to reduce the impact of the HCV epidemic. Therefore we initiated the nationwide retrieval project CELINE, aiming to achieve HCV micro-elimination in previously diagnosed but LTFU HCV patients.
Methods: LTFU patients were identified by consulting laboratory and patient records of up to 15 years old in hepatitis treatment centres and, when possible, public health or primary care laboratories and other hospitals. Subsequently, the Municipal Personal Records database was consulted to identify patients eligible for retrieval, defined as being alive and having a known Dutch residence. These patients were invited for a screening visit at their local hepatitis treatment centre. Primary endpoint was the number of LTFU patients successfully re-linked to care.
Results: So far, 28 centres have finished the identification phase and initiated the retrieval phase, whereas in a further 10 centres CELINE has been approved. This includes 35 of 47 (74%) hepatitis treatment centres and 3 other centres. Of 14,942 potential ever chronically infected patients, 65% had already been cured or were still in care and only 8% (n=1,261) were LTFU and eligible for retrieval. Currently, 867 patients have been invited for re-evaluation: 25% of these had been successfully treated, 5% had either severe comorbidity, moved abroad or were deceased precluding treatment, 9% refused to be re-evaluated and in 43% contact has not (yet) been established. So far, 151 patients (18%) have been screened or have an outpatient care appointment scheduled. At their screening visit, these patients were mostly male (68%), median 58 years old (IQR 53-63), LTFU for median 7 years (IQR 4-11) and intravenous drug use was the predominant HCV transmission route (68%). At re-evaluation, 83% tested HCV RNA positive and none HIV positive. Of those HCV RNA positive, 30% had a Fibroscan measurement indicating advanced fibrosis or cirrhosis (≥9.5 kPa). So far, 78% of RNA-positive retrieved patients have commenced HCV treatment.
Conclusion: The majority of ever diagnosed HCV patients in the Netherlands has already been cured, while only 8% is LTFU and eligible for retrieval. So far, we have re-linked 151 patients to care, with 30% of HCV RNA positive patients showing signs of at least advanced fibrosis. This demonstrates that retrieval of LTFU HCV patients is feasible and worthwhile.

End of treatment HBsAg, HBcrAg and HBV RNA levels predict risk of off-treatment ALT flares in patients with chronic hepatitis B

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Background: Since ALT flares after therapy withdrawal are associated with adverse outcomes, risk stratification is of major clinical importance. We aimed to study whether serum levels of novel biomarkers at end of treatment (EOT) are associated with occurrence of off-treatment flares.
Methods: We studied chronic hepatitis B patients who participated in three global randomized trials of peginterferon-based therapy (99-01 [PEG-IFN alone vs PEG-IFN + lamivudine], PARC [PEG-IFN alone vs PEG-IFN with ribavirin] and ARES [ETV with PEG-IFN add-on]). HBV RNA, hepatitis B surface antigen (HBsAg) and hepatitis B core related antigen (HBcrAg) were quantified at EOT. Associations between biomarker levels and ALT flares were assessed using continuous data and after categorization (<3/>3 log for HBsAg, undetectable/detectable for HBV RNA, and for HBcrAg <3/>3 log for HBeAg-negative and <6/>6 log for HBeAg-positive patients). SCALE-B score (comprising HBsAg, HBcrAg, age and ALT) was also calculated and patients were categorized using previously reported cut-offs (<260 , 260-320, ≥320). ALT flares were defined as an ALT ≥5x ULN during the first 6 months after therapy cessation. Sustained response was defined as HBV DNA levels <2,000 IU/mL six months post-treatment.
Results: A total of 344 patients with EOT data were enrolled; 230 HBeAg-positive and 114 HBeAg-negative. Patients were predominantly Caucasian (77.0%) and had genotype A/B/C/D in 23.3/7.3/13.4/52.3%. During follow-up, 122 patients (35.5%) experienced an ALT flare. Flares were associated with lower rates of sustained response (3.5% vs 26.8% among patients with and without a flare; p<0.001). Higher HBsAg (OR 1.586, 95% CI 1.231-2.043, p<0.001), HBV RNA (OR 1.695, 95% CI: 1.371-2.094, p<0.001) and HBcrAg (OR 1.518 95% CI: 1.324-1.740, p<0.001) levels at EOT were associated with higher risks of ALT flares. Combinations of biomarkers, e.g. HBV RNA with HBsAg or the SCALE-B score, further improved risk stratification: for example, among 69 patients with both high HBV RNA and HBsAg levels, 36 (52.2%) experienced a flare, compared to 0/42 patients (0.0%) with low HBV RNA and HBsAg levels (p<0.001). Findings were consistent in multivariate analysis adjusted for potential predictors including HBeAg-status and EOT response (HBV DNA <200 IU/mL).
Conclusion: Off-treatment flares were not associated with favourable virological outcomes. Higher EOT serum HBsAg, HBcrAg and HBV RNA levels are associated with a higher risk of ALT flares after therapy withdrawal. These findings can be used to guide decision-making regarding therapy discontinuation and intensity of off-treatment follow-up.

Autoimmune hepatitis – primary biliary cholangitis variant often treated outside Paris criteria with similar results

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Background: In patients with features of both autoimmune hepatitis and primary biliary cholangitis (AIH-PBC variant syndrome) fulfilling the Paris criteria, treatment with glucocorticoids and ursodeoxycholic acid (UDCA) is advised. Aim of this study was to evaluate the use of the Paris criteria in clinical practice and compare treatment response and outcome between AIH-PBC patients inside and outside Paris criteria and to AIH and PBC patients.
Methods: All clinically diagnosed AIH-PBC patients treated with combination therapy of glucocorticoids and UDCA were included in a multicenter multinational cohort. Characteristics were compared to control cohorts of 396 AIH patients and 860 PBC patients.
Results: Only 22 of the included 83 (27%) AIH-PBC patients fulfilled the Paris criteria. Treatment response for the AIH component was not different at 12 months of treatment between patients inside and outside the Paris criteria (35% Paris vs 54% non-Paris; p=0.200) and comparable to AIH patients (47%; p=0.821). Treatment response for the PBC component was reached in 32 (56%) of AIH-PBC patients (50% Paris vs 61% non-Paris; p=0.454) which was comparable with PBC patients (55%; p=0.867). Ten year transplant free survival was 87.3% (95% CI 78.9% - 95.7%) in AIH-PBC patients which was not significantly different from AIH (p=0.086) and PBC (p=0.572).
Conclusion: In clinical practice AIH-PBC patients are frequently treated with UDCA and glucocorticoids outside the Paris criteria. Treatment response and long-term outcome are comparable to patients inside the Paris criteria, and to AIH and PBC patients.

Single cell RNA sequencing identifies distinct intestinal inflammation patterns in primary sclerosing cholangitis associated colitis compared to ulcerative colitis

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Background: Primary sclerosing cholangitis (PSC) is an inflammatory disorder of the biliary tract. Roughly 60-80% of PSC patients have concomitant inflammatory bowel disease (IBD). PSC-IBD is phenotypically different from ulcerative colitis (UC-IBD) with predominantly right-sided disease and a higher risk for colorectal cancer. The etiology of PSC-IBD is unknown, but it is hypothesized that intestinal barrier dysfunction plays a role in the translocation of gut bacteria to the liver, causing inflammation in the bile ducts (1). In this study we aim to find distinct PSC-IBD pathomechanisms by comparing mucosal cell composition and expressional pathways between PSC-IBD and UC-IBD using single-cell RNA sequencing.
Methods: A total of 47 samples, of which 28 paired inflamed and non-inflamed, were collected from the colon of subjects with either PSC-IBD (n=24), UC-IBD (n=18) or non-IBD control (n=5). Whole biopsies were cryopreserved and dissociated into single cells using collagenase digestion. Cells were loaded onto the 10x V3 chip with V3 reagents for library preparation. Sequencing was performed on an MGI2000 sequencer, featuring 100bp paired-end reads. After demultiplexing, Cellranger was used to create count matrices. Seurat was used for quality control of cells (>200 genes and <60% of mitochondrial reads per cell), and further data analyses. Differential expression was performed using MAST and comparison between disease sets was done using permutation analysis.
Results: A total of 74.022 cells passed quality control, which could be clustered into 36 distinct cell types. Similar patterns of cell type composition were observed between PSC-IBD and UC-IBD. However, we observed marked changes in gene expression between inflamed and non-inflamed samples, which were specific for PSC-IBD in DUOX2+ enterocytes, enteroendocrine cells and immature goblet cells. UC-IBD inflammation, on the other hand, was specifically characterized by a large number of differentially expressed genes in BEST4+ enterocytes, IgG plasma cells, and several fibroblast-subsets. Furthermore, the PSC risk genes in the HLA region were differentially expressed in absorptive enterocytes in inflamed as compared to non-inflamed samples in PSC-IBD, but not UC-IBD. In addition, follicular B cells and IgA plasma cells expressed genes involved in stress in PSC-IBD inflammation, but not in UC-IBD.
Conclusion: Here we show that intestinal inflammation in PSC-IBD is characterized by distinct cell specific gene expression patterns compared to UC-IBD. This study provides insight in cellular mechanisms underlying intestinal disease in PSC, and may be used to identify potential therapeutic targets.

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Homeostatic function and inflammatory activation of ileal CD8+ tissue-resident (CD69+CD103+) T-cells is dependent on mucosal location

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Background: Tissue-resident memory T-cells (Trm), both of the CD4 and CD8 lineage, have been implicated in disease flares in inflammatory bowel disease. However, data is conflicting regarding the profile of human $CD8^+$ Trm, with studies suggesting both pro-inflammatory and regulatory functions. It is crucial to understand the functional profile of these cells with (new) therapeutic strategies aimed at targeting (trafficking of) gut T-cells.
Methods: Here we compared lamina propria and intraepithelial $CD103^+CD69^+CD8^+$ T-cells in healthy controls and patients with active ileal Crohn's disease employing flow cytometry, RNA-sequencing and tissue imaging mass cytometry (CyTOF).
Results: Lamina propria $CD103^+CD69^+CD8^+$ T-cells have a classical Trm profile with active pathways for regulating cell survival/death and cytokine signaling, whereas intraepithelial $CD103^+CD69^+CD8^+$ T-cells display an enhanced cytotoxic profile. During chronic inflammation, especially intraepithelial $CD103^+CD69^+CD8^+$ T-cells displayed a pro-inflammatory profile with concurrent loss of homeostatic functions such as vitamin A metabolism.
Conclusion: Altogether, these compartmental and inflammation-induced differences indicate that therapeutic strategies could have a different impact on the same immune cells depending on the local compartment and presence of an inflammatory milieu, and should be taken into account when investigating short- and long-term effects of new gut T-cell targeting drugs.

Activated, cytotoxic CD27+PD1+ CD8-T cells in RCDII duodenum

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Background: Refractory Celiac Disease type II (RCDII) is a rare indolent lymphoma, hypothetically caused by chronic inflammation in the small intestine. Next to its immunological hallmark of a clonally expanded intra-epithelial iCD3+sCD3-CD7+CD56- aberrant cell population, RCDII pathogenesis is ill-defined. To obtain a better understanding of the underlying immune dysregulation in RCDII, we aimed at unbiased single-cell characterization of the innate and adaptive immune system in RCDII.
Methods: We collected paired small intestinal and blood samples from 12 RCDII patients and 6 healthy controls. Obtained CD45+ cells were stained and with a 39 cell surface marker antibody panel for single-cell CyTOF (scCyTOF). Additionally, we performed single-cell RNA-seq (scRNA-seq) on duodenal CD45+ cells of 2 RCDII patients.
Results: In both our scCYTOF and scRNA-seq data, we observed the presence of CD27+PD1+ memory CD8 T cells in RCDII duodenum. These cells are CD69+ tissue-resident cells with a suggested location in the lamina propria since they were negative for CD103. We found that these cells are activated (*HLA-DR, CD74, LAG3, HAVCR2*) and display a cytotoxic profile (*GZMH, GZMK, NKG7*). Additionally, we observed the presence of *CD70* on the expanded aberrant cell population in RCDII duodenum, a marker known to be frequently expressed by various lymphoma's.
Conclusion: We observed the presence of activated, cytotoxic CD27+PD1+ memory CD8 T cells in RCDII duodenum. These CD27+PD1+ CD8 T cells may be specific for a yet unknown antigen expressed by the aberrant cells, and as such be involved in the control of the aberrant cells population. We speculate that the interaction between these cells and the aberrant cells is enhanced by the CD27-CD70 T-cell co-stimulatory pathway. These findings contribute to better understanding of RCDII pathogenesis and, with further research, may be exploited for new treatment options for RCDII.

Addition of neutralizer to duodenoscope samples increases yield of cultures acquired after high level disinfection

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Background: A reliable culturing method is necessary to properly monitor contamination of duodenoscopes. The CDC advises addition of neutralizers to culture samples to neutralize remaining detergents or disinfectants. However, evidence that this method promotes appropriate outcomes of culturing and circumvents false negative results is not available. This study compares the yield of cultures with and without addition of a neutralizer.
Methods: We found two brand new duodenoscopes of the same type (DEC ED34-i10T2, Pentax) to show persistent contamination after they were subjected to simulated ERCP procedures with an artificial test soil (ATS2015, Healthmark) containing a very high concentration (10^8 CFU/mL) of gut flora. The soiling was followed by manual cleaning, high level disinfection (HLD) and overnight storage in a drying cabinet. Samples of duodenoscope 1 were collected after HLD or drying and samples of duodenoscope 2 were collected at both points. Sampling included a swab of the distal tip and a flush-brush-flush of the working channel. Only samples of duodenoscope 2 were supplemented with Dey-Engley neutralizing broth.
Results: Duodenoscope 1 completed 70 tests (38 samples after HLD, 32 after drying). Duodenoscope 2 completed 60 tests. Of duodenoscope 2, significantly (P< 0,001) more samples collected immediately after HLD were positive compared to samples of duodenoscope 1, respectively 57 (95%) and 3 (7.9%). There was no significant difference in samples collected after drying, 23 (71.9%) positive tests in duodenoscope 1 and 49 (81.7%) in duodenoscope 2 (P=0.278).
Conclusion: The difference in yield of samples collected directly after HLD is likely due to false negative cultures in those samples not treated with neutralizers. No increased yield was found in samples collected with or without a neutralizer after overnight storage. Neutralizers should be added to samples collected of wet duodenoscopes to avoid false negative culture results. Neutralizers are not needed when sampling dried duodenoscopes.

Gut mucosa dissociation protocols influence cell type proportions and single-cell gene expression levels

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Background: Single-cell RNA sequencing (scRNA-seq) has revolutionized the study of the cellular landscape of the gut. Most single-cell protocols require fresh material, which limits sample size of experiments, and consequently, introduces batch effects. This is especially true for samples acquired through complex medical procedures, such as intestinal mucosal biopsies. Moreover, the tissue dissociation procedure required for obtaining single cells is a major source of noise; different dissociation procedures applied to different compartments of the tissue induce artificial gene expression differences between cell subsets.
Methods: To overcome these challenges, we have developed a one-step dissociation protocol and demonstrated its use on cryopreserved gut mucosal biopsies. Using flow cytometry and scRNA-seq analysis, we compared this one-step dissociation protocol to the current gold standard, two-step collagenase dissociation, and an adaptation of a recently published alternative, three-step cold-active protease digestion.
Results: Both cell viability and cell type composition were comparable between the one-step and two-step collagenase dissociation, with the former being more time-efficient and introducing less batch effects. The cold protease dissociation resulted in equal cell viability, rendering high numbers of epithelial cells, and low counts in the mesenchymal compartment. The multi-step protocols affected cell types spanning multiple compartments differently. Cell type-specific gene expression differences exist.
Conclusion: In summary, we show that a one-step dissociation protocol using cryopreserved gut mucosal biopsies can overcome the logistical challenges and batch effects in large scRNA-seq studies without compromising other aspects. Furthermore, the presented protocol now allows using cryopreserved cells, enabling large scale scRNA-seq, flow cytometry, organoid generation and intraepithelial lymphocyte expansion.

Loss-of-response to anti-TNFα critically depends on treatment duration in patients with inflammatory bowel disease

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Background: Inflammatory bowel disease (IBD) is often managed with anti-tumor necrosis factor-α (anti-TNFα) compounds, but only few studies have reported on long-term outcomes. We aimed to determine whether the incidence of loss-of-response decreases with longer treatment duration.
Methods: In a multicenter, retrospective cohort study of patients with IBD who received anti-TNFα for at least 4 months between 2011-2019, we compared incidence rates of loss-of-response between different intervals of treatment duration and performed parametric survival modelling to assess significant changes with longer treatment duration. Cox regression analysis was performed to identify predictors of loss-of-response. Secondary outcomes included overall anti-TNFα discontinuation and dose escalations.
Results: We included 900 anti-TNFα treatment episodes in 746 individual patients, providing 2398 patient-years of follow-up. Loss-of-response was observed in 231 (25.7%) episodes, with occurrence of anti-drug antibodies in 67 (29%) cases of loss-of-response. Within the first year, the incidence of loss-of-response was threefold higher than after four years of treatment (17.3% versus 4.7% per patient-year, p<0.001). The incidence of overall drug discontinuation (28.6% versus 14.0% per patient-year, p<0.001) and dose escalations (36.5% versus 6.4% per patient-year, p<0.001) also decreased significantly from the first year to after four years, respectively. Risk factors for loss-of-response included stricturing or penetrating Crohn's disease (adjusted hazard ratio [aHR] 1.67, 95% CI 1.14 – 2.44), while male sex (aHR 0.74, 95% CI 0.56 – 0.98) and concomitant immunomodulators (aHR 0.73, 95% CI 0.54 – 0.98) were protective.
Conclusion: Long-term use of anti-TNFα maintenance treatment is associated with a reduced risk of loss-of-response in patients with IBD.

Comparison of linear versus circular-stapled gastroenterostomy in Roux-en-Y gastric bypass: a nationwide population-based cohort study

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Background: When performing Roux-en-Y gastric bypass (RYGB), the gastroenterostomy can be constructed in a circular stapled or linear stapled way. Both stapling techniques are frequently used worldwide and importantly, these techniques vary in anastomotic size. A larger anastomotic diameter allows more passage of food and theoretically, this may lead to insufficient weight loss, or regaining weight in the long-term (i.e., non-response). The aim of this study was to assess non-response rates after bariatric surgery and examine the impact of the stapling technique.
Methods: This is a nationwide, population-based cohort study of patients that received primary RYGB in the Netherlands. Data originates from the Dutch Audit of Treatment of Obesity (DATO). The primary outcome was the impact of stapling technique on the rate of non-response defined as significant weight regain (≥20% of a patients' lost weight) after initial successful weight loss (≥15% TWL) 2-4 years after RYGB. Secondary outcomes were the rate of response, defined as successful weight loss (≥15% TWL) within 1.5 years after RYGB, the incidence of postoperative complications and the progression of obesity related comorbidities.
Results: In a cohort of 15024 patients (n=1026 circular, n= 13998 linear), non-response was observed in 2554 patients. This was equally distributed between the two groups (20.2% circular; 19.2% linear). No differences in response rate, nor total weight loss were observed up to 4 years after surgery. Patients in the circular stapled group experienced more short-term complications, specifically major bleedings (2.6% circular; 1.2% linear; p <.001). No differences were found in the worsening of comorbidities, nor in de novo developed comorbidities. Multivariate logistic regression analysis demonstrated that stapling technique was not associated with non-response.
Conclusion: No beneficial effect in weight loss outcomes was found when reviewing stapling techniques used in the construction of the gastroenterostomy during RYGB surgery. Based on short-term complications, the linear stapled technique appears to be safer. Future studies, preferably randomized controlled, with extensive follow-up may further demonstrate superiority of one of these stapling techniques.

Update on Incidence, Prevalence Treatment and Survival of Patients with Small bowel Neuroendocrine Neoplasms in The Netherlands

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Background: Small bowel neuroendocrine neoplasms (SB-NEN) are a rare cancer with relatively high survival rates compared to other cancers. Population-based studies are ideal to study this kind of indolent disease, as long time periods and large patient numbers are covered. The aim of this study is to provide an update on Dutch data by exploring trends in epidemiology, treatment and survival outcomes of patients with SB-NEN.
Methods: All patients with SB-NEN diagnosed between 2005 and 2015 were included from the Netherlands Cancer Registry (NCR). Corresponding histopathology reports were requested from The Nationwide Network and Registry of Histo- and Cytopathology in The Netherlands (PALGA). Age-adjusted incidence rates were calculated based on age groups according to Statistics Netherlands (CBS) using the direct standardization method. Descriptive statistics were used to present the distribution of data. Survival analyses were performed with the Kaplan-Meier method and the Cox proportional hazards model was used to identify factors associated with survival.
Results: A total of 1451 patients were identified, of which 975 were included. The age-adjusted incidence rate of SB-NEN increased from 0.52 to 0.81 per 100.000 persons years between 2005 and 2015 and males were more represented than females (incidence of 0.93 versus 0.69 per 100.000 person years in 2015). Mean follow-up was 61 (±38) months, and all-cause mortality was 33%. Most patients had a grade 1 tumour (83%). Surgery was performed in 86%, of which 99% had undergone resection of the primary tumour. Administration of somatostatin analogues (SSAs) increased from 5 to 22% for stage III and from 27 to 63% for stage IV.
Conclusion: This study showed an increase in the incidence of SB-NEN. A predominant role of surgery was found with an increased use of SSAs over time.

ATP tests after manual cleaning do not predict the presence of microorganisms on duodenoscopes and linear echoendoscopes after high level disinfection

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Background: Microbiological culturing is the gold standard in monitoring contamination of endoscopes, but has a considerable turnaround time. Adenosine triphosphate (ATP) tests promise to detect any biological material on endoscopes quickly, however, their reliability to detect contamination is not conclusively proven. We investigated the value of ATP tests after manual cleaning to predict the presence or absence of microorganisms shown by culture after high level disinfection (HLD) in duodenoscopes and linear echoendoscopes (DLE).
Methods: ATP surface and water tests (Clean-Trace, 3M Company) were performed on samples taken from the cap, forceps elevator and flush of the working channels of DLEs after manual cleaning. These results were compared to the growth of any microorganisms in cultures acquired after HLD. ATP tests with >200 relative light units (RLU) were considered positive. ROC curves were used to compare the RLU levels with presence of microorganisms in the cultures.
Results: In total, 901 tests were performed involving 26 different DLEs. The forceps elevator had a positive ATP test in 306 tests (34.0%), the cap in 146 tests (45.3%) and the channel in 116 tests (12.9%). The ATP test was false-negative in 219 (36.8%) of the forceps elevator samples, in 37 (21%) of the cap samples, and in 257 (32.9%) of the channel samples. Irrespective of the type of microorganisms, type of DLE and sample site, no correlation was found between ATP test results after manual cleaning and microbial growth in cultures acquired after HLD. The area under the curves of different ROC curves were low, with a maximum of 0.607.
Conclusion: We found no evidence that ATP tests performed after manual cleaning can predict the presence or absence of microorganisms after HLD as shown by culture. This cannot be explained by the effect of HLD alone, since there was also a high number of false-negative ATP tests.

Crohn's Disease fistula show skewed lymphoid/myeloid balance and altered myeloid cell profiles

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Background: A fistula is an abnormal tract connecting two epithelialized surfaces, for example the intestine and the skin. Perianal fistula are a common complication of patients suffering Crohn's Disease (CD), but also occur in non-IBD patients in the form of cryptoglandular fistula. Around one third of all CD patients develop fistula at some point during their disease course. Fistula are often refractory to therapy, both due to the anatomically complex nature of these tracts and poor wound healing responses. In contrast, cryptoglandular fistula often respond to standard therapy. The biological background of this difference is unknown, and comparative studies between the two groups are lacking. The aim of this study was to characterize the cellular composition in fistula tracts of CD and cryptoglandular patients.
Methods: Curettage material of perianal fistula tracts was obtained during surgical intervention from patients with CD (n=15) and cryptoglandular fistulas (n=5). Single-cell suspensions were stained with a 35-antibody panel, focusing on myeloid and T-cell markers and were analysed using mass cytometry (CyTOF).
Results: The main cellular component fistula tracts consisted of CD66a+ granulocytes (average 64 +/- 24%), irrespective of diagnosis or the presence of a seton. However, the remaining mononuclear compartment differed significantly between Crohn and cryptoglandular fistula. In CD, the majority was of lymphoid nature (CD3+ T cells 57 +/-21%, CD19+ B cells 14 +/-15%), while in cryptoglandular tracts, the majority consisted of cells of myeloid origin (61+/- 15%). No effect of a seton in situ was observed in the lymphoid/myeloid balance.
Within the T cell compartment, as expected, the majority of cells was CD45RO+, indicating activation. No clear difference was observed between diagnoses. In contrast, presence of a seton increased the proportion of CD45RO+ T cells, in particular in CD4+ cells. In the myeloid compartment, CD14high/HLA-int monocytes, CD14int/HLA-high inflammatory macrophages and CD14high/CD163+ resident macrophages were identified. Interestingly, CD patient samples contained less monocyte-like cells, and substantially more resident macrophages compared to cryptoglandular samples. This feature tended to be even more enhanced in the presence of a seton, although this did not reach statistical significance.
Conclusion: Despite granulocytes being the main contributor to the cellular composition of fistula tracts, striking differences were found between Crohns and cryptoglandular fistula, both in lymphoid/myeloid balance, and in the presence of resident macrophages. These differences may contribute to the lack of response to therapy in CD.

Perspectives on treatment of inflammatory bowel diseases in older patients; gut-feeling or evidence-based medicine? – a qualitative study in professionals and patients

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Background: The older inflammatory bowel disease (IBD) population is challenging to treat as they are characterized by heterogeneity in geriatric characteristics, such as functional, social, mental status or frailty. Literature has found a difference in applied treatment strategies in older patients as compared to adult patients. To unravel underlying considerations contributing to this difference we aimed to create a conceptualization of therapy goals and frailty in older patients with IBD.
Methods: We conducted semi-structured interviews in 15 professionals and 15 older patients aged ≥65 years with IBD. All participants were selected using purposive sampling and interviews were analyzed inductively.
Results: Several elements regarding different therapy goals in older versus adult patients were identified in both professionals and patients. Professionals strived more towards clinical remission and put lower priority on endoscopic remission in older patients. Patients themselves were also focused on clinical remission but valued objective confirmation of remission as a reassurance. In both professionals and patients, the prevention of long term complications was mentioned to be of less importance. Some professionals said that they therefore tended to treat older patients less aggressively. Some professionals said to opt for surgery earlier in IBD treatment course in older patients, while older patients themselves strived towards prevention of surgery due to fear of becoming dependent. Professionals differed remarkably regarding corticosteroid therapy: some stated to allow low dose maintenance therapy in older patients, while others were reluctant to even prescribe short corticosteroid courses. Patients were more uniform in avoiding corticosteroids, mainly due to negative experiences in the past. In both professionals and patients, we found a shift towards geriatric goals in frail patients with IBD, such as maintaining independency. Furthermore, professionals mentioned to apply different treatment strategies in frail patients. However, none of the professionals assessed frailty systematically but judged a patients frailty status by applying a clinical view.
Conclusion: The large variation in professionals' treatment preferences reflects a lack of evidence regarding treatment of older patients with IBD. There is a need for clinically applicable evidence on frailty in IBD as, although professionals base therapy goals on frailty status, frailty judgement is based on a clinical view. Bridging this gap of evidence could aid tailored treatment of frail patients with IBD.

Societal cost-of-illness of inflammatory bowel disease has rapidly increased over the years and differs between continents: a systematic review

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Background: With increasing incidence of Inflammatory Bowel Disease (IBD) in developing countries and increasing prescription rates for biologics globally, knowledge on the cost burden of IBD and cost drivers is essential for health policy makers worldwide. We conducted a systematic review to determine cost-of-illness of IBD and assess time trends and geographical differences.
Methods: A systematic review of population-based studies that estimated cost-of-illness of IBD and were published in Embase, Medline, Web of Science and Google Scholar. Studies on interventions and those reporting costs for a subset of patients defined by phenotype or treatment were excluded, as these do not give a representative estimate of the cost-of-illness of IBD. Only studies published in English were included. Methodology of all included studies was assessed and costs were adjusted to 2018 US dollars.
Results: In total, 4,837 unique studies were screened on title and abstract and 4,730 excluded. After full-text screening, 64 of the remaining 107 studies were included in the systematic review. The study methodologies differed considerably, with large differences in perspective, valuation method and source population. Mean annual healthcare costs for prevalent Crohn´s disease (CD) cases in the last 10 years were in Asia $4,463; Europe $12,396 and North America $17,508. Costs for prevalent ulcerative colitis (UC) patients in the same period were $1,654, $7,206 and $13,569 respectively. For CD, the cost drivers moved from inpatient (61% of total costs) in 1995 to medication costs (77%) in 2016. Similar trends were identified for UC (1998: 50% and 36% versus 2016: 9%, and 82% for inpatient and medication costs, respectively). This cost trend is primarily attributable to an increase in medication costs in all four geographical areas, while in- and outpatient costs were relatively stable during the same time period. The annual costs of absenteeism and presenteeism per prevalent case of CD were $5,638 in Asia and $6,485 in Europe. For UC these costs were $4,828 and $6,414 respectively. Annual costs of absenteeism and presenteeism in North America were $20,074 per patient for a combined cohort of UC and CD patients.
Conclusion: Per patient costs for IBD are increasing worldwide, with highest costs in North America and lowest in Asia. This is primarily due to an increase in medication costs. Productivity costs are substantial and might even exceed healthcare costs. Biologic therapy was expected to decrease inpatient costs by reducing hospitalisations and surgery, but this does not appear to be the case. Continuing growth of these costs can lead to an intolerable burden on healthcare systems worldwide.

Incidence and predictive factors of biliary complications in patients presenting with uncomplicated gallstone disease. Results from three prospective multicentre cohort studies.

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Background: A wait-and-see policy is justified in patients with gallstones and non-specific biliary pain to better select patients for cholecystectomy. However, the incidence and predictive factors for the development of biliary complications are unclear.
Methods: A prospective multicentre cohort study is performed with data from the SECURE-, SUCCESS-, and PERFECT-trial. Patients with abdominal pain and gallstones, without a history of complicated gallstone disease, eligible for cholecystectomy were included. The primary outcome was the incidence of biliary complications, or between first presentation and 6 months of follow-up or cholecystectomy. A biliary colic was classified as a minor complication. Cholecystitis, biliary pancreatitis, cholangitis or choledocholithiasis were classified major complications. The secondary outcome was the time interval between first presentation and the development of a biliary complication. We developed and validated a multivariable regression model to predict the occurrence of a biliary complication and assess factors associated with a complication free period. Cox regression analyses were performed to analyze variables associated with outcome. A p-value < 0.05 was considered statistically significant. Analyses were performed using SPSS statistics version 25.0 (IBM) and R version 3.6.3; R Foundation for Statistical Computing, Vienna, Austria with package ‘rms’.
Results: Between February 2014 and June 2019 a total of 1956 patients were eligible for inclusion in 29 Dutch hospitals. A biliary event occurred in 4.6% patients (89/1956) prior to surgery. Complications were classified as minor in 42.7% (38/89) and major in 57.3% of patients (51/89). In 2.2% the patients (43/1956) a complication occurred within 30 days. The incidence of cholecystitis, choledocholithiasis or biliary pancreatitis prior to surgery was 2.6% (50/1956). Use of pain medication for pain attacks was associated with a biliary complication (OR 1.7, 95%CI 1.1 – 2.8, p = 0.011). Male sex was associated with major complications (OR 2.0, 95%CI 1.1 – 3.5, p = 0.020). No further associations were found.
Conclusion: The 2.6% risk of cholecystitis, choledocholithiasis or biliary pancreatitis in patients who present with initially uncomplicated cholecystolithiasis is not negligible. The only factor associated with biliary complications was use of pain medication. Male sex was associated with occurrence of a major biliary complication. When a wait-and-see policy is advocated, 4.6% of patients develop a biliary complication prior to surgery and within the first six months after presentation. The risk for a major complication is 2.6%.

Risk of Barrett's Esophagus and Esophageal Adenocarcinoma among Patients Diagnosed with Breast Cancer – a Nationwide Study

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Background: As the risk of esophageal adenocarcinoma (EAC) in women is lower than in men, routine endoscopic screening for EAC or its precursor Barrett's esophagus (BE) of all women is not recommended. Insight into female-specific risk factors is warranted to develop tailored screening recommendations for women at increased risk for BE and EAC. As breast cancer and EAC share risk factors and molecular mechanisms of carcinogenesis, we hypothesized that women with a previous breast cancer diagnosis might be at an increased risk for EAC. We therefore aimed to determine the risk of BE and EAC in a nationwide cohort of breast cancer patients with long-term follow-up.
Methods: In this population-based cohort study, all female patients diagnosed with breast cancer without distant metastases between 2000 and 2017 were identified using the nationwide Netherlands Cancer Registry (NCR). Patients were followed up until BE/EAC diagnosis, death, or end of study follow-up. EAC cases after breast cancer were retrieved from the NCR and cases of BE with or without dysplasia were identified through linkage to PALGA: the Dutch Pathology Registry. Age- and period-adjusted standardized incidence ratios (SIRs) were calculated to compare BE and EAC risks after a breast cancer diagnosis with the risk in the general population. Cumulative incidences for BE and EAC were estimated using Fine and Gray analyses adjusted for death as competing risk.
Results: We identified 250 627 women with a first diagnosis of breast cancer who were followed for a median duration of 6.7 (IQR 2.8-10.5) years. After a median of 4.5 (IQR 2.0–8.8) years, 155 patients developed EAC. The risk of EAC was higher after a breast cancer diagnosis than in the general population (SIR 1.27; 95%CI 1.08–1.49; p=0.004). Breast cancer diagnosis was not significantly associated with nondysplastic BE (SIR 1.07; 95%CI 0.93–1.22; p=0.33), BE with low-grade dysplasia (SIR 1.09; 95%CI 0.81–1.44; p=0.57), and BE with high-grade dysplasia (SIR 1.36; 95%CI 0.79–2.17; p=0.23). The 10-year cumulative incidences for EAC was 0.08% (95%CI 0.06–0.09). In multivariate competing risk analyses, increasing age at breast cancer diagnosis was associated with EAC risk (sub hazard ratio 1.04; 95%CI 1.03–1.05; p<0.001). The risk of EAC was not affected by the use of radiotherapy, chemotherapy, or hormonal treatment for breast cancer.
Conclusion: In this population-based study, breast cancer is marginally associated with EAC, but not with BE. Although the risk of EAC after breast cancer is increased by 27% compared with the general population, the absolute cumulative risk of BE/EAC remains low. We therefore advise against endoscopic screening for BE and EAC of breast cancer survivors.

Effect of Family History on the Risk of Barrett's Esophagus and Esophageal Adenocarcinoma: Systematic Review and Meta-analysis

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Background: Current guidelines recommend different screening approaches for individuals with a family history of Barrett's esophagus (BE) or esophageal adenocarcinoma (EAC), varying from no screening to screening of all individuals with a positive family history. A systematic review and meta-analysis was performed to determine evidence-based risk estimates for individuals with a family history of BE or EAC.
Methods: We systematically searched Pubmed, Embase, and Cochrane Library until April 2020 to identify all studies that reported on the association between family history and the risk of developing BE and EAC. Pooled summary estimates of adjusted relative risks and prevalence of familial BE/EAC with 95% confidence intervals (CI) were calculated using a random-effects model.
Results: Fourteen studies comprising 16,189 BE/EAC patients were analyzed. Familial clustering was seen in 5.86% (95%CI: 3.35–10.04) of patients with BE or EAC. Offering screening to first-degree relatives of patients with BE or EAC, especially those with concurrent reflux symptoms, would have resulted in an average diagnostic yield of 23.5% (95%CI: 13.4–37.9) for BE. Individuals with a first-degree relative with BE or esophageal cancer were 2.47 (95%CI: 1.40–4.34) times more likely to have BE or EAC compared with individuals with no family history.
Conclusion: This systematic review and meta-analyses shows that familial aggregation of BE and EAC is observed in a small but important subgroup of patients with BE and EAC and identifies a family history of BE or EAC as a strong risk factor for both disorders. The review emphasizes the importance of obtaining a careful family history in all patients with BE or EAC to identify high-risk individuals who may benefit from early detection strategies to prevent EAC-related mortality. Nonetheless, as the risk appears to be lower than previously suggested, this review does not clearly support endoscopic screening of all first-degree relatives of patients with BE or EAC.

The Workgroup Serrated Polyps and Polyposis (WASP) classification for optical diagnosis of diminutive colorectal polyps using iScan

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Background: The Workgroup Serrated Polyps and Polyposis (WASP) is a classification system for endoscopic differentiation between adenomas (ADs), hyperplastic polyps (HPs) and sessile serrated lesions (SSLs) to be used with narrow band imaging. The WASP classification has never been evaluated using other virtual chromoendoscopy techniques, nor has it been updated since the revised WHO 2019 criteria for colorectal tumors. The aims of this study were: 1) to improve the optical diagnosis of diminutive colorectal polyps, after participating in an interactive training, when applying the WASP classification using iScan and 2) to evaluate whether optical diagnosis using the WASP classification is still feasible after implementation of the revised WHO 2019 criteria.
Methods: Endoscopists predicted polyp histology, including their level of confidence, based on 30 videos of diminutive polyps, before and after participating in an interactive training (T_0 and T_1). After three months, these endoscopists were invited to score a new set of 30 videos (T_2). The primary outcome was the overall diagnostic accuracy at T_0, T_1 and T_2. All polyp specimens were histopathologically scored according to the WHO 2010 and WHO 2019 criteria, respectively. Secondary outcomes included accuracy specifically for SSLs.
Results: Overall diagnostic accuracy was 0.58 (95% CI 0.55-0.62) at T_0, and significantly improved to 0.63 (95% CI 0.60-0.66, p=0.004) at T_1. For polyps diagnosed with high confidence, accuracy was 0.70 (95% CI 0.64-0.75) at T_0 and 0.74 (95% CI 0.69-0.78, p=0.166) at T_1. Accuracy for SSLs was 0.51 (95% CI 0.46-0.56) at T_0 and 0.55 (95% CI 0.49-0.60, p=0.119) at T_1. Accuracy for high confidence SSLs was 0.57 (95% CI 0.48-0.66) at T_0 and 0.62 (95% CI 0.56-0.69, p=0.383) at T_1. After three months, the overall accuracy was 0.58 (95% CI 0.54-0.62, p=0.787, compared to T0). The accuracy for SSLs At T_2 was 0.48 (95% CI 0.42-0.55, p=0.520). After revision of all polyps specimens according to the WHO 2019 guideline, accuracy rates of all polyps, and SSLs specifically, significantly declined at T_0 and T_1, regardless of confidence levels. Reversely, at T_2 all accuracy rates significantly increased.
Conclusion: Optical diagnosis of colorectal diminutive polyps significantly improves after participating in a training on the use of the WASP classification using iScan; however, this improvement was not found for SSLs, nor was it any longer present after three months. The application of the recently revised WHO criteria for histopathological diagnosis drastically changed the diagnostic value of the WASP classification, likely making its future use in clinical practice less reliable.

The small bowel is protected by the presence of luminal preservation solution during cold storage in a brain-dead rat model

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Background: Small bowel (SB) transplantation is performed a handful of times a year, and graft survival rates are disappointing. Thus, animal models are needed to understand the mechanisms occurring before, during and after the procedure. The SB, donated after brain death (DBD), is viable for up to 10 hours of storage, shorter than other abdominal organs which are preserved in the same way. There have also been no developments in the way the graft is treated, stored and transported. The protective effects of luminal perfusion (LP) with an ice-cold solution have been consistent in previous studies in small and large animals, but none of these models include DBD. The aim of our study is to investigate whether the beneficial effects of LP occur also in a DBD model.
Methods: Wistar rats (N=9) underwent brain death induction by inflation of a balloon at 1 ml/hr for 30 minutes and kept stable for 2 hours. Donor vessels were then perfused with University of Wisconsin solution (UW) and the SB explantated. The bowel was then divided into three pieces for cold storage (CS). One segment was kept empty (control), and the rest were filled with 0.06 ml/cm of either UW (UW/UW) or polyethylene glycol 3350 (UW/PEG). All segments were then tied shut and stored in ice-cold UW. Analysis time points were procurement (t=0) and after 4 and 8 hours of CS (t=4, t=8 respectively). Samples were evaluated by histopathological scoring of preservation injury (IPI; median [range]; Kruskall-Wallis and Dunn's statistics, p < 0.05 for significance), percentage of absent epithelial lining and presence of oedema. More analyses are to be performed.
Results: Basal score at t=0 shows a median value of 2 [0-3]. IPI results from control samples were 4 [2-5] (t=4) and 2 [2-6] (t=8). UW/UW at t=4 had less damage, 2 [2-3, p < 0.005) and all other samples showed a tendency to lower damage but no statistical significance. 50% of the epithelial lining is detached from t=4 in control, while in UW/UW is 30%. Increasing amounts of oedema beneath the epithelial layer in the UW/UW reflects the largely conserved mucosal surface in comparison to other groups.
Conclusion: Luminal perfusion of the small bowel is protective of the mucosa in the brain-dead rat. The LP solution with the best effect is UW for up to 4 hours of static cold storage. These results show less effect of LP than previously described, when using non-DBD models. More attention should be paid to the effect of DBD in the grafts viability on further studies.

Adaptation and content validity of the Dutch Crohn's Life Impact Questionnaire

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Background: Crohn's disease (CD) can have a profound impact on patients' lives. Quality of life (QoL) improvement is currently an important clinical and scientific endpoint. The Crohn's Life impact Questionnaire (CLIQ) is a CD-specific patient reported measure for QoL, developed together with CD patients and validated in the United Kingdom. We aim to adapt the CLIQ for use in the Netherlands and evaluate its content validity.
Methods: A Dutch version was developed by a consecutive bilingual and lay panel. Five bilingual Dutch natives excluding health care professionals or professional translators produced conceptual equivalent Dutch options for all sentences in the CLIQ. A lay panel of six Dutch natives with a low to average educational level produced a preliminary version. Both panel sessions were led by a Dutch moderator and an English member from the original development team. Next, cognitive debriefing interviews were held with 12 purposively selected CD patients to test the comprehensibility, relevance and comprehensiveness of the Dutch CLIQ. In an audio recorded meeting the Dutch CLIQ was completed, followed by a guide led interview. Analysis was performed by summarizing the results of the interview guide per section as interviews progressed and an altered version was tested in subsequent interviews when necessary.
Results: The bilingual panel (2:3 M:F, aged 31 to 72) produced 1 to 4 Dutch options for each sentence in the CLIQ. The lay panel (1:2 M:F, aged 32 to 75) was very decisive and choose the best Dutch option for each sentence. Their version was approved by the original development team. Twelve cognitive debriefing interviews were held in CD patients (1:1 M:F, aged 25 to 77) who reported mild (n=5), moderate (n=5) or quite severe (n=2) disease. The CLIQ as a whole was found clear and easy to understand by 10/12 patients. One item was misinterpreted and altered for the final version that was tested in the latter 5 interviews. Only minor revisions were made to that final version. All patients found the CLIQ as a whole relevant and no individual items were repeatedly mentioned as irrelevant. Half the patients mentioned missing aspects of their disease, though none were mentioned more than twice, except for work/school related aspects (n=3). This was left unaltered, as these aspects might not be applicable to all CD patients.
Conclusion: The Dutch CLIQ appears to be conceptual equivalent to the original and has satisfactory content validity according to Dutch CD patients. Currently our study is moving forward to investigate other measurement properties of the Dutch CLIQ in a large multicentric consecutive outpatient sample in the Netherlands.

Self-reported Health-Related Quality of Life and Disease Control of Patients with Inflammatory Bowel Disease during the COVID-19 pandemic in The Netherlands

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Background: To learn from the current crisis caused by the COVID-19 pandemic and be prepared for future pandemics, it is important to investigate the impact of this extraordinary period on the wellbeing of patients with inflammatory bowel disease (IBD). Therefore, the aim of this research was to describe the self-reported Health-Related Quality of Life (HRQoL) and disease control of patients with IBD from the start of the COVID-19 pandemic and measures in The Netherlands.
Methods: This was a prospective study initiated on March 17, 2020 until July 1st, 2020. All patients aged 18 years and older with IBD that visited the Erasmus MC (Rotterdam, The Netherlands) outpatient clinic between March 2019 to February 2020 received up to date information on COVID-19. Patients were invited to complete online questionnaires at week 0, 2, 6 and 12. The Inflammatory Bowel Disease Questionnaire (IBDQ), the Inflammatory Bowel Disease control-8 (IBD-control-8), Numeric Rating Scale (NRS) on fatigue and the Manitoba IBD index (MIBDI) were used. The evolution of the different outcomes over time was measured using mixed models.
Results: Of 1151 invited patients, 851 participants (67% CD and 33% UC or IBD-U) completed one or more questionnaires (response rate 74%). No relevant changes in total scores were found over time for the IBDQ (effect estimate 0.006, 95% CI [-0.003-0.015]) and IBD-control-8 (effect estimate 0.004, 95% CI [0.998-1.011]). There was a slight, increasing trend in fatigue scores over time (effect estimate 0.011, 95% CI [0.004, 0.019]).
Conclusion: This first lock down due to the COVID-19 pandemic in The Netherlands did not impact the HRQoL of patients with IBD. Up to date information may have contributed to a stable HRQoL in IBD patients even in an extreme period with restrictions and insecurities.

Efficacy of Permacol injection for perianal fistulas in a tertiary referral population: poor outcome in patients with complex fistulas

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Background: Injection of Permacol collagen paste can be used as a sphincter-sparing treatment for perianal fistulas. Outcome data in complex anal fistulas are scarce, and the available evidence is based on studies which are limited in sample size (i.e. < 50 patients). Hence, we sampled a series of consecutive patients referred to a specialist centre for treatment of mainly complex perianal fistulas, aiming to evaluate: 1) short- and long term efficacy of Permacol injection; 2) clinical and fistula related factors associated with recurrence after Permacol injection.
Methods: Retrospective analysis of consecutive patients with perianal fistulas treated with Permacol injection between June 2015-April 2019. Endoanal ultrasonography was systematically analysed post-hoc, blinded to treatment outcome. Recto- and anovaginal fistulas were excluded. Healed fistulas were defined as absent anal symptoms and a closed external opening on physical examination, at minimum follow up of 6 months. Regression analyses were performed to identify factors associated with unhealed fistulas.
Results: Ninety-five patients (53 males; median age 45 years) were analysed. Seventy-six (80.0%) patients had complex perianal fistulas (>1/3 of sphincter involvement, multiple tracks or Crohn's). After single Permacol injection, fistulas were healed in 20 (21.1%) patients at 3 months follow up, and in 19 (20.0%) patients at a median follow up of 31 months (IQR 16-37). Of the remaining patients with unhealed fistulas, 9 (11.8%) patients had significant symptom improvement. Simple fistulas were unhealed in 11/18 (61.1%) and complex fistulas in 65/77 (84.4%) patients; complex fistulas were significantly associated with unhealed fistulas (OR 3.45 [95%CI 1.11–10.67]; *p*=0.032). The rate of persisting fistulas was high after previously performed mucosal advancement flap (*n*=13/14 [92.9%]), LIFT procedure (*n*=10/12 [83.3%]), fistula laser closure (*n*=6/6 [100%]), and also in patients with a diagnosis of Crohn's disease (*n*=4/5 [80.0%]). Permacol injection was numerically more likely to fail in patients without pre-Permacol seton drainage (32/36 [88.9%]) compared to those with pre-surgical drainage (44/59 [74.6%]), *p*=0.099. Twenty-three patients underwent subsequent Permacol injections, which were successful in seven (30.4%) patients: after one (*n*=4) or two (*n*=3) additional injections.
Conclusion: This largest study to date in patients with mainly complex perianal fistulas demonstrated that long term efficacy of a single Permacol injection was only 20%. Complex fistulas were associated with poor outcome. Hence, Permacol injection should be considered a treatment option in simple fistulas only.

The complexities of analysis for APC mosaicism

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Background: Mosaic mutations in the *APC* gene have been identified as a common cause (25%) for unexplained polyposis in patients with >20 adenomas. The frequency of *APC* mosaicism remains unknown in patients with milder phenotypes.
Methods: To test for *APC* mosaicism, multiple lesions of patients with unexplained colonic polyposis were tested for *APC* using Next Generation Sequencing. Additionally, patients with milder phenotypes, like 10-20 adenomas aged between 60 and 70, less than 5 adenomas before the age of 50 or more than 20 adenomas aged >70, were included in this study as well.
Results: The true mosaicism detection rate was 12% (26/218) in the entire cohort, 7.7% in patients with <10 adenomas (2/26) and 7.4% in those with 10-20 adenomas (7/94). Stratified for age, 3.1% (1/32) of patients aged >70 showed with a true mosaicism. Besides true mosaicism, 21% (46/218) of patients showed a so-called hybrid mosaicism, where an identical variant was shared by multiple, but not all lesions. Interestingly, 43% (20/46) of hybrids have a specific *APC* splice variant c.835-8A>G in multiple lesions. This *APC* variant and 7 other recurring variants were compatible with the recently described mutational signature caused by colibactin, a compound produced by *pks+ E.coli.* In total, 21 patients showed such a variant in a hybrid pattern. The possible influence of colibactin in these patients needs further exploration. Therfore, we are now performing additional analyses like Whole Genome Sequencing.
Conclusion: Our results indicate that *APC* mosaicism also plays a role in patients with milder polyposis phenotypes. Furthermore, a substantial proportion of patients in our cohort had a hybrid mosaicism of which the clinical consequences are not yet clear. No universal explanation could be identified and therefore case by case evaluation is required.
Besides, the presence of *pks+ E.coli* might be an additional explanation for unexplained polyposis patients. This especially applies to the large proportion of patients carrying variants fulfilling the *pks+ E.coli* mutational signature in multiple lesions.

Ustekinumab for Crohn's Disease: Two-Year Results of the Initiative on Crohn and Colitis (ICC) Registry, a Nationwide Prospective Observational Cohort Study

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Background: Ustekinumab is a monoclonal antibody that selectively targets p40, a shared subunit of the cytokines interleukin (IL)-12 and IL-23. It is registered for the treatment of Crohn's disease (CD) and ulcerative colitis. We assessed the two-year efficacy and safety of ustekinumab in a real world, prospective cohort of CD patients.
Methods: CD patients who started ustekinumab in regular care were prospectively enrolled in the nationwide Initiative on Crohn and Colitis Registry. At week 0, 12, 24, 52 and 104, clinical remission (HBI ≤ 4 points), biochemical remission (fecal calprotectin (FC) ≤200 μg/g and/or CRP ≤5 mg/L), peri-anal fistula remission, extra-intestinal manifestations, ustekinumab dosage and safety outcomes were determined. Patients starting therapy less than two years ago were excluded for the current evaluation. The primary outcome was corticosteroid-free clinical remission at week 104.
Results: In total, 252 CD patient with at least two years of follow up were included. The proportion of patients in corticosteroid-free clinical remission at week 12, 24, 52 and 104 was 32.3% (81/251), 41.4% (104/251), 39% (97/249) and 34.0% (84/247), respectively. Of the 97 patients in corticosteroid free clinical remission at week 52, 58 (59.8%) were still in corticosteroid-free clinical remission at week 104. The proportion of patients with combined corticosteroid-free clinical and biochemical remission was 5.2% (13/252), 7.6% (19/251), 12.4% (31/251), 17.7% (44/249) and 15.8% (39/247) at week 0, 12, 24, 52 and 104 respectively. The proportion of patients in corticosteroid-free clinical remission was not significantly different at week 52 and 104 between patients on a q8w or a q12w interval, 45.2% (q8w) vs 35.4 (q12w) P= 0.80 and 39.7% (q8w) vs 29.3% (q12w) P=0.68, respectively. The probability of remaining on ustekinumab treatment after 52 and 104 weeks was 64.3% and 54.8%, respectively. There were no predictive factors associated with corticosteroid-free clinical remission at week 104 on univariate and multivariate analysis. Most common adverse events were headache, skin reaction and musculoskeletal complaints. Two patients stopped ustekinumab due to an infection after 8 and 30 weeks of treatment (mild fever syndrome and moderate upper airway infection, respectively). The main reason for discontinuing treatment after 52 weeks was loss of response (66.7%).
Conclusion: Ustekinumab was effective and relatively safe in our real world, prospective cohort of CD patients. After 104 weeks of ustekinumab treatment, one third of patients were in corticosteroid-free clinical remission.

Acceptance and perceived control are independently associated with quality of life in inflammatory bowel disease: introduction of a new segmentation model

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Background: Segmentation of patients based on psychological determinants of subjective health may allow new ways of personalisation of care. The cross-disease segmentation model developed by Bloem & Stalpers discriminates patients based on disease acceptance and perceived control. We aimed to study the validity of the segmentation model, compare the characteristics and outcomes of patients per segment and evaluate whether the model independently correlates with quality of life in patients with inflammatory bowel disease (IBD).
Methods: This is a cross-sectional cohort study of adult IBD patients in a secondary care IBD centre with questionnaires on quality of life (32-item IBDQ) and acceptance and perceived control (6-items with 7-point Likert scale). Patients were divided in four segments based on acceptance and perceived control score (cut-off > 5).
Results: We included 686 of 1282 patients who were approached for the study. Four segments were formed: segment I high acceptance and control (N = 264), segment II high acceptance and low control (N = 96), segment III low acceptance and high control (N = 63) and segment IV low acceptance and low control (N = 263). The acceptance and perceived control scale showed a unidimensional structure (83% and 85% of the total variability explained by the first factor), were internally consistent (Crohnbach's alpha 0.90 and 0.91) and correlated positively with HRQoL (Spearman rho 0.65, p < 0.001 and 0.51, p < 0.001). The four segments differed significantly in age (p < 0.001), smoking behaviour (p = 0.015), type of IBD (p = 0.013), disease duration (p = 0.045), extra-intestinal manifestations (p = 0.011), type of IBD-medication (p < 0.001), clinical disease activity (p < 0.001) and quality of life (p < 0.001). Multiple linear regression analyses showed socio-demographic, clinical and treatment-related factors explained 25% of variance in quality of life. The explained variance in quality of life significantly increased to 45% when the patients' segment was added to the model (ΔR^2 20%, p < 0.001). Both acceptance and perceived control were positively correlated with quality of life. The strongest correlation was found between segment IV (low acceptance and low perceived control) and quality of life (ß -.52, p < 0.001). The correlation between clinically active disease and quality of life was less strong (ß -.27, p < 0.001).
Conclusion: The segmentation model based on disease acceptance and perceived control is valid in IBD patients, discriminates patients that differ clearly from one another in characteristics and disease outcomes, and correlates independently with quality of life. This may open new strategies for patient care.

Exclusive enteral nutrition or prednisolone induction treatment: clinical and endoscopic evaluation of new-onset luminal paediatric Crohn's disease.

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Background: To induce remission in luminal paediatric Crohn's Disease (CD) the ESPGHAN 2020 guideline recommends treatment with exclusive enteral nutrition (EEN) or oral prednisolone. To maintain remission azathioprine (AZA) usually is started. We hypothesize that induction by EEN or prednisolone followed by AZA maintenance often provides insufficient disease control in children with moderate-to-severe paediatric CD.
Methods: Induction of remission by conventional treatment was a secondary outcome of parameter in the "TISKIDS" study. All patients treated with conventional treatment were included in this study.[1] Inclusion criteria were; age 3-17 years and new-onset, untreated luminal CD with weighted paediatric CD activity index (wPCDAI) >40. Induction treatment consisted of EEN (polymeric feeding for 6–8 weeks after which normal diet was reintroduced within 2–3 weeks) or oral prednisolone (1 mg/kg daily with a maximum of 40 mg for 4 weeks, followed by tapering). At the same time AZA as maintenance treatment was introduced in all patients. The choice for EEN or prednisolone was up to the patient and parents, in accordance with the treating physician. Patients with loss of response during AZA monotherapy stepped up to infliximab therapy.. Ten weeks after treatment initiation, rates of clinical remission (wPCDAI <12.5), endoscopic remission by endoscopy (SES-CD <3) and faecal calprotectin (FC) levels (<250 ug/g) were assessed. Treatment success at 14 weeks was defined as clinical remission without treatment escalation at this time point.
Results: 27/47 patients received EEN and 20/47 prednisolone. At baseline, demographics and disease activity were similar in the two treatment groups. At 10 weeks, 9/26 (35%) patients treated with EEN and 8/20 (40%) patients treated with prednisolone (p=0.71) were in clinical remission. At this time point, 29/47 (62%) consented to repeat endoscopy. Endoscopic remission rates were 3/16 (19%) in EEN treated patients and 1/13 (8%) in prednisolone treated patients (p=0.945). Likewise, a minority of patients had FC levels < 250 µg/g (EEN: 4/21 (19%) vs. prednisolone: 4/16 (25%) p=0.66). At 14 weeks, 13/27 (48%) EEN and 5/20 (25%) prednisolone treated patients received additional CD related therapy (p=0.11). In univariate analysis ESR and CRP levels at baseline were both prognostic for treatment success at week 14 (p=0.05 and p=0.05).
Conclusion: Children with newly diagnosed moderate-to-severe CD had low clinical, biochemical and endoscopic remission rates at 10 weeks following initiation of EEN or prednisolone induction treatment. Our data suggest that patients with higher inflammatory markers at baseline are less likely to achieve treatment success at 14 weeks.

De-escalation of biological therapy in inflammatory bowel disease patients following prior escalation

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Background: There are limited data available on de-escalation of biological therapy after prior escalation in inflammatory bowel disease (IBD) patients. This study aimed to assess the frequency and outcomes of de-escalation of biological therapy in IBD patients after prior dose escalation and evaluate which measures are used prior to de-escalation.
Methods: This multicentre, prospective, cohort study enrolled IBD patients treated with infliximab (IFX), adalimumab (ADA) or vedolizumab (VEDO) in whom therapy was de-escalated at least once after prior biological escalation. De-escalation based on objective disease measures was defined as faecal calprotectin ≤ 200 µg/g and/or trough levels were therapeutic or supratherapeutic and/or radiologic or endoscopic remission. Successful de-escalation was defined as remaining on the same or lower biological dose for ≥6 months after de-escalation.
Results: In total, 206 IFX users, 85 ADA users and 55 VEDO users underwent therapy escalation. Of these, 34 (17%) patients on IFX, 18 (21%) patients on ADA and 9 (16%) patients on VEDO had received at least one subsequent de-escalation. De-escalation was successful in 91% of IFX patients, 89% of ADA patients and 100% of VEDO patients. The probability of remaining on the de-escalated regimen or further de-escalation after 1 year was 85% for IFX, 62% for ADA and 89% for VEDO. De-escalation based on objective measures was performed in 60% of all de-escalations. Objective de-escalations were successful in 98% versus 81% of subjective de-escalations.
Conclusion: De-escalation after biological escalation is successful in the majority of patients. Objective markers of remission increase the likelihood of successful de-escalation.

Safety and drug survival of methotrexate versus tioguanine after failure of conventional thiopurines in Crohn's disease

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Background: Dutch IBD guidelines recommend tioguanine (TG) treatment as next in line therapy for Crohn's disease after failure of conventional thiopurines as an alternative to methotrexate (MTX). It is unclear how safety and effectiveness compare for both therapies. This study aimed to compare the tolerability, effectiveness, and drug survival of MTX and TG therapy after failure of conventional thiopurines in patients with Crohn´s disease.
Methods: We conducted a retrospective, multi-centre study in three Dutch hospitals between January 1st, 2012 and January 1st, 2020, including patients initiating MTX or TG for Crohn's disease after failure of conventional thiopurines. Patients with prior MTX or TG use, MTX or TG not primarily prescribed for Crohn's disease (e.g., rheumatic disease), or patients receiving concomitant biological treatment at baseline were excluded. The follow-up duration was 24 months or until treatment discontinuation. The primary outcome was the discontinuation rate due to AE. Secondary outcomes included ongoing treatment without initiation of biological treatment and total drug survival.
Results: In total, 141 patients with failure of conventional thiopurine treatment and subsequent therapy with either MTX (n=65) or TG (n=76) were included. Median follow-up was 21 months (IQR 6-24). Thirty-seven patients (26.2%) (MTX: 38.5%, TG: 15.8%, p=0.002) discontinued their treatment due to AE during follow-up. The median time until discontinuation due to AE was 20.6 weeks (IQR: 8.5 – 44.8) for MTX and 28.1 weeks (IQR: 9.7-58.9) for TG (p=0.411). MTX use was associated with a significantly higher risk of treatment failure due to AE (OR: 3.18 [95% CI: 1.42–7.14] p=0.005). No other risks were identified. The most frequent reasons for discontinuation were nausea for MTX (N=6) and abdominal pain for TG (N=4). Eight serious adverse events (SAE) occurred in the MTX group and 5 in the group using TG. Infections comprised the majority of all SAE, respectively 50% (n=4) and 80% (n=4). Elevated liver enzymes appeared in 3 MTX and 4 TG patients as reason for discontinuation. There were no observed cases of nodular regenerative hepatitis, liver fibrosis, or cirrhosis. Initiation of concomitant biological therapy was not significantly different. Total monotherapy drug survival after 24 months was 43% for TG and 30% for MTX (p=0.050).
Conclusion: Thirty-nine percent of MTX patients, compared to 16% of TG patients, discontinued therapy due to AE in patients with Crohn's disease with prior failure of conventional thiopurines. These data may aid the selection of subsequent therapy after failure of conventional therapy.

Switching within or out of class are the most effective strategies in IBD patients with immunogenicity against anti-TNF antibodies

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Background: Immunogenicity to anti-TNF agents is associated with loss of response. The efficacy of different strategies to restore favourable pharmacokinetics and clinical response upon the detection of anti-drug antibodies (ADA) has not been widely studied. We aimed to evaluate the success of different clinical approaches.
Methods: IBD patients with ADA against infliximab or adalimumab were identified through an electronic database search of a single tertiary IBD centre between 2004 and 2019. ADA were measured using a drug-sensitive assay and levels >12 AU/ml were considered positive. Clinical, biochemical and endoscopic data were retrospectively collected. Criteria for success of a therapeutic intervention, following ADA detection, were clinical remission 1 year after the intervention without further change of treatment.
Results: Two-hundred-and-ten IBD patients (172 Crohn's disease) were identified (115 receiving infliximab, 95 adalimumab). At ADA detection, median ADA level was 68 AU/ml; 53% of patients were in clinical remission. Therapeutic strategies at ADA detection were as follows: I) 41/210 (20%) patients continued the same dose anti-TNF, II) 41/210 (20%) patients underwent anti-TNF dose intensification, III) 24/210 (11%) continued the same anti-TNF with concomitant optimisation of immunomodulators, IV) 13/210 (6%) had both anti-TNF dose intensification and optimization of immunomodulators, V) 42/210 (20%) switched to another anti-TNF treatment, VI) 30/210 (14%) discontinued all biologic treatment, VII) 11/210 (5%) switched to a biologic out of class and VIII) 8/210 (4%) patients underwent surgery. Switching biological agents, both within and out of class, were the most successful strategies in terms of clinical remission at 1 year. Of the strategies that continued the same anti-TNF, dose intensification with concomitant immunomodulator optimization had the fastest beneficial effect (median 3 months (IQR 2-5), p=0.03) and was the most effective (62%, p=0.05) strategy to suppress ADA to undetectable levels. Patients that continued with same dose anti-TNF or de-escalated to conventional treatment were often already in clinical remission at ADA detection, but often deteriorated within 1 year, in 29%, (p=0.004) and 30% (p=0.02) of patients, respectively.
Conclusion: Switching within or out of class are the most successful strategies to regain and maintain clinical remission upon detection of ADA. Intensification of anti-TNF dosing with concomitant optimization of immunomodulatory therapy is the fastest strategy to suppress ADA formation.

Long-term outcomes following a swith from originator Adalimumab to the biosimilar SB5 (IMRALDI) in a real-world IBD cohort

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Background: Since 2017 multiple adalimumab (ADA) biosimilars, such as SB5 (Imraldi) and ABP501 (Amgevita), have been approved for use in IBD. Although several studies confirmed the efficacy and safety of the biosimilar infliximab, data about the switch to the biosimilar ADA are scarce. We therefore aimed to investigate the long-term outcomes following a switch from the ADA originator (Humira) to the biosimilar SB5 in IBD patients.
Methods: We performed a retrospective cohort study in a tertiary IBD referral centre. All IBD patients in our centre treated with Humira underwent an elective switch to the biosimilar SB5 regardless of IBD phenotype, disease activity and ADA dosing. We identified all these patients in a biologic prescription database that prospectively registered all ADA start and stop dates including brand names. Data on IBD phenotype, CRP, drug survival, ADA drug and antibody levels, and fecal calprotectin (FCAL), were collected.
Results: 228 IBD patients switched from Humira to SB5, including 204 patients with CD (89.5%) and 24 with UC/IBDU. 118 patients were male (n=51.8%) and median IBD duration was 9 years (IQR 5-16). 104/228 (46.0%) patients used infliximab before ADA. Patients were treated for a median of 33 months (IQR 18-58) with Humira prior to switching. At Humira - SB2 switch, 62.1% (141/228) received 40mg ADA every other week and 37.4% (85/228) once weekly. The median duration of follow up on SB5 treatment until last GI-related contact or drug discontinuation was 13 months (IQR 10-14). 178/201 (89.8%) and 93/140 (78.0%) patients remained on SB5 at week 26 and week 52, respectively. 75/228 patients (33.0%) discontinued SB5 treatment due to secondary loss of response (n=37, 49.3%), adverse events (n=32, 42.7%) or long-term remission (n=3, 4.0%). Pain at the injection site was the most frequently reported adverse event (n=25); all these patients switched to Amgevita.
No significant differences were seen regarding biochemical remission (CRP < 5 mg/l; p=0.45; FCAL < 250; p=0.17) between baseline, week 26 and week 52 following switch. Median ADA trough levels at baseline, week 26 and week 52 were 11.0 ug/ml (IQR 7.0-18.0), 11.7 ug/ml (IQR 8.2-17.4) and 9.2 ug/ml (IQR 5.1-12.0), respectively. ADA drug antibodies were present in 8/68 (11.8%) patients at baseline, in 8/56 (14.3%) at week 26 and in 8/33 (24.2%) at week 52.
Conclusion: In this real-world IBD cohort 78.0% of patients continued SB5 beyond 1 year after switching from Humira to SB5. No differences in biochemical remission were found between baseline, week 26 and week 52. ADA trough levels remained stable after the switch. These data confirm that switching to SB5 does not affect treatment efficacy and safety.

Gut microbiome and proteomic changes as biomarker of response to vedolizumab in patients with inflammatory bowel disease

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Background: Approximately half of the patients with IBD respond favourably to the a4b7-integrin inhibitor vedolizumab. Currently, adequate biomarkers of therapy response to vedolizumab are lacking in IBD. Here we aimed to predict vedolizumab response in IBD based on clinical characteristics, the gut microbiota and circulating proteins.
Methods: We prospectively collected clinical data, faecal and blood samples prior to and 14 weeks after vedolizumab treatment in 50 IBD-patients. Shot-gun metagenomic sequencing was performed on the faecal samples to characterize bacterial abundances and metabolic functions. A multiplex immunoassay enabled analysis of 92 inflammation related protein biomarkers (Olink- Inflammation panel) from the serum of these patients. Response to vedolizumab was based on the assessment of the treating physician as well as making use of clinical disease activity scores and faecal calprotectin measurements. Differences in gut microbiota and circulating proteins were assessed in the baseline and paired follow-up samples in relation to treatment response. A machine learning prediction model was built by using random forests, dividing the cohort into 75% training set and 25% test set, and general linear models.
Results: 27/50 patients showed response to vedolizumab. At baseline, five differences were identified in clinical characteristics, i.e. responders were older, had a longer disease duration, used more antibiotics, had more bowel resections and had lower leukocyte values as compared to non-responders (p < 0.05, Wilcoxon test). When analysing the microbial features and circulating proteins individually, no differences were identified between responders and non-responders at baseline. However, when we combined the above-mentioned clinical characteristics and the top 3 differentially abundant circulating proteins TNFSF12, LTA and MMP-10 in our prediction model at baseline, we were able to predict treatment response with an area under the curve of 0.76. Next, we analysed changes over time in gut microbial features and circulating proteins, thereby identifying in responders an increase in gut microbial a-diversity (p = 0.0494) and altered abundance of seven proteins (FDR < 0.1, CD5, CST5, IL10RB, SCF, TNFRSF9, DNER and MCP-4). Finally, we analysed whether the gut microbiota could influence the circulating proteins. We identified that the protein Oncostatin M showed the largest interaction with the gut microbiota.
Conclusion: Our study revealed the predictive potential of clinical characteristics, the gut microbiota and circulating proteins in response to vedolizumab treatment in patients with IBD. These findings may ultimately help to assign vedolizumab to eventual responders in IBD.

Pregnant women with perianal Crohn's disease: the current guideline on delivery method needs improvement

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Background: Pregnant women with active perianal Crohn's disease, have an indication for a caesarean section according to the current ECCO guidelines. This advice is based on the assumption that vaginal delivery leads to exacerbation of perianal disease and to worsening of faecal continence. However, there is no strong evidence to support this. Moreover studies have suggested that vaginal delivery has no influence on faecal incontinence. This study aims to examine the effects of delivery method on perianal disease progression and faecal incontinence in women with perianal Crohn's disease.
Methods: In this retrospective cohort study, 240 women were selected from a large IBD database within a tertiary hospital in the Netherlands. All women are aged >18 years, had Crohn's disease and perianal disease, and have at least one child. In addition, 102 women of this cohort completed a questionnaire. Faecal continence was scored using the Vaizey-score. Descriptive analysis was performed using SPSS and differences between groups were analysed using linear regression analysis. p-values <0,05 were considered statistically significant.
Results: After exclusion of 31 patients, the medical records of 209 patients were analysed. The caesarean section rate within this cohort was 27,8%, which is, as expected, high when compared to the caesarean section rate of 14% of the general Dutch population. The questionnaire cohort consists of 102 women, the median interval between the questionnaire and the most recent childbirth was 15 years (range 0-55). Within the group of women who delivered at least one child vaginally (n=84), 12,7% reported an alteration of faecal continence, compared to 7,5% of the women who never had a vaginal delivery (n=18). Within the total cohort of women (n=102) 24,5% reported altered faecal continence after the deliveries. Using linear regression the relation between delivery method and faecal continence (Vaizey score) was analysed. The outcome was corrected for the years after delivery. No significant relation between mode of delivery and faecal continence was found (B 0,97 [-1,19-3,14] p 0,375).
Conclusion: Faecal continence after delivery in women with Crohn's disease is not significantly influenced by the delivery method in this retrospective cohort. Based on our study and literature, we believe that it should be possible to lower the caesarean section rate in these patients. When determining the mode of delivery in women with Crohn's disease and perianal fistulas, the location of the fistula should be held in consideration. To draw solid conclusions, better registration of fistula location and objective documentation of fistula activity (using PDAI-score) is needed.

Optimal timing of rectal diclofenac in preventing post-ERCP pancreatitis

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Background: Rectal nonsteroidal anti-inflammatory drug (NSAID) prophylaxis reduces the incidence of post- endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis. The optimal timing of administration in relation the ERCP procedure is unknown. We assessed whether the timing of rectal NSAID prophylaxis (before or after the ERCP) affects the incidence of post-ERCP pancreatitis in moderate- to high-risk patients.
Methods: Patients with a moderate- to high-risk to develop post-ERCP pancreatitis, selected from the patients included in the randomized clinical trial (FLUYT trial, June 2015 to June 2019), that received rectal NSAID monotherapy 100mg prophylaxis within 30 minutes before or after the ERCP procedure were included. The primary endpoint was the development of post-ERCP pancreatitis. Secondary endpoints included the severity of pancreatitis, ERCP-related complications, length of hospitalization, and intensive care unit (ICU) admittance.
Results: From the 409 included patients, 346 patients received the rectal NSAID before and 63 patients after the ERCP procedure. No differences in baseline characteristics were observed. The incidence of post-ERCP pancreatitis was lower in the group that received the rectal NSAID preprocedural, compared to postprocedural, respectively: 8% vs. 18% (relative risk: 2.32; 95% confidence interval: 1.21 to 4.46, P = 0.017). Hospital stay was significantly longer in the patients who received postprocedural prophylaxes (1 (1-2) vs. 1 (1-4) days; P = 0.02). Additionally, an increased ICU admission rate was observed in the postprocedural group (1 vs. 4; P = 0.002).
Conclusion: The administration of rectal NSAIDs before the ERCP procedure reduces the incidence of post-ERCP pancreatitis, compared to administration after the procedure in moderate- to high-risk patients. (ISRCTN registry: ISRCTN13659155).

Evaluation of Gastroscopy Referrals in Primary Care in the Netherlands

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Background: The number of gastroscopies has increased since the introduction of open-access endoscopy. Nonetheless, up to 40% of gastroscopy referrals by general practitioners have been suggested not to meet referral criteria. We aimed to evaluate the appropriateness of gastroscopy referrals in a large general practice (GP) database.
Methods: We accessed the ELAN database containing GP patients in the region Leiden/Den Haag. Patients that were referred for open-access gastroscopy between 2016 and 2018 were identified through the use of selection criteria in the encoded database. Demographics, clinical data and details on medication use were collected by reviewing medical records. Appropriateness of open-access gastroscopy referrals was scored according to the Dutch College of General Practitioners guideline 'Upper gastrointestinal symptoms' (version 2013).
Results: A total of 148,926 adult patients from 27 primary care general practices were assessed. We identified 153 patients that were referred for open-access gastroscopy between 2016 and 2018. Median age was 55 years (IQR 42-66) of whom 67% were female. At the time of referral, almost all patients (n=141, 92%) already used acid suppressants and more than half (n=89, 58%) already had *Helicobacter pylori* tested. However, in the majority of patients (n=106, 69%) the duration of gastric symptoms was less than three months. In 66 patients (43%) the endoscopy referral was considered inappropriate, whereof 74% (n=49) had complaints less than three months. The outcome of gastroscopy was unknown in 57 patients (39%). Of the patients in which the outcome was known, the majority showed no clinically significant findings (n=70, 80%). Half of the patients (n=28, 54%) that consulted their GP for the gastroscopy result, were nonetheless referred to a gastroenterology outpatient clinic afterwards.
Conclusion: The indication for open-access gastroscopy was inappropriate in almost half (43%) of GP referrals, with more than half of patients (54%) still being referred to a gastroenterology outpatient clinic afterwards. Better counseling of patients and setting of indications could avoid inappropriate gastroscopy referrals, especially in patients with a shorter duration of symptoms.

Endoscopic Papillectomy; a Delphi consensus

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Background: Consensus regarding an optimal endoscopic treatment algorithm for papillary adenomas has not been established. This is likely due to low patient numbers and lack of high-level scientific studies. We aimed to assess the existing degree of consensus among international experts and develop further concordance by means of a Delphi process.

Methods: A total of 52 international experts with either significant scientific contributions or internationally recognised high volume clinical practice in the field of endoscopic papillectomy were invited to participate. Data were collected between August and December 2019 using an online survey platform. A total of three rounds were conducted and after each round the responses were summarized and anonymously redistributed for discussion in the next round(s). Consensus was defined as ≥70% agreement. Based on these results a consensus-based treatment algorithm is proposed. Strength of the consensus statements was based on the level of evidence of the supporting literature collected after systematic review, according to the definitions of the Oxford Centre for Evidence-Based Medicine.

Results: Twenty-eight experts (54%) joined the first round, 17 the second (33%) and 16 the final round (31%). Consensus was achieved on 47 of the final 79 statements (59%). Percentages showing the level of agreement. Diagnostic work-up should include at least an upper endoscopy using a duodenoscope (100%) and biopsies (94%). Additional abdominal imaging should only be performed on indication (75-81%). Patients with (suspected) papillary malignancy or over 1 cm ingrowth in the pancreatic duct (PD) or common bile duct (CBD) should be referred for surgical resection (76%). To prevent pancreatitis, rectal nonsteroidal anti-inflammatory drugs should be administered prior to resection (82%) and a pancreatic stent should be placed (100%). A biliary stent is indicated in case of ongoing bleeding from the papillary region (76%) or concerns for a (micro) perforation after resection (88%). Follow-up should be commenced 3-6 months after initial papillectomy and repeated every 6-12 months for at least 5 years (75%).

Conclusion: Useful expert consensus statements on endoscopic treatment for papillary adenoma were derived from this Delphi process. This is the first step in developing an international consensus-based algorithm for endoscopic management of papillary adenomas. There were surprisingly many areas where consensus could not be achieved, no scientific data exists, and a wide variety in daily practice continues. These treatment aspects should be the focus of future studies.

Endoscopic expert revision of previous histological confirmed flat low-grade dysplasia in Barrett's esophagus

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Background: The strongest histologic predictor for progression to high-grade dysplasia (HGD) or esophageal adenocarcinoma (EAC) in Barrett's esophagus (BE) is expert confirmed diagnosis of low-grade dysplasia (LGD). However, previous studies showed that up to 85% of LGD diagnosis were downstaged to non-dysplastic BE during revision. Therefore, Dutch guidelines advise to only refer patients with confirmed LGD to a Barrett's Expert Center (BEC). Aim was to assess if a finding of confirmed LGD in BE without visible lesions (VL), diagnosed in a community setting, is an indicator for higher grades of dysplasia and if referral to a BEC is indeed necessary.
Methods: Endoscopic therapy for BE neoplasia in NL is centralized in 9 BECs with trained endoscopists and pathologists. Upon community hospital LGD diagnosis, a national expert pathology panel reviews biopsy specimens. If LGD is confirmed, patients are referred for dedicated imaging endoscopy with high-definition white light- and virtual chromoendoscopy, followed by target/Seattle biopsies, in a BEC <3 months. We collected data from patients with confirmed LGD in random biopsies, without VL, referred between Jan 2017 and Oct 2019, since the guideline was introduced in 2017. Primary outcome was worst baseline histology established in a BEC, either in random biopsy specimen or in endoscopic resection specimen, reviewed by an expert pathologist.
Results: 222 patients with confirmed LGD without detected VL were referred to a BEC. Time between community and BEC endoscopy was 3mo (IQR 0-3). In 54/222 patients (24%; 95%CI 19-31), higher grade of neoplasia was found: HGD (n=30), EAC (n=24). The majority of these patients (43; 80%) had a VL. Eleven (20%) had HGD in random biopsies. 53/54 patients (98%) had curative endoscopic treatment, one patient (2%) had deep submucosal invasion and required esophagectomy. LGD was reconfirmed in 147 patients (66%; 95%CI 60-72). In the remaining 21 patients (10%; 95%CI[6-14]) biopsies showed non-dysplastic BE (NDBE). The majority of LGD patients received endoscopic treatment (125/147;85%) of which 119 (95%) achieved complete endoscopic eradication. 20/21 NDBE and 22/147 LGD patients were not treated and underwent surveillance. During median FU of 19mo (IQR 12-24), 3/42(7%) patients progressed to HGD.
Conclusion: After expert panel LGD confirmation in BE without VL diagnosed in a community hospital, dysplasia was reproduced in >90% upon BEC endoscopy. In 24% of patients, higher grades of dysplasia were found, often with VL. Our results endorse the current advice to confirm LGD, and to refer patients with confirmed LGD, even without VL, to an expert center.

Poor healing and poor squamous regeneration after radiofrequency ablation therapy for early Barrett's neoplasia: incidence, risk factors, and outcomes

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Background: Although endoscopic eradication therapy (EET) with radiofrequency ablation (RFA) is effective in the majority of patients with Barrett's Esophagus (BE), a subgroup is unable to achieve complete eradication of BE (CE-BE). Some might experience delayed healing with visible ulcerations ("poor healing"; PH) and/or regeneration with BE mucosa ("poor squamous regeneration"; PSR). Since little data is available for PH/PSR, we aimed to evaluate the incidence, risk factors, and outcomes of patients with PH/PSR after RFA.
Methods: We included all patients with at least 1 RFA treatment from a nationwide Dutch registry consisting of all patients who underwent EET for early BE neoplasia. Treatments were performed according to a joint treatment and follow-up protocol. PH was defined as visible ulcerations ≥3 months post-RFA; PSR as <50% regression after complete healing. Treatment success was defined as CE-BE.
Results: 1,386 patients (median BE C2M5) underwent EET for LGD (27%), HGD (30%), or early cancer (43%). PH occurred in 10% of patients (134/1,386) and additional time +/- acid suppression resulted in complete healing in all patients. Upon complete healing, normal squamous regeneration was seen in 50% (67/134) and 97% (65/67) achieved CE-BE. Overall, 5% of patients had PSR (74/1,386), preceded by PH in 92% (67/74). 64% (47/74) of PSR patients failed CE-BE. 70% (33/47) of failures had persisting BE that was free of neoplasia, and 30/33 underwent endoscopic follow-up. During mean 42 months 23% (7/30) progressed to neoplasia and all underwent curative repeat EET. The remaining 30% of failures (14/47) had persisting neoplasia. Overall, patients with PSR had a higher risk for progression to advanced cancer that exceeded boundaries for endoscopic treatment as compared to patients without PSR (15% vs <1% resp, P<0.01). Risk factors for PSR included <50% squamous regeneration after baseline endoscopic resection (OR 13.1 [95% CI 6.8-25.9]), presence of reflux esophagitis (OR 7.1 [2.9-16.6]), longer BE segments (OR 1.3 [1.2-1.4]), and higher BMI (OR 1.1 [1.0-1.2]).
Conclusion: PH and/or PSR occurs in 10% of patients after RFA. PH may be managed with additional time and acid suppression. Half of the patients will then have normal squamous regeneration with excellent success rates. However, if PSR occurs, the risk for treatment failure and progression to advanced disease is significant. We therefore recommend, upon detection of PSR, to carefully balance continuation of ablative therapy versus alternative treatment options. Endoscopic surveillance is a valid alternative in remaining BE with no neoplasia, whereas esophagectomy may be considered at early stages if advanced neoplasia is present.

Endoscopic submucosal dissection for Barrett's related neoplasia in the Netherlands: results of a nationwide cohort of 130 cases

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Background: Endoscopic resection (ER) is the standard of care for early neoplasia in Barrett's esophagus (BE). Generally, (piecemeal) ER is used to remove early neoplasia, yet the use of endoscopic submucosal dissection (ESD) is expanding. We aimed to report outcomes of all ESDs for BE neoplasia, performed in a setting of centralized care in the Netherlands.
Methods: Endoscopic therapy for BE neoplasia in the Netherlands is centralized in 9 expert centers with specifically and jointly trained endoscopists and pathologists. Uniformity is further ensured by a joint protocol and regular group meetings. ESD is performed for large and bulky lesions that cannot be removed with cap-based ER and/or in case of suspicion for submucosal (sm) invasion. Prospectively collected treatment/FU data are registered in a uniform database. We report efficacy and safety outcomes of all successfully completed ESD-BE cases treated in the Netherlands since 2008. En-bloc resection was defined as complete resection of the delineated target lesion in a single piece, R0-resection as absence of cancer in the vertical and lateral margin.
Results: A total of 130 ESDs was performed for lesions with a median diameter of 30mm (IQR 10-40) over 30% of the circumference (25-50). During median 121 min (90-180), 126/130 were removed en-bloc (97%). The remaining 4 were completely removed in piecemeal fashion. Pathology was m-EAC (48%) or sm-EAC (52%; 19% sm1 and 33% ≥sm2). Stratified for depth of invasion, the combined rate for en-bloc and R0 resection was 87% for T1a lesions (95%CI 77-94) and 49% (95%CI 37-62) for T1b lesions. After R1 resection, 29% of patients (10/34) had residual cancer at first FU, all of which were detected during the 8-12 weeks follow-up endoscopy. The remaining 71% (24/34) had no residual cancer in esophagectomy specimen (n=4) or during a median endoscopic FU of 9 months (4-22) (n=20). A total of 76 patients with en-bloc and R0 resection underwent endoscopic FU during median 17 months (IQR 8-30), with a local recurrence risk of 0% [95% CI 0-5]. In one patient, a small perforation occurred (1% [95% CI 0-4]), successfully treated with a clip. Post-procedural bleeding occurred in 4 patients (3% [95% CI 1-7]); esophageal stricture in 18 (13%, [95% CI 8-20]), resolved after median 3 (IQR 1-12) endoscopic dilatations.
Conclusion: In expert hands, ESD is safe and allows for effective removal of mucosal and submucosal esophageal adenocarcinoma. Our data suggest that histopathological R1 resection does not necessarily imply residual cancer and need for additional surgery, and underline the importance of endoscopic restaging to identify patients who do have residual cancer.

Disruption or disconnection of the pancreatic duct in patients with severe acute pancreatitis: a large prospective multi-center cohort

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Background: Disruption or disconnection of the pancreatic duct is a common finding following severe pancreatitis. Data and guidelines are currently lacking on the exact incidence and clinical impact.
Methods: A total of 927 consecutive patients with severe acute pancreatitis as defined by the revised Atlanta Classification were evaluated for a disrupted/disconnection pancreatic duct. We assessed patient characteristics, diagnostic modalities, invasive interventions and clinical impact of disruption/disconnection of the pancreatic duct. Generalized linear models were used to adjust for pre-specified confounders.
Results: Disruption or disconnection of the pancreatic duct was diagnosed in 261/927 patients (28%). An association was found for male gender (OR 1.5, 95% CI 1.1 – 2.1, p=0.008) and parenchymal necrosis (OR 4.6, 95% CI 3.2 – 6.7, p<0.001). An independent effect of a disrupted/disconnected pancreatic duct on readmission (adjusted OR 1.8, 95% CI 1.2 – 2.7, p=0.003), need for invasive intervention (adjusted OR 10.6, 95% CI 5.5 – 20.5, p<0.001) and organ failure (adjusted OR 1.7, 95% CI 1.2 – 2.4, p=0.003), with no independent effect on mortality beyond the first week (adjusted OR 0.7, 95% CI 0.4 – 1.1, p = 0.143), was found. We found an independent association with abdominal compartment syndrome (adjusted OR 3.1, 95% CI 1.3 – 7.4, p=0.009).
Conclusion: Around one third of patients with severe acute pancreatitis develop a disrupted or disconnected pancreatic duct. Diagnostic modalities and treatment strategies vary widely and the clinical impact is considerable. Efforts should be made to define an optimal diagnostic work-up and treatment strategy to improve outcomes.

Lumen-apposing metal stents versus double-pigtail plastic stents in the endoscopic step-up approach for infected necrotizing pancreatitis

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Background: Infected necrotizing pancreatitis is a potentially lethal disease that generally requires invasive intervention. The endoscopic step-up approach is preferred over a surgical step-up approach in eligible patients. LAMS might optimize endoscopic drainage and reduce the need for endoscopic necrosectomy. Nevertheless, some safety concerns, particularly the risk of bleeding, remain. We conducted a multicenter prospective study to investigate the clinical outcome of LAMS in patients with infected necrotizing pancreatitis.
Methods: Patients with infected necrotizing pancreatitis, eligible for endoscopic drainage with LAMS, were prospectively enrolled, and were compared to 51 patients assigned to the endoscopic step-up approach with DPS in the multicenter TENSION trial with identical in- and exclusion criteria. LAMS were removed within 6 weeks after placement. Primary endpoint was the need for endoscopic necrosectomy. Secondary endpoints included mortality, major complications, total number of interventions, length of intensive care and hospital stay during 6 months of follow-up.
Results: A total of 53 patients were prospectively enrolled in 16 hospitals. The primary endpoint did not differ between the LAMS-group and DPS-group (64% vs. 57%; RR 1.13, 95%CI 0.83-1.54, P=0.55). After correction for age, gender, SIRS, CRP, and use of antibiotics, the odds ratio for endoscopic necrosectomy in the LAMS vs. DPS-group was 1.14 (95%CI 0.44-2.90, P=0.78).
No differences were observed in mortality (11% vs. 18%; RR 0.64, 95%CI 0.25-1.67, P= 0.41), new-onset organ failure (17% vs. 14%; RR 1.24 95%CI 0.50-3.07, P=0.79), or other major complications. Bleeding, requiring endoscopic, surgical or radiologic intervention, occurred in 9% in the LAMS vs. 22% in the DPS-group (RR 0.44, 95%CI 0.16-1.17, P=0.11) after a median of 20 days (IQR 14-26) and 25 days (IQR 18-55), respectively (P=0.54). Length of intensive care stay was equal in both groups (median 0 days [IQR 0-4] vs. 0 days [IQR 0-9], P=0.49) and hospital stay did not differ (median 34 days [IQR 16-52] vs. median 35 days [IQR 22-71], P=0.23). The median number of drainage procedures was 1 (IQR 1-3) in the LAMS-group vs. 1 in the DPS-group (IQR 1-3) (P=0.44), and the median number of necrosectomies was 1 (IQR 0-3) vs. 1 (IQR 0-2) (P=0.37). The LAMS was removed after a median of 41 days (IQR 34-50).
Conclusion: The use of LAMS did not reduce the need for endoscopic necrosectomy compared with DPS in the step-up endoscopic approach for infected necrotizing pancreatitis. Additionally, no increased risk of complications, in particular bleeding, was observed.

Postponed or immediate drainage of infected necrotizing pancreatitis (POINTER): a multicenter randomized trial

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Background: Infected necrotizing pancreatitis is a potentially lethal disease that usually requires invasive intervention. Although current treatment guidelines advise to postpone drainage of infected necrosis for several weeks to await full encapsulation, the optimal timing of intervention for infected necrosis is debated.
Methods: We conducted a multicenter randomized trial in patients with infected necrotizing pancreatitis, to determine whether immediate catheter drainage is superior to postponed catheter drainage. Immediate catheter drainage included treatment with antibiotics and catheter drainage within 24 hours after patients were diagnosed with infected necrosis. Postponed catheter drainage included treatment with antibiotics and supportive treatment, aimed to postpone the drainage procedure until necrosis became walled-off. The primary end point was the Comprehensive Complication Index, combining all complications during 6 months of follow-up. Outcomes were assessed by a blinded adjudication committee.
Results: In total, 104 patients were randomly assigned to immediate catheter drainage (55 patients) or postponed catheter drainage (49 patients) in 22 Dutch hospitals. Immediate catheter drainage was performed after a median of 24 days (IQR 20-30), and postponed catheter drainage after a median of 29 days (IQR 24-40) after onset of symptoms of acute pancreatitis (P=0.004).
The primary end point CCI did not differ between the immediate and postponed drainage groups: the median CCI was 56.46 (IQR 34.46-80.47) and 48.22 (IQR 39.05-83.29), respectively (P=0.97). No significant difference between the immediate and postponed drainage group was observed in the rate of new-onset organ failure (25% and 22%; RR 1.13, 95%CI 0.57-2.26) and death (13% and 10%; RR 1.25, 95%CI 0.42-3.68). The median number of interventions for infected necrosis was 4 (IQR 2-6) and 1 (IQR 0-5) (P<0.001). The length of intensive care stay was equal in both groups (median 0 days [IQR 0-8] vs. 0 days [IQR 0-8], P=0.76) and total hospital did not differ significantly (median 48 days [36-83] vs. 35 days [21-66], P=0.07). In the postponed drainage group, 19 patients (39%) were successfully treated with antibiotics alone, without need for catheter drainage or necrosectomy during follow-up.
Conclusion: Immediate catheter drainage in patients with infected necrotizing pancreatitis is not superior to postponed catheter drainage in reducing complications. With a postponed catheter drainage strategy including antibiotic treatment, less interventions for infected necrosis are required, and more than one-third of patients may be treated conservatively.