NVGE
NEDERLANDSE VERENIGING
VOOR GASTRO-ENTEROLOGIE

DIGESTIVE DISEASE DAYS - DDD

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

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

**INHOUDSOPGAVE** **pag.**



**Tijdstippen diverse ledenvergaderingen donderdag:**

| | | |
|---|---|---|
| Nederlandse Vereniging voor Hepatologie | 22 maart | 09.00 uur – Auditorium |
| Nederlandse Vereniging voor Gastroenterologie | 22 maart | 11.30 uur – Brabantzaal |
| NVMDL i.o. | 22 maart | 12.00 uur – Zaal 55-57 |
| Netwerk verpleegkundig specialisten MDL | 22 maart | 13.30 uur – Zaal 52 |
| Nederlandse Vereniging voor Gastrointestinale Chirurgie | 22 maart | 14.30 uur – Brabantzaal |

**INHOUDSOPGAVE** **pag.**



**Tijdstippen diverse ledenvergaderingen vrijdag:**

| | | |
|---|---|---|
| Nederlandse Vereniging van Maag-Darm-Leverartsen | 23 maart | 08.00 uur – Zaal 82-83 |
| V&VN MDL | 23 maart | 09.20 uur – Brabantzaal |
| Sectie Gastrointestinale Oncologie | 23 maart | 11.00 uur – Zaal 80 |
| Sectie Kinder-MDL | 23 maart | 13.30 uur – Zaal 20 |

**Belangrijke mededeling**
**over de aanwezigheid van farmaceutische industrieën**

NVGE
NEDERLANDSE VERENIGING
VOOR GASTRO-ENTEROLOGIE

*Aan alle deelnemers tijdens het Digestive Disease Days op 22 en 23 maart 2018*

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

De Geneesmiddelenwet zegt dat - onder strikte voorwaarden - de farmaceutische industrie alleen reclame mag maken voor receptgeneesmiddelen voor personen die bevoegd zijn om dergelijke geneesmiddelen voor te schrijven. Alle andere personen (inclusief bijvoorbeeld verpleegkundigen, endoscopie-assistenten en biochemici) worden beschouwd als “publiek”. De farmaceutische industrie mag geen reclame maken voor receptgeneesmiddelen voor publiek.
De Nederlandse Vereniging voor Gastroenterologie is een wetenschappelijke vereniging voor personen die beroepsmatig betrokken zijn bij zorg, onderwijs en onderzoek ten behoeve van patiënten met maag-, darm- en leveraandoeningen. Dat betekent dat ook personen die geen arts zijn, lid van de NVGE zijn.
De aanwezigheid van artsen, niet-artsen en farmaceutische industrieën tijdens het congres kan de NVGE ongewild in aanraking brengen met de inspectie voor de gezondheidszorg, sectie reclametoezicht, en daarmee in diskrediet worden gebracht. Dat willen wij uiteraard voorkomen.

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

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

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

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

Het bestuur van de NVGE

## Voorwoord

Hierbij treft u het volledige programma aan van de Digestive Disease Days op 22 en 23 maart a.s. in NH Conference Center Koningshof te Veldhoven. Zoals gebruikelijk wordt ons congres vooraf gegaan door het cursorisch onderwijs op woensdag 21 maart, deze keer over infecties.

Ook dit voorjaar weer aandacht voor het basale onderzoek. De Sectie Experimentele Gastroenterologie organiseert meerdere abstract sessies zowel op de donderdag als op de vrijdag. Het overige "heet van de naald" wetenschappelijk onderzoek uit MDL Nederland is te vinden in de verschillende abstractsessies op beide dagen.
Het programma georganiseerd door de NVGIC vindt op donderdag plaats. De onderwerpen die aan bod komen zijn onder meer de behandeling van zowel maligne als benigne colon en rectum aandoeningen, ook de lopende trials in Nederland worden voor het voetlicht gebracht.

Op donderdagochtend een symposium over de behandeling van complicaties van cirrose. Het programma op donderdagochtend kent verder een terugblik op de ECCO en er vinden 2 meet the expert sessies plaats over acute endoscopie en over de behandeling van leverfalen. Omdat het interactieve karakter van de sessies zeer gewaardeerd worden duren deze sessies nu 1 uur, de tweede expert sessie zal plaatsvinden net na de lunch  Het NVGE symposium over de behandeling van ischemie kent een internationaal karakter met als spreker Prof. S. Acosta, Vaatchirurg, uit Malmö. Na de President Select met de prijsuitreikingen en de bekendmakingen van de verstrekte NVGE subsidies volgt de uitreiking van de Frieda den Hartog Jagerprijs aan Prof. dr. G.J. A. Offerhaus, titel van de aansluitende presentatie is: Van Mens naar Muis (en terug..).

Op de vrijdagochtend start het programma van de V&VN MDL in de Brabantzaal en tevens op vrijdagochtend een programma van de sectie endoscopie met als titel: Battle in endoscopy. Halverwege de ochtend een kinder-MDL/NVGE symposium over Jong gekregen, Oud gehouden ziektes. Parallel hieraan het NESPEN symposium. In de middag een oncologie symposium over immunotherapie inclusief de bijwerkingen van deze therapie en een symposium over de behandeling van hepatitis C in de klinische praktijk.

Een plezierig congres gewenst.

Prof. dr. C.J. van der Woude, secretaris NVGE

# Programma donderdag 22 maart 2018

| Donderdag | Brabantzaal | Auditorium | Baroniezaal | Parkzaal |
|---|---|---|---|---|
| 08.30 - 09.30 | Ontvangst en koffie/thee | | | |
| 09.30 - 11.30 | Symposium NVGIC<br>Maligne colon/rectum | NVH Symposium<br>Behandeling van complicaties van cirrose | Symposium IBD Terugblik ECCO<br>met aansluitend casuïstiek<br>*Aanvang 10.00 uur* | Abstractsessie<br>Ned. Vereniging voor Gastrointestinale Chirurgie I<br>*Aanvang 09.15 uur* |
| | *pagina 10* | *pagina 14* | *pagina 19* | *pagina 22* |
| 11.30 - 12.00 | Ledenvergadering NVGE | Geen programma i.v.m. Ledenvergadering NVGE | Geen programma i.v.m. Ledenvergadering NVGE | Geen programma i.v.m. Ledenvergadering NVGE |
| 12.00 - 13.00 | Lunch in expositiehal | | | |
| 13.00 - 15.00 | Symposium NVGIC<br>Benigne colon/rectum | Abstractsessie<br>Sectie Inflammatoire Darmziekten I | Symposium NVGE<br>Clinical update of Chronic Mesenteric Ischemia | Abstractsessie<br>Ned. Vereniging voor Gastrointestinale Chirurgie II |
| | *pagina 11* | *pagina 15* | *pagina 20* | *pagina 24* |
| 15.00 - 15.30 | Theepauze | | | |
| 15.30 - 17.00 | Symposium NVGIC<br>Grenzen @ GI Spoedzorg n.a.v. nieuwe richtlijn rondom spoedoperaties en juridische consequenties | Abstractsessie<br>Sectie Inflammatoire Darmziekten II | DEG sessie I: Key note speaker en abstracts | Abstractsessie Nederlandse Vereniging voor Gastroenterologie I |
| | *pagina 11* | *pagina 17* | *pagina 21* | *pagina 26* |
| 17.00 - 17.30 | Voordrachten President Select | | | |
| 17.30 - 17.45 | Uitreiking NVGE Subsidies | | | |
| 17.45 - 18.00 | Uitreiking NVGE Gastrointestinale Researchprijs 2017 | | | |
| 18.00 - 18.30 | Frieda den Hartog Jagerprijs:<br>Johan Offerhaus<br>'Van Mens naar Muis (en terug…)' | | | |
| 18.30 - 19.30 | Borrel in expositiehal | | | |
| 19.30 - 22.00 | Diner Beneluxzaal | | | |
| 22.00 - 22.30 | Koffie en opening tentoonstelling 'Inside Art' Meierij foyer | | | |
| 22.30 - 00.00 | Borrel | | | |

| Donderdag | Zaal 80 | Zaal 81 |
|---|---|---|
| 09.30 - 10.30 | Meet the expert leverfalen | Meet the expert spoed endoscopieën |
| 13.00 - 14.00 | Meet the expert leverfalen | Meet the expert spoed endoscopieën |
| 15.30 - 17.00 | Abstractsessie Sectie Gastrointestinale Endoscopie I<br>*pagina 29* | |

# Programma vrijdag 23 maart 2018

| Vrijdag | Auditorium | Baroniezaal | Parkzaal | Zaal 80 |
|---|---|---|---|---|
| 08.30 - 09.30 | Ontvangst en koffie | | | |
| 09.30 - 11.00 | Symposium Sectie Gastrointestinale Endoscopie - Battle in endoscopy MDL-arts en chirurg | DEG sessie II: Battle en abstracts | Abstractsessie Sectie Gastrointestinale Oncologie | Abstractsessie NESPEN/IBD |
| | *pagina 31* | *pagina 33* | *pagina 36* | *pagina 42* |
| 11.00 - 11.30 | Koffiepauze expo | | | |
| 11.30 - 13.00 | Symposium Kinder-MDL/NVGE: 'Jong gekregen, oud gehouden' | DEG-sessie III: Keynote speaker en abstracts + prijsuitreiking | Abstractsessie Sectie Gastrointestinale Endoscopie II | Symposium NESPEN: Nieuwe voedingsconcepten in ziekenhuizen: optimalisering voedingszorg en minder ondervoeding? Uitreiking NESPEN proefschriftprijs |
| | *pagina 31* | *pagina 34* | *pagina 38* | *pagina 44* |
| 13.00 - 14.00 | Lunch in expositiehal | | | |
| 14.00 - 16.00 | Symposium Immunotherapy in GI malignancies and its GI related side-effects | "How do I do it", sessie over de real-life behandeling van hepatitis C en B | Abstractsessie Nederlandse Vereniging van Gastroenterologie II | |
| | *pagina 32* | *pagina 35* | *pagina 40* | |

## V&VN programma vrijdag 23 maart 2018 - Ochtend

| Vrijdag | Brabantzaal | Zaal 63/64 |
|---|---|---|
| 09.00 - 09.20 | Ontvangst en koffie | |
| 09.20 - 10.00 | Algemene ledenvergadering V&VN MDL | |
| 10.00 - 11.10 | Programma I - MDL algemeen | |
| 11.10 - 11.40 | Koffiepauze | |
| 11.40 - 13.00 | Programma II - Endoscopie | Programma III - MDL algemeen |
| 13.00 - 14.00 | Lunch in expositiehal | |

## V&VN programma vrijdag 23 maart 2018 - Middag

| Vrijdag | Brabantzaal | Zaal 63/64 | Zaal 82/83 | Zaal 80 | Zaal 81 |
|---|---|---|---|---|---|
| 14.00 - 15.45 | Programma I<br>Endoscopie | Programma II<br>Verpleegkundig Endoscopisten | Programma III<br>Inflammatoire Darmziekten | Programma IV<br>Lever | Programma V<br>Oncologie en Chirurgie |
| 15.45 - 16.30 | Borrel | | | | |

*Woensdag 21 maart 2018*

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

Cursuscommissie
Dr. B. Oldenburg, MDL-arts, UMCU, Utrecht, voorzitter
Dr. C.M. Bakker, MDL-arts, Slotervaart Ziekenhuis, Amsterdam
Dr. I.L. Holster, aios MDL, Erasmus MC, Rotterdam
Dr. M.A.J.M. Jacobs, MDL-arts, VUmc, Amsterdam
Prof. dr. J.F. Lange, chirurg, UMCG, Groningen
Dr. A.M.J. Langers, MDL-arts, LUMC, Leiden
Dr. B.J. Veldt, MDL-arts, Reinier de Graaf Gasthuis, Delft
Dr. L. van Vlerken, aios MDL, UMCU, Utrecht

## Infectieziekten in de MDL

***Voorzitters:*** *Marco Bruno, Lisanne Holster*

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14.30 – 14.45 *Helicobacter pylori*: valkuilen in de diagnostiek en behandeling
*Dr. Lisette Capelle, MDL-arts, Meander MC, Amersfoort*

14.50 – 15.05 Cholangitis, leverabces
*Dr. Frans Cuperus, MDL-arts, UMCG, Groningen*

15.10 – 15.25 Icterus na tropenbezoek
*Dr. Sophie Willemse, MDL-arts, AMC, Amsterdam*

15.30 – 15.45 Infecties en endoscopen
*Prof. dr. Marco Bruno, MDL-arts, Erasmus MC, Rotterdam*

15.50 – 16.10 Pauze

***Voorzitters:*** *Bas Oldenburg, Lotte van Vlerken*

16.10 – 16.25 Infecties bij de immuungesupprimeerde patiënt
*Prof. dr. Geert D'Haens, MDL-arts, AMC, Amsterdam*

16.30 – 16.45 Acute infectieuze diarree bij reizigers en thuisblijvers
*Dr. Martijn Bauer, internist-infectioloog, LUMC, Leiden*

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

***Voorzitters:*** *Rogier de Ridder, Eveline Rondagh*

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16.50 – 17.05 Parasitaire infecties
*Dr. Pieter Jan Haas, microbioloog, UMCU, Utrecht*

17.10 – 17.40 Pauze

17.45 – 18.00 PEG gerelateerde infectieuze complicaties
*Dr. Rogier de Ridder, MDL-arts, MUMC, Maastricht*

18.05 – 18.20 Fecestransplantatie: indicaties en technieken
*Dr. Josbert Keller MDL-arts, Haaglanden MC, Den Haag*

18.25 – 18.40 Immuunsuppressie: screening en vaccinaties
*Dr. Ad van Bodegraven, MDL-arts, Zuyderland MC, Heerlen/Sittard-Geleen*

18.45 Einde cursus, diner

De cursuscommissie verwacht van de MDL-artsen i.o. dat ze de Cursus Klinische Hepatologie (Dutch Liver Week) éénmaal bezoeken in het tweede deel van de MDL-opleiding (jaar vier tot zes).

Op het cursorisch onderwijs zijn conform de eisen van het Centraal Register Kort Beroepsonderwijs leveringsvoorwaarden van toepassing. Informatie vindt u op de onderwijspagina van www.mdl.nl en www.nvge.nl.

**Symposium Nederlandse Vereniging voor Gastrointestinale Chirurgie I** **Brabantzaal**

**Voorzitters:** T. van Loon en H.L. van Westreenen

**Maligne colon/rectum**

09.30 Laat optredende naadlekkages en chronische pre-sacrale sinus vorming na low anterior resecties: resultaten van de Rectum Snapshot studie
*Dr. W.A.A. Borstlap, chirurg, AMC, Amsterdam*

09.55 Leidt stentplaatsing bij linkszijdig obstructief coloncarcinoom inderdaad tot slechtere lange termijn uitkomsten? De uitkomsten van een systematic review en meta-analyse.
*Drs. F. Amelung, Meander MC / UMCU, Utrecht*

10.20 Leidt robot chirurgie versus laparoscopische bij lage rectum operaties tot een betere kwaliteit van leven?
*Drs. A. Couwenberg, arts-onderzoeker, UMCU, Utrecht*

10.45 'Wait and see' beleid bij volledige respons neo-adjuvante behandeling van rectumcarcinomen: stand van zaken
*Prof. dr. G.L. Beets, chirurg, Antoni van Leeuwenhoek, Amsterdam*

11.10 Highlights rectumca trials anno 2018
*Dr. J.B. Tuynman, chirurg, VUmc, Amsterdam*

11.30 Aanvang algemene ledenvergadering NVGE

**Algemene ledenvergadering - NVGE** **Brabantzaal**

11.30 Aanvang algemene ledenvergadering NVGE

12.00 Lunchpauze in expositiehal

**Symposium – Nederlandse Vereniging voor Gastrointestinale Chirurgie II** **Brabantzaal**

**Voorzitters:** J. Leijtens en V.M.W.T. Klemann

**Benigne colon/rectum**

13.00 Kan een klysma volstaan als darm voorbereiding bij lage rectum chirurgie? Vergelijking van een hoog opgaand klysma versus volledige darmvoorbereiding, kijkend naar de colon mobiliteit.
*Drs. T. Burghgraef, arts-onderzoeker, Meander MC, Amersfoort*

13.25 Ongecompliceerde diverticulitis met een belletje vrij lucht op CT: reden voor paniek?
*Drs. H.E. Bolkenstein, Meander MC, Amersfoort*

13.50 Behandeling van geperforeerde diverticulitis Hinchey 3 of 4: lange termijn resultaten van de LADIES trial.
*Drs. D. Lambrichts, Erasmus MC, Rotterdam*

14.10 IBD chirurgie: stand van zaken
*Prof. dr. L.P.S. Stassen, chirurg, MUMC, Maastricht*

14.30 Algemene ledenvergadering NVGIC

15.00 Theepauze

**Symposium – Nederlandse Vereniging voor Gastrointestinale Chirurgie III** **Brabantzaal**

**Voorzitter:** T. Karsten en M. Ditzel

**Grenzen @ GI Spoedzorg**
**n.a.v. nieuwe richtlijn rondom spoedoperaties en juridische consequenties**

15.30 Introductie tot nieuwe richtlijn en relatie tussen de uitkomst van een spoedoperatie en beschikbaarheid operatiekamer en ervaring van het team.
*Prof. dr. M. Boermeester, chirurg, AMC, Amsterdam*

Hoelang kan een operatie voor acute colon obstructie uitgesteld worden zonder negatieve gevolgen?
*Dr. D. Wasowicz, chirurg, Tweesteden Ziekenhuis, Tilburg*

Hoelang kan een cholecystectomie voor acute cholecystitis worden uitgesteld?
*Dr. P.R. de Reuver, chirurg, Radboudumc, Nijmegen*

Juridische consequenties van de nieuwe richtlijn rondom spoedoperaties

17.00 Einde programma

## President Select — Brabantzaal

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

*Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten*

17.00 The Natural Course and Long-term Consequences of Untreated Eosinophilic Esophagitis in a Large Cohort (p. 51)
*R.A.B. Oude Nijhuis[1], M.J. Warners[1], L.R.H. de Wijkerslooth[2], A.J.P.M. Smout[1], A.J. Bredenoord[1]. [1]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Isala, Zwolle, The Netherlands.*

17.10 Duodenal mucosal resurfacing elicits improvement in glycemic and hepatic parameters in type 2 diabetes: complete 1 year results from the first multicenter study (p. 52)
*A.C.G. van Baar[1], M. Nieuwdorp[3], F. Holleman[4], J. Deviere[5], L. Crenier[6], R. Haidry[7], R. Batterham[8], L. Rodriguez Grunert[9], M. Galvao Neto[10], P. Vignolo[9], G. Costamagna[11], J.J.G.H.M Bergman[1]. [1]Gastroenterology & Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [3]Internal and Vascular Medicine, Academic Medical Center, Amsterdam, The Netherlands. [4]Internal Medicine, Academic Medical Center, Amsterdam, The Netherlands. [5]Gastroenterology, Erasmus University Hospital, Brussels, Belgium. [6]Endocrinology, Erasmus University Hospital, Brussels, Belgium. [7]Gastroenterology, University College Hospital, London, United Kingdom. [8]Center for Obesity Research, Dept. of Medicine, University College Hospital, London, United Kingdom. [9]CCO Clinical Center for Diabetes, Obesity and Reflux, Santiago, Chile. [10]Bariatric Endoscopy Service, Gastro Obeso Center, Sao paulo, Brazil. [11]Digestive Endoscopy, Policlinico Gemelli, Catholic University of Rome, Rome, Italy.*

17.20 Body composition and growth in children with intestinal failure receiving long-term parenteral nutrition (p. 53)
*E. Neelis[1], J. Olieman[2], S. Kouwenhoven[3], M. Tabbers[4], C. Jonkers[5], R. Wijnen[6], E. Rings[1], B. de Koning[1], J. Hulst[1]. [1]Dept. of Pediatric Gastroenterology, Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands. [2]Dept. of Dietetics, Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands. [3]Dept. of Pediatrics, VU Medical Center, Amsterdam, The Netherlands. [4]Dept. of Pediatric Gastroenterology, AMC-Emma Children's Hospital, Amsterdam, The Netherlands. [5]Dept. of Dietetics, AMC-Emma Children's Hospital, Amsterdam, The Netherlands. [6]Dept. of Pediatric Surgery, Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands.*

**NVGE subsidies** **Brabantzaal**

17.30 **Bekendmaking toegekende NVGE-subsidies**:
- *Subsidies Gastrostart*
- *Subsidies voor multidisciplinaire en instelling-overstijgende onderzoeksinitiatieven of werkgroepen.*

**Prijsuitreiking** **Brabantzaal**

17.45 **NVGE Gastrointestinale Researchprijs 2018**
*Uitreiking door Dr. L.J.W. van der Laan, voorzitter van de jury.*
*De prijsuitreiking wordt gevolgd door een korte voordracht door de winnaar.*

**Frieda den Hartog Jager prijs** **Brabantzaal**

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

18.00 'Van Mens naar Muis (en terug….)'
*Prof. dr. G.J.A. Offerhaus, patholoog, UMCU, Utrecht*

18.30 Congresborrel in expo

20.00 Buffet Beneluxzaal

**Nederlandse Vereniging voor Hepatologie** **Auditorium**

09.00 Algemene Ledenvergadering Nederlandse Vereniging voor Hepatologie

**Symposium – Nederlandse Vereniging voor Hepatologie** **Auditorium**

**Voorzitters:** U.H.W. Beuers en H.J. Metselaar

**Behandeling van complicaties van cirrose**

09.30 Standaard en nieuwe ontwikkelingen in preventie en behandeling van varicesbloedingen
*Dr. M.J. Coenraad, MDL-arts, LUMC, Leiden*

09.50 Diagnose en behandeling van hepatopulmonaal syndroom en portopulmonale hypertensie
*Dr. A. Boonstra, longarts, VUmc, Amsterdam*

10.10 Behandeling van refractaire ascites, hydrothorax, AKI-HRS
*Dr. R.B. Takkenberg, MDL-arts, AMC, Amsterdam*

10.30 Experimental Young Investigator Award 2018 (3 x 5 min pitch / battle)
*'Battle' met de 3 TOP auteurs 2017*

11.00 Timing van levertransplantatie
*Prof. dr. H.J. Metselaar, MDL-arts, Erasmus MC, Rotterdam*

11.20 Uitreiking Experimental Young Investigator Award 2018

11.30 Aanvang algemene ledenvergadering NVGE in de Brabantzaal

12.00 Lunchpauze

**Abstractsessie – Sectie Inflammatoire Darmziekten I** **Auditorium**

**Voorzitters :** M.J. Pierik en C. Spooren

*Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten*

13.00 Post-inflammatory polyps do not predict colorectal neoplasia in patients with inflammatory bowel disease: a multinational retrospective cohort study (p. 54)

*R. Mahmoud[1], S.C. Shah[2], J.R. ten Hove[1], J. Torres[3], E. Mooiweer[1], D. Castaneda[2], J. Glass[2], J. Elman[4], A. Kumar[2], J. Axelrad[5], T. Ullman[2], J.F. Colombel[2], B. Oldenburg[1], S.H. Itzkowitz[2]. I.C.C. Initiative on Crohn & Colitis. [1]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands. [2]Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, United States of America. [3]Division of Gastroenterology, Hospital Beatriz Ângelo, Loures, Portugal. [4]Dept. of Medicine, Icahn School of Medicine at Mount Sinai, New York, United States of America. [5]Division of Digestive and Liver Diseases, Columbia University Medical Center, New York, United States of America.*

13.10 Long-term risk of advanced neoplasia after colonic low-grade dysplasia in patients with inflammatory bowel disease: a nationwide cohort study (p. 55)

*M.E. de Jong[1], S.B. van Tilburg[1], L.H.C. Nissen[2], W. Kievit[1], I.D. Nagtegaal[3], F. Hoentjen[4], L.A.A.P. Derikx[1]. [1]Dept. of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Jeroen Bosch Hospital, 's Hertogenbosch, The Netherlands. [3]Dept. of Pathology, Radboud University Medical Center, Nijmegen, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, The Netherlands.*

13.20 **MLDS voordracht**

IgA immune complexes in the lamina propria drive inflammation in the human intestine through metabolic reprogramming of human CD103+ dendritic cells (projectnr. CDG 12-10) (p. 56)

*J. den Dunnen. Academic Medical Center, Amsterdam, The Netherlands.*

13.30 Whole-exome sequencing study identifies novel variants in NUDT15 that contribute to thiopurine-induced myelosuppression in Europeans (p. 57)

*M.D. Voskuil[1], G.J. Walker[2], J.W. Harrison[3], G.A. Heap[2], J. Koskela[4], E.A.M. Festen[1], M.J. Daly[4], R.K. Weersma[1], R. Ward[3], M.N. Weedon[3], J.R. Goodhand[2], N.A. Kennedy[2], T. Ahmad[2]. [1]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [2]Dept. of Gastroenterology, Royal Devon and Exeter Hospital, Garcia Exeter, United Kingdom. [3]University of Exeter Medical School, Exeter, United Kingdom. [4]Broad Institute of Harvard University and MIT, Cambridge, United States of America.*

13.40 Using whole exome sequencing to expand the genetic architecture of inflammatory bowel disease (p. 58)

*R.K. Weersma[1], M.A. Rivas[2], C. Stevens[3], B. Avila[3], J. Koskela[4], T. Ahmad[5], S. Brant[6], J. Cho[7], A. Franke[8], B. Glase[9], D. McGovern[10], A. Palottie[11], J. Rioux[12], H. Sokol[13], D. Turner[14], H. Winter[15], R.J. Xavier[16], M.J. Daly[17]. [1]Dept. of Gastroenterology and Hepatology University Medical Center Groninggen, Groningen, The Netherlands. [2]Biomedical Data Science, Stanford University, San Francisco, United States of America. [3]The Broad Institute of Harvard and MIT, Cambridge, United States of America. [4]Institute for Molecular Medicine, Helsinki, Finland. [5]University of Exeter, Exeter, United Kingdom. [6]Meyerhoff Inflammatory Bowel Disease Center, Dept. of Medicine, School of M, Baltimore, United States of America. [7]Charles Bronfman Institute for Personalized Medicine Icahn School of Medicine, New york, United States of America. [8]Nstitute of Clinical*

*Molecular Biology, Christian-Albrechts-University of Kiel, Kiel, Germany. [9]Endocrinology and Metabolism Service, Hadassah-Hebrew University Hospital, Jerus, Jerusalem, Israel. [10]Cedars-Sinai Medical Center, Los angeles, United States of America. [11]Institute for Molecular Medicine Finland (FIMM), Helsinki, Finland. [12]Montreal Heart Institute and Université de Montréal, Montreal, Canada. [13]Gastroenterology Dept., Saint-Antoine Hospital, APHP, Paris, France. [14]Shaare Zedek Medical Center, Jerusalem, Israel. [15]Pediatric Medical Services, Massachusetts General Hospital, Boston, United States of America. [16]Gastrointestinal Unit, Massachusetts General Hospital, Boston, United States of America. [17]Analytic and Translational Genetics, Massachusetts General Hospital, Boston, United States of America.*

13.50 Tacrolimus suppositories as induction therapy for refractory ulcerative proctitis: a randomized controlled trial (p. 59)

*M.R.K.L. Lie[2] , J.E. Kreijne[1], G. Dijkstra[3], M. Löwenberg[4], G. van Assche[5], R.L. West[6], D. van Noord[6], A.E. van der Meulen-de Jong[7], B. Hansen[2], A.C. de Vries[2], C.J. van der Woude[2]. [1]Dept. of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands. [2]Dept. of Gastroenterology and Hepatology Erasmus Medical Center, Rotterdam, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [5]Dept. of Gastroenterology and Hepatology, University Hospitals Leuven, Leuven, Belgium. [6]Dept. of Gastroenterology and Hepatology, Franciscus Gasthuis & Vlietland, Rotterdam, The Netherlands. [7]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands.*

14.00 Effect of disease duration and location on clinical remission in Crohn's disease patients treated with filgotinib, a selective JAK1 inhibitor: post-hoc analysis from the Phase 2 FITZROY study (p. 60)

*M. Löwenberg[1], G.R.A.M. D'Haens[1], A. van der Aa[2], C. Jamoul[2], C. Tasset[2], P. Harrison[2], S. Vermeire[3]. [1]Academic Medical Center, Dept. of Gastroenterology, Amsterdam, The Netherlands. [2]Galapagos NV, Mechelen, Belgium. [3]University Hospitals Leuven, Dept. of Gastroenterology, Leuven, Belgium.*

14.10 Long-Term Drug Survival of Thioguanine in Inflammatory Bowel Disease among Two Real-Life Cohorts (p. 61)

*M. Simsek[1], D. Deben[2], M.V. Bénard[1], H.J.C. Buiter[3], M.L. Seinen[1], C.J.J. Mulder[1], D.R. Wong[2], K.H.N. de Boer[1], A.A. van Bodegraven[4]. [1]Dept. of Gastroenterology and Hepatology, VU Medical Center, Amsterdam, The Netherlands. [2]Dept. of Clinical Pharmacy and Toxicology, Zuyderland Medical Center, Sittard-geelen, The Netherlands. [3]Dept. of Clinical Pharmacy, VU Medical Center, Amsterdam, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, Zuyderland Medical Center, Sittard-Geelen, The Netherlands.*

14.20 Drug survival of vedolizumab-treated inflammatory bowel disease patients in a nationwide observational cohort study: case series (p. 62)

*V.B.C. Biemans[1], C.J. van der Woude[2], G. Dijkstra[3], A.E. van der Meulen-de Jong[4], B. Oldenburg[5], N.K.H. de Boer[6], C.Y. Ponsioen[7], A.C. de Vries[2], J.J.L. Haans[8], M.J. Pierik[8], F. Hoentjen[1]. [1]Dept. of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands. [5]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands. [6]Dept. of Gastroenterology and Hepatology, VU Medical Center, Amsterdam, The Netherlands. [7]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [8]Dept. of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, The Netherlands.*

14.30 Ustekinumab for crohn's disease: a nationwide real-life observational cohort study (p. 63)

*V.B.C. Biemans[1], A.E. van der Meulen-de Jong[2], C.J. van der Woude[3], N.K.H. de Boer[4], G. Dijkstra[5], B. Oldenburg[6], C.Y. Ponsioen[7], P.W.J. Maljaars[2], J.J.L. Haans[8], M.J. Pierik[8], F. Hoentjen[1]. [1]Dept. of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, VU Medical Center, Amsterdam, The Netherlands. [5]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [6]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands. [7]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [8]Dept. of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, The Netherlands.*

14.40 Use of Compplementary and Alternative Medicine use does not influence adherence to regular IBD medication (p. 64)

*N. Dekkers[1], S. van der Marel[1], A.E. van der Meulen-de Jong[1], T. Markus- de Kwaadsteniet[2], D. Van der Horst[2], J. Maljaars[1]. [1]Gastroenterology-Hepatology, LUMC, Leiden. [2]CCUVN, Woerden, The Netherlands.*

14.50 Clinical feasibility of dried blood sampling for infliximab in IBD-patients (p. 65)

*S.E. Berends[1], G.R.A.M. D'Haens[2], K. Bloem[3], J. Schaap[4], A. de Vries[4], T. Rispens[3], R.A. Mathôt[1]. [1]Dept. Hospital Pharmacy, Academic Medical Center, Amsterdam, The Netherlands, Amsterdam, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [3]Dept. of Immunopathology, Sanquin Research and Landsteiner Laboratory, Amsterdam, The Netherlands. [4]Biologicals Lab, Sanquin Diagnostic Services, Amsterdam, The Netherlands.*

15.00 Theepauze

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**Abstractsessie – Sectie Inflammatoire Darmziekten II** **Auditorium**

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**Voorzitters :** D. Leemreis en A.E van der Meulen

*Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten*

15.30 Dutch translation and validation of the IBD-control: a questionnaire to assess patient-reported disease control in IBD patients (p. 66)

*M.E. de Jong[1], E. Taal[2], E. Slotman[3], R.L. West[4], T.E. Römkens[5], J.M. Jansen[6], F. Hoentjen[7], M.G. Russel[3]. [1]Dept. of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen. [2]Faculty of behavioural, Management and Social Sciences, University of Twente, Enschede.[3]Dept. of Gastroenterology and Hepatology, Medical Spectrum Twente, Enschede. [4]Dept. of Gastroenterology and Hepatology, Sint Franciscus &Vlietland, Rotterdam. [5]Dept. of Gastroenterology and Hepatology, Jeroen Bosch Hospital, 's-Hertogenbosch, [6]Dept. of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam. [7]Dept of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, The Netherlands.*

15.40 The direct healthcare costs of Crohn's disease increased over the last two decades in a Dutch population-based cohort study (p. 67)

*R.C.A. Lalisang[1], D. Wintjens[1], M. Romberg-Camps[2], A. van Bodegraven[2], L. Oostenbrug[2], J. Haans[1], A. Masclee[1], D. Jonkers[1], M. Pierik[1]. [1]Maastricht University Medical Center+, Dept. of Internal Medicine, Maastricht, [2]Zuyderland Medical Center, Dept. of Gastroenterology and Hepatology, Sittard-Geleen/Heerlen, The Netherlands.*

15.50 Home-based Vedolizumab infusions: A suitable alternative to routine hospital infusions (p. 68)

*J.A. Nieuwstraten[1], N.M.S. Peek-Kuijt[1], L.C. van Ginkel[2], P.W.J. Maljaars[1], A.E. van der Meulen-de Jong[1]. [1]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands. [2]Dept. of Care Registration, Leiden University Medical Center, Leiden, The Netherlands.*

16.00 A first pregnancy seems associated with a positive effect on the course of Inflammatory Bowel Disease: Data from a prospective pregnancy cohort (p. 69)

*J. van der Giessen, S.L. Kanis, G.M. Fuhler, C.J. van der Woude. Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands.*

16.10 Does mucosal inflammation drive recurrence of PSC in liver transplant recipients with Ulcerative Colitis? (p. 70)

*N. Dekkers[1], M. Westerouen van Meeteren[1], A. Inderson[1], W. Laleman[2], B. Desschans[2], B. van Hoek[1], A.E. van der Meulen-de Jong[1], J. Sabino[2], S. Farina Sarasqueta[3], S. Vermeire[2], J. Maljaars[1]. [1]Gastroenterology-Hepatology, LUMC, Leiden, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, University Hospital Leuven, Leuven, Belgium. [3]Pathology, LUMC, Leiden, The Netherlands.*

16.20 Persistent mesorectal inflammatory activity is associated with complications after proctectomy in Crohn's Disease (p. 71)

*J.H.M. van der Meer[1], E.J. de Groof[2], P.J. Tanis[2], J.R. de Bruyn[1], O. van Ruler[2], G.R.A.M. D'Haens[3], G.R. van den Brink[3], W.A. Bemelman[2], M.E. Wildenberg[1], C.J. Buskens[2]. [1]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Surgery, Academic Medical Center, Amsterdam, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands.*

16.30 Ultrasound for assessing disease activity in ulcerative colitis: development of a novel ultrasonographic disease activity index (p. 72)

*S.J.A. Bots[1], K. Nylund[2], M.L. Löwenberg[1], K.B. Gecse[1], O.H. Gilja[2], G.R. D'Haens[1]. [1]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [2]National Center for Ultrasound in Gastroenterology, Haukeland Hospital, Bergen, Norway.*

16.40 High prevalence of severe liver fibrosis in patients with longstanding IBD (p. 73)

*M.E.J. Steenhuis, S. van der Marel, T.W.A. van Deijnen, M.E. Tushuizen, A. van der Meulen-de Jong, P.W.J. Maljaars. Dept. of Gastroenterology, LUMC, Leiden, The Netherlands.*

16.50 Vedolizumab versus ustekinumab for crohn's disease: comparative effectiveness in a real-life observational cohort study (p. 74)

*V.B.C. Biemans[1], C.J. van der Woude[2], A.E. van der Meulen-de Jong[3], G. Dijkstra[4], N.K.H. de Boer[5], B. Oldenburg[6], C.Y. Ponsioen[7], A.C. de Vries[2], D.S.J. Wintjens[8], F. Hoentjen[1], M.J. Pierik[8]. [1]Dept. of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [5]Dept. of Gastroenterology and Hepatology, VU Medical Center, Amsterdam, The Netherlands. [6]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands. [7]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [8]Dept. of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, The Netherlands.*

17.00 Plenair programma in de Brabantzaal

18.30 Borrel in expo

20.00 Buffet in Beneluxzaal

**Symposium IBD – Terugblik ECCO** **Baroniezaal**

**Voorzitters:** A.E. van der Meulen en B. Oldenburg

10.00 Prediagnostiek IBD en tight control
*Dr. B. Oldenburg, MDL-arts, UMCU, Utrecht*

10.15 Epidemiologie en farmaco epidemiologie
*Dr. M.J. Pierik, MDL-arts, MUMC, Maastricht*

10.30 Resultaten Trials van (potentiële) nieuwe therapie
*Dr. P.W.J. Maljaars- MDL-arts, LUMC, Leiden*

10.45 Peri-operatief nieuws
*Dr. J.F. Lange, chirurg, UMCG, Groningen*

**Casuïstiek IBD** **Baroniezaal**

11.00 Casuïstiek ahv expertpanel
*Onder leiding van dr. K.H.N. de Boer, MDL-arts, VUmc, Amsterdam*

Oncologie en IBD medicatie
*L.H.C. Nissen, MDL-arts, Jeroen Bosch ziekenhuis, Den Bosch*

Timing chirurgie colitis ulcerosa
*Dr. K.C.M.J. Peeters, chirurg, LUMC, Leiden*

11.30 Aanvang algemene ledenvergadering NVGE in de Brabantzaal

**Symposium** **Baroniezaal**

**Voorzitter:** Prof. dr. M.J. Bruno

**Symposium: Clinical update of Chronic Mesenteric Ischemia**

13.00 Opening
*Prof. dr. M.J. Bruno, MDL-arts, Erasmus MC, Rotterdam*

13.05 "Many questions. Where are the answers?"
*Dr. O.J. Bakker, vaatchirurg, Franciscus Gasthuis & Vlietland, Rotterdam*

13.20 "Chronic arterial and venous mesenteric ischemia, a guide for gastroenterologists"
*Prof. dr. J.J. Kolkman, MDL-arts, Medisch Spectrum Twente, Enschede*

13.40 "How and when to intervene in chronic mesenteric ischemia"
*Prof. dr. R.H. Geelkerken, vaatchirurg, Medisch Spectrum Twente, Enschede*

14.00 "Endovascular access techniques in mesenteric ischemia"
*Dr. A. Moelker, interventie radioloog, Erasmus MC, Rotterdam*

14.20 "Acute mesenteric ischemia, an update for gastroenterologists and GI surgeons"
*Prof. S. Acosta, vaatchirurg, Malmö, Zweden*

14.50 "Clinical trials and future prospectives"
*Drs. L.J.D. van Dijk, arts-onderzoeker, Erasmus MC, Rotterdam*

15.00 Theepauze

**Abstractsessie – Sectie Experimentele Gastroenterologie I** **Baroniezaal**

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

*Voordrachten in het Engels, spreektijd 7 minuten, discussietijd 3 minuten*

15.30 'Up and coming therapies in IBD, targets and mechanisms'
*Dr. E.A.M. Festen, MDL-arts, UMCG, Groningen*

16.00 Commonly used medication is associated with the composition and function of the gut microbiota (p. 75)
*A. Vich Vila[1], V. Collij[1], S. Sanna[2], F. Imhann[1], Z. Mujagic[3], D. Jonkers[3], J. Fu[2], C. Wijmenga[2], S. Zhernakova[2], R.K. Weersma[1]. [1]Dept. of Gastroenterology and Hepatology, UMCG, Groningen, The Netherlands. [2]Dept. of Genetics, UMCG, Groningen, The Netherlands. [3]Division Gastroenterology-Hepatology, Maastricht University Medical Center+, Maastricht, The Netherlands.*

16.10 Macrophage IL10 signaling is required for the therapeutic effect of anti-TNFa therapy in IBD (p. 76)
*P.J. Koelink[1], F.M. Bloemendaal[1], L. Westera[1], A.B. van 't Wout[2], A.K. Gloudemans[2], B. Li[3], T.L. Geiger[3], G.R.A.M. D'Haens[4], M.E. Wildenberg[1], G.R. van den Brink[1]. [1]Academic Medical Center, Tytgat Institute, Amsterdam, The Netherlands. [2]Janssen Prevention Center of Janssen Vaccines & Prevention BV, Leiden, The Netherlands. [3]Dept. of Pathology, St. Jude Children's Research Hospital, Memphis, United States of America. [4]Amsterdam Medical Center, Dept. of Gastroenterology, Amsterdam, The Netherlands.*

16.20 Sympathetic activity regulates macrophages via the β2-adrenergic receptor (p. 77)
*R.A. Willemze[1], L.E. Nijhuis[1], O. Welting[1], J. Folgering[2], H. Darwinkel[2], J. Seppen[1], S.E.M. Heinsbroek[1], W.J. de Jonge[1]. [1]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, The Netherlands. [2]Brains On-line B.V., Groningen, The Netherlands.*

16.30 Development of reliable, valid and responsive scoring systems for endoscopy and histology in animal models for inflammatory bowel disease (p. 78)
*P.J. Koelink[1], M.E. Wildenberg[1], L.W. Stitt[2], B.G. Feagan[2], A.K. Gloudemans[3], A.B. van 't Wout[3], J.F. Brandse[4], A.A. te Velde[5], G.R.A.M. D'Haens[4], G.R. van den Brink[1]. [1]Academic Medical Center, Tytgat Institute, Amsterdam, The Netherlands. [2]Robarts Clinical Trials Inc, Amsterdam, The Netherlands. [3]Janssen Prevention Center of Janssen Vaccines & Prevention BV, Leiden, The Netherlands. [4]Dept. of Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands. [5]Academic Medical Center, Tytgat Institute, Amsterdam, The Netherlands.*

16.40 Integration of whole exome sequencing and RNA sequencing of intestinal biopsies in inflammatory bowel disease identifies inflammation dependent effects (p. 79)
*R. Barbieri[1], W.T.C. Uniken Venema[1], A. Vich Vila[1], L. Yang[2], F. Lude[2], F. van Dijk[2], N. de Klein[2], M. Swertz[2], S. Sanna[2], M.D. Voskuil[1], M. Rivas[3], R. Xavier[3], M. Daly[3], E.A.M. Festen[1], R.K. Weersma[1]. [1]Dept. of Gastroenterology, University Medical Center Groningen, Groningen, The Netherlands. [2]Dept. of Genetics, University Medical Center Groningen, Groningen, The Netherlands. [3]Broad Institute of MIT and Harvard, Cambridge, Cambridge, United States of America.*

16.50 The pathophysiology of human obstructive cholestasis is mimicked in cholestatic Gold Syrian hamsters (p. 80)

*R.F. van Golen[1], L.R. de Haan[2], P.B. Olthof[1], R.J. Coelen[1], R. Weijer[2], D.R. de Waart[3], A.B.P. van Kuilenburg[4], A. Pechlivanis[5], J. Verheij[6], M. Heger[7]. [1]Experimental Surgery, AMC, Amsterdam, The Netherlands. [2]Experimental Surgery, Amsterdam, The Netherlands. [3]Tytgat Institute, Amsterdam, The Netherlands. [4]Laboratory Genetic Metabolic Disorders, Academic Medical Center, Amsterdam, The Netherlands. [5]Division of Computational, Systems and Digestive Medicine, Imperial College, London, United Kingdom. [6]Pathology, Academic Medical Center, Amsterdam, The Netherlands. [7]Experimental Surgery, AMC, Amsterdam, The Netherlands.*

18.30 Borrel in expo

20.00 Buffet in Beneluxzaal

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**Abstractsessie – Nederlandse Vereniging voor Gastrointestinale Chirurgie I** **Parkzaal**

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**Voorzitters :** J.W. Haveman en A.T. Ruys

*Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten*

09.50 Risk factors for refractory anastomotic strictures after esophageal atresia repair: a multicenter study (p. 81)

*F.W.T. Vergouwe[1], J. Vlot[2], H. IJsselstijn[2], M.C.W. Spaander[1], J. van Rosmalen[3], M.W.N. Oomen[4], J.B.F. Hulscher[5], M. Dirix[6], M.J. Bruno[1], M. Schurink[7], R.M.H. Wijnen[2]. [1]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands. [2]Dept. of Pediatric Surgery, Erasmus University Medical Center-Sophia, Rotterdam, The Netherlands. [3]Dept. of Biostatistics, Erasmus University Medical Center, Rotterdam, The Netherlands. [4]Dept. of Pediatric Surgery, Academic Medical Center, Amsterdam, The Netherlands. [5]Dept. of Pediatric Surgery, University Medical Center Groningen-Beatrix, Groningen, The Netherlands. [6]Dept. of Pediatric Surgery, Maastricht University Medical Center, Maastricht, The Netherlands. [7]Dept. of Pediatric Surgery, Radboud University Medical Center, Nijmegen, The Netherlands.*

10.00 Minimally Invasive versus Open Distal Pancreatectomy (LEOPARD): Multi-center Patient-Blinded Randomized Controlled Trial (p. 82)

*T. de Rooij[1], J. van Hilst[1], H.C. van Santvoort[2], P.B. van den Boezem[3], F. Daams[4], R.M. van Dam[5], C.H. Dejong[5], M.G. Dijkgraaf[6], E.B. van Duyn[7], C.H. van Eijck[8], S. Festen[9], M.F. Gerhards[9], B. Groot Koerkamp[8], C.J. van Laarhoven[10], I.H. de Hingh[11], G. Kazemier[4], J.M. Klaase[7], R.H. de Kleine[12], M.D. Luyer[11], G.A. Patijn[13], P. Steenvoorde[7], M. Suker[8], M. Abu Hilal[14], O.R. Busch[15], M.G. Besselink[15], F.O.R.T.H Dutch Pancreatic Cancer Group[16]. [1]Dept. of Surgery, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Surgery, St. Antonius Hospital, Nieuwegein, The Netherlands. [3]Dept. of Surgery, Radboud Nijmegen University Medical Center, Nijmegen, The Netherlands. [4]Dept. of Surgery, VU Medical Center, Amsterdam, The Netherlands. [5]Dept. of Surgery, Maastricht University Medical Center, Maastricht, The Netherlands. [6]Clinical Research Unit, Academic Medical Center, Amsterdam, The Netherlands. [7]Dept. of Surgery, Medisch Spectrum Twente, Enschede, The Netherlands. [8]Dept. of Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands. [9]Dept. of Surgery, OLVG, Amsterdam, The Netherlands. [10]Dept. of Surgery, Radboud Nijmegen University Medical Center, Nijmegen, The Netherlands. [11]Dept. of Surgery, Catharina Hospital, Eindhoven, The Netherlands. [12]Dept. of Surgery, University Medical Center Groningen, Groningen, The Netherlands. [13]Dept. of Surgery, Isala Clinics, Zwolle, The Netherlands. [14]Dept. of Surgery, Southampton University Hospital NHS Foundation Trust, Southampton, United Kingdom. [15]Dept. of Surgery, Academic Medical Center, Amsterdam, The Netherlands. [16]Dutch Pancreatic Cancer Group, Amsterdam, The Netherlands.*

10.10 The introduction of minimally invasive surgery for distal and total gastrectomy: a propensity score matched analysis (p. 83)

*E.C. Gertsen, H.J.F. Brenkman, M.F.J. Seesing, L. Goense, J.P. Ruurda, R. van Hillegersberg. Dept. of Surgery, Universitair Medisch Centrum Utrecht, Utrecht, The Netherlands.*

10.20 Portal vein embolization does not result in microvascular flow differences between the embolized and non-embolized liver lobes in humans (p. 84)

*Z. Uz[1], C. Ince[2], B. Ergin[2], D.P. Veelo[3], T. van Gulik[4]. [1]Dept. of Surgery, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Translational Physiology, Academic Medical Center, Amsterdam, The Netherlands. [3]Dept. of Anesthesiology, Academic Medical Center, Amsterdam, The Netherlands. [4]Dept. of Surgery, Academic Medical Center, Amsterdam, The Netherlands.*

10.30 Outcomes of Salvage Surgery in patients with recurrent esophageal cancer after definite chemoradiotherapy (p. 85)

*A.E. Slaman[1], W.J. Eshuis[2], W.A. Draaisma[2], S.S. Gisbertz[2], J.J.G.H.M Bergman[3], H.W.M. Van Laarhoven[4], M.C.C.M. Hulshof[5], S.L. Meijer[6], M.I. Van Berge Henegouwen[2]. [1]Dept. of Surgery, Academisch Medisch Centrum, Amsterdam, The Netherlands. [2]Dept. of Surgery, Academic Medical Center, Amsterdam, The Netherlands. [3]Dept. of Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands. [4]Dept. of Oncology, Academic Medical Center, Amsterdam, The Netherlands. [5]Dept. of Radiotherapy, Academic Medical Center, Amsterdam, The Netherlands. [6]Dept. of Pathology, Academic Medical Center, Amsterdam, The Netherlands.*

10.40 Can a surgeon perform a macroscopic inspection of a gallbladder? (p. 86)

*B.J.G.A. Corten[1], S. Alexander[2], P. Zwam[3], R.M.H. Roumen[2], G.D. Slooter[2]. [1]Dept. of Surgery, Máxima Medical Center, Veldhoven, The Netherlands. [2]Dept. of Surgery, Máxima Medical Center, Veldhoven, The Netherlands. [3]Foundation PAMM laboratories for pathology and medical microbiology, Eindhoven, The Netherlands.*

10.50 Epidural analgesia after minimally invasive esophagectomy: efficacy and complication profile (p. 87)

*B.F. Kingma[1], E. Visser[1], M. Marsman[2], J.P. Ruurda[1], R. Van Hillegersberg[1]. [1]Dept. of Surgery, University Medical Center Utrecht, Utrecht, The Netherlands. [2]Dept. of Anesthesiology, University Medical Center Utrecht, Utrecht, The Netherlands.*

11.00 Long-term quality of life in patients after McKeown versus Ivor Lewis esophagectomy (p. 88)

*E. Jezerskyte[1], S.S. Gisbertz[1], M.I. van Berge Henegouwen[1], L.M. Saadeh[2], M. Scarpa[2], M. Sprangers[3]. [1]Surgery, AMC, Amsterdam, The Netherlands. [2]Surgery, Veneto Oncological Institute, Padova, Italy. [3]Medische psychologie, AMC, Amsterdam, The Netherlands.*

11.10 Eye-tracking as a tool to differentiate physicians with different grades of experience in performing laparoscopic pancreaticoduodenectomy (p. 89)

*D.J. Brinkman[1], W.J. van der Vliet[2], M.G. Besselink[3], K. Bosscha[4], O.R. Busch[3], R.M. van Dam[2], S. Festen[5], J. van Hilst[3], I.H.J.T. de Hingh[6], T.M. Karsten[5], D.J. Lips[7], T. de Rooij[3], Y. Song[8], M.D.P. Luyer[1]. [1]Dept. of Surgery, Catharina Hospital, Eindhoven, The Netherlands. [2]Dept. of Surgery, Maastricht University Medical Center, Maastricht, The Netherlands. [3]Dept. of Surgery, Academic Medical Center, Amsterdam, The Netherlands. [4]Dept. of Surgery, Dept. of Surgery, Jeroen Bosch Hospital, 's hertogenbosch, The Netherlands. [5]Dept. of Surgery, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands. [6]Dept. of Surgery, Catharina Ziekenhuis, Eindhoven, The Netherlands. [7]Dept. of Surgery, Jeroen Bosch Hospital, 's hertogenbosch, The Netherlands. [8]Dept. of Technical Design and Engineering, Technical University Delft, Delft, The Netherlands*

11.20 Comparing the costs before and after the learning curve of laparoscopic gastrectomy for gastric cancer in a Western referral center (p. 90)
*T.T.T. Tweed, J.J.W. Tegels, M.N. Sosef, E.H.J. Belgers, K.W.E. Hulsuwé, J.H.M.B. Stoot. Dept. of Surgery, Zuyderland Medical Center, Geleen, The Netherlands.*

11.30 Aanvang algemene ledenvergadering NVGE

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**Abstractsessie – Nederlandse Vereniging voor Gastrointestinale Chirurgie II Parkzaal**

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**Voorzitters :** A.G. den Hartog en J. Melenhorst

*Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten*

13.00 The effect of preoperative optimization of nutritional status in patients with significant bowel obstruction (p. 91)
*C.S. van Kessel[1], A.B. Smits[2], D. Smeeing[2]. [1]Dept. of Surgery, St Antonius Hospital Nieuwegein, Nieuwegein, The Netherlands. [2]St Antonius Hospital Nieuwegein, Nieuwegein, The Netherlands.*

13.10 Hartmann's procedure or sigmoidectomy with primary anastomosis for perforated diverticulitis with purulent or fecal peritonitis: results of the international, multiCenter, parallel-group, randomised, open-label LADIES trial (p. 92)
*D.P.V. Lambrichts[1], S. Vennix[2], G.D. Musters[2], I.M. Mulder[1], H.A. Swank[2], J. Vermeulen[1], S. van Dieren[3], W.A. Bemelman[2], J.F. Lange[1]. [1]Dept. of Surgery, Erasmus Medical Center, Rotterdam, The Netherlands. [2]Dept. of Surgery, Academic Medical Center, Amsterdam, The Netherlands. [3]Clinical Research Unit, Academic Medical Center, Amsterdam, The Netherlands.*

13.20 Achievements in colorectal cancer care during 8 years of auditing in the Netherlands (p. 93)
*M.P.M. de Neree tot Babberich[1], R. Detering[2], J.W.T. Dekker[3], M. Elferink[4], R.A.E.M. Tollenaar[5], M.W.J.M. Wouters[6], P.J. Tanis[7]. [1]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Surgery, Academic Medical Center, Amsterdam, The Netherlands. [3]Dept. of Surgery, Reinier de Graaf Hospital, Delft, The Netherlands. [4]Dept. of Research, Netherlands Comprehensive Cancer Organization (IKNL), Utrecht, The Netherlands. [5]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands. [6]Dept. of surgical oncology, Netherlands Cancer Institute-Antoni van Leeuwen, Amsterdam, The Netherlands. [7]Dept. of surgery, Academic Medical Center, Amsterdam, The Netherlands.*

13.30 Population based comparative study of postoperative outcomes of screen-detected colorectal cancer (p. 94)
*M.P.M. de Neree tot Babberich[1], N.C.A. Vermeer[2], M.W.J.M. Wouters[3], W.M.U. Van Grevenstein[4], K.C.M.J. Peeters[2], E. Dekker[1], P.J. Tanis[5]. [1]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands. [3]Dept. of surgical oncology, Netherlands Cancer Institute-Antoni van Leeuwenhoek, Amsterdam, The Netherlands. [4]Dept. of Surgery, Utrecht University Medical Center, Utrecht, The Netherlands. [5]Dept. of surgery, Academic Medical Center, Amsterdam, The Netherlands.*

13.40 Postoperative Risks after Surgical Treatment for Submucosal Invasive Colorectal Cancer: a National Cohort Study (p. 95)

*N.C.A. Vermeer[1], Y. Backes[2], E. Bastiaannet[1], H.S. Snijders[3], G.J. Liefers[1], L.M. Moons[2], C.J.H. Van de Velde[1], K.C.M.J. Peeters[1]. [1]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands. [3]Dept. of Surgery, Groene Hart ziekenhuis, Gouda, The Netherlands.*

13.50 Therapy refractory ulcerative colitis patients may benefit from appendectomy; long-term clinical results from a multicenter prospective cohort series (p. 96)

*M.E. Stellingwerf[1], S. Sahami[1], D.C. Winter[2], H.E. Mulcahy[2], G.A. Doherty[2], G. Cullen[2], S. Martin[2], G.R. D'Haens[3], W.A. Bemelman[1], C.J. Buskens[1]. [1]Dept. of Surgery, AMC, Amsterdam, The Netherlands. [2]Center for Colorectal Disease, St Vincent's University Hospital, Dublin, Ireland. [3]Dept. of Gastroenterology and Hepatology, AMC, Amsterdam, The Netherlands.*

14.00 Interobserver variability in the classification of appendicitis during laparoscopy (p. 97)

*E.M.L. de Wijkerslooth[1], K.A.L. Mauff[2], I. Dawson[3], C.C. Rossem[4], B.R. Toorenvliet[5], B.P.L. Wijnhoven[1]. [1]Dept. of Surgery, Erasmus Medical Center, Rotterdam, The Netherlands. [2]Dept. of Biostatistics, Erasmus Medical Center, Rotterdam, The Netherlands. [3]Dept. of Surgery, IJsselland Ziekenhuis, Capelle a/d ijssel, The Netherlands. [4]Dept. of Surgery, Maasstad Ziekenhuis, Rotterdam, The Netherlands. [5]Dept. of Surgery, Ikazia Ziekenhuis, Rotterdam, The Netherlands.*

14.10 Influence of conversion and anastomotic leakage on survival in rectal cancer surgery; a large retrospective cross-sectional study (p. 98)

*E.J.B. Furnee[1], T.S. Aukema[2], S.J. Oosterling[3], W.A.A. Borstlap[4], W.A. Bemelman[4], P.J. Tanis[4]. [1]Dept. of Surgery, University Medical Center Groningen, Groningen, The Netherlands. [2]Dept. of Surgery, Meander Medical Center, Amersfoort, The Netherlands. [3]Dept. of Surgery, Spaarne Gasthuis, Haarlem, The Netherlands. [4]Dept. of Surgery, Academic Medical Center, Amsterdam, The Netherlands.*

14.20 Patient blood management in colorectal cancer patients: a survey among Dutch gastroenterologists, surgeons and anesthesiologists (p. 99)

*M.J. Wilson[1], A. Koopman-van Gemert[2], J.J. Harlaar[3], J. Jeekel[4], J.J. Zwaginga[5], M. Schipperus[6]. [1]Dept. of Surgery, Erasmus Medical Center, Rotterdam, The Netherlands. [2]Dept. of Anesthesiologie, Albert Schweitzer Hospital, Dordrecht, The Netherlands. [3]Dept. of Surgery, VU Medical Center, Amsterdam, The Netherlands. [4]Dept. of Neuroscience, Erasmus Medical Center, Rotterdam, The Netherlands. [5]Dept. of Immunohematology and Blood Transfusion, LUMC, Leiden, The Netherlands. [6]Dept. of Hematology, Haga Teaching Hospital, Den haag, The Netherlands.*

14.30 Endoscopic features of response to chemoradiation for rectal cancer (p. 100)

*M.E. van der Sande[1], M. Maas[2], J. Melenhorst[3], S.O. Breukink[4], R.G.H. Beets-tan[2], M.E. van Leerdam[5], G.L. Beets[1]. [1]Dept. of Surgery, Antoni van Leeuwenhoek, Amsterdam, The Netherlands. [2]Dept. of Radiology, Antoni van Leeuwenhoek, Amsterdam, The Netherlands. [3]Dept. of Surgery, Maastricht Univeristy Medical Center, Maastricht, The Netherlands. [4]Dept. of Surgery, Maastricht University Medical Center, Maastricht, The Netherlands. [5]Dep of Gastroenterology, Antoni van Leeuwenhoek, Amsterdam, The Netherlands.*

14.40 The effect of intestinal manipulation on healing of the intestinal anastomosis (p. 101)

*E.G. Peters[1], D.J. Brinkman[1], O. Welting[2], H.P. van Hamersveld[2], W.J. de Jonge[3], M.D.P. Luyer[4]. [1]Dept. of Surgery, Catharina Ziekenhuis, Eindhoven, The Netherlands. [2]Tytgat Institute for liver and intestinal research, AMC, Amsterdam, The Netherlands. [3]Tytgat Institute for liver and intestinal research, AMC, Amsterdam, The Netherlands. [4]Dept. of surgery, Catharina Ziekenhuis, Eindhoven, The Netherlands.*

**Abstractsessie – Nederlandse Vereniging voor Gastroenterologie** **Parkzaal**

**Voorzitters :** A.J. Bredenoord en J.J. Keller

*Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten*

15.30 Durability of radiofrequency ablation for treatment of esophageal squamous cell neoplasia: 5 year follow-up of a prospective study in China (p. 102)

*S.N. van Munster[1], X. Yu[2], Y. Zhang[2], L. Xue[3], D.E. Fleischer[4], N. Lv[3], S.M. Dawsey[5], J.J.G.H.M Bergman[6], G.Q. Wang[2]. [1]Dept. of Gastroenterology and Hepatology,Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of endoscopy, CICAMS hospital, Beijing, China. [3]Dept. of pathology, CICAMS hospital, Beijing, China. [4]Dept. of Gastroenterology & Hepatology, Mayo Clinic, Scottsdale, United States of America. [5]Dept. of Cancer Epidemiology & Genetics, National Cancer Institute, Bethesda, United States of America. [6]Dept. of Gastroenterology & Hepatology, Academic Medical Center, Amsterdam, The Netherlands.*

15.40 Clinical and endoscopic predictors of neoplastic progression in Barrett's esophagus surveillance: a multi-center community based prospective cohort study (p. 103)

*E. Klaver[1], A. Bureo Gonzalez[1], R. Mallant[2], L.C. Baak[3], C. Böhmer[4], A.H. van Oijen[5], A.H. Naber[6], P. Scholten[7], L.C. Duits[1], J.J. Bergman[1], R.E. Pouw[1]. [1]Dept. of Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Gastroenterology, Flevohospital, Almere, The Netherlands. [3]Dept. of Gastroenterology, OLVG Oost, Amsterdam, The Netherlands. [4]Dept. of Gastroenterology, Spaarne Hospital, Hoofddorp, The Netherlands. [5]Dept. of Gastroenterology, Northwest Clinics, Alkmaar, The Netherlands. [6]Dept. of Gastroenterology, Tergooi Hospital, Hilversum, The Netherlands. [7]Dept. of Gastroenterology, OLVG West, Amsterdam, The Netherlands.*

15.50 Development of an Updated Score Chart to Predict the Risk of Chronic Mesenteric Ischemia based on a Multicenter Cohort of 666 Patients (p. 104)

*L.J.D. van Dijk[1], D. van Noord[2], R.H. Geelkerken[3], J. Harki[1], S.A. Berendsen[1], A.C. de Vries[1], A. Moelker[4], Y. Vergouwe[5], H.J.M. Verhagen[6], J.J. Kolkman[7], M.J. Bruno[1]. [1]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Franciscus Gasthuis & Vlietland, Rotterdam, The Netherlands. [3]Dept. of Surgery, Medical Spectrum Twente, Enschede, The Netherlands. [4]Dept. of Radiology, Erasmus University Medical Center, Rotterdam, The Netherlands. [5]Dept. of Public Health, Erasmus University Medical Center, Rotterdam, The Netherlands. [6]Dept. of Vascular Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands. [7]Dept. of Gastroenterology and Hepatology, Medical Spectrum Twente, Enschede, The Netherlands.*

16.00 Incidence of colorectal cancer in young adults in Europe (p. 105)

*F.E.R. Vuik[1], M. Bardou[2], E.J. Kuipers[1], M.C.W. Spaander[1]. [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Public Health, Erasmus MC, Rotterdam, The Netherlands.*

16.10 Aberrant intra-epithelial lymphocytes in refractory celiac disease type II cause villous atrophy by granzyme-B mediated apoptosis of enterocytes via CD103-E-cadherin-interaction (p. 106)

*J.M.W. van de Water[1], D.A.R. Castelijn[1], L.R. de Baaij[1], F. Koning[2], G.J. Bouma[1], C.J.L.M. Meijer[3], H.J. Bontkes[4], C.J.J. Mulder[1], S.A.G.M. Cillessen[3]. [1]Dept. of Gastroenterology and Hepatology, VU Medical Center, Amsterdam, The Netherlands. [2]Dept. of Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, The Netherlands. [3]Dept. of Pathology, VU Medical Center, Amsterdam, The Netherlands. [4]Dept. of Medical Immunology, VU Medical Center, Amsterdam, The Netherlands.*

16.20 Mast cell activation syndrome (mcas) in patients with rapid onset of food induced symptoms of dyspepsia, ibs, diarrhea, nausea or vomiting reacts favorably on histamine 1 or 2 blockers or cromoglycate. An observational study (p. 107)

*M.H. Otten[1], H. Akol[1], M. Oudkerk Pool[1], G. Tan[2], T.C.M.A. Schreuder[1]. [1]Dept. of Gastroenterology and Hepatology, Medisch Centrum de Veluwe, Apeldoorn, The Netherlands. [2]Dept. of Gastroenterolgy and Hepatology, Mediscch Centrum de Veluwe, Apeldoorn, The Netherlands.*

16.30 Development of a core outcome set for infant gastroesophageal reflux disease (p. 108)

*R. Rexwinkel[1], M.M.J. Singendonk[2], C. DiLorenzo[3], L. Ferris[4], A. Staiano[5], N.F. Steutel[2], N. Thapar[6], Y. VandenPlas[7], M.P. van Wijk[2], M.A. Benninga[2], M.M. Tabbers[2]. [1]Dept. of Pediatric Gastroenterology and Nutrition, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Pediatric Gastroenterology and Nutrition, Academic Medical Center, Amsterdam, The Netherlands. [3]Dept. of Pediatrics, Ohio State University College, Columbus, ohio, United States of America. [4]Gastroenterology Unit, Women's and Children's Health Network, School of Medicine, North adelaide, Australia. [5]Dept. of Translational Medical Science, University of Naples Federico II, Naples, Italy. [6]Great Ormond Street Hospital for Children, London, United Kingdom. [7]Dept. of Pediatrics, UZ Brussel, Vrije Universiteit Brussel, Brussel, Belgium.*

16.40 Detection of Gastrointestinal Ischemia by Means of Endoscopic Visible Light Spectroscopy after Luminal Feeding (p. 109)

*L.J.D. van Dijk[1], J. Harki[1], D. van Noord[2], A.C. de Vries[1], A. Moelker[3], H.J.M. Verhagen[4], E.J. Kuipers[1], M.J. Bruno[1]. [1]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Franciscus Gasthuis & Vlietland, Rotterdam, The Netherlands. [3]Dept. of Radiology, Erasmus University Medical Center, Rotterdam, The Netherlands. [4]Dept. of Vascular Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands.*

16.50 Differentiation between paediatric irritable bowel syndrome and inflammatory bowel disease based on faecal scent: proof of principle study (p. 110)

*S. Bosch[1], N. van Gaal[1], R.P. Zuurbier[2], J.A. Covington[3], A.N. Wicaksono[3], M.H. Biezeveld[4], M.A. Benninga[5], C.J.J. Mulder[1], N.K.H. de Boer[1], T.G.J. de Meij[6]. [1]Dept. of Gastroenterology and Hepatology, VU Medical Center, Amsterdam, The Netherlands. [2]Dept. of paediatrics, Spaarne Gasthuis, Hoofddorp, The Netherlands. [3]School of engineering, University of Warwick, Coventry, United Kingdom. [4]Dept. of paediatrics, OLVG, Amsterdam, The Netherlands. [5]Dept. of paediatric gastroenterology, Emma Children's Hospital, AMC, Amsterdam, The Netherlands. [6]Dept. of paediatric gastroenterology, VU Medical Center, Amsterdam, The Netherlands.*

18.30 Borrel in expo

20.00 Buffet in Beneluxzaal

**Meet the expert** **Zaal 80**

09.30 – 10.00 uur – sessie I
13.00 – 14.00 uur – sessie II

## Thema: Leverfalen

*De sessies – waarvoor tevoren moet worden ingeschreven - worden verzorgd door Prof. dr. H.J. Metselaar en Dr. E.T.T.L. Tjwa*

**Meet the expert** **Zaal 81**

09.30 – 10.00 uur – sessie I
13.00 – 14.00 uur – sessie II

## Thema: Spoed endoscopieën

*De sessies - waarvoor tevoren moet worden ingeschreven - worden verzorgd door Dr. H.M. van Dullemen en Prof. dr. F. Vleggaar*

**Abstractsessie – Sectie Gastrointestinale Endoscopie I** **Zaal 80**

**Voorzitters :** B. Bastiaansen en J-W. Poley

*Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten*

15.30 Improved barrett's neoplasia detection using computer assisted multi-frame analysis of volumetric laser endomicroscopy images (p. 111)

*M.R. Struyvenberg[1], A. Rikos[2], F. van der Sommen[2], P.H. de With[2], S. Zinger[2], W.L. Curvers[3], J.J. Bergman[1]. [1]Dept. of Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Electrical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands. [3]Dept. of Gastroenterology, Catharina Hospital, Eindhoven, The Netherlands.*

15.40 The argos project: first results of the development of a computer aided detection system for barrett`s neoplasia (p. 112)

*A.J. de Groof[1], J. van der Putten[2], F. van der Sommen[2], S. Zinger[2], W.L. Curvers[3], R. Bisschops[4], O. Pech[5], A. Meining[6], H. Neuhaus[7], E.J. Schoon[3], P.H.N. de With[2], J.J.G.H.M Bergman[1]. [1]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Electrical Engineering, VCA group, Eindhoven University of Technology, Eindhoven, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven, Germany. [4]Dept. of Gastroenterology and Hepatology, University Hospital Leuven, Leuven, Belgium. [5]Gastroenterology and interventional Endoscopy, Krankenhaus Barmherzige Brüder, Regensburg, Germany. [6]Center of Internal Medicine, Ulm University, Ulm, Germany. [7]Internal Medicine, Evangelisches Krankenhaus, Düsseldorf, Germany.*

15.50 Safety, tolerability and dosimetry of a novel Swipe Cryoballoon device (90°-SCBA) for ablation of dysplastic Barrett's esophagus (p. 113)

*S.N. van Munster[1], A. Overwater[2], G.M. Raicu[3], C.A. Seldenrijk[3], W.B. Nagengast[4], E.J. Schoon[5], J.J.G.H.M Bergman[1], B.L.A.M. Weusten[2]. [1]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, St. Antonius Hospital, Nieuwegein, The Netherlands. [3]Dept. of Pathology, St. Antonius Hospital, Nieuwegein, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [5]Dept. of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven, The Netherlands.*

16.00 Self-sizing radiofrequency ablation balloon for eradication of Barrett's esophagus: results of an international multicenter randomized trial comparing three different treatment regimens (p. 114)

*K. Belghazi[1], R.E. Pouw[1], S.N. van Munster[1], A.D. Koch[2], B.L.A.M. Weusten[3], E.J. Schoon[4], W.L. Curvers[4], A.W. Gotink[3], R.J. Haidry[5], O. Pech[6], J.J.G.H.M Bergman[1], R. Bisschops[7]. [1]Dept. of Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Gastroenterology, Erasmus Medical Center, Rotterdam, The Netherlands. [3]Dept. of Gastroenterology, st. Antonius Hospital, Nieuwegein, The Netherlands. [4]Dept. of Gastroenterology, Catharina Hospital, Eindhoven, The Netherlands. [5]Dept. of Gastroenterology, University College Hospital NHS Foundation Trust, London, United Kingdom. [6]Dept. of Gastroenterology and Interventional Endoscopy, St. John of God Hospital, Regensbergg, Germany. [7]Dept. of Gastroenterology, UZ gasthuisberg, Leuven, Belgium.*

16.10 Long-term follow-up results of a randomized trial comparing radiofrequency ablation versus endoscopic surveillance in Barrett's esophagus patients with low-grade dysplasia (p. 115)

*E. Klaver[1], K.N. Phoa[1], F.G. van Vilsteren[1], B.L. Weusten[2], R. Bisschops[3], E.J. Schoon[4], O. Pech[5], H. Manner[5], K. Ragunath[6], J. Ortiz[6], G. Fullarton[7], M. Di Pietro[8], W. Januszewicz[8], N. Ravi[9], D. O'Toole[9], J.J. Bergman[1], R.E. Pouw[1]. [1]Dept. of Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Gastroenterology, St. Antonius Hospital, Nieuwegein, The Netherlands. [3]Dept. of Gastroenterology, University Hospital Leuven, Leuven, Belgium. [4]Dept. of Gastroenterology, Catharina Hospital, Eindhoven, The Netherlands. [5]Dept. of Gastroenterology, Helios dr. Horst Schmidt Clinics, Wiesbaden, Germany. [6]Dept. of Gastroenterology, Queens Medical Center, Nottingham, United Kingdom. [7]Dept. of Surgical Gastroenterology, Glasgow Royal Infirmary, Glasgow, United Kingdom. [8]Medical Research Council, Cancer Unit, Cambridge, United Kingdom. [9]Dept. of Clinical Medicine and Gastroenterology, St. James's Hospital, Dublin, Ireland.*

16.20 Cryoballoon ablation of dysplastic Barrett's esophagus causes shorter duration and less severe post-procedural pain as compared to radiofrequency ablation (p. 116)

*S.N. van Munster[1], A. Overwater[2], R. Haidry[3], R. Bisschops[4], J.J.G.H.M Bergman[5], B.L.A.M. Weusten[2]. [1]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Gastroenterology & Hepatology, st. Antonius hospital, Nieuwegein, The Netherlands. [3]Dept. of Gastroenterology, University College London Hospital, London, United Kingdom. [4]Dept. Of Gastroenterology, University Hospital Leuven, Leuven, Belgium. [5]Dept. of Gastroenterology & Hepatology, Academic Medical Center, Amsterdam, The Netherlands.*

16.30 EUS-guided keyhole biopsies for diagnosis of sub-endothelial tumors: technique description, histological diagnostic yield and safety (p. 117)

*M.J.A. Westerouen van Meeteren, L.E. Perk. Dept. of Gastroenterology, Haaglanden Medisch Centrum, Den Haag, The Netherlands.*

16.40 Endosonographic measurements of tumor thickness and surface area to evaluate tumor response after neoadjuvant chemoradiotherapy in patients with esophageal cancer; a multicenter prospective cohort study (p.118)

*R.D. van der Bogt[1], B.J. Noordman[2], K.K. Krishnadath[3], C.A.M. Roumans[1], E.J. Schoon[4], L.E. Oostenbrug[5], P.D. Siersema[6], F.P. Vleggaar[7], J.J.B. van Lanschot[2], M.C.W. Spaander[1]. [1]Dept. of Gastroenterology, Erasmus Medical Center, Rotterdam, The Netherlands. [2]Dept. of Surgery, Erasmus Medical Center, Rotterdam, The Netherlands. [3]Dept. of Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands. [4]Dept. of Gastroenterology, Catharina Hospital, Eindhoven, The Netherlands. [5]Dept. of Gastroenterology, Zuyderland Medical Center, Heerlen, The Netherlands. [6]Dept. of Gastroenterology, Radboud University Medical Center, Nijmegen, The Netherlands. [7]Dept. of Gastroenterology, University Medical Center Utrecht, Utrecht, The Netherlands.*

16.50 Long-term outcome of dilatation and stenting of anastomotic and non-anastomotic biliary strictures after liver transplantation (p.119)

*B. van Hoek[1], A.C. den Dulk[1], A. Inderson[1], A.R. van Erkel[2], J. Dubbeld[3], D. van der Helm[1], M.J. Coenraad[1], H.W. Verspaget[1]. [1]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands. [2]Dept. of Radiology, Leiden University Medical Center, Leiden, The Netherlands. [3]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands.*

18.30 Borrel in expo

20.00 Diner in de Beneluxzaal

**Symposium – Battle in endoscopy** **Auditorium**

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

**Symposium "Battles in Endoscopy"**

09.30 Galwegdrainage: Radiologisch middels PTC versus Endoscopisch middels EUS
*Dr. E.P.A. Vonken, afdeling Radiologie in UMCU vs prof. dr. F.P. Vleggaar, afdeling MDL, UMCU*

10.00 Behandeling van T1 coloncarcinomen: Chirurgisch versus Endoscopisch
*Dr. J.B. Tuynman, afdeling Heelkunde VUmc vs dr. B.A.J. Bastiaansen, afdeling MDL, AMC*

10.30 Behandeling Chronische pancreatitis: Chirurgisch versus Endoscopisch
*Prof. dr. M.G.H. Besselink, afdeling Heelkunde AMC, Amsterdam vs prof. dr. M.J. Bruno, afdeling MDL, Erasmus MC Rotterdam*

11.00 Koffiepauze in de expositiehal

**Symposium – Sectie Kinder MDL en NVGE** **Auditorium**

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

**Symposium: Jong gekregen, oud gehouden**

11.30 'Eens Crohn, altijd Crohn?'
*Prof. dr. J.C. Escher, kinderarts-MDL, Erasmus MC-Sophia, Rotterdam*
*Prof. dr. C.J. van der Woude, MDL-arts, Erasmus MC, Rotterdam*

12.00 'Galgangatresie: een leven lang zorg(en)'
*Prof. dr. R.H.J. Houwen, kinderarts-MDL, UMCU/WKZ, Utrecht*
*Dr. K.J. van Erpecum, MDL-arts, UMCU, Utrecht*

12.30 'Oud worden met coeliakie'
*Drs. M.M.S. Wessels, kinderarts-MDL, Rijnstate, Arnhem*
*Prof. dr. G. Bouma, MDL-arts in VUmc, Amsterdam.*

13.00 Lunchpauze in expo

**Symposium – Immunotherapy in GI malignancies** **Auditorium**

**Voorzitters:** J. van Dieren en E.J Gielisse

14.00 Opkomst immuuntherapie algemene oncologie praktijk. Wees voorbereid MDL-artsen!
*Prof. dr. H.J.M. Groen, longarts, UMCG, Groningen*

14.25 De rol van immuuntherapie bij de behandeling van gastrointestinale tumoren
*Drs. M. Chalabi, oncoloog, AVL, Amsterdam*

14.50 Immuuntherapie geïnduceerde colitis
*Dr. K.F.J. de Boer, MDL-arts, VUmc, Amsterdam*

15.15 Immuuntherapie geïnduceerde hepatitis en heeft IT ook een rol bij de behandeling van HCC?
*Dr. D. Sprengers, hepatoloog, Erasmus MC, Rotterdam*

15.40 Panel discussie

16.00 Einde sessie

**Abstractsessie – Sectie Experimentele Gastroenterologie II** **Baroniezaal**

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

*Voordrachten in het Engels, spreektijd 7 minuten, discussietijd 3 minuten*

09.30 'Stromal-Epithelial interactions in CRC'
*Prof. J.C.H. Hardwick, MDL-arts, LUMC, Leiden*

09.50 AP1 components ATF2 and ATF7 are dispensable for the intestinal epithelium during homeostasis (p. 120)
*B.J. Meijer[1], B. Baan[1], J.H.M. van der Meer[1], J. Heijmans[1], V. Muncan[1], G.R. van der Brink[2]. [1]Tytgat institute for Liver and Intestinal Research, Amsterdam, The Netherlands. [2]GlaxoSmithKline, Medicines Research Center, Stevenage, United Kingdom.*

10.00 An unbiased proteomic screen identifies CtBP2 as an ER stress dependent regulator of intestinal epithelial stemness (p. 121)
*B.J. Meijer[1], B.F. Westendorp[1], J.H.M. van der Meer[1], V. Muncan[1], J. Heijmans[1], G.R. van der Brink[2]. [1]Tytgat institute for Liver and Intestinal Research, Amsterdam, The Netherlands. [2]GlaxoSmithKline, Medicines Research Center, Stevenage, United Kingdom.*

10.10 Aberrant lipid metabolism in patients with DGAT1 deficiency (p. 122)
*D.Y. van Haaften-Visser[1], J.M. van Rijn[1], R.C. Ardy[2], A. Kansu[3], B. Härter[4], M. van Hoesel[1], A.H.M. van Vugt[1], M. Ng[2], Z. Kuloglu[3], M. Keçeli Basaran[5], F. Ozcay[6], H. van der Doef[7], P.J. Coffer[8], T. Müller[9], G. van Haaften[10], R.H.J. Houwen[11], A.R. Janecke[9], S. Middendorp[1], K. Boztug[2]. [1]Dept. of Pediatric Gastroenterology, Wilhelmina Children's Hospital, Utrecht, The Netherlands. [2]Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases, Vienna, Austria. [3]Dept. of Pediatric Gastroenterology, Ankara University, Ankara, Turkey. [4]Dept. of Visceral, Transplant and Thoracic Surgery, University of Innsbruck, Innsbruck, Austria. [5]Pediatric Gastroenterology Dept., Akdeniz University Medicine Hospital, Antalya, Turkey. [6]Dept. of Pediatric Gastroenterology, Baskent University, Ankara, Turkey. [7]Dept. of Pediatric Gastroenterology, University Medical Center Groningen, Groningen, The Netherlands. [8]Regenerative Medicine Center, University Medical Center Utrecht, Utrecht, The Netherlands. [9]Dept. of Pediatrics I, Medical University of Innsbruck, Innsbruck, Austria. [10]Dept. of Medical Genetics, University Medical Center Utrecht, Utrecht, The Netherlands. [11]Dept. of Pediatric Gastroenterology, Wilhelmina Children's Hospital, Utrecht, The Netherlands.*

10.20 Intestinal fetal organoids as a model of intrinsic postnatal epithelial maturation (p. 123)
*M. Navis[1], T. Martins Garcia[1], I.B. Renes[2], G.R. van den Brink[1], J.L.M. Vermeulen[1], S. Meisner[1], M.E. Wildenberg[1], R.M. van Elburg[3], V. Muncan[1]. [1]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, The Netherlands. [2]Nutricia Research, Utrecht, The Netherlands. [3]Dept. of Pediatrics, Academic Medical Center, Amsterdam, The Netherlands.*

10.30 UPR transcription factors ATF6 and XBP1s reduce colorectal cancer cell proliferation and stemness through interaction with PERK (p. 124)
*C.N. Spaan, W.L. Smit, J.F. van Lidth de Jeude, B. Meijer, V. Muncan, G.R. van den Brink, J. Heijmans. Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, The Netherlands.*

10.40 Colonic CD90+ crypt-based fibroblasts secrete semaphorins to support epithelial growth (p. 125)

*B.F. Westendorp[1], O.N. Olga[1], J. Koster[2], S. Meisner[1], V. Muncan[1], M.E. Wildenberg[1], G.R. Brink, van den[3]. [1]Tytgat Institute for Liver and Intestinal Research, Amsterdam, The Netherlands. [2]Dept. of Oncogenomics and Emma Children's Hospital, Amsterdam, The Netherlands. [3]Tytgat Institute for Liver and Intestinal Research and Dept. of Gastroenterology, Amsterdam, The Netherlands.*

10.50 Preoperative biliary drainage reverses cholestasis-associated inflammatory and fibrotic gene signatures in patients with perihilar cholangiocarcinoma (p. 126)

*R.F. van Golen[1], M.J. Reiniers[1], L.R. de Haan[1], R. Weijer[1], J.K. Wiggers[1], P.D. Moerland[2], L.K. Alles[1], T.M. van Gulik[1], M. Heger[1]. [1]Experimental Surgery, Academic Medical Center, Amsterdam, The Netherlands. [2]Bioinformatics Laboratory, Academic Medical Center, Amsterdam, The Netherlands.*

11.00 Theepauze

**Abstractsessie – Sectie Experimentele Gastroenterologie III** **Baroniezaal**

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

*Voordrachten in het Engels, spreektijd 7 minuten, discussietijd 3 minuten*

11.30 Battle Junior Research Award 2017

12.00 Autologous neoantigen-specific T cell responses in low mutation burden colorectal cancers (p. 127)

*J. van den Bulk[1], D. Ruano[1], M. Visser[2], R. van der Breggen[1], K.C.M.J. Peeters[3], M.E. IJsselsteijn[1], S.H. van der Burg[2], E.M.E. Verdegaal[2], N.F. de Miranda[1]. [1]Dept. of Pathology, Leiden University Medical Center, Leiden, The Netherlands. [2]Dept. of Clinical Oncology, Leiden University Medical Center, Leiden, The Netherlands. [3]Dept of Surgery, Leiden University Medical Center, Leiden, The Netherlands.*

12.10 TRAIL produced by SMAD4 deficient tumors stimulates BMP2 production by ibroblasts and enhances colorectal cancer invasiveness (p. 128)

*S. Ouahoud[1], P.W. Voorneveld[1], L.R.A. van der Burg[1], G. van Pelt[2], W. Meskers[2], L.J.A.C. Hawinkels[1], J.C.H. Hardwick[1]. [1]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands. [2]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands.*

12.20 Synergistic inhibition of tumor growth by combined endoglin and PD1 targeting in colorectal cancer (p. 129)

*M.J.A. Schoonderwoerd[1], R. Angela[2], M. Paauwe[1], E.S.M. de Jonge-Muller[1], C.P. Theuer[3], C.F.M. Sier[4], J.C.H. Hardwick[1], M.F. Fransen[5], L.J.A.C. Hawinkels[1]. [1]Dept. of Gastroenterology-Hepatology, Leiden University Medical Center, Leiden, The Netherlands. [2]Dept. of Gastroenterology-Hepatology, Leiden University Medical Center, Leiden, Leiden, The Netherlands. [3]TRACON pharmaceuticals, San diego, United States of America. [4]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands. [5]Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, The Netherlands.*

12.30 Altered arginine metabolism in hyperproliferative intestinal epithelium: a potential role in tumorigenesis and wound healing (p. 130)

*J.H.M. van der Meer[1], B.J. Meijer[1], W.L. Smit[1], C.N. Spaan[1], E.A. Struys[2], S. Meisner[1], P.J. Koelink[1], L.J.A.C. Hawinkels[3], T.B.M. Hakvoort[1], M.A. Boermeester[4], G.R. van den Brink[5], V. Muncan[1]. [1]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, The Netherlands. [2]Metabolic Unit, Clinical Chemistry, VU Medical Center, Amsterdam, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands. [4]Dept. of Surgery, Academic Medical Center, Amsterdam, The Netherlands. [5]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands.*

12.40 Mutations of the adenoma to carcinoma sequence control an increased cellular capacity of global translation in the intestine (p. 131)

*W.L. Smit[1], C.N. Spaan[1], B.J. Meijer[1], J.H. van der Meer[1], V. Muncan[1], G.R. van den Brink[2], J. Heijmans[1]. [1]Tytgat Institute for Liver and Intestinal Research, Amsterdam, The Netherlands. [2]GlaxoSmithKline, Medicines Research Center, Stevenage, United Kingdom.*

12.50 Anti-BMP2/4 lama-derived antibodies promote neo-squamous re-epithelization at the squamo-columnar junction in a novel cryo-ablation mouse model (p. 132)

*A. Correia[1], S. Calpe[1], D. Straub[2], S. Hoefnagel[1], K.K. Kausilia[3]. [1]Center of Experimental & Molecular Medicine, Academic Medical Center, Amsterdam, The Netherlands. [2]Center of Experimental & Molecular Medicine, Academic Medical Center, Amsterdam, The Netherlands. [3]Dept. of Gastroenterology & Hepatology, Academic Medical Center, Amsterdam, The Netherlands.*

13.00 Lunchpauze in Expo

**Symposium – How do I do it – behandeling hepatitis B en C** **Baroniezaal**

**Voorzitters :** L.C. Baak en R.B. Takkenberg

14.00 Ervaringen en vragen vanuit de hepatitis behandelcentra

15.30 Einde sessie

**Abstractsessie – Sectie Gastrointestinale Oncologie** **Parkzaal**

**Voorzitters :** M. Bigirwamungu en N. Lelyveld

*Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten*

09.30 Increased levels of the systemic immune-inflammation index and risk of incident cancer: results from a population-based cohort study (p. 133)

*J. Fest[1], R. Ruiter[2], B. Groot Koerkamp[1], M.A. Ikram[2], B.H. Stricker[2], C.H.J. van Eijck[1]. [1]Dept. of Surgery, Erasmus Medical Center, Rotterdam, The Netherlands. [2]Dept. of Epidemiology, Erasmus Medical Center, Rotterdam, The Netherlands.*

09.40 Features of incident CRC in Lynch syndrome (p. 134)

*T.E. Argillander[1], M. Bigirwamungu-Bargeman[2], S. de Boer[3], M.A.J.M. Jacobs[4], J.J. Koornstra[5], M. van Kouwen[6], A.M. Langers[7], P.C. van de Meeberg[3], F.M. Nagengast[6], S. Sanduleanu[8], J. Vecht[9], M. Verhulst[10], W. de Vos tot Nederveen Cappel[9], P.J. van der Schaar[11], E. Dekker[12], P. van Duijvendijk[13], H. Vasen[7]. [1]Netherlands Foundation for the Detection of Hereditary Tumors, Leiden, The Netherlands. [2]Dept. of Gastroenterology & Hepatology, Medisch Spectrum Hospital, Enschede, The Netherlands. [3]Dept. of Gastroenterology & Hepatology, Slingeland Hospital, Doetinchem, The Netherlands. [4]Dept. of Gastroenterology & Hepatology, VU Medical Center, Amsterdam, The Netherlands. [5]Dept. of Gastroenterology & Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [6]Dept. of Gastroenterology & Hepatology, Radboud University Medical Center, Nijmegen, The Netherlands. [7]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands. [8]Dept. of Gastroenterology & Hepatology, University Medical Center Maastricht, Maastricht, The Netherlands. [9]Dept. of Gastroenterology & Hepatology, Isala Clinics, Zwolle, The Netherlands. [10]Dept. of Gastroenterology & Hepatology, Maxima Medical Center, Eindhoven, The Netherlands. [11]Dept. of Gastroenterology & Hepatology, Antonius Hospital, Nieuwegein, The Netherlands. [12]Dept. of Gastroenterology & Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [13]Dept. of Surgery, Gelre Hospitals, Apeldoorn, The Netherlands.*

09.50 Comparison of two brands of fecal immunochemical tests within the Dutch nationwide CRC screening program (p. 135)

*E. Wieten[1], C.M. de Klerk[2], A. van der Steen[3], C. Ramakers[4], E.J. Kuipers[5], B. Hansen[1], I. Lansdorp-Vogelaar[6], P.M. Bossuyt[7], E. Dekker[2], M.C.W. Spaander[1]. [1]Dept. of Gastroenterology & Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands. [2]Dept. of Gastroenterology & Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [3]Regional organization for Population Screening South-West Netherlands, Rotterdam, The Netherlands. [4]Dept. of Clinical Chemistry, Rotterdam, The Netherlands. [5]Dept. of Gastroenterology & Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands. [6]Dept. of Public Health, Erasmus University Medical Center, Rotterdam, The Netherlands. [7]Dept. of Clinical Epidemiology, Academic Medical Center, Amsterdam, The Netherlands.*

10.00 Effect of oral anticoagulants and NSAIDs on the accuracy of a fecal immunochemical test (FIT) within a colorectal cancer screening program - A systematic review and meta-analysis (p. 136)

*S.A.V. Nieuwenburg[1], F.E. Vuik[1], M.J.H.A. Kruip[2], E.J. Kuipers[1], M.C.W. Spaander[1]. [1]Dept. of Gastroenterology & Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands. [2]Dept. of Hematology, Erasmus Medical Center, Rotterdam, The Netherlands.*

10.10 Endoscopic resection of large non-pedunculated colorectal neoplasms (LNPCPs): outcomes in the Dutch colorectal cancer (CRC) screening program (p. 137)

*Q.E.W. van der Zander[1], A.J.P. van de Wetering[1], R.M.M. Bogie[1], B. Winkens[2], A. Reumkens[1], L.W.T. Meulen[1], H.R. Cheng[3], J.W.A. Straathof[3], E. Keulen[4], C.M. Bakker[4], R. de Ridder[1], C.V. Hoge[1], A.A.M. Masclee[1], S. Sanduleanu-Dascalescu[1]. [1]Div. of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, The Netherlands. [2]Dept. of Methodology and Statistics, Maastricht University Medical Center, Maastricht, The Netherlands. [3]Dept. of Internal Medicine, Maxima Medical Center, Veldhoven, The Netherlands. [4]Dept. of Internal Medicine and Gastroenterology, Zuyderland Medical Center, Heerlen, The Netherlands.*

10.20 Optical diagnosis of diminutive polyps in the Dutch CRC screening program: Are we ready to start? (p. 138)

*A.J.P. van de Wetering[1], R.M.M. Bogie[1], A. Reumkens[2], Q.E.W. van der Zander[1], L.W.T. Meulen[1], B. Winkens[3], H.R. Cheng[4], J.W.A. Straathof[4], E. Keulen[2], C.M. Bakker[2], C.H.V. Hoge[1], R. de Ridder[1], A.A.M. Masclee[1], S. Sanduleanu[1]. [1]Dept. of Internal Medicine, Maastricht University Medical Center, Maastricht, The Netherlands. [2]Dept. of Internal Medicine and Gastroenterology, Zuyderland Medical Center, Heerlen, The Netherlands. [3]Dept. of Methodology and Statistics, Maastricht University, Maastricht, The Netherlands. [4]Dept. of Gastroenterology, Máxima Medical Center, Veldhoven, The Netherlands.*

10.30 Histological model to improve the assessment of the indication for surgery in pedunculated T1 colorectal carcinomas: a multicenter cohort-nested matched case control study (p. 139)

*Y. Backes[1], S.G. Elias[2], J.N. Groen[3], M.P. Schwartz[4], F.H.J. Wolfhagen[5], J.M.J. Geesing[6], F. ter Borg[7], J. van Bergeijk[8], B.W.M. Spanier[9], W.H. de Vos tot Nederveen Cappel[10], K. Kessels[11], C.A. Seldenrijk[12], M. Raicu[12], A.N. Milne[13], M. Kerkhof[14], T.C.J. Seerden[15], P.D. Siersema[16], F.P. Vleggaar[1], G.J.A. Offerhaus[1], M.M. Lacle[1], L.M.G. Moons[1]. [1]University Medical Center Utrecht, Utrecht, The Netherlands. [2]Julius Center for Health Sciences, Utrecht, The Netherlands. [3]Sint Jansdal Harderwijk, Harderwijk, The Netherlands. [4]Meander Medical Center, Amersfoort, The Netherlands. [5]Albert Schweitzer Hospital, Dordrecht, The Netherlands. [6]Diakonessenhuis, Utrecht, The Netherlands. [7]Deventer Hospital, Deventer, The Netherlands. [8]Gelderse Vallei, Ede, The Netherlands. [9]Rijnstate Hospital, Arnhem, The Netherlands. [10]Isala Clinics, Zwolle, The Netherlands. [11]Flevo Hospital, Almere, The Netherlands. [12]Sint Antonius Hospital, Nieuwegein, The Netherlands. [13]Dept. of Pathology, Diakonessenhuis, Utrecht, The Netherlands. [14]Groene Hart Hospital, Gouda, The Netherlands. [15]Amphia Hospital, Breda, The Netherlands. [16]Radboud University Medical Center, Nijmegen, The Netherlands.*

10.40 Magnetic resonance imaging for response assessment after neoadjuvant chemoradiotherapy in oesophageal cancer: can we select complete responders? (p. 140)

*S.E. Vollenbrock[1], F.E.M. Voncken[2], D.M.J. Lambregts[1], M. Maas[1], J.M. van Dieren[3], L.C. ter Beek[1], B.M.P. Aleman[2], R.G.H. Beets-Tan[1], A. Bartels-Rutten[1]. [1]Dept. of Radiology, Antoni van Leeuwenhoek, Amsterdam, The Netherlands. [2]Dept. of Radiation Oncology, Antoni van Leeuwenhoek, Amsterdam, The Netherlands. [3]Dept. of Gastroenterology, Antoni van Leeuwenhoek, Amsterdam, The Netherlands.*

10.50 Prediction in surveillance of Barrett's esophagus: The effect of multiple measurements of biomarkers on the estimated neoplastic progression risk (p. 141)

*C.A.M. Roumans[1], M.C.W. Spaander[2], I. Lansdorp-Vogelaar[1], K. Biermann[3], M.J. Bruno[2], E.W. Steyerberg[1], D. Rizopoulos[4]. On behalf of ProBar study group. [1]Dept. of Public Health, Erasmus University Medical Center, Rotterdam, The Netherlands. [2]Dept. of Gastroenterology & Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands. [3]Dept. of Pathology, Erasmus University Medical Center, Rotterdam, The Netherlands. [4]Dept. of Biostatistics, Erasmus University Medical Center, Rotterdam, The Netherlands.*

11.00 Korte ledenvergadering Sectie Gastrointestinale Oncologie
Aansluitend koffiepauze in de expositiehal.

**Abstractsessie – Sectie Gastrointestinale Endoscopie II** **Parkzaal**

**Voorzitters :** E.J. Schoon en B.L.A.M. Weusten

*Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten*

11.30 Safety and efficacy of using lumen apposing metal stents in the management of post-operative fluid collections (POFC): a large, international, multicenter study (p. 142)

*F.P. Vleggaar[1], J. Yang[2], J.H. Kaplan[3], A. Sethi[3], E. Dawod[4], R.Z. Sharaiha[4], A. Chiang[5], T. Kowalski[5], J. Nieto[6], R. Law[7], H. Hammad[8], S. Wani[8], M. Wagh[8], D. Yang[9], A. Messallam[10], Q. Cai[10], V. Kushnir[11], A. Mir Ahmed[12], A. Anderloni[13], D. Adler[14], S. Nagula[15], I. Raijman[16], S. Irani[17], C. Robles-Medranda[18], A. Hamid El Chafic[19], R. Pawa[20], M. Gabr[21], M.A. Kashab[2]. [1]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands. [2]Division of Gastroenterology and Hepatology, Johns Hopkins Medical Institution, Baltimore, United States of America. [3]Division of Digestive and Liver Disease, Columbia University Medical Center, New York, United States of America. [4]Division of Gastroenterology and Hepatology, Weill Cornell Medical Center, New York, United States of America. [5]Division of Gastroenterology and Hepatology, Thomas Jefferson University, Philadelphia, United States of America. [6]Division of Gastroenterology and Hepatology, Borland Groover Clinic, Jacksonville, United States of America. [7]Division of Gastroenterology, University of Michigan, Ann arbor, United States of America. [8]Division of Gastroenterology and Hepatology, University of Colorado Anschutz Med, Aurora, United States of America. [9]Division of Gastroenterology and Hepatology, University of Florida, Gainesville, United States of America. [10]Division of Digestive Disease, Emory University School of Medicine, Atlanta, United States of America. [11]Divsion of Gastroenterology, Washington University in Saint Louis, United States of America. [12]Division of Gastroenterology and Hepatology, University of Alabama at Birmingham, Mountain brook, United States of America. [13]Division of Gastroenterology, Digestive Endoscopy Unit, Milan, Italy. [14]Division of Gastroenterology and Hepatology, University of Utah, Salt Lake City, United States of America. [15]Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, United States of America. [16]Division of Gastroenterology, Greater Houston Gastroenterology, Houston, United States of America. [17]Division of Gastroenterology and Hepatology, Virginia Mason Medical Center, Seattle, United States of America. [18]Gastroenterology and Endoscopy Division, Guayaquil, Equador. [19]Division of Gastroenterology, Ochsner Medical Center, New Orleans, United States of America. [20]Division of Gastroenterology, Dept. of Internal Medicine, Wake Forest Schoo, Winston salem, United States of America. [21]Division of Gastroenterology, Beth Israel Deaconess Medical Center, Boston, United States of America.*

11.40 Comprehensive Analysis of Adverse Events Associated with Endoscopic Ultrasound drainage of Pancreatic Fluid Collection using lumen-apposing metal stents: An International Multicenter Study (p. 143)

*F.P. Vleggaar[1], P. Fockens[2], A. Bogte[3], R. Voermans[2], A. Fugazza[4], A. Sethi[5], C. Packey[5], A. Trindade[6], P.C. Benias[6], J. Devlin[7], Y. El-Sherif[7], M.A. Kashab[8], C. Paiji[9], I. Tarantino[10], D. Ligresti[10], P.H. Deprez[11], C. Fabbri[12], C. Binda[12], J.R. Aparicio Tormo[13], B. Martinez[13], U. Will[14], G. Vanbiervliet[15], A. Charanchon[16], D. Adler[17], A. Repici[18], A. Anderloni[4]. [1]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, UMCU, Utrecht, The Netherlands. [4]Digestive Endoscopy Unit, Departement of Gastroenterology, Humanitas Research Ho, Milan, Italy. [5]Division of Digestive and Liver Disease, Columbia University Medical Center, New York, United States of America. [6]Long Island Jewish Medical Center, Hofstra Northwell School of Medicine, New York, United States of America. [7]Kings College Hospital, Londen, United Kingdom. [8]Therapeutic Endoscopy, Johns Hopkins Hospital, Baltimore,*

*United States of America. [9]Therapeutic Endoscopy, Johns Hopkins Hospital, Division of Gastroenterology, Baltimore, United States of America. [10]Dept. of Diagnostic and Therapeutic Services, IRCCS-ISMETT, Palermo, Italy. [11]Dept. of Hepatogastroenterology, Cliniques universitaires Saint-Luc, Brussel, Belgium. [12]Unit of Gastroenterology and Digestive Endoscopy, AUSL Bologna Bellaria-Maggiore, Bologna, Italy. [13]Endoscopy Unit, Digestive Service, Alicante University General Hospital, Alicante, Spain. [14]Dept. of Gastroenterology, Municipal Hospital, Gera, Germany. [15]Digestive Endoscopy Unit, l'Archet University Hospital, Nice, France. [16]Service d'Hépato-gastro-entérologie, CH Princesse Grace, Monte Carlo, Monaco. [17]University of Utah School of Medicine, Division of Gastroenterology and Hepatolo, Salt Lake City, United States of America. [18]Humanitas University, Milaan, Italy.*

11.50 Safety and efficacy of the new 20 mm lumen apposing metal stent (LAMS) for endoscopic treatment of pancreatic and peripancreatic fluid collectios (PPFCS): a large, international, multicenter study (p. 144)

*F.P. Vleggaar[1], M. Perez Miranda[2], M. Dollhopf[3], R. Kunda[4], A. Anderloni[5]. [1]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands. [2]Dept. of Gastroenterology, Valladolid, Spain. [3]Klinikum Munchen, Munchen, Germany. [4]Dept. of Gastroenterology, Aarhus University, Aarhus, Denmark. [5]Division of Gastroenterology, Digestive Endoscopy Unit, Milan, Italy.*

12.00 Long term evaluation of Endoscopic Transpapillary Pigtail Gallbladder Stenting in patients with symptomatic gallbladder disease: a singleCenter retrospective study (p. 145)

*M.K. Toneman[1], L.E. Perk[1], G.J.D. van Acker[2]. [1]Dept. of Gastroenterology, Haaglanden Medisch Centrum, Den Haag, The Netherlands. [2]Dept. of Surgery, Haaglanden Medisch Centrum, Leidschendam, The Netherlands.*

12.10 A novel tool for fast and effective endoscopic removal of pancreatic necrosis (p. 146)

*S.E. van der Wiel, J.W. Poley, M.J.A.L. Grubben, M.J. Bruno, A.D. Koch. Dept. of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands.*

12.20 Technical feasibility and safety of suck-and-snare EMR for treatment of difficult colorectal polyps (p. 147)

*V. van der Voort[1], L.M.G. Moons[1], W. de Graaf[2], R. Schrauwen[3], W.L. Hazen[4], T.C.J. Seerden[5], F.P. Vleggaar[1], P. Didden[1]. [1]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, Bernhoven Hospital, Uden, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, Elisabeth-TweeSteden Hospital, Tilburg, The Netherlands. [5]Dept. of Gastroenterology and Hepatology, Amphia Hospital, Breda, The Netherlands.*

12.30 The therapeutic yield of repeated colonoscopy for delayed bleeding after endoscopic mucosal resection of large colorectal polyps (p. 148)

*S. van der Star[1], L.M.G. Moons[1], R.J. Ouwehand[1], J.M.J. Geesing[2], W.H. de Vos tot Nederveen Cappel[3], F. ter Borg[4], J.D. van Bergeijk[5], M.P. Schwartz[6], F.H.J. Wolfhagen[7], J.N. Groen[8], F.P. Vleggaar[1], P. Didden[1]. [1]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Diakonessenhuis, Utrecht, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, Isala, Zwolle, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, Deventer Hospital, Deventer, The Netherlands. [5]Dept. of Gastroenterology and Hepatology, Gelderse Vallei Hospital, Ede, The Netherlands. [6]Dept. of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, The Netherlands. [7]Dept. of Gastroenterology and Hepatology, Albert Schweitzer Hospital, Dordrecht, The Netherlands. [8]Dept. of Gastroenterology and Hepatology, Sint Jansdal Hospital, Harderwijk, The Netherlands.*

12.40 Deep mural injury after colorectal endoscopic mucosal resection (EMR): occurrence, risk factors and outcome of endoscopic clip placement (p. 149)

*S. van der Star[1], L.M.G. Moons[1], R.J. Ouwehand[1], J.M.J. Geesing[2], W.H. de Vos tot Nederveen Cappel[3], F. ter Borg[4], J.D. van Bergeijk[5], M.P. Schwartz[6], F.H.J. Wolfhagen[7], J.N. Groen[8], F.P. Vleggaar[1], P. Didden[1]. [1]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Diakonessenhuis, Utrecht, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, Isala, Zwolle, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, Deventer Hospital, Deventer, The Netherlands. [5]Dept. of Gastroenterology and Hepatology, Gelderse Vallei Hospital, Ede, The Netherlands. [6]Dept. of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, The Netherlands. [7]Dept. of Gastroenterology and Hepatology, Albert Schweitzer Hospital, Dordrecht, The Netherlands. [8]Dept. of Gastroenterology and Hepatology, Sint Jansdal Hospital, Harderwijk, The Netherlands.*

12.50 Lunchpauze in expo

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**Abstractsessie – Nederlandse Vereniging voor Gastroenterologie II** **Parkzaal**

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

*Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten*

14.00 Antibiotic Prophylaxis in Percutaneous Transhepatic Cholangiography and Biliary Drainage (PTCD), a retrospective multicenter study (p. 150)

*A.S. Turan[1], S.F.M. Jenniskens[2], L.J. Schultze Kool[3], J.M. Martens[4], M.J.C.M. Rutten[5], L.S.F. Yo[6], M.J.L. van Strijen[7], P.D. Siersema[1], E.J.M. van Geenen[1]. [1]Dept. of Gastroenterology, Radboudumc, Nijmegen, The Netherlands. [2]Dept. of Radiology and Nuclear Medicine, Radboudumc, Nijmegen, The Netherlands. [3]Dept. of Radiology and Nuclear Medicin, Radboudumc, Nijmegen, The Netherlands. [4]Dept. of Radiology, Rijnstate Hospital, Arnhem, The Netherlands. [5]Dept. of Radiology, Jeroen Bosch Hospital, Den Bosch, The Netherlands. [6]Dept. of Radiology, Catharina Hospital, Eindhoven, The Netherlands. [7]Dept. of Radiology, St Antonius Hospital, Nieuwegein, The Netherlands.*

14.10 Pancreatic cyst surveillance imposes low psychological burden: preliminary results of the pacyfic study (p. 151)

*K.A. Overbeek[1], A. Kamps[1], P.A. van Riet[1], M.C. di Marco[2], G. Zerboni[3], J.E. van Hooft[4], S. Carrara[5], C. Ricci[2], T.A. Gonda[6], E. Schoon[7], M. Polkowski[8], G. Beyer[9], P. Honkoop[10], L.A. van der Waaij[11], R. Casadei[2], G. Capurso[3], M.J. Bruno[1], E.M.A. Bleiker[12], D.L. Cahen[1]. [1]Dept. of Gastroenterology & Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands. [2]Dept. of Medical Science and Surgery, University of Bologna, Bologna, Italy. [3]Digestive and Liver Disease Unit, Sant Andrea Hospital, Rome, Italy. [4]Dept. of Gastroenterology & Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [5]Dept. of Gastroenterology, Humanitas Research Hospital, Rozzano, Italy. [6]Dept. of Medicine, Columbia University Medical Center, New York, United States of America. [7]Dept. of Gastroenterology & Hepatology, Catharina Hospital, Eindhoven, The Netherlands. [8]Dept. of Gastroenterological Oncology, M.Sklodowska-Curie Institute, Warsaw, Poland. [9]Dept. of Medicine, Ludwig-Maximilians-University Hospital, Munich, Germany. [10]Dept. of Gastroenterology, Albert Schweitzer Hospital, Dordrecht, The Netherlands. [11]Dept. of Gastroenterology & Hepatology, Martini Hospital, Groningen, The Netherlands. [12]Division of Psychosocial Research, The Netherlands Cancer Institute, Amsterdam, The Netherlands.*

14.20 The Dutch national ERCP quality registration with RAF-E does not correlate with clinical ERCP outcome (p. 152)

*S.C. Meijer, L.P.L. Gilissen. Dept. of Gastroenterology and Hepatology, Catharina Ziekenhuis, Eindhoven, The Netherlands.*

14.30 Reducing pancreatic cyst surveillance: development of the dutch american risk stratification tool (dart-i) to identify ipmn with low risk to progress and fulfill resection criteria (p. 153)

*K.A. Overbeek[1], M. Alblas[2], V. Gausman[3], P. Kandel[4], C. Brooks[5], P.A. van Riet[1], M.B. Wallace[4], T.A. Gonda[5], D.L. Cahen[1], M.J. Bruno[1]. [1]Dept. of Gastroenterology & Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands. [2]Dept. of Public Health, Erasmus University Medical Center, Rotterdam, The Netherlands. [3]Dept. of Medicine, NYU-Langone Medical Center, New York, United States of America. [4]Dept. of Gastroenterology & Hepatology, Mayo Clinic, Jacksonville, United States of America. [5]Dept. of Medicine, Columbia University Medical Center, New York, United States of America.*

14.40 Influence of antibiotic duration in cholangitis after successful drainage by ERCP (p. 154)

*B. ten Böhmer[1], S. Haal[1], S. Balkema[2], A.C.T.M. Depla[3], P. Fockens[1], J.E. van Hooft[1], J. Jansen[4], S.D. Kuiken[4], B.I. Liberov[5], E. van Soest[6], R.P. Voermans[1]. [1]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Gastroenterology, Westfriesgasthuis, Hoorn, The Netherlands. [3]Dept. of Gastroenterology, MC Slotervaart, Amsterdam, The Netherlands. [4]Dept. of Gastroenterology and Hepatology OLVG, Amsterdam, The Netherlands. [5]Dept. of Internal medicine, Zaans Medisch Centrum, Zaandam, The Netherlands. [6]Dept. of Gastroenterology, Spaarne Gasthuis, Hoofddorp, The Netherlands.*

14.50 Durable Response in Markers of Cholestasis Through 24 Months of Open-Label Extension with Obeticholic Acid in Patients in the Benelux with Primary Biliary Cholangitis (p. 155)

*K.J. van Erpecum[1], J.P.H. Drenth[2], U.H.W. Beuers[3], C.M.J. van Nieuwkerk[4], R. Pencek[5], E. Smoot Malecha[5], L. MacConell[5], F. Nevens[6]. [1]University Medical Center Utrecht, Utrecht, The Netherlands. [2]Radboud University Medical Center, Nijmegen, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, VU Medical Center, Amsterdam, The Netherlands. [5]Clinical Development, Intercept Pharmaceuticals, San Diego, United States of America. [6]Dept of Gastroenterology, UZ Leuven, Leuven, Belgium.*

15.00 Increased risk of death and liver transplantation in autoimmune hepatitis, results from a national cohort study (p. 156)

*F.F. van den Brand[1], K.S. van der Veen[1], Y.S. de Boer[1], N.M.F. van Gerven[1], B.J. Verwer[1], B.I. Lissenberg-Witte[2], B. van Hoek[3], K.J. van Erpecum[4], U.H.W. Beuers[5], H.R. van Buuren[6], J.P.H. Drenth[7], J.W. den Ouden[8], R.C. Verdonk[9], G.H. Koek[10], J.T. Brouwer[11], M.M.J. Guichelaar[12], J.M. Vrolijk[13], C.J.J. Mulder[1], C.M.J. van Nieuwkerk[1], G. Bouma[1]. [1]Dept. of Gastroenterology and Hepatology, VU Medical Center, Amsterdam, The Netherlands. [2]Dept. of Epidemiology and Biostatistics, VU Medical Center, Amsterdam, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands. [5]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [6]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands. [7]Dept. of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, The Netherlands. [8]Dept. of Gastroenterology and Hepatology, Haga Hospital, The Hague, The Netherlands. [9]Dept. of Gastroenterology and Hepatology, St. Antonius Hospital, Nieuwegein, The Netherlands. [10]Dept. of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, The Netherlands. [11]Dept. of Gastroenterology and Hepatology, Reinier de Graaf Hospital, Delft, The Netherlands. [12]Dept. of Gastroenterology and Hepatology, Medisch Spectrum Twente, Enschede, The Netherlands. [13]Dept. of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, The Netherlands.*

15.10 **MLDS-voordracht**

Drug utilization in patients with cirrhosis in ambulatory care: a retrospective cohort study, (projectnr. CDG 12-10) (p. 157)

*R.A. Weersink[1], K. Taxis[2], S.D. Borgsteede[1]. [1]Dept. of Clinical Decision Support, Health Base Foundation, Houten, The Netherlands. [2]Dept. of PharmacoTherapy, -Epidemiology & -Economics, University of Groningen, Groningen, The Netherlands.*

15.20 Einde sessie

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**Abstractsessie – Sectie NESPEN / Inflammatoire Darmziekten** **Zaal 80**

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**Voorzitters :** A. Bodelier en C.F. Jonkers

*Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten*

09.30 Drug survival and immunogenicity after switching from Remicade® to biosimilar CT-P13 in inflammatory bowel disease patients: Two year follow-up of a prospective observational cohort study (p. 158)

*L.J.T. Smits[1], L.A.A.P. Derikx[2], A.A.J. van Esch[1], J.P.H. Drenth[1], R.S. Boshuizen[3], D.J. de Jong[1], F. Hoentjen[1]. [1]Dept. of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Jeroen Bosch hospital, 's Hertogenbosch, The Netherlands. [3]Biologics Laboratory, Sanquin Diagnostic Services, Amsterdam, The Netherlands.*

09.40 Latent cytomegalovirus infection does not influence disease course in Inflammatory Bowel Disease (p. 159)

*K.W.J. van der Sloot[1], M.D. Voskuil[1], R.K. Weersma[1], M.C. Visschedijk[1], E.A.M. Festen[1], H.M. van Dullemen[1], C. van Leer-Buter[2], B.Z. Alizadeh[3], G. Dijkstra[1]. [1]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [2]Dept. of Medical Microbiology, University Medical Center Groningen, Groningen, The Netherlands. [3]Dept. of Epidemiology, University Medical Center Groningen, Groningen, The Netherlands.*

09.50 Gallstone disease necessitating cholecystectomy after ileal or ileocecal resection in Crohn's disease: a nationwide cohort study in the Netherlands (p. 160)

*E.M.J. Beelen[1], J.C. Goet[1], K. Biermann[2], A.H. Gijsbers[3], W.R. Schouten[4], C.J. van der Woude[1], A.C. de Vries[1]. [1]Dept. of gastroenterology and hepatology, Erasmus Medical Center, Rotterdam, The Netherlands. [2]Dept. of pathology, Erasmus Medical Center, Rotterdam, The Netherlands. [3]Stichting PALGA, Houten, The Netherlands. [4]Dept. of surgery, Erasmus Medical Center, Rotterdam, The Netherlands.*

10.00 The gut microbiome can distinguish inflammatory bowel disease from healthy controls and irritable bowel syndrome (p. 161)

*R. Gacesa[1], A. Vich Vila[1], F. Imhann[1], V. Collij[1], Z. Mujagic[2], A. Kurilshikov[3], M.J. Bonder[3], E.F. Tigchelaar[3], J. Dekens[3], V. Peters[1], M.D. Voskuil[1], M.C. Visschedijk[1], H.M. van Dullemen[1], M.A. Swertz[1], E.A.M. Festen[1], G. Dijkstra[1], R.G. Xavier[4], J. Fu[3], C. Wijmenga[3], D.M.A.E. Jonkers[2], A. Zhernakova[3], R.K. Weersma[1]. [1]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [2]Maastricht University Medical Center, Division for Gastroenterology-Hepatology, Maastricht, The Netherlands. [3]Dept. of Genetics, University Medical Center Groningen, Groningen, The Netherlands. [4]Center for Microbiome Informatics and Therapeutics, MIT, Cambridge, United States of America.*

10.10 The 1000IBD project: multi-omics data of 1000 inflammatory bowel disease patients; Data release 1 (p. 162)

*F. Imhann[1], K.J. van der Velde[2], R. Barbieri[1], R. Alberts[1], M.D. Voskuil[1], A. Vich Vila[1], V. Collij[3], L.M. Spekhorst[3], K.W.J. van der Sloot[1], V. Peters[1], H.M. van Dullemen[1], M.C. Visschedijk[1], E.A.M. Festen[1], M.A. Swertz[2], G. Dijkstra[3], R.K. Weersma[3]. [1]Dept. of Gastroenterology, UMCG, Groningen, The Netherlands. [2]Dept. of Genetics, UMCG, Groningen, The Netherlands. [3]Dept. of Gastroenterology, Groningen, The Netherlands.*

10.20 Increased abundance of gut microbial virulence genes and pro-inflammatory pathways during Crohn's disease exacerbations (p. 163)

*M.A.Y. Klaassen[1], F. Imhann[2], V. Collij[2], A. Vich Vila[2], R. Gacesa[2], J. Fu[2], A. Zhernakova[2], C. Wijmenga[3], R.K. Weersma[2]. [1]University Medical Center Groningen, Groningen, The Netherlands. [2]Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [3]Dept. of Genetics, University Medical Center Groningen, Groningen, The Netherlands.*

10.30 How to measure environmental exposures (the exposome) in Inflammatory Bowel Disease? (p. 164)

*K.W.J. van der Sloot[1], B.Z. Alizadeh[2], G. Dijkstra[1]. [1]Dept. of Gastroenterology and Hepatology, Groningen, The Netherlands. [2]Dept. of Epidemiology, Groningen, The Netherlands.*

10.40 Evaluation of Quality of life and caregiver burden in home parenteral nutrition patients: a cross sectional study (p. 165)

*J.M. Beurskens[1], G.J. Huisman de Waal[2], G. Wanten[1]. [1]Radboudumc, Nijmegen, The Netherlands. [2]Radbouduniversity / IQ healthcare, Nijmegen, The Netherlands.*

10.50 Anti-inflammatory dietary recommendations based on the relation between food and the gut microbiome composition in 1424 individuals (p. 166)

*L.A. Bolte[1], F. Imhann[1], A. Vich Vila[2], V. Collij[1], V. Peters[1], J. Fu[3], E.F. Tigchelaar[2], A. Kurilshikov[2], M.J.E. Campmans-Kuijpers[1], G. Dijkstra[1], C. Wijmenga[2], A. Zhernakova[2], R.K. Weersma[1]. [1]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [2]Dept. of Genetics, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands. [3]Dept. of Pediatrics, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands.*

11.00 Theepauze

**Symposium – Sectie NESPEN** **Zaal 80**

**Voorzitters :** I. Gisbertz en C.F. Jonkers

**Symposium: nieuwe voedingsconcepten in ziekenhuizen: optimalisering voedingszorg en minder ondervoeding?**

11.30 Screening en behandeling van ondervoeding in het ziekenhuis
*Mw. dr. Gerdien Ligthart-Melis, dietist, freelance*

11.50 Nieuw voedingsconcept ziekenhuis Bernhoven
*Mw. dr. Ingrid Gisbertz, MDL Bernhoven*

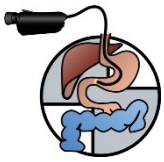
12.10 Food for care
*Mw. drs. Dorian Dijxshoorn, Radboudumc, Nijmegen*

12.30 Elke patiënt gelijke voeding of tailormade voedingsconcept?
*Mw. Cheyenne Gouwenrok, AMC, Amsterdam*

12.50 Proefschriftprijs 2018 NESPEN uitreiking en presentatie
*Mw. Dr. Kirsten van der Beek*

13.00 Afsluiting

## V&VN MDL - Ochtendprogramma 1 — Brabantzaal



**Voorzitter:** Mw. T.A. Korpershoek

### MDL algemeen

10.05 Welkom
*Mw. T.A. Korpershoek*

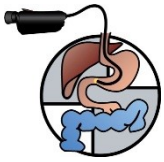
10.10 ACNES
*Dr. F.H.J. Wolfhagen, MDL-arts, Albert Schweitzer ziekenhuis, Dordrecht*

10.30 Therapietrouw / E-health
*Mw. dr. A.J. Linn, assistent professor in gezondheidswetenschap, UVA, Amsterdam*

10.50 Feces transplantatie
*Dr. J.J. Keller, MDL-arts, Haaglanden MC, Den Haag*

11.10 Theepauze

## V&VN MDL - Ochtendprogramma II — Brabantzaal



**Voorzitter:** n.t.b.

### Endoscopie

11.40 Onderzoek digitaal zorgpad voor colonoscopie
*Mw. W. Adriaans, verpleegkundig specialist MDL, Maxima Medisch Centrum, Veldhoven*

12.00 ERCP en cholangitis
*Mw. S.E.S. Smulders, verpleegkundig specialist, LUMC, Leiden*

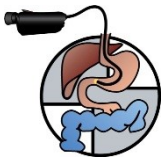
12.20 Bariatrische endoscopie / chirurgie
*Dr. M.J.M. Groenen, MDL-arts, Ziekenhuis Rijnstate, Arnhem*

12.40 Ontstaan en behandeling van angiodysplasieën
*Drs. K. Grooteman, aios MDL, Radboudumc, Nijmegen*

13.00 Lunchpauze in Expo

## V&VN MDL - Ochtendprogramma III — Zaal 63/64

V&VN Beroepsvereniging van zorgprofessionals
Maag Darm Lever



**Voorzitter:** Mw. T.A. Korpershoek

**MDL algemeen**

11.40 IBD en chirurgie
*Dr. T.S. Aukema, chirurg, Meander MC, Amersfoort*

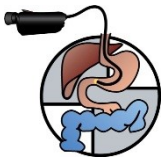
12.00 Toegangen voor enterale voeding
*Dr. G.J.A. Wanten, MDL-arts, Radboudumc, Nijmegen*

12.20 Short bowel syndroom
*Prof. dr. G. Dijkstra, MDL-arts, UMCG, Groningen*

12.40 Beeldvorming bij het colorectaalcarcinoom (CRC)
*Dr. M.J. Lahay, radioloog, Antoni van Leeuwenhoek, Amsterdam*

13.00 Lunchpauze in Expo

## V&VN MDL - Middagprogramma I — Brabantzaal



**Voorzitter:** Mw. E. Sprong

### Endoscopie

14.00 Klinisch redeneren op de endoscopie
*Mw. H. Straver-ten Velde, verpleegkundig specialist, Diakonessenhuis, Utrecht*

14.20 Barret slokdarm
*Dr. F. Oort, MDL-arts, Alrijne ziekenhuis, Leiderdorp*

14.40 Diagnostiek en behandeling IPMN (intraductaal papillair mucineuze neoplasie)
*Dr. N.C.M. van Huijgevoort, MDL-arts, AMC, Amsterdam*

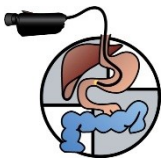
15.00 Poliepen: EMR, ESD, endoscopische fullthickness resectie
*Prof. dr. J.C. H. Hardwick, MDL-arts, LUMC, Leiden*

15.20 Verpleegkundigen interventies bij endoscopische complicaties
*Mw. A. Boersen, verpleegkundig endoscopist, Noordwest ziekenhuis, Alkmaar*

15.40 Afronding

15.45 Borrel

## V&VN MDL - Middagprogramma II — Zaal 63/64



**Voorzitter:** Mw. A. Boersen

### Verpleegkundig Endoscopisten

14.00 Kwaliteitsindicatoren bij een scopie
*Dr. J.Y.L. Lai, MDL-arts, Haaglanden MC, Den Haag*

14.20 Lichamelijke belasting bij een scopie
*Dr. R.J. Robijn, MDL-arts, Rijnstate ziekenhuis, Arnhem*

14.40 Pijnloze scopie / loopmanagement
*Dr. A.M.J. Langers, MDL-arts, LUMC, Leiden*

15.00 Sessiel serrated leasie: wat is dat en doet het er toe?
*Prof. dr. E. Dekker, MDL-arts, AMC, Amsterdam*

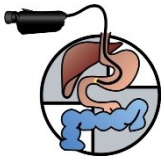
15.20 Effectiviteit voorbereiding bij coloscopie (onder voorbehoud)

15.40 Afronding

15.45 Borrel

## V&VN MDL - Middagprogramma III — Zaal 82/83

Beroepsvereniging van zorgprofessionals
Maag Darm Lever



**Voorzitter:** Mw. M. Verwey

**IBD**

14.00 Echografie bij IBD patiënten
*Mw. M. de Jong, verpleegkundig specialist IBD, AMC, Amsterdam*

14.20 Thiopurines
*Mw. M. Simsek, arts-onderzoeker MDL, VUmc, Amsterdam (onder* voorbehoud)

14.40 Incontinentie bij de IBD patiënt
*Mw. N.A. Boontje, verpleegkundig specialist MDL, UMCU, Utrecht*

15.00 Maligniteit en IBD
*Dr. F. Hoentjen, MDL-arts, Radboudumc, Nijmegen*

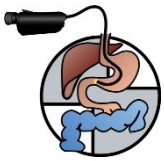
15.20 Zwangerschap en IBD
*Mw. P.C.W.M. Hurkmans, verpleegkundig specialist MDL, Amphia ziekenhuis, Breda*

15.40 Afronding

15.45 Borrel

## V&VN MDL - Middagprogramma IV — Zaal 80

v&vn
Beroepsvereniging van zorgprofessionals
Maag Darm Lever



**Voorzitter:** n.t.b.

**Lever**

14.00 Diagnose en klinische verschijnselen van encefalopathie
*Dr. M. Kramer, MDL-arts, Radboudumc, Nijmegen*

14.20 Behandeling: medicatie bij encefalopathie
*Dr. M. Kramer, MDL-arts, Radboudumc, Nijmegen*

14.40 Verpleegkundige aspecten: voorlichten van de patiënt en familie en het gebruik van het “encefalopathie dagboek”
*Mw. M. Heide, verpleegkundig specialist i.o., UMCG, Groningen*

15.00 Hepatische encefalopathie na TIPS plaatsing
*Dhr. K. de Wit, MD PhD-student, AMC, Amsterdam*

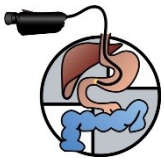
15.20 Klinisch redeneren bij hepatische encefalopathie
*(spreker volgt)*

15.40 Afronding

15.45 Borrel

**V&VN MDL - Middagprogramma V** **Zaal 81**

Beroepsvereniging van zorgprofessionals
Maag Darm Lever



**Voorzitter:** N. Ipenburg

**Oncologie / chirurgie**

14.00 Levermetastasen bij coloncarcinoom
*Dr. M. Vermaas, gastro-intestinaal chirurg, IJsselland ziekenhuis, Capelle aan de IJssel*

14.20 Shared decision making binnen de oncologie
*Dr. D. Ubbink, principal investigator arts en klinisch epidemioloog, AMC, Amsterdam*

14.40 LAR syndroom
*Mw. S. de Bruijn, verpleegkundig specialist, Reinier de Graaf ziekenhuis, Delft*

15.00 T1 colocarcinoom en nu?
*Mw. M. Bloedjes, verpleegkundig specialist, Noordwest Ziekenhuisgroep, Alkmaar*

15.20 HIPEC bij maagcarcinoom: de stand van zaken
*Drs. W. Koemans, arts-onderzoeker, Antoni van Leeuwenhoek, Amsterdam*

15.40 Afronding

15.45 Borrel

## The Natural Course and Long-term Consequences of Untreated Eosinophilic Esophagitis in a Large Cohort

*R.A.B. Oude Nijhuis[1], M.J. Warners[1], L.R.H. de Wijkerslooth[2], A.J.P.M. Smout[1], A.J. Bredenoord[1]. [1]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Isala, Zwolle, The Netherlands.*

Background: Eosinophilic esophagitis (EoE) is a chronic inflammatory disease that eventually may lead to stricture formation. Current guidelines encourage chronic maintenance therapy in order to reduce the risk of long-term complications. However, due to the paucity of observational studies in large cohorts over a considerable period of time, data on the natural course and long-term consequences of EoE are scarce. Hence the level of evidence, supporting the view that long-term complications outweigh the burden of chronic drug use, is low. Therefore, we aimed to investigate the natural course of EoE and to evaluate the association between untreated disease and the occurrence of complications over two decades in a large cohort.

Methods: We retrospectively analyzed charts of patients diagnosed with EoE between 1996–2015, collected from 15 hospitals throughout the Netherlands. Histologic, clinical and endoscopic characteristics were identified and stratified by age and diagnostic delay, an indicator of untreated disease.

Results: We included 721 patients (524 males, 117 children (≤18 years). Dysphagia and food impactions were more common in adults whereas children more often presented with vomiting and abdominal pain (all $p<0.001$). The prevalence of fibrotic endoscopic features was higher in adults (76%) than in children (39%), and children more frequently presented with inflammatory endoscopic features (both $p<0.001$). The percentage of patients with fibrotic features increased with prolonged duration of diagnostic delay from 56% (≤2 years of diagnostic delay) to 92% (≥21 years diagnostic delay). Likewise, prevalence of strictures (from 19% to 52%) and food impactions (from 24% to 57%) increased as time of untreated disease progressed (all $p<0.001$). In a multivariate logistic regression model, diagnostic delay of ≥ 5 years (odds ratio (OR) = 3.5; 95% confidence interval (CI) = 2.3-5.4) and male gender (OR=2.5; 95% CI=1.5-4.1) were major independent risk factors for stricture formation.

Conclusion: Our data, collected from the largest long-term follow-up study thus far, demonstrated that the natural course of EoE progresses from feeding difficulties and inflammatory endoscopic features in young children towards dysphagia, food impaction and fibrotic endoscopic features in adults. Additionally, we demonstrated that prolonged untreated disease leads to esophageal stricture formation, and is associated with an increased risk of food impactions requiring endoscopic bolus dislodgement. These findings suggest that effective treatment of esophageal inflammation is essential and based on our results we encourage the use of chronic maintenance therapy in EoE.

## Duodenal mucosal resurfacing elicits improvement in glycemic and hepatic parameters in type 2 diabetes: complete 1 year results from the first multicenter study

*A.C.G. van Baar[1, 2], M. Nieuwdorp[3], F. Holleman[4], J. Deviere[5], L. Crenier[6], R. Haidry[7], R. Batterham[8], L. Rodriguez Grunert[9], M. Galvao Neto[10], P. Vignolo[9], G. Costamagna[11], J.J.G.H.M Bergman[1]. [1]Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. The Netherlands. [3]Internal and Vascular Medicine, Academic Medical Center, Amsterdam, The Netherlands. [4]Internal Medicine, Academic Medical Center, Amsterdam, The Netherlands. [5]Gastroenterology, Erasme University Hospital, Brussels, Belgium. [6]Endocrinology, Erasme University Hospital, Brussels, Belgium. [7]Gastroenterology, University College Hospital, London, United Kingdom. [8]Center for Obesity Research, Dept. of Medicine, University College Hospital, London, United Kingdom. [9]CCO Clinical Center for Diabetes, Obesity and Reflux, Santiago, Chile. Florida International University, Miami, [10]Bariatric Endoscopy Service, Gastro Obeso Center, Sao Paulo, Brazil. [11]Digestive Endoscopy, Policlinico Gemelli, Catholic University of Rome, Rome, Italy.*

Introduction: Abnormalities in duodenal mucosa, nutrient absorption and enteroendocrine cells are thought to play a pathophysiological role in the development of insulin resistance in type 2 diabetes (T2D) patients. Duodenal exclusion via bariatric surgery confers an insulin sensitizing metabolic benefit, partially weight-independent. Duodenal Mucosal Resurfacing (DMR) is an endoscopic procedure that resurfaces duodenal mucosa through hydrothermal ablation and may confer similar metabolic benefits using a less invasive procedure. We report the 12 month efficacy data of the first multicenter study involving DMR.

Methods: We conducted a single arm, open label, multicenter study in which T2D patients (HbA1c 7.5-10.0%; age 25-75y; BMI 24-40kg/m$^2$; oral glucose lowering medication) received a single DMR procedure. DMR consists of balloon catheter based circumferential mucosal lifting followed by hydrothermal ablation. Glucose lowering medication was kept stable for ≥6mo post DMR but could be adjusted according to care guidelines thereafter. Efficacy was assessed by analyzing HbA1c, fasting plasma glucose (FPG), Homeostasis Model Assessment index (HOMA-IR), hepatic transaminases and weight up to 12mo post DMR compared to baseline (Δ) in the whole cohort and in the ample β-cell reserve (fasting plasma insulin [FPI] >15uU/ml) subgroup using repeated measures ANOVA Bonferroni correction and correction for 3mo weight loss. Data are mean±SE.

Results: We included 46 subjects (weight 91±2kg; HbA1c 8.6±0.1%; FPG 196±7 mg/dL; HOMA-IR 7.87±0.8). ΔHbA1c was -1.3±0.2 (p=0.007) and -1.0±0.2% (p=0.008) at 9 and 12mo. ΔFPG was -40±11 (p=0.016) and -41±10 mg/dL (p=0.007) at 9 and 12mo. 12mo ΔHOMA-IR was -4.0±1.1 (p=0.018). Δ weight was -3.4±0.7 and -3.1±0.8kg (p=0.012) at 3 and 6mo with some rebound at 12mo: -2.1±1.0kg (p=0.43). ΔALT was -10±3 (p=0.024) and -8±3 (p=0.137) at 3 and 12mo. ΔAST was -5±2 (p=0.053) and -5±2 U/L (p=0.058) at 9 and 12mo. 12mo changes in the ample β-cell reserve subgroup (n=19) were ΔHbA1c -1.4±0.4%, ΔFPG -48±9 mg/dL, ΔHOMA-IR -6.2±1.0. In the tertile subjects with highest transaminases at baseline 12mo ΔALT was -21±7U/L and ΔAST -11±2U/L.

Conclusion: Single DMR procedure produced sustained reductions in HbA1c, FPG, and HOMA-IR and observed reductions in transaminase levels up to 12 months, with more evident glycemic effects in patients with preserved β-cell function and more evident hepatic effects in patients with high baseline ALT and AST. A randomized controlled study is planned to further establish efficacy, safety and durability of the metabolic DMR effects and a mechanistic study is being conducted to elucidate the mechanism of action of DMR.

**Body composition and growth in children with intestinal failure receiving long-term parenteral nutrition**

*E. Neelis[1], J. Olieman[2], S. Kouwenhoven[3], M. Tabbers[4], C. Jonkers[5], R. Wijnen[6], E. Rings[1], B. de Koning[1], J. Hulst[1]. [1]Dept. of Pediatric Gastroenterology, Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands. [2]Dept. of Dietetics, Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands. [3]Dept. of Pediatrics, VU Medical Center, Amsterdam, The Netherlands. [4]Dept. of Pediatric Gastroenterology, AMC-Emma Children's Hospital, Amsterdam, The Netherlands. [5]Dept. of Dietetics, AMC-Emma Children's Hospital, Amsterdam, The Netherlands. [6]Dept. of Pediatric Surgery, Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands.*

Background: Current growth monitoring and estimation of nutritional requirements of children with intestinal failure (IF) is mostly based on weight and height parameters. Information about body composition of these children is not widely available. Our aim was to assess body composition of children with IF on long-term parenteral nutrition (PN).
Methods: A cross-sectional study in children with IF who received PN for ≥6 months in 2 centers. Body mass index (BMI), height for age (HFA), weight for age (WFA) and weight for height (WFH) standard deviation scores (SDS) were calculated with Dutch reference data. Body composition was assessed using air displacement plethysmography (BOD POD®, for children >2 years). In contrast to other methods, this method has no large inter-observer variability and material such as the central venous catheter can be calibrated. Percent fat mass (%FM) and absolute fat free mass (FFM) SDS were estimated using Dutch reference values measured with DEXA (available >4 years).
Results: Twenty-two patients underwent body composition measurement at a median age of 7.2 years (range 2.1-16.8); 19 patients were still PN dependent. Median PN duration was 5.4 years (IQR 1.3-8.3). Patients with IF were significantly lighter (median WFA SDS -0.7, p=0.003) and shorter (median HFA SDS -1.3, p<0.001) when compared to the reference population (Table 1). WFH and BMI SDS were not different from the reference population. Ten patients (46%) were growing below their target height range. For 19 patients %FM and FFM SDS could be calculated; patients had significantly more %FM (median %FM SDS 1.4, p<0.001) and less FFM (median FFM SDS -1.7, p<0.001) than the reference population. No significant differences were found according to PN dependency or type of IF. Significant positive correlations were found between FFM SDS and all anthropometric parameters; WFA SDS (Spearman's rho 0.784, p<0.001), HFA SDS (0.584, p=0.009) and BMI SDS (0.558, p=0.013). No significant correlations were found between anthropometric parameters and %FM SDS.
Conclusion: Despite close monitoring of weight and height and follow-up in a multidisciplinary team, children with IF on long term PN show significant abnormalities of body composition with higher FM and lower FFM compared to healthy children. Strikingly, WFH and BMI of these children were normal, suggesting that the use of these frequently used parameters is not valid in assessing fat mass in clinical practice. Further studies should evaluate the effect of a patient tailored approach including nutritional advice based on body composition together with advice regarding physical activity.

## Post-inflammatory polyps do not predict colorectal neoplasia in patients with inflammatory bowel disease: a multinational retrospective cohort study

*R. Mahmoud[1], S.C. Shah[2], J.R. ten Hove[1], J. Torres[3], E. Mooiweer[1], D. Castaneda[2], J. Glass[2], J. Elman[4], A. Kumar[2], J. Axelrad[5], T. Ullman[2], J.F. Colombel[2], B. Oldenburg[1], S.H. Itzkowitz[2]. I.C.C. Initiative on Crohn and Colitis. [1]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands. [2]Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York City, United States of America. [3]Division of Gastroenterology, Hospital Beatriz Ângelo, Loures, Portugal. [4]Dept. of Medicine, Icahn School of Medicine at Mount Sinai, New York City, United States of America. [5]Division of Digestive and Liver Diseases, Columbia University Medical Center, New York City, United States of America.*

Background: Patients with inflammatory bowel disease (IBD) who have post-inflammatory polyps (PIPs) are considered to be at higher risk of colorectal neoplasia (CRN). Using limited evidence from older, case-control studies, European gastroenterological societies proposed increasing the frequency of surveillance colonoscopies in patients with PIPs from every 5 to every 2-3 years in absence of other risk factors. We aimed to define the risk of CRN and colectomy in IBD patients with PIPs in the modern era.

Methods: We conducted a multinational, retrospective cohort study of patients with IBD undergoing CRN surveillance at a tertiary care center in the United States or a consortium of 7 hospitals in the Netherlands between 2000-2015. Eligible patients had confirmed colonic disease duration <u>></u> 8 years (or any duration if concomitant primary sclerosing cholangitis (PSC)), <u>></u>2 surveillance colonoscopies with biopsies, and no prior history of advanced CRN (ACRN; high-grade dysplasia or colorectal cancer) or colectomy. Primary outcomes were occurrence of ACRN, low-grade dysplasia (LGD), indefinite dysplasia (IND) or colectomy according to PIP status (survival analysis). Secondary outcomes were predictors of ACRN (Cox regression analysis) and factors associated with PIPs (multiple logistic regression).

Results: Among 1582 eligible patients, 462 (29.2%) had PIPs. PIPs were associated with more severe histologic inflammation (adjusted odds ratio (aOR) 1.42; 95%CI: 1.23 – 1.64) and greater disease extent (aOR 1.69; 95%CI: 1.21 – 2.36), but lower frequency of PSC (aOR 0.39; 95%CI: 0.27 - 0.56). Presence of PIPs did not predict ACRN (adjusted hazard ratio (aHR) 1.05; 95%CI 0.54 – 2.05), but multivariate regression analysis revealed that ACRN was significantly and independently predicted by PSC (aHR 2.22; 95%CI 1.01 – 4.87), prior IND or LGD (aHR 4.91; 95%CI 2.60 – 9.24), histologic inflammation (aHR 2.34; 95%CI 1.55 – 3.54), disease duration (aHR 1.05; 95%CI 1.01 – 1.08) and caecal intubation during surveillance (aHR 0.09; 95%CI 0.01 – 0.70). During a median follow-up of 4.8 years, time to ACRN (p=0.41), LGD (p=0.97) or IND (p=0.13) was not decreased in patients with PIPs. Subgroup analyses stratified by cohort, presence of PSC, IBD phenotype or prior IND or LGD did not significantly alter these results. Time to colectomy was significantly shorter in patients with PIPs (p=0.01).

Conclusion: PIPs were associated with greater severity and extent of colonic inflammation, and higher rates of colectomy, but did not independently predict the development of CRN. These findings suggest that intervals for CRN surveillance should not be shortened solely based on presence of PIPs.

**Long-term risk of advanced neoplasia after colonic low-grade dysplasia in patients with inflammatory bowel disease: a nationwide cohort study**

*M.E. de Jong[1], S.B. van Tilburg[1], L.H.C. Nissen[2], W. Kievit[1], I.D. Nagtegaal[3], F. Hoentjen[4], L.A.A.P. Derikx[1]. [1]Dept. of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Jeroen Bosch Hospital, 's Hertogenbosch, The Netherlands. [3]Dept. of Pathology, Radboud University Medical Center, Nijmegen, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, The Netherlands.*

Background: Patients with inflammatory bowel disease (IBD) bear an increased colorectal cancer (CRC) risk. This risk is further increased following colonic low-grade dysplasia (LGD). Endoscopic surveillance programs aim to reduce CRC risk by detecting and removing precancerous lesions like LGD. Long-term risk of high-grade dysplasia (HGD) or CRC after LGD is relatively unknown, since most available studies are small and cover a relatively short follow-up period. We established a nationwide cohort of IBD patients with LGD to determine long-term cumulative advanced neoplasia (HGD and/or CRC) incidence, and to identify risk factors for advanced neoplasia development

Methods: All IBD patients with LGD between 1991 and 2005 in the Netherlands were identified using the Dutch National Pathology Registry (PALGA). Follow-up data were collected until January 2016. The cumulative incidence of advanced neoplasia was determined by Kaplan Meier curves, censoring patients at the end of colorectal surveillance or (sub)total colectomy. Risk factors for developing advanced neoplasia were identified with multivariable Cox regression analysis.

Results: We identified 2738 patients with colonic LGD with a median follow-up of 9.5 years (IQR 4.2-13.7) after initial LGD diagnosis (1981 (72.4%) ulcerative colitis, 541 (19.8%) Crohn's disease, 216 (7.9%) indeterminate colitis). 423 (15.5%) Patients underwent (sub)total colectomy. Advanced neoplasia was detected in 397 of 2738 patients, including 240 patients with CRC. The cumulative incidence of advanced neoplasia was 3.5%, 9.1%, 14.4%, 21.9% and 29.9% after 1, 5, 10, 15 and 20 years, respectively (Figure 1). Median time to develop advanced neoplasia after LGD was 4.7 years (IQR 1.3-10.0). Multivariable analyses identified a higher age (<u>></u> 55 years) at initial LGD (hazard ratio (HR) 1.87; 95% confidence interval (CI) 1.53-2.30), an IBD duration > 5 years before LGD (HR 1.46; 95% CI 1.13-1.90) and male gender (HR 1.37; 95% CI 1.10-1.71) as independent risk factors for advanced neoplasia following LGD.

Conclusion: In a large nationwide cohort of IBD patients with LGD with median follow-up of almost 10 years, the cumulative incidence of advanced neoplasia was 21.9% after 15 years. Older age at LGD (<u>></u> 55 years), longer IBD duration (>5 years) before LGD, and male gender were independent risk factors for advanced neoplasia development after initial LGD. These results may aid in risk stratification for endoscopic surveillance after LGD in patients with IBD.

**IgA immune complexes in the lamina propria drive inflammation in the human intestine through metabolic reprogramming of human CD103+ dendritic cells –**
*MLDS voordracht, projectnr. CDG 12-10*

*J. den Dunnen. Academic Medical Center, Amsterdam, The Netherlands.*

In various tissues, recognition of pathogens by immune cells through pathogen-sensing receptors is sufficient for the induction of pro-inflammatory responses. However, in tissues characterized by high presence of commensal microorganisms, such as the gastrointestinal tract, sensing of microorganisms is a steady state phenomenon, and a “second signal” is required to discriminate between homeostatic conditions and infection. Here, we set out to identify these additional signals that triggers inflammation in the human intestine. We provide evidence that in the human intestine the presence of IgA immune complexes, as a result of bacterial opsonization, acts as one of these second danger signals. We show that the presence of IgA immune complexes in the lamina propria converts the intestinal response from tolerogenic to pro-inflammatory through activation of a key subset of human intestinal dendritic cells that express the marker CD103. This pro-inflammatory response is characterized by selective amplification of particular pathogenic pro-inflammatory cytokines such as TNFα, IL-1β, and IL-23, which subsequently promotes T helper 17 responses (counteracting bacteria) and activates type 3 innate lymphoid cells (mediating tissue repair). Mechanistically, we identified that cytokine amplification is mediated by IgA-sensing receptor Fc alpha receptor I (FcαRI) through enhanced gene translation and caspase-1 activation, which critically depends on FcαRI-induced metabolic reprogramming through signaling via kinases Syk, PI3K, and TBK1/IKKε. These data demonstrate that formation of IgA immune complexes in the human lamina propria provides an environmental cue for the conversion of a tolerogenic to an inflammatory response in the intestine. While the physiological function of this phenomenon most likely is to provide protective immunity against invading micro-organisms, the nature of the inflammatory response strongly suggests that this process also constitutively occurs in patients suffering from inflammatory bowel disease (IBD) and celiac disease (CD). Therefore, from a therapeutic point of view, targeting of this pathway may be a valuable approach to attenuate inflammation in IBD and CD.

## Whole-exome sequencing study identifies novel variants in NUDT15 that contribute to thiopurine-induced myelosuppression in Europeans

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Background: Thiopurines are commonly used drugs for inflammatory bowel disease (IBD) but this is limited by myelosuppression in 7% of patients. Thiopurine S-methyltransferase (TPMT) variants only explain 26% of thiopurine-induced myelosuppression (TIM) in Europeans, suggesting the presence of other genetic determinants. Genetic variants in NUDT15 have been identified as risk factor for TIM in Asians, but the impact of NUDT15 genetic variation in Europeans is unknown. We aimed to identify novel variants associated with TIM through a combined genome-wide association study (GWAS) and exome sequencing study.
Methods: We recruited 491 IBD patients with TIM and 742 thiopurine-tolerant IBD controls from 86 hospitals in 6 countries. Inclusion criteria included drug exposure in the 7 days prior to TIM, leukocytes $<2.5x10^9$/L, or neutrophils $<1.0x10^9$/L and that TIM necessitated dose reduction/drug withdrawal. An independent cohort comprising 73 TIM cases and 840 controls, with the exact same inclusion criteria and sequence platform, was used for replication. To asses both common and rare genetic variants we generated both genotype array and exome sequencing data for a total of 2,146 patients, resulting in ~30 million variants.
Results: We first confirmed an association of TIM with TPMT in an initial GWAS. We then, using exome sequencing, discovered a novel 6bp in-frame deletion (rs746071566; AGGAGTC/A, p.Gly17_Val18del) at chromosome 13 in exon 1 of NUDT15 (5.8% of cases, 0.2% of controls OR = 38.2; $P = 1.3 \times 10^{-8}$). We replicated this in the independent cohort (2.7% of cases, 0.2% of controls, OR=11.8, P=0.034). All NUDT15 variants were validated by Sanger sequencing. Multivariable logistic regression demonstrated that weight-adjusted dose (OR=2.2, $P=9.4x10^{-11}$), NUDT15 genotype (OR 21.7, $P=2.8x10^{-8}$) and TPMT genotype (OR 2.2, $P=2.6x10^{-4}$ for MUT/WT and OR 51.2, $P=1.8x10^{-4}$ for MUT/MUT) were independent risk factors for TIM.
Conclusion: We conducted the largest ever clinical and genetic analysis of TIM identifying NUDT15 coding variants, including a novel 6bp deletion; carriage of any coding variant confers a 22-fold increase in the odds of TIM, independent of TPMT genotype and thiopurine dose. Although NUDT15 variants are less common than TPMT variants, their effect size for heterozygotes is greater. The number of patients needed to genotype to prevent TIM due to NUDT15 coding variant heterozygosity is 100. The estimated absolute risk of TIM in NUDT15 heterozygotes is 59%. A future clinical decision tool incorporating NUDT15 and TPMT genotypes will offer personalized thiopurine therapy and prevent the considerable morbidity and costs associated with myelosuppression.

## Using whole exome sequencing to expand the genetic architecture of inflammatory bowel disease

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Crohn's disease (CD) and ulcerative colitis (UC) are debilitating, inflammatory diseases of the gastrointestinal tract, collectively known as the inflammatory bowel diseases (IBD). Among complex diseases, genetics has been particularly successful in IBD, with genome-wide association studies (GWAS) over the past decade defining confirmed association to 250 gene loci. A handful of these associations have led to specific validated functional variants highlighting intracellular response to microbes and regulation of adaptive immunity in the pathogenesis of IBD. For the vast majority, however, the specific implicated gene and causal functional variants have not been identified, limiting near-term insights into pathogenesis and longer-term ability to convert associations into actionable therapeutic hypotheses. This limitation is commonplace – the emerging challenge for human genetics is no longer discovering genetic associations, it is deducing how identified genes and corresponding alleles exert influence on biology in health and disease.

With support from the Helmsley Charitable Trust and partnership with IBD researchers around the world, we launched an exome sequencing initiative in 2014 with a goal to define the full allelic spectrum of protein-altering variation in genes associated to CD and/or UC, assess their role in clinical course and response to therapy, and to determine whether truncating variants confer risk or protection in each IBD gene in order to highlight opportune therapeutic targets. We have completed exomes of 13,000 IBD cases providing a high-resolution view of coding variation at each GWAS hit and demonstrated a convincing excess of rare exome signal. The cases are drawn from individual substudies focusing on isolated populations (Ashkenazi, Finnish, French-Canadian), admixed populations and clinical extremes, each providing unique opportunities for discovery.

Early findings from the effort include novel protective truncating variants, the complete allelic series (including unique founder population alleles), non-additive inheritance models at known genes such as NOD2, overlooked low-frequency coding variants that explain GWAS hits (PRDM1 and ADAM15) and novel alleles for thiopurine-induced myelosuppression. The integration of low frequency and rare functional variants with GWAS is moving us closer to a complete genetic architecture of IBD. Association results for all variants through will be made available to the research community through a web-based exome browser as analyses are completed.

## Tacrolimus suppositories as induction therapy for refractory ulcerative proctitis: a randomized controlled trial

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Background: The treatment of 5-ASA refractory ulcerative proctitis (UP) remains challenging. Previous studies have shown that topical tacrolimus is effective for the treatment of refractory UP. However, the efficacy of tacrolimus as induction therapy compared to topical corticosteroids is unknown.

Methods: We conducted a multicenter double-blind randomized controlled trial in7 hospitals (EUDRACT 2013-001259-11). We randomly allocated adult patients (pts) with refractory UP in a 1:1 ratio, using a sealed envelope method, to either tacrolimus 2mg suppositories OD (TSP) or beclomethasone 3mg suppositories OD (BSP). Primary outcome was combined clinical remission, defined as Colitis Activity Index (CAI) ≤4 and endoscopic remission, defined as Mayo score of 0 after 4 weeks. Secondary outcomes were clinical response defined as a decrease of CAI≥3 from baseline, endoscopic response defined as a decrease in Mayo score ≥1 and/or decrease ≥5cm extend of inflammation, and safety. All analyses were intention to treat. Outcomes were compared using $X^2$ test or Mann-Whitney U test as appropriate.

Results: Between February 2014 and November 2017, 88 pts were included (66% F, mean age 41.8yrs (SD14), median disease duration 7.1 years [IQR 2.8-13.6]). After randomisation, 45 pts received TSP and 43 pts BSP. Concomitant treatments in 53 pts (60%) were comparable for TSP and BSP (5-ASA 17 vs 23; immunomodulators 12 vs 5; biologics 5 vs 4), respectively (p>0.05). Primary outcome was achieved in 6/45 (13.3%) pts receiving TSP vs 6 /43 (13.9%) pts who received BSP(p=0.93). Clinical remission rate at week 4 was similar between the TSP group (53.3%, n=24) and BSP group (58.1% n=25) (p=0.35). Endoscopic remission at week 4 was achieved in 24.4% (n=11) TSP pts vs 13.9% (n=6) BSP pts (p=0.11). Secondary outcome clinical response was achieved in 64.4% (n=29) TSP pts and in 67.4% (n=29) BSP pts (p=0.46). Endoscopic response was seen in 55.6% (n=25) TSP pts vs 58.1% (n=25) BSP pts (p=0.47). Adverse events were reported in 22 (48.8%) TSP pts vs 13 (30.2%) BSP pts (p=0.05). Serious adverse events occurred in 5 pts(3 TSP, p=0.68).

Conclusion: In pts with 5-ASA refractory UP efficacy of topical tacrolimus was not statistically different compared to beclomethasone for inducing combined clinical and endoscopic remission, despite the observation of a higher rate of endoscopic remission after topical TSP. No differences were observed in clinical and endoscopic response rates. Fewer adverse effects were observed in the BSP treated pts. Overall, our results demonstrate that tacrolimus suppositories could be considered as an alternative induction strategy for refractory UP. (ZonMw Grant 836011003)

**Effect of disease duration and location on clinical remission in Crohn's disease patients treated with filgotinib, a selective JAK1 inhibitor: post-hoc analysis from the Phase 2 FITZROY study**

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Introduction: Safety and efficacy of filgotinib (FIL), an oral, selective Janus kinase 1 (JAK1) inhibitor, was evaluated in a 20-week Phase 2 study in patients with active Crohn's disease (CD) (FITZROY). The primary endpoint (CDAI remission at Week 10) was met with an acceptable safety profile. In this post-hoc analysis, the effect of disease duration and location on the primary endpoint was assessed.
Methods: 174 patients with moderate-to-severely active CD (CDAI: 220 - 450) and ulcerations confirmed by centrally read endoscopy were randomized 3:1 to receive 200mg FIL or placebo (PBO) QD for 10 weeks. Immunosuppressants (i.e. azathioprine, methotrexate, 6-mercaptopurine) were discontinued prior to initiation, but corticosteroids remained on a stable dose until Week 10 (W10). Patients were naïve to anti-TNF therapy or previously exposed to anti-TNF with no response or loss-of-response. Clinical remission at W10 was analysed by disease duration (<5 years (y), 5-10y and >10y) and historical location (ileal, ileo-colonic, colonic).
Results: Baseline disease characteristics were similar in both groups (mean CDAI 293, mean SES-CD 14.6, mean CRP 15.6 mg/L, 41% >10mg/L, oral corticosteroids use 51%, mean daily dose 22 mg). Forty-two % of patients were anti-TNF naïve. Forty-three % were diagnosed for less than 5y, 30% between 5 and 10y and 27% for >10y. Most anti-TNF naïve patients (63%) had <5y CD, whereas 71% of anti-TNF non-responders were diagnosed >5 y. Sixty-two % had ileo-colonic disease, 18% only ileal involvement and 20% only colonic involvement. The percentage of FIL-treated patients in clinical remission at W10 was not impacted by longer disease duration (53%, 43% and 43% for <5y, 5-10y and >10y, respectively), while for PBO-treated patients the percentage of remitters was lower in case of longer (i.e. > 10y) disease duration: 24%, 27% and 17% for <5y, 5-10y and >10y, respectively. In FIL-treated patients, higher remission rates in both anti-TNF naïve and (to a lesser extent) anti-TNF non-responders were seen, independent of disease duration (anti-TNF naïve: 59%, 60%, 62%; anti-TNF non-responders: 42%, 37%, 32%, for <5y, 5-10y and >10y, respectively). Clinical remission after FIL treatment was also confirmed across disease locations, although a higher percentage of remitters was observed in the subgroup with colonic disease (FIL: 42%, 41% and 68%, and PBO: 14%, 26% and 17% for ileal, ileo-colonic and colonic disease, respectively).
Conclusion: This post-hoc analysis of the Phase 2 FITZROY study demonstrated that JAK1 inhibition with FIL in CD patients was associated with clinical remission at week 10, independent of disease duration and location.

**Long-Term Drug Survival of Thioguanine in Inflammatory Bowel Disease among Two Real-Life Cohorts**

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Background: Thioguanine (TG), a non-conventional thiopurine, has shown promising therapeutic results in the treatment of inflammatory bowel disease (IBD). Especially in IBD-patients who failed prior conventional thiopurine therapy, TG is a valuable alternative considering its favorable risk profile. Long-term tolerability and safety of TG have been poorly studied. In this study, we aimed to assess the long-term drug survival and clinical outcomes of TG therapy among two real-life cohorts.
Methods: In this two-center retrospective study, IBD-patients treated with TG between January 2001 and June 2017 were identified by hospital pharmacy dispensing records. Success of therapy was defined as clinical remission (based on physician's global assessment, laboratory and endoscopic findings) without corticosteroids, surgical intervention or addition of anti-TNF therapy. Rates and reasons for TG treatment failure, withdrawal or adverse events were collected. Hepatotoxicity was defined as liver enzymes of ≥ 2 the upper limit of normal and myelotoxicity as presence of leucopenia or thrombocytopenia.
Results: In total, 125 patients were included with a median TG treatment duration of 54 months (range: 0-203 months) and a median daily dose of 20 mg (range: 10-40 mg). Of these, 60% was female, 64% had Crohn's disease and 91% had previously failed conventional thiopurines. TG was discontinued in 21 patients (17%) due to intolerance (n = 11), refractoriness (n = 2), maintained remission (n = 3) or other reasons (n = 5). The percentage of patients still using TG at 12, 24, 60 and 120 months was 95%, 93%, 88% and 83%, respectively. Clinical remission was observed in 67% (84/125) of the patients at 6 months TG therapy. Endoscopic remission was revealed in 69% (54/78) at follow-up. Median 6-thio-guanine-nucleotides were higher in the clinical responders (385 [104-962] vs. 257 [125-750] pmol/8×$10^8$ red blood cells, P < 0.05). Hepatotoxicity and myelotoxicity occurred in 16% and 2%, respectively, and were transient in 80% of the cases. Pancreatitis did not reoccur in all patients (n = 14) with prior thiopurine-induced pancreatitis. There were no cases of sympto-matic nodular regenerative hyperplasia (i.e. with clinical or radiological manifestations) in this cohort.
Conclusion: Prolonged TG therapy was well-tolerated and effective as a maintenance treatment for IBD with approximately 80% of patients continuing TG during a median duration of almost 5 years. Pancreatitis, a common adverse event associated with conventional thiopurines, did not (re)occur during TG therapy.

## Drug survival of vedolizumab-treated inflammatory bowel disease patients in a nationwide observational cohort study: case series

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Background: Vedolizumab (VDZ) is a monoclonal antibody blocking the α4β7 integrin. Obtaining clinical response can take up to 3 to 6 months but once obtained seems to be well maintained at least throughout week 52. However, real-life drug survival data beyond week 52 is currently scarce. We therefore aimed to assess the drug survival in our 2 year nationwide observational cohort (Case Series) of VDZ-treated inflammatory bowel disease (IBD) patients.
Methods: IBD patients who started VDZ from October 2014 in 7 university medical centers were included. Patients were followed for 2 years or until VDZ was discontinued using a systematic follow-up according to a pre-defined protocol. We registered clinical disease activity (Harvey Bradshaw Index and Short Clinical Colitis Activity Index (SCCAI)), inflammatory biomarkers (CRP and faecal calprotectin), hospital admissions, surgery, adverse events, and VDZ discontinuation. The mean difference was tested by dependent t-test, a Wilcoxon-signed rank test was used as well.
Results: We enrolled 266 patients: 172 CD (110 female, mean age 39.5±14.4 years, mean disease duration 13.6±10.7 yrs) and 94 UC (41 female, mean age 43.3±16.3 yrs, mean disease duration 10.4±9.2 yrs). 98.8% (CD) and 80.3% (UC) were biological-experienced. At baseline 63.2% of IBD patients used concomitant medication. A total of 121 (45.4%, CD 83, UC 38) IBD patients discontinued VDZ after a median follow-up of 25.7 (IQR 16.6-44.9) weeks for CD and 20.4 (14.9-30.4) weeks for UC. Main reason was primary non-response (71.1%), while adverse events required discontinuation in 5%. Drug survival of VDZ did not differ significantly between CD and UC patients (p=0.49). VDZ discontinuation occurred for 66 IBD patients (CD: 33 no response, 2 adverse events, UC: 22 no response, 1 adverse event) before 26 weeks of treatment. Beyond 52 weeks, 19 (7.1%) IBD patients discontinued VDZ treatment, 17 CD (9 loss of response) and 2 UC (1 loss of response). UC patients who discontinued VDZ due to non-response had less decrease of SCCAI at week 12 compared to those who continued VDZ until end of follow-up (mean decrease in SCCAI (3.4 (±3) vs. 0.5 (3.7) (p=0.001)). While the median treatment duration was 20.4 weeks for UC primary non-responders (IQR 16.9-28.6).
Conclusion: In a real-life IBD cohort, discontinuation rates for VDZ were 24.8% at week 26, 38.3% at week 52, and only 7.1% beyond week 52. The main reason was primary non-response (71.1%) in contrast to adverse events (5%). A decrease in SCCAI at week 12 was predictive of clinical response to VDZ. Our long-term VDZ data show a reassuring drug survival and safety profile beyond 52 weeks in daily clinical practice.

## Ustekinumab for crohn's disease: a nationwide real-life observational cohort study

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Background: Ustekinumab (UST) targets the p40 unit of interleukin-12 and interleukin-23 and is approved for treatment of Crohn's disease (CD). The majority of CD patients included in the registration trials are highly selected patients from referral centers, satisfying strict inclusion/exclusion criteria and following detailed protocols that do not accurately reflect routine care. We therefore designed a nationwide cohort (Case Series) of UST-treated CD patients in the Netherlands in order to systematically assess real-life effectiveness and safety.
Methods: CD patients who started UST from November 2016 in 7 university medical centers were included. We used a predefined follow-up (0-12-24-52-104 weeks) and assessed systematically clinical disease activity (Harvey Bradshaw (HBI), inflammatory biomarkers (C-Reactive protein and faecal calprotectin)), hospital admissions, IBD-related surgery and adverse events. Clinical remission was defined as HBI < 5. Wilcoxon signed-rank test was used.
Results: We enrolled 125 CD patients (82 female, mean age 40.2 ± 13.4 years) with a mean disease duration of 14.1 ± 9.9 years. At baseline 67 (53.6%) had a history of IBD-related surgery, 124 (99.2%) had failed at least one biological and 61 (48.8%) had used vedolizumab. 32 (25.6%) patients had stricturing disease, 14 (11.2%) penetrating disease, and 23 (18.4%) perianal disease. Concomitant medication at baseline included corticosteroids (n=24), immunosuppressants (thiopurines or methotrexate, IMM, n=24) and 8 used the combination. The median follow-up was 17.1 (IQR: 8-24) weeks. After 12 weeks of treatment, disease activity (HBI) decreased by median 8 (IQR: 4-12) vs. 5 (2-9) p<0.001 and biochemical markers (CRP: median 11 (IQR 4-25) vs. 5 (1-13) p<0.001, faecal calprotectin median 598 (IQR 275-1607) vs. 393 (142-393) p=0.002). At week 24, 43.6% was in clinical remission (Median HBI: 4.5 (IQR 2-7)) with a median CRP of 3 (2-11), 70.1% of subjects had the injection interval every 8 weeks or less. No anti-drug antibodies were detected in 29 (23.2%) patients who underwent pharmacokinetic evaluation. UST was discontinued in 17.6% of the subjects after a median treatment duration of 18.8 (IQR: 13-25.5) weeks, 77.3% due to primary non-response and 9.1% due to adverse events including one infusion reaction. Four severe infections requiring hospital admission were reported.
Conclusion: Our nation-wide real-life data on UST showed that 43.6% of CD patients were in clinical remission after 24 weeks accompanied by a reduction in inflammatory markers. Two serious adverse events required discontinuation of therapy and 4 severe infections resulting in hospital admission were reported.

**Use of Compplementary and Alternative Medicine use does not influence adherence to regular IBD medication**

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Background: Many IBD patients use Complementary and Alternative Medicine (CAM). Recently, concerns have been raised on the adherence to conventional medicine in CAM users. For the present study, we aimed to study 1. the prevalence of CAM use, 2. patients' characteristics associated with CAM use, 3. the effect of CAM use on adherence to regular IBD medication, and comparing this to adherence to CAM-products (if used), 4. the relationship between disability and use of CAM.
Methods: This cross-sectional survey studied the current use of CAM for IBD in the patient panel of the Dutch IBD patient organisation CCUVN. This panel consisted of 1813 volunteers. The survey included questions concerning the use of three CAM categories (Products, Health-providers and Actions/Activities), the adherence to CAM-Products and conventional medicine (if used). Additionally, IBD status (scored 1-10), general health status (1-10) subjective disability (using questions inspired by the IBD-Disk) and socio-demographic information were assessed.
Results: 549 (30.3%) participants completed the survey, of which 545 were included. Of the responders, 61.7% currently use CAM for their IBD. 42,5% of responders used products (e.g. supplements), 37.4% used actions (sports, diet) and 17.6% visited a health provider. CAM users were younger (mean age 49.0 vs 54.8 years, p=<0.01) and more often female (76.7% vs 60.6%, p=<0.001); financial situation did not affect CAM use. CAM users rated the state of their IBD (7.10/10 vs 7.47/10 p=0.036) and general health (6.60/10 vs 6.95/10 p=0.019) lower than non-users, and had a higher degree of disability in all fields except 'others'. No significance difference was found concerning adherence to conventional medicine between the CAM-users and non-users. Additionally, CAM-users conveyed a higher subjective dependency on their conventional medicine than non-users. Finally, participants using both products and conventional medicine felt more adherent, knowledgeable and dependent concerning their conventional medicine compared to their products.
Conclusions: More than 60% of the studied population used CAM for their IBD. CAM use is highest in females and younger age. CAM users showed high levels of disability. In this study, no significant relationship was found between CAM use and a lower adherence to conventional medicine. Instead, those using both conventional medicine and products showed to be more adherent, knowledgeable and subjectively dependent on conventional medicine than on CAM-products. Our findings do not support the hypothesis that CAM use is a marker for low adherence to conventional medication.

## Clinical feasibility of dried blood sampling for infliximab in IBD-patients

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Background: Therapeutic drug monitoring (TDM) is important to optimize outcome of infliximab (IFX) treatment in inflammatory bowel disease (IBD). Dried blood spot (DBS) sampling using capillary blood obtained via a finger prick could facilitate TDM, since patients can administer this finger prick themselves at any time and away from the hospital. We investigated the predictive performance and the feasibility of DBS for measuring IFX concentrations in IBD patients.
Methods: We studied 40 adult IBD patients receiving IFX therapy according to standard guidelines. From each patient blood was obtained simultaneously via venepuncture and DBS via finger prick by a trained employee at 3 different timepoints (trough, peak, 3-5 weeks after infusion). One week before IFX infusion (timepoint 4), patients performed DBS at home and the sample was directly sent to Sanquin laboratories, Amsterdam, The Netherlands. The corresponding serum concentration for this time point was estimated using Bayesian pharmacokinetic analysis. Capillary blood was obtained by a microsampling device developed by Neoteryx™. Hematocrit (Hct) values of each individual patient were used to convert DBS eluate results to values which can be compared to (venous) serum concentrations. Spearman's correlation coefficient was used to assess correlation and bias was calculated.
Results: Forty IBD patients were included with median [interquartile range] age: 41 [32-50], albumin: 43 mg/L [41-45], and CRP: 1.3 mg/L [0.4-4.4]. IFX concentrations obtained from the DBS method correlated strongly with serum results from the same patient for IFX trough- and mid-interval concentrations (Spearman correlation coefficient >0.88) and moderately for IFX peak concentrations (Spearman correlation coefficient = 0.69). IFX serum concentrations from the DBS performed at home showed strong correlation with the concentrations obtained by Bayesian analysis (Spearman correlation coefficient = 0.71). No structural bias was shown.
Conclusion: DBS via finger prick can be used for the assessment of serum IFX concentrations. More importantly, we showed the feasibility of using DBS via finger prick at home. This method greatly facilitates the use of TDM in the treatment of IBD patients using IFX.

## Dutch translation and validation of the IBD-control: a questionnaire to assess patient-reported disease control in IBD patients.

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Background: Patient-reported outcome measures (PROMs) are promising tools in inflammatory bowel disease (IBD) care. Nevertheless, the use of PROMs is not widespread in daily practice, which suggests a lack of efficiency and clinical relevance. The 'IBD-control', a short IBD-specific questionnaire measuring disease control from the patient's perspective, was successfully validated and implemented in clinical practice in the United Kingdom and is recommended by the International Consortium for Health Outcomes Measurement (ICHOM). In this study, we aimed to translate and validate the Dutch version of the IBD-control in IB-DREAM, a prospective multicenter registry of IBD patients.
Methods: The IBD-control comprises 13 categorical items and a visual analogue scale (VAS 0-100). It was forward-backward translated into Dutch by bilingual translators. Subsequently, acceptability and lack of ambiguity was tested in a pilot patient group (n=5). Prospective validation was performed using IB-DREAM, a prospective online IBD registry which is currently used in 5 IBD centers in The Netherlands. At baseline we assessed prospectively the IBD-control, short IBDQ, Short Form-36 (SF-36) and clinician assessment by Harvey-Bradshaw Index(HBI) or Simple Clinical Colitis Activity Index(SCCAI) and Physician Global Assessment(PGA). Reliability was measured by test-retest (2 week repeat).
Results: 384 patients with Crohn's disease (CD) and 110 patients with ulcerative colitis (UC) completed the questionnaires. Mean age was 41.5 years (SD<u>+</u>15 years) for CD and 43.7 years(<u>+</u>16) for UC. Mean HBI and SCCAI scores were 3.0(<u>+</u>4.1) and 2.3(<u>+</u>2.5), respectively. Internal consistency (Cronbach's alpha) for the subset of 8 items (IBD-control-8) was 0.81. Correlation between IBD-control-8 score and the IBD-control VAS score was high (Spearman's rho= 0.66). Construct validity analyses showed moderate to strong correlations between the IBD-control-8 score and the other instruments: short IBDQ (r= 0.81), HBI (r= -0.62), SCCAI (r= -0.54), PGA (r=-0.55), SF-36 physical component (r=0.62) and mental component(r= 0.52). Test-retest reliability was high with an intraclass correlation coefficient for the IBD-control-8 score of 0.96 and for IBD-control-VAS score of 0.92 (n=34). Mean IBD-control-8 scores differed (ANOVA, p<0.001) between the following PGA categories: remission (13.1<u>+</u>3.2, n=207), mild (10.0<u>+</u>4.0, n=84) and moderate/severe (5.5<u>+</u>3.5, n=40).
Conclusion: The Dutch version of the IBD-control is a short, reliable and valid instrument for measuring IBD disease control from a patient's perspective. The reliability and user-friendliness make IBD-control a promising tool for Dutch clinical IBD practice.

**The direct healthcare costs of Crohn's disease increased over the last two decades in a Dutch population-based cohort study**

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Background: Due to the widespread use of biologicals, medication replaced hospitalisation as major cost driver in Crohn's Disease (CD). Whether the use of biologicals merely led to a shift of costs, or also to changes in total costs is unclear. Therefore, we aimed to assess direct costs of CD over the past two decades within the population-based IBD South Limburg (IBDSL) cohort.
Methods: CD patients registered in the IBDSL cohort with ≥ 1 year of follow-up were included. Three eras were distinguished based on year of diagnosis: '91–'98, '99–'05 and '06–'11. Patients were followed up to 5 years from diagnosis, till end of follow-up or end of data collection (2014). Resource utilization (i.e. hospitalisation, surgery, diagnostics and medication) was assessed by scrutinizing patient files. Cost estimates were calculated in Euro (€) by multiplying resource use with Dutch reference prices for the corresponding era. Prices were corrected for inflation using consumer price indices. Differences between eras were analysed by one-way ANOVA and Tukey's HSD for post-hoc analysis. Cost differences between years of follow-up were analysed by paired samples t-tests. Log-transformation was used to correct for skewed data.
Results: In total, 1108 CD patients were included and 786 (277 in era '91–'98, 345 in era '99–'05 and 164 in era '06–'11) completed the five-year follow-up. For each separate era, costs were higher in the first year compared to the subsequent years (all $p<0.001$). After year 1, costs remained relatively stable, but were higher for each consecutive era ($p<0.001$). Mean total costs in the first year were € 5,915, € 6,658 and € 6,027 for era '91-'98, '99-'05 and era '06-'11, respectively, and were not significantly different from each other. Three years from diagnosis and onwards, significant differences in mean cumulative total costs (CTCs) were found between the eras. Post-hoc analysis showed significant increases in mean CTCs between the first and the other two eras, but not between the second and third era. Mean CTCs after 5 years were € 12,688, € 19,447 and € 24,191 for era '91–'98, '99–'05 and '06–'11 respectively. Mean costs per year (calculated over 5 years follow-up) were € 2,538, € 3,889 and € 4,838, for the consecutive eras. Median CTCs were substantially lower than mean CTCs, confirming the skewness of our cost data.
Conclusion: In this population-based study, direct healthcare costs after the first year were higher for each consecutive era, leading to an increase in total CD-related direct costs over time. Studies assessing whether this increase is compensated by a decrease in indirect costs (e.g. decreased work disability) are warranted.

**Home-based Vedolizumab infusions: A suitable alternative to routine hospital infusions**

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Objective: Vedolizumab maintenance treatment for patients with inflammatory bowel disease (IBD) consists of intravenous infusions that are often given at 8-week intervals in an outpatient setting in the hospital. We aimed to evaluate whether home-based infusions offer a useful and safe alternative for the care of IBD patients.
Methods: Adult IBD patients receiving Vedolizumab maintenance treatment were invited to receive infusions at home for the duration of 1 year. Inclusion criteria were clinical remission and the absence of adverse events during all previous infusions. During this year, patients received 5 infusions at home and 2 infusions at the hospital, with a 6-month interval between the 2 hospital infusions. Patient satisfaction and costs were analysed and compared with hospital-based infusions.
Results: A total of 17 (65%) of 26 invited patients participated. Mean age of patients was 49 years, 53% of patients were female and 11 patients (65%) had ulcerative colitis. Eight patients (47%) did not work full-time. One patient had an allergic reaction after infusion 5 and was withdrawn. Regarding average patient satisfaction on a scale of 1-10, no difference was found between home infusions (9.1) and hospital infusions (8.6).
Before starting this project 83% of patients (completely) agreed with the statement that they expected to save time with home infusions. Afterwards this percentage remained unchanged. Patients were also asked if they expected home infusions to be satisfying. Beforehand, 88% (completely) agreed with this statement. Afterwards, 93% (completely) agreed. All patients (completely) agreed that home infusions were easy to receive and that there was sufficient support present. A significant difference (p=0.02) was found in average reported missed hours of work when comparing home infusions (mean 1.6 hours, median 0.2) to hospital infusions (mean 2.1 hours, median 1). The self-reported costs for home infusions were significantly (p=0.000) lower (€0,32; median €0,00) than hospital infusions (€11,06; median €8,73). Healthcare costs for home care were €1400 for 5 infusions, including medication delivery at home. Hospital infusions cost €300 each time. This leads to a saving of €100 per patient per year.
Conclusion: Home-based Vedolizumab infusions are a safe alternative for hospital infusions. Satisfaction was the same for home-care and hospital infusions. Patient expectations for satisfaction and time-efficiency were met or exceeded. Home infusions significantly reduces sick leave from work by patients and the self-reported expenses are lower for the individual patient. General healthcare costs are also lower in the home-care setting.

**A first pregnancy seems associated with a positive effect on the course of Inflammatory Bowel Disease: Data from a prospective pregnancy cohort**

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Background: The effect of pregnancy on the course of inflammatory bowel disease (IBD) remains controversial. Data is limited and inconsistent. In order to gain insight into the disease course before and after a first pregnancy in patients with IBD, we investigated the number of relapses.
Methods: We analyzed data from our ongoing prospectively followed-up pregnancy cohort, obtained pre-, during and post-pregnancy. Only patients with a minimal follow-up of 7 yrs (4 yrs before pregnancy to 3 after) were included, to exclude short term effects of the intensive follow-up of patients at the pre-conception clinic. Relapse was defined as endoscopic SES-CD score of ≥ 7 (CD) or Mayo score ≥ 2 (UC) and/or fecal calprotectin >200 µg/g, medication adjustment and/or resections due to exacerbation of disease. Statistical analysis was performed using Wilcoxon signed test. Possible factors associated with a higher relapse rate after delivery (disease activity during pregnancy, maternal age, smoking before/during and after pregnancy, prepregnancy BMI, mode of delivery, thiopurine and/or biological use during pregnancy, breastfeeding, IBD diagnosis) were compared using Mann Whitney U tests for continuous data and Chi-square tests for categorical data.
Results: Sixty-five primigravida patients (46 Crohn's Disease [CD; 71%] and 19 Ulcerative Colitis [UC; 29%]) were included. Age and mean disease duration at conception were 30 yrs (0.6, SD) and 8 yrs (0.6, SD). All 65 pregnancies resulted in live birth. Seven patients (11%) had a new relapse during pregnancy. A drastic decrease in relapses was observed in the years prior to pregnancy, with a small increase directly after delivery. Overall, the mean number of relapses/person/year was 0.41+/-0.06 and 0.28+/-0.05 respectively before and after pregnancy (p=.037). This significant decrease in relapses was only seen for CD patients (N=46, 0.35+/-0.06 before and 0.24+/-0.06 after delivery, p=.021). In the post-partum period more UC patients seemed to have a relapse compared to CD patients (68% vs 39%, p=.032).
Conclusions: In this prospective observational cohort study, we found a lower rate of relapses in the 3 years after a first pregnancy compared to the 4 years before delivery. Post-partum, UC patients are more likely to experience a elapse compared to CD patients. We speculate that pre-conception care reduces the number of relapses.In order to perform logistic regression and determine all possible factors associated with relapse after delivery, more patients need to be included in this study.

**Does mucosal inflammation drive recurrence of PSC in liver transplant recipients with Ulcerative Colitis?**

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Primary Sclerosing Cholangitis (PSC) is a progressive fibroinflammatory disease of the biliary tract. PSC is in 70-80% of the patients associated with a form of IBD, mostly ulcerative colitis (UC). A liver transplantation (LT) remains the only effective treatment for PSC as no disease-modifying treatment is available. After transplant, PSC recurrence (rPSC) occurs in 11-25% of patients. UC is a risk factor for rPSC, and this effect may be attenuated by colectomy but the mechanism behind this effect is unclear. This study primarily aimed to assess whether mucosal inflammation is a risk factor for developing rPSC. In addition, other patient-and graft-related risk factors were studied.

In this retrospective cohort study, all UC and non-IBD patients that underwent LT for PSC in the participating hospitals were included. Follow-up started at transplantation and ended at death, rPSC or graft failure due to other causes. The following risk factors were assessed: presence of UC, degree of colonic mucosal inflammation, cytomegalovirus (CMV) infections, recipient age at transplant, gender, gender mismatch and age difference between donor and recipient, rejection, non-heart-beating procedures, (timing of) colectomy, cholangiocarcinoma prior to transplant and type of immunosuppressant used. The histological Geboes score was used for assessment of colonic mucosal inflammation. Subsequent Geboes scores were analysed using a Time-Dependent Covariate, which allows for changing scores during follow up. Right- and left-sided inflammation was analysed separately, and the highest score was analysed.

In total 81 patients were included, of which 62 (76.5%) were diagnosed with UC. Seventeen patients (21.0%) developed rPSC during a median follow-up time of 5.2 years. In a subset of 42 patients ( 11 patients with rPSC) colon biopsies were available for analysis of Geboes scores. In this population, no association was found between the degree of mucosal inflammation and rPSC, using both original Geboes scores and a cut-off point of 3. In the full cohort of 81 patients, CMV infections post-LT (HR: 4.576, 95% CI 1.688-12.403) and younger receiver age (age at LT: (HR: 0.934, 95% CI 0.881-0.990)) were independently associated with an increased risk of rPSC, whereas a NHB procedure was not ( HR: 4.258, 95% CI 0.989-18.329, p=0.052). In univariate analysis, rPSC increased the risk for graft loss (HR: 6.4 95% CI 2.122-19.906, p= 0.001)

In this multicenter retrospective cohort study, no association was found between degree of histological inflammation and occurrence of rPSC. Both a CMV infection post-LT and a younger receiver age at LT are associated with an increased risk of rPSC.

**Persistent mesorectal inflammatory activity is associated with complications after proctectomy in Crohn's Disease**

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Background: Rectal resection in inflammatory bowel disease (IBD) is frequently complicated by disturbed perineal wound healing. Close rectal dissection, where the mesorectum remains in situ, is hypothesized to reduce complications by minimizing dead space compared to total mesorectal excision. The aim of this study was to analyse postoperative outcomes of both techniques in ulcerative colitis and Crohn's disease. In addition, immune-activity in mesorectal tissue was assessed.
Methods: Perineal complications and healing were retrospectively assessed in a consecutive series of 74 IBD patients undergoing proctectomy using close rectal dissection or total mesorectal excision. Mesorectal tissue of 15 patients was analysed by FACS, immunofluorescence and in situ hybridisation. Based on the combined clinical and in vitro findings, a novel surgical approach for Crohn's patients with disturbed perineal healing after proctectomy was developed and assessed in a case series of 8 patients.
Results: In Crohn's disease, perineal complications were more frequent after close rectal dissection than after total mesorectal excision (59.5% versus 17.6%;p=0.007) with lower healing rates (51.4% versus 88.2%;p=0.014). No significant differences were observed in ulcerative colitis. Compared to ulcerative colitis as well as non-IBD controls, the mesorectal tissue of Crohn's disease patients contained enhanced numbers of macrophages with a pro-inflammatory phenotype, including high expression of CD14, production of TNF-alpha and decreased expression of the wound healing associated marker CD206. As these results suggest a pro-inflammatory status of the mesorectum in Crohn's disease, mesorectal excision with omentoplasty was performed in 8 patients with persistent presacral abscess after close rectal dissection. This procedure resulted in complete perineal wound closure in 6/8 patients and partial closure in the remaining 2 patients. Evaluation of the mesorectal tissue indeed showed ongoing inflammatory characteristics despite prior removal of the affected bowel in these patients.
Conclusion:In Crohn's disease, close rectal dissection resulted in increased numbers of perineal complications, associated with a pro-inflammatory immune status of the mesorectal tissue. Excision of this pro-inflammatory mesenteric tissue resulted in strong improvement in perineal healing rates.

**Ultrasound for assessing disease activity in ulcerative colitis: development of a novel ultrasonographic disease activity index**

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Introduction: Trans-abdominal ultrasound (US) is useful for detection of inflammation in ulcerative colitis (UC) patients. Up to now, no validated disease severity index exists. We aimed to develop an ultrasonographic activity index using endoscopy as reference standard.
Methods: UC patients undergoing endoscopy in standard care were eligible for inclusion. US was performed within 3 weeks from endoscopy without treatment change. Endoscopists and ultrasonographers were blinded for the other examination. The recorded US parameters included bowel wall thickness (BWT), Doppler signal (DS), colonic haustrations, wall layer stratification (WLS) fatty wrapping and presence of reactive lymph nodes. DS was categorized as absent, small spots or large spots/stretches. Disease activity was categorized according to the endoscopic Mayo score. US and endoscopic findings were compared for each colon segment except for the rectum. Normally distributed parameters were compared with unpaired T-tests. Categorical parameters were compared with logistic regression. ROC curves were made to determine optimal cutoff values for BWT. The most predictive parameters and cutoff values were used to construct a point based UC-US index. The index was calculated for each patient and compared with the overall Mayo score using the Spearman's rank correlation test.
Results: Sixty patients were included and 208 colon segments were endoscopically explored. Mean BWT was significantly different between all Mayo categories, except for Mayo 2 vs 3. BWT > 2.1 mm was best to discriminate between Mayo 0 and Mayo 1-3 (Sens 83.5%; Spec 91.5% ), a cutoff of 3.2 mm was best to discriminate between Mayo 0-1 and Mayo 2-3 (Sens 93.5%; Spec 91.8%) and BWT >3.9mm was best for detection of Mayo 3 (Sens 86.2;%; Spec 82.7%). DS was predictive for active (i.e. ≥ Mayo 1) disease (OR 25.1; 95%CI 10.5-60.2). Large spots/stretches of DS were associated with Mayo 2-3 (OR 48.6; 95%CI 11.0-214.8). Loss of haustrations was associated with active disease but did not discriminate between Mayo categories (OR 144.0; 95%CI 41.1-504.1). Presence of fatty wrapping was associated with severe disease (OR 39.6; 95%CI 6.7-233.3). The UC-US score was calculated for each patient by adding points for BWT (1-3), DS (1-2), loss of haustrations (1) and presence of fatty wrapping (1). The global UC-US score showed high correlation with overall endoscopic disease activity (Þ = 0.844; p<0.001).
Conclusions: An ultrasonographic UC disease activity index was developed that showed excellent correlation with endoscopic disease activity. This index needs to be validated in future prospective studies and tested for sensitivity to change.

## High prevalence of severe liver fibrosis in patients with longstanding IBD

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Increased occurrence of NAFLD is observed in patients with IBD. Age, obesity, insulin resistance and other metabolic conditions are common risk factors, but recent data also point to IBD related factors such as disease activity, duration, steroid use and prior surgical intervention, in the development of NAFLD. Overall, chronic inflammation, impaired intestinal barrier function and microbial disturbances could play an important role in both IBD and NAFLD pathogenesis. NAFLD is associated with a worse prognosis due to occurrence of cardiovascular events, especially when severe liver fibrosis is present. Recent data also suggest a relation between severe liver fibrosis and IBD. Consecutive IBD patients were evaluated. Data was collected by questionnaires (Harvey-Bradshaw index, partial mayo score, Mediterranean Diet Score), laboratory (HbA1C, CRP, liver enzymes and fecal calprotectin) and physical examination. A fibroscan® was used to assess steatosis and fibrosis, whereby CAP in d/Bm was used as measurement of steatosis and liver stiffness in kPa for fibrosis. 84 patients were included, mean age 44yrs and 44 patients had Crohn's disease (52% of patients). NAFLD (CAP>247 d/Bm) was found in 35 (42%) patients, of which 18 (21%) had relevant NAFLD (CAP >279 d/Bm). Relevant Fibrosis (≥F2) was seen in 16 (19%) patients and 7 (8%) patients had severe fibrosis (≥F3/F4). Patients with relevant NAFLD had significantly higher waist-hip ratio (0.87 versus 0.83, p=0.046), higher ALAT (36.72 U/L versus 17.51 U/L, p=0.036) and more fibrosis (7.50 kPa versus 4.83 kPa, p=0.020) than IBD patients without NAFLD. Patients with severe fibrosis and IBD more often had surgery (5 versus 2, p=0.047), a longer disease duration (26yrs versus 15yrs, p=0.026), higher waist circumference (98cm versus 87cm, p=0.013), higher hip circumference (111cm versus 103cm, p=0.013), higher body mass index (27.66kg/$m^2$ versus 24.69kg/$m^2$, p=0.001), lower fecal calprotectin (42.17µg/g versus 352.48µg/g, p=0.000) and more mesalazine use in the past (6 versus 1, p=0.048) than IBD patients without severe fibrosis. No multivariate analysis was done due to too small numbers. This prospective IBD cohort demonstrated a NAFLD prevalence comparable to the general population, but a high prevalence of severe fibrosis ( 8%; ≥F3/F4). Duration of IBD and intestinal surgery, which can be considered a marker for more severe IBD, were related to the presence of severe fibrosis, in addition to markers related to the metabolic syndrome. These data suggest a need for active control of liver health in patients with longstanding severe IBD.

## Vedolizumab versus ustekinumab for crohn's disease: comparative effectiveness in a real-life observational cohort study

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Background: The anti-adhesion antibody vedolizumab (VDZ) and the interleukin inhibitor ustekinumab (UST) can both be considered for Crohn's disease (CD) when conventional and anti-TNF medication fail. However, head to head trials are not available and methodological issues limit the indirect comparison based on the registration studies. Propensity-score matching allows for reducing the effects of treatment-selection bias or confounding using observational data when estimating the effects of treatments. Therefore, our aim was to compare VDZ and UST treated CD patients in a systematic observational cohort, the Case Series.
Methods: CD patients who received either VDZ or UST in standard care were followed using predefined follow-up visits (0-12-24-52-104 weeks) while documenting CD characteristics, clinical disease activity (Harvey Bradshaw Index (HBI)), inflammatory markers (CRP, faecal calprotectin), hospital admissions, CD related surgery and adverse events. Clinical remission was defined as HBI <5. To compare the treatments, we excluded patients with a history of both studied treatments and used propensity score analysis to match while correcting for hospital of admission, gender, disease duration, location and behaviour, prior CD and peri-anal surgery, and number of failed biologicals. The mean difference was tested with a dependent t-test, $chi^2$ test was used.
Results: Out of 172 VDZ and 125 UST patients we matched 42 patients starting VDZ with 42 starting UST. Baseline characteristics were comparable (66.7% female, mean age 39.9±13.6 yrs., mean disease duration 14.1 ± 9.8 yrs., 98.8% biological experienced, 53.6% IBD surgery, 21.4% perianal surgery, 29.8% structuring and 16.7% penetrating disease, 17.9% perianal disease, mean HBI at baseline 8.4±5.4) except for number of patients with concomitant medication at baseline (VDZ 32 vs. UST 22 p=0.02). Reduction of HBI was significant for both VDZ and UST after 12 weeks but did not further decrease beyond 12 weeks (week 12: VDZ mean HBI -2.9 (± 5.1) p=0.002, UST -4.2 (5.6) p<0.001). The mean difference of HBI decrease between VDZ and UST at week 12 (p=0.346) and 24 did not differ (mean -3.9 VDZ (± 6.0) vs. -4.6 UST (6.5) p=0.72). After 24 weeks, 46.2% VDZ and 57.9% UST patients were in corticosteroid-free clinical remission (p=0.44). The rate of adverse events was comparable.
Conclusion: Our ongoing nationwide cohort of VDZ and UST-treated patients demonstrated high rates of clinical corticosteroid-free remission after 24 weeks (VDZ 46.2%, UST 57.9%). Propensity-score matching demonstrated that clinical remission and adverse events were comparable between treatments after 24 weeks.

**Commonly used medication is associated with the composition and function of the gut microbiota**

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Introduction: In the recent years, there has been an increasing interest in understanding the role of the gut microbiota in human health. Commonly used medication such as proton pump inhibitors (PPIs) and antibiotics have shown to disturb the microbial gut composition and as a consequence, increase the risk for infections and other health complications. In this study, we show the impact of commonly used medication on the composition of the gut microbiota and its functional changes.
Methods: We collected microbiome data from three shotgun metagenomics sequenced cohorts: 1.patients with inflammatory bowel diseases (n=454) 2.case-control irritable bowel syndrome cohort (n=289) and 3.a population based cohort (n=1140). Fecal samples were collected and DNA was isolated using the same standardized procedures. Microbial composition characterization and functional profiling were performed using MetaPhlAn2 and HUMAnN2 tools. Associations between medication use and microbial signatures were studied using non-zero inflated linear models. Information about sex, age, BMI, sequencing Dept.h and use of 41 different medications groups were used as covariates in our analyses. Subsequently, results obtained per cohort were meta-analyzed. The heterogeneity Cochran's-Q test was performed to identify results driven by a single cohort. To account for multiple testing, we used a false discovery rate <5% to declare significance.
Results: In concordance with previous studies, participants using PPIs had an increased relative abundance of Streptococcus species and a decrease in Bifidobacterium longum abundance. In addition, participants who use beta-blockers had an increased abundance of the glycolytic bacteria Bacteroides uniformis, while laxative users had a decreased abundance of Coprococcus catus and an increased abundance of Alistipes indistinctus. Changes in the host metabolism induced by medication also affected bacterial pathways, the use of metformin was associated with an enrichment of bacterial pathways involved in carbohydrates and amino acid metabolism. The use of vitamin K antagonists was associated with a decrease in pathways involved in vitamin and carbohydrate biosynthesis. Moreover, methanogenic bacterial pathways were increased in oral steroids supplementation users.
Conclusion: In the present study, 16 different medication groups were associated with changes in composition and function of the gut microbiota, with PPIs, metformin, antibiotics and laxatives having the largest impact. Together these results improve current knowledge on the pharmacodynamics of certain types of medication and provide the basis for further investigation and correction of side-effects

**Macrophage IL10 signaling is required for the therapeutic effect of anti-TNFa therapy in IBD**

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Background: Interleukin(IL)10 is an important anti-inflammatory cytokine for the maintainance of gut homeostasis. Defects in the IL10 signalling pathway in macrophages leads to disregulation of regulatory (M2) type macrophages and subsequent inflammatory bowel disease (IBD). IBD patients are frequently succesfully treated with anti-TNFα antibody therapy, although not all patients are responsive.
Methods: We determined the effect of anti-TNFα therapy in both IL10 knock-out (KO) mice and in the CD4+CD45Rb high T-cell transfer model of colitis. Macrophage populations were quantified using qPCR analysis for CD206 and iNOS and flow cytometry for CD206. IL10 mRNA and protein levels were analysed with qPCR and ELISA.
Results: Colitis in the IL10 KO mice was completely resistant to anti-TNFα therapy, in sharp contrast to the colitis in SCID or Rag1 KO mice upon transfer of CD4+CD45Rb high T-cells, which was significantly reduced by anti-TNFα therapy. Succesfull anti-TNFα therapy was accompanied by an increase of IL10 levels and an increase of regulatory (M2) type macrophages in the intestine. Blocking IL10 signaling, with an IL10 Receptor blocking antibody, diminshed the therapeutic efficacy of anti-TNFα therapy. Anti-TNFα therapy was also effective in RAG1 KO mice that received a transfer with IL10 Receptor KO CD4+CD45Rb high T-cells, indicating that IL10 signaling in T-cells was not important for the therapeutic efficacy of anti-TNFα. In contrast, LysMCre IL10Ra flox/flox Rag1 KO, mice defective in macrophage IL10 signaling, were unresponsive to anti-TNFα therapy upon receiving CD4+CD45Rb high T-cells. In these mice there was also no increase of intestinal M2 macrophages.
Conclusion: IL10 signaling in macrophages is pivotal for the therapeutic efficacy of anti-TNFα therapy in animal models for IBD. Defects in the IL10 pathway may also play a role in anti-TNFα non-responders which is subject of further investigation.

**Sympathetic activity regulates macrophages via the β2-adrenergic receptor.**

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Background: The autonomic nervous system is an important immune regulator. It has been established in-vitro that norepinephrine, the main sympathetic neurotransmitter, has anti-inflammatory effects. Furthermore, a loss of sympathetic innervation in the intestine of patients with inflammatory bowel disease has been described.
To study the role of sympathetic innervation on immune function, we applied sympathetectomy in T-cell transfer colitis and tested the immune regulatory function of adrenergic receptor activation on myeloid cells in-vitro and in-vivo.
Methods: In $Rag1^{-/-}$ mice, chemical sympathectomy was achieved using 6-hydroxydopamine, followed by a transfer of $CD45RB^{high}$ T-cells. In a follow-up study, surgical selective sympathectomy (sx) was achieved by cutting the superior mesenteric nerve in $Rag1^{-/-}$ mice. Two weeks after sx, colitis was evaluated by histology, endoscopy and intestinal cytokine mRNA levels, along with clinical parameters such as weight loss and colon weight. Intestinal norepinephrine levels were measured by mass spectrometry. Furthermore, intestinal macrophages were sorted and analysed on flow cytometry and cytokine mRNA levels.
In-vitro, LPS-stimulated bone-marrow derived macrophages (BMDM) were pre-treated with norepinephrine or salbutamol, a β2-adrenergic receptor agonist. After 18 hours, cytokine protein levels were determined in the supernatant and cytokine mRNA levels in the cell lysates.
Results: Chemical sympathectomy had no effect on the course of T-cell transfer colitis. However, in $Rag1^{-/-}$ mice without T-cell transfer it elicited elevated colitis. Subsequently, sx caused a significant decrease of intestinal norepinephrine levels in $Rag1^{-/-}$ mice. Sx caused weight loss and a significant increase in colon weight and histology score in $Rag1^{-/-}$ mice compared to $Rag1^{-/-}$ mice after a sham operation. Furthermore, there was a significant increase of the pro-inflammatory cytokines in the colon after sx compared to sham, reflecting spontaneous colitis. In agreement, colonic myeloid cells of $Rag1^{-/-}$ mice expressed elevated inflammatory cytokines compared to sham.
In-vitro, pre-treatment of LPS-stimulated BMDM with norepinephrine or salbutamol led to a decrease in cytokines compared to no pre-treatment or pre-treatment combined with the beta-blocker propranolol.
Conclusion: In immune comprised $Rag1^{-/-}$ mice, intestine-selective sympathectomy leads to a decrease in intestinal norepinephrine, causing spontaneous colitis. Furthermore, we show that sympathetic activity regulates macrophage reactivity in-vitro and in-vivo. Our data reveal a strong modulatory potential of the sympathetic nervous system on the intestinal immune system.

**Development of reliable, valid and responsive scoring systems for endoscopy and histology in animal models for inflammatory bowel disease**

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Background and Aims: Although several endoscopic and histopathologic indices are available to evaluate severity of inflammation in mouse models of colitis, the reliability of these scoring instruments is unknown. Our aim was to evaluate the reliability of the individual items in the existing indices and develop new scoring systems by selection of the most reliable index items.
Methods: Two observers scored the histological slides (n=224) and endoscopy videos (n=201) from treated and untreated Interleukin(IL)-10 knock-out and T-cell transferred SCID mice. Intra-rater and inter-rater reliability for endoscopy and histology scores, and each individual item, were measured using intraclass correlation coefficients (ICCs). The Mouse Colitis Histology Index (MCHI) and Mouse Colitis Endoscopy Index (MCEI) were developed using the most reliable items. Both were correlated to the colon density and to each other and were evaluated for their ability to detect changes in pathobiology.
Results: Inter-rater ICCs (95% CIs) for the total histology and endoscopy scores were 0.90 (0.87-0.92) and 0.80 (0.76-0.84), respectively. The MCHI and MCEI were highly correlated with colon density with a Spearman Rho=0.81(0.75-0.85) and 0.73 (0.66-0.79) respectively, and with each other, Spearman Rho=0.71 (0.63-0.77). The MCHI and MCEI were able to distinguish among the experimental groups within the models with pairwise differences between the treated and untreated groups being statistically significant ($P<0.001$)
Conclusions: These histological and endoscopic indices are valid and reliable measures of intestinal inflammation in mice, that are responsive to treatment effects in pre-clinical studies.

**Integration of whole exome sequencing and RNA sequencing of intestinal biopsies in inflammatory bowel disease identifies inflammation dependent effects**

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Background: Inflammatory bowel disease (IBD), consisting of Crohn's disease (CD) and Ulcerative Colitis (UC), is a chronic relapsing inflammatory disease with increasing prevalence. In recent years, 215 genetic loci have been associated with both CD and UC. The effect of genetic variation on gene expression (defined as expression quantitative trait loci – eQTLs) has been studied by combining GWAS and transcriptome data from peripheral blood. Biological processes, such as inflammation, may modulate eQTLs by altering the transcriptome regulation, which could favour the onset of disease. To study the context and tissue dependent effects of genetic variants in IBD, we correlated Whole Exome Sequencing (WES) of whole blood samples to RNA-sequencing of inflamed and non-inflamed intestinal biopsies from IBD patients.
Methods: We performed cis-eQTL analyses on 165 corresponding RNA-sequencing and WES samples: I) Within IBD-associated genetic regions II) Whole-exome wide. In addition, we assessed the effect of inflammation on eQTLs in paired inflamed and non-inflamed biopsies from 75 patients. All analyses were done using the R package Matrix-eQTL, correcting for possible confounding factors (batch, sex, age, tissue, diagnosis). An eQTL was defined significant using an FDR threshold of 0.05. We identified 96 gut mucosal eQTLs in known associated IBD loci and 1479 eQTLs exome-wide.
Results: We identified 378 inflammation-specific eQTLs, of which 18 in known IBD-associated loci. Two top inflammation-specific eQTLs are IL21 and IL17RC. IL21 is well known to play an important role in IBD, and it is known to be overexpressed in intestinal mucosa in IBD. IL21 is expressed by T and B cells, and it acts on intestinal epithelium helping to maintain Th1 inflammation and Th17 differentiation, hallmarks of IBD intestinal inflammation. IL17RC encodes the IL17RC receptor, which is structurally similar to the IL17RA receptor both of which bind IL17A and IL17F. However, while the IL17RA receptor that has a higher affinity for IL17A, which regulates inflammation, IL17RC has a higher affinity for IL17F, which exacerbates inflammation, and was recently implicated in IBD development. Anti-IL17A drugs were shown to be ineffective in the treatment of IBD, but based on these data one could consider targeting IL17F or IL17RC.
Conclusions: In this study we show the following: I) We identified 18 eQTLs that affect gene expression in the intestine during inflammation only. II) Perturbation of the genes involved in inflammation-dependent eQTLs is likely associated to alter disease activity in IBD. These inflammation-specific eQTLs are potential leads for drug targeting in IBD.

## The pathophysiology of human obstructive cholestasis is mimicked in cholestatic Gold Syrian hamsters

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Background and Aims: Obstructive cholestasis causes liver injury via accumulation of toxic bile acids (BAs). Therapeutic options for cholestatic liver disease remain limited, partially because the available murine disease models lack translational value in that they too rapidly proceed to severe liver injury and do not capture the human compensatory mechanisms to obstructive cholestasis such as the hepatic induction of fibroblast growth factor 15 (Fgf15, FGF19 in humans). Male gold Syrian hamsters mimic human lipid metabolism. The aim was to study whether gold Syrian hamsters reflect the human response to obstructive cholestasis.
Methods: Male gold Syrian hamsters were subjected to bile duct ligation (BDL) and were sacrificed after 0.25 to 28 days of obstructive cholestasis. Cholestasis-induced hepatocellular injury was studied by clinical chemistry (transaminases, alkaline phosphatase, bilirubin) and liver histology (H&E, picrosirius red, Fouchet, and copper stains). Pro-inflammatory changes were studied by PCR. Hepatic and plasma bile salt pool composition was studied by high-performance liquid chromatography and ultra-performance liquid chromatography tandem mass spectrometry. The hepatic expression of genes related to bile salt transport and bile salt signaling was studied by PCR and ELISA.
Results: Profiling of time-related changes following (BDL) in Gold Syrian hamsters revealed a biochemical response similar to cholestatic patients in terms of BA pool composition, alterations in hepatocyte BA transport and signaling, suppression of BA production, and elimination of BAs through phase II conjugation. Hamsters tolerated cholestasis well for up to 28 days and progressed relatively slowly to fibrotic liver injury, whereas hepatocellular necrosis was absent. The histological response to cholestasis in hamsters was similar to the changes seen in 17 patients with prolonged obstructive cholestasis caused by bile duct cancer. Hamsters moreover upregulated hepatic fibroblast growth factor 15 (Fgf15, FGF19 in humans) expression in response to BDL, which is a cytoprotective adaptation to cholestasis that hitherto had only been documented in cholestatic human livers.
Conclusion: Male gold Syrian hamsters embody the human response to obstructive cholestasis, including the compensatory induction of hepatic Fgf15 expression. Hamster models should therefore be added to the repertoire of animal models used to study the pathophysiology of cholestatic liver disease.

**Risk factors for refractory anastomotic strictures after esophageal atresia repair: a multicenter study**

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Background: Esophageal atresia (EA) is a rare congenital anomaly (1:3500 live births) and requires surgical correction soon after birth. Dedicated centers have reported survival rates up to 95%. However, anastomotic stricture formation is still the most frequent post-operative complication (17%-59%), occurring mostly in the first year of life. We aimed to determine the incidence of refractory anastomotic strictures after EA repair and to identify risk factors associated with refractory stricture formation.
Methods: Retrospective multicenter study in EA patients born between 1999-2013, treated in five centers in the Netherlands. Exclusion criteria were isolated fistula, inability to obtain esophageal continuity, death prior to discharge, and follow-up <6 months. A refractory esophageal stricture was defined as an anastomotic stricture requiring ≥5 dilations at maximally four-week intervals. Risk factors for development of refractory anastomotic strictures after EA repair were identified with multivariable logistic regression analysis.
Results: We included 454 children (61% male, 7% isolated EA (Gross type A)). End-to-end anastomosis was performed in 436 (96%) children. Anastomotic leakage occurred in 13%. Fifty-eight percent of children with an end-to-end anastomosis developed an anastomotic stricture, requiring a median of 3 (range 1-34) dilations. Refractory strictures were found in 32/436 (7%) children and required a median of 10 (range 5-34) dilations. Isolated EA (OR 5.7; p=0.012), anastomotic leakage (OR 5.0; p=0.001) and the need for esophageal dilation within 28 days after EA repair (OR 15.9; p<0.001) were risk factors for development of a refractory anastomotic stricture.
Conclusions: The incidence of refractory strictures of the end-to-end anastomosis in children treated for EA was 7%. Risk factors were isolated EA, anastomotic leakage and the need for esophageal dilation within 28 days after EA repair. Children showing one or more of these factors may benefit from supportive care (e.g. adequate acid suppression) aiming to prevent development of a severe refractory stricture.

## Minimally Invasive versus Open Distal Pancreatectomy (LEOPARD): Multicenter Patient-Blinded Randomized Controlled Trial

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Background: Minimally invasive distal pancreatectomy (MIDP) is gaining popularity as observational studies suggest superior outcomes compared with open distal pancreatectomy (ODP). Randomized studies are, however, lacking. We aimed to assess whether MIDP reduces the time to functional recovery, as compared to ODP.

Methods: In this multicenter randomized controlled trial, we assigned adult patients with tumors confined to the left-sided pancreas to MIDP or ODP by trained surgeons in 17 Dutch centers. Patients were blinded for 5 days with a large abdominal dressing and treated according to an enhanced recovery pathway. Primary endpoint was postoperative time to functional recovery (defined as: independently mobile, pain control with oral medication alone, maintaining >50% daily required intake, no intravenous fluids, and no infection). Follow-up was until 90 days postoperatively. Analyses were according to intention-to-treat.

Results: A total of 108 patients were enrolled, 51 were assigned to MIDP and 57 to ODP. Time to functional recovery was 4 days (IQR 3-6) with MIDP vs. 6 days (IQR 5-8) with ODP (P<0.001). MIDP was associated with an improvement of each individual component of the primary endpoint as well as length of hospital stay (6 vs. 8 days, P<0.001). For MIDP, 10% was robot-assisted and 8% converted to ODP. Operative blood loss was less after MIDP (150 (IQR 50-350) vs. 400 (IQR 200-775) mL, P<0.001), whereas operative time was longer (217 (IQR 135-277) vs. 179 (IQR 129-231) min, P=0.005). Grade B/C postoperative pancreatic fistula was seen in 37% vs. 21% of patients (P=0.06), without difference in radiological drainage (22% vs. 20%, P=0.73) and re-operation (2% vs. 5%, P=0.62). Grade B/C delayed gastric emptying was seen less frequently after MIDP (4% vs. 20% (P=0.01). Clavien-Dindo grade ≥3 complications were seen in 25% vs. 38% (P=0.21) and mortality in 0% vs. 2% (P>0.99), for MIDP and ODP respectively.

Conclusions: Patients recover faster after MIDP, as compared to ODP. MIDP reduced operative blood loss, delayed gastric emptying and hospital stay. Clavien-Dindo grade ≥3 complications and mortality were comparable.

This investigator-initiated study was funded by Ethicon Endo-Surgery and registered in the Netherlands Trial Registry (NTR5188).

**The introduction of minimally invasive surgery for distal and total gastrectomy: a propensity score matched analysis**

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Background: Recent population based studies suggest that minimally invasive gastrectomy (MIG) was safely introduced in various countries. However, these studies do not differentiate between distal and total gastrectomy, procedures with a different complexity. The aim of this study was to evaluate the safety of MIG for distal and total gastrectomy.
Methods: In the Netherlands all patients who undergo elective gastrectomy with curative intent for gastric adenocarcinoma are registered in the Dutch Upper GI Cancer Audit. From this audit, patients were included from 2011-2016. Postoperative outcomes (morbidity, mortality and hospital stay) and short-term oncological outcomes (radicality and lymph node yield) were appraised. Propensity score matching (PSM) was applied to create comparable groups of patients receiving open gastrectomy (OG) versus MIG, either total or distal gastrectomy. Factors used for PSM were patient and tumor characteristics, year of surgery and hospital volume. Categorical parameters were compared using the Chi-square test and the student's t-test was used for continuous variables. Logarithmic transformation was applied for variables with a non-parametric distribution.
Results: Of the 1970 eligible patients, 1138 underwent distal gastrectomy and 832 underwent total gastrectomy. After PSM in the distal gastrectomy group, 390 open gastrectomy patients were matched to 288 minimally invasive gastrectomy patients. Conversions occurred in 9% of patients during MIG. Although overall postoperative morbidity (37% vs. 34%, p=0.422) and mortality (3% vs. 3%, p=0.806) were comparable, patients who underwent MIG encountered less intra-abdominal abscesses (4% vs. 1%, p=0.039), wound infections (6% vs. 2%, p=0.021) and fascia dehiscence (2% vs. 0%, p=0.034). The median hospital stay was shorter after MIG (9 vs. 7 days, p<0.001) . The radicality and lymph node yield were comparable.
In the total gastrectomy group, 581 patients remained after PSM, 323 receiving open gastrectomy and 258 receiving minimally invasive gastrectomy. Conversions occurred in 11% of patients during MIG. Overall postoperative morbidity (45% vs. 47%, p=0.643) and mortality (6% vs. 8%, p=0.219) were comparable, whereas the anastomotic leakage rate was higher in the MIG group (17% vs. 11%, p=0.030). The length of hospital stay was comparable between both groups, as were radicality and lymph node yield.
Conclusion: Benefits of MIG during the early introduction can be demonstrated for distal gastrectomy but not for total gastrectomy. The outcomes of centers operating in their learning curve of MIG may be partly responsible for these results, which warrants further analysis.

**Portal vein embolization does not result in microvascular flow differences between the embolized and non-embolized liver lobes in humans.**

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Background: Preoperative portal vein embolization is used to increase future remnant liver volume enabling extended resections. The microvascular effects occurring after unilateral portal venous occlusion are however, poorly understood. This study aimed to assess the microvascular changes in the embolized and the non-embolized lobes after right portal vein embolization (PVE).
Methods: Videos of the hepatic microcirculation in patients undergoing right hemihepatectomy following PVE were recorded using a handheld vital microscope based on incident dark field imaging; the CytoCam (Braedius Medical). Hepatic microcirculation was measured in the embolized and the non-embolized lobe after laparotomy. The same measurements were obtained on the right and left liver lobe after laparotomy in a control group (patients without PVE). AVA software v. 3.2 (Automated, Vascular Analysis) was used to obtain the following microcirculatory parameters: total vessel density (TVD), sinusoidal diameter (Sd), microcirculatory flow index (MFI) and absolute red blood cell velocity (RBCv), Systemic parameters were recorded during the operations.
Results: 8 patients were included after PVE (4 males, 4 females, age 66±7 years) and 8 patients were included in the control group (5 males, 3 females, age 60±13 years). TVD and the Sd were significantly higher in the hypertrophic lobe compared to the embolized lobe and the control lobes (i.e. (TVD hypertrophic 40±9 vs atrophic 26.8±4.6 and control 29.9±5.5, P:0.001)( Sd hypertrophic 9.3±1.8 vs atrophic 6.4±0.9 and control 7.0±0.6 mm, P:0.01)). The MFI and RBCv were not significantly different between the lobes indicating similar microvascular flow despite the difference in vessel density. No differences were found in the systemic and demographic variables.
Conclusion: The non-embolized lobe has a significantly higher microvascular density (TVD and Sd), however without differences in microvascular flow (MFI and RBCv). The overall microvascular flow is not affected by PVE which casts doubts on the portal flow differential in inducing the hypertrophy response in the non-embolized lobes

**Outcomes of Salvage Surgery in patients with recurrent esophageal cancer after definite chemoradiotherapy**

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Background: Definite chemoradiotherapy for cancer of the esophagus can be chosen as primary treatment in selected patients. In patients who have recurrent disease curative surgery is a treatment option, but evidence for this 'salvage' surgery is limited. Some researchers suggest that short- and long-term outcomes after salvage esophagectomy are similar to curative esophagectomy following neoadjuvant chemoradiation for cancer of the esophagus. The aim of this study was to evaluate the clinical outcomes of salvage esophagectomy after definite chemoradiotherapy as compared to curative esophagectomy following neoadjuvant chemoradiotherapy.
Methods: A prospectively maintained database was used to select patients who underwent esophagectomy for recurrent cancer of the esophagus after definite chemoradiotherapy ('salvage esophagectomy') and patients who underwent curative esophagectomy following neoadjuvant chemoradiation ('curative esophagectomy') between January 2009 and December 2017. Proximal tumors were excluded. During salvage esophagectomy, patients underwent resection alone without reconstruction or a direct reconstruction was made. Chi square tests or Fisher's exact tests were used to compare p-values between groups.
Results: A total of 558 patients underwent curative esophagectomy and 17 patients underwent salvage esophagectomy in the study period. Curative surgery showed better results than salvage surgery concerning R0-resections (96% versus 65%, p<0.001). Morbidity was similar (60% versus 77%, p=0.211), but complications were more severe after salvage surgery resulting in a higher combined 30-days and in-hospital mortality (29% versus 3%, p<0.001). There was no significant difference in recurrences after 1 year (26% after curative surgery versus 46% after salvage surgery, p=0.163) and in the 3-year overall survival (45% after curative surgery versus 25% after salvage surgery, p=0.239) between groups.
Conclusion: Salvage surgery is associated with a substantial higher postoperative mortality rate, lower R0-resection rate, a similar morbidity rate and similar 3-year overall survival.

**Can a surgeon perform a macroscopic inspection of a gallbladder?**

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Aims: Routine histopathologic gallbladder examination after cholecystectomy has been a point of discussion for several decades. Recent changes in national guidelines suggest a selective histopathologic examination gallbladders. The aim of this study was to evaluate the macroscopic examination by the surgeon in relation to the final histology outcome.
Methods: A prospective study was conducted in a Dutch teaching hospital to investigate the practice of macroscopic gallbladder examination by a surgeon compared to routine histopathology by a pathologist. All consecutive cholecystectomies were included between November 2009 and February 2011. Patient characteristics, operative procedure, conversions to laparotomy, macroscopic examination of the gallbladder mucosa, alleged necessity for microscopic analysis and final histopathology of the gallbladder were analyzed.
Results: A total of 319 consecutive cholecystectomies were performed. Twenty-nine patients were treated for acute cholecystitis. Of all macroscopic examinations the surgeon identified 62 gallbladders with macroscopic abnormalities, ranging from polyps to wall thickening or ulcers. Including acute cholecystitis a total of 55 (17,2%) could have had reasons for further microscopic evaluation by the pathologist. Macroscopic examination agreement between surgeon and the pathologist was rated as “strong agreement” ($\kappa = 0,822$). The surgeon and the pathologist had disagreement on the macroscopic examination of 18 gallbladders. In these gallbladders, however, the additional histology was not relevant to clinical outcome.
Conclusions: The present prospective study shows that the surgeon is capable of adequate macroscopic gallbladder examination postoperatively. We suggest to only perform selective microscopic gallbladder examination, which can result in about 80% reduction of this kind of routine histology.

**Epidural analgesia after minimally invasive esophagectomy: efficacy and complication profile**

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Introduction: Adequate postoperative pain management is essential to facilitate uneventful recovery after esophagectomy. Although epidural analgesia is currently the gold standard in this context, it is not satisfactory in all patients. The aim of this study was to describe the efficacy and complications profile of epidural analgesia after minimally invasive esophagectomy.
Methods: Patients that underwent a robot-assisted minimally invasive McKeown esophagectomy for esophageal cancer were selected from a single center prospective database (2012-2015). The number of patients that could receive epidural analgesia, the range of epidural block per day, the number of epidural top-ups, the need for escape pain mediation (i.e. intravenous opioids), the highest pain score per day (numeric rating scale (NRS), 0-10), and epidural-related complications were assessed until postoperative day (POD) 4.
Results: A total of 108 patients were included. Epidural catheter placement was achieved in 101 patients (94%). In the patients that received epidural analgesia a complete block was found in 49% (POD1), 42% (POD 2), 20% (POD3), and 30% (POD4). Reinforcement of epidural analgesia by epidural top-up was performed in 26 patients (24%), which was successful in 22 patients. Intravenous opioids were given at least once in 49 out of 108 patients (45%) on either POD 1, 2, 3, or 4. Median highest pain scores on the corresponding days were NRS 2, 4, 3, and 4. Epidural related complications were encountered in 20 patients (19%) and included catheter problems (n=11), hypotension (n=6), bradypnea (n=2), and reversible tingling in the legs (n=1).
Conclusion: Epidural analgesia is insufficient in nearly half of patients undergoing minimally invasive esophagectomy. In order to optimize pain control, alternative pain management modalities should be evaluated.

**Long-term quality of life in patients after McKeown versus Ivor Lewis esophagectomy**

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Background: Treatment of distal esophageal and gastroesophageal junction (GEJ) cancers is challenging. The therapy for these cancers mainly consist of (neo)adjuvant chemo(radio)therapy and surgery. There are different surgical approaches possible for these patients: transthoracic esophagectomy with a cervical anastomosis (McKeown) or an intrathoracic anastomosis (Ivor Lewis). However, there is no evidence which is the preferred approach in terms of oncology, morbidity and quality of life. The aim of this study was to investigate the difference in the long-term quality of life in patients undergoing McKeown (McK) versus Ivor Lewis (IL) esophagectomy in a tertiary referral center.
Methods: Consecutive patients after either McK or IL for distal oesophagus, GEJ or proximal gastric carcinoma were asked to fill in EORTC QLQ-C30 and EORTC QLQ-OG25 questionnaires to evaluate quality of life during the period of January 2014 – December 2017. EORTC QLQ-INFO25 quality of life questionnaire was used to evaluate information needs of patients in both groups. All answers with a long follow up (> 1 year) after surgery were analysed.
Results: In the McK group 62 and in the IL group 110 patients were included. Median follow up was 3 years for McK and 2 years for IL. Median age was 62,4 years. Cognitive functioning was significantly better in the IL group (p=0.038). Complaints of dyspnoe (p=0.004) and dysphagia (p=0.028) were significantly higher in the McK group. Patients after IL had significantly less trouble with eating with others (p=0.003), trouble with taste (p=0.032), chocking when swallowing (p=0.022) and trouble with talking (p=0.038). There was no significant difference in global health status or physical, role, social or emotional functioning. Furthermore there was no difference in symptoms of nausea, fatigue, pain, discomfort or information scores between McK and IL groups.
Conclusion: After a follow up of > 1 year no differences in global health status or physical, role, social or emotional functioning scales between McK and IL esophagectomy were found. However, significant differences in some symptom scales and cognitive functioning were observed in favor of IL. These findings should be taken into consideration when deciding between a McK and IL esophagectomy in patients where both procedures are feasible

**Eye-tracking as a tool to differentiate physicians with different grades of experience in performing laparoscopic pancreaticoduodenectomy**

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Background: Laparoscopic pancreaticoduodenectomy (LPD) is currently introduced in the Netherlands. However, LPD is a technically complex procedure and associated with a learning curve. Reduction of the learning curve by training is important to reduce learning curve associated morbidity and mortality. However, it remains unclear what the differences are in surgical performance between experts and trainees. Eye-tracking is a novel tool that may be used for objective measure of surgical performance. This aim of this study was to investigate whether eye-tracking can be used to differentiate between physicians with different grades of experience in performing LPD.
Methods: Subjects were recruited and allocated in groups based on their experience in performing LPD; laparoscopic experts, open experts, surgical residents and novices. Eye movement and gaze measurements were captured using eye-tracking as subjects were presented with three videos of critical steps of LPD. Outcome measures included fixation time, number of fixations, saccade length and distribution of measurements within groups.
Results: Twenty-seven physicians were included. There was a high person correlation coefficient between the three videos, which indicates a consistent performance of the physicians. Laparoscopic experts (n=8) had the least number of fixations, longer mean eye fixation time and larger standard deviation of eye fixation time, which indicate that they are able to find regions of interest and quickly collect contextual information. Open experts (n=3) had the largest number of fixations, which implies that they focus on many different locations in the videos. Surgical residents (n=7) frequently move their eyes across a large part of the screen to search information, as shown by longer saccade length and larger distributions. Generally, in all measures, the measurement results of laparoscopic experts and novices (n=9) are close, which could be explained by the fact that novices mainly follow surgical instruments.
Conclusion: This pilot study shows that eye-tracking can demonstrate differences in fixation and eye gaze between physicians with different grades of experience in performing LPD. Future studies should therefore be carried out to investigate if eye tracking can be used as a tool to monitor progress during surgical training in LPD.

**Comparing the costs before and after the learning curve of laparoscopic gastrectomy for gastric cancer in a Western referral center.**

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Background: Laparoscopic gastrectomy for gastric cancer has shown benefits over open surgery and might be more cost effective. This laparoscopic approach is a complex procedure and requires a certain learning curve. The aim of this study is to evaluate the costs of laparoscopic gastrectomy before and after the learning curve.
Methods: All patients who underwent laparoscopic gastrectomy for histologically proven gastric cancer from January 2013 through July 2017, with curative intent, were prospectively included in this study. Primary outcomes were costs concerning surgery and hospital stay.
Results: Group one, representing those operated before the learning curve consisted of 51 (49.5%) patients. Group two, representing those operated after the learning curve consisted of 52 (50.5%) patients. No statistical significant cost reduction was found concerning operation duration, surgical materials and hospital stay after the learning curve. Mean operation duration cost before the learning curve was €3685 ± 599 compared to the average cost after the learning curve of €3805 ± 611, p = 0.317. Costs of surgical materials did not differ between groups, €2454 ± 459 vs. €2572 ± 650, p = 0.316. Complication and conversion rates showed no difference between the two groups.
Conclusion: No cost reduction was found for laparoscopic gastrectomy for gastric cancer after the learning curve, with respect to surgical and admission costs.

**The effect of preoperative optimization of nutritional status in patients with significant bowel obstruction**

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Background: Bowel obstruction is a frequent complication of both malignant and benign bowel diseases. Obstruction is often preceded by symptoms like abdominal pain, nausea and anorexia, resulting in weight loss and malnutrition. Traditionally, these patients receive (semi-)acute surgery with associated high complication and mortality rates as those patients often are in poor condition and nutritional status. We hypothesized that these symptoms are due to bowel distension caused by the faeces that has to pass a stenotic part of the bowel. The purpose of this study was to introduce a new preoperative feeding protocol for patients with signs of bowel obstruction in order to reduce bowel distension. Thereby we aimed to perform elective laparoscopic surgery with high rates of primary anastomosis.
Methods: From February 2013 all patients with signs and symptoms of bowel obstruction were included in a prospective database, except for patients with a (near) blow-out requiring emergency surgery. All patients received one of the following diets depending on the severity of obstructive symptoms: residue low diet with protein enriched drinks, complete diet of protein enriched drinks, enteral nutrition (EN) through a nasoenteral tube, or total parenteral nutrition (TPN). Patients were evaluated for relieve of obstructive symptoms and weight gain and were subsequently operated in an elective setting.
Results: 61 patients were included (17 benign indication, 44 malignant indication). Median weight loss was 6 kg. Patients were treated with a residue low diet (n=14), a complete diet of protein enriched drinks (n=18), EN (n=19) or TPN (n=10). 4/61 patients received emergency surgery as obstructive symptoms progressed. 57/61 patients received elective surgery. Laparoscopy was possible in 40/57 patients (70.2%) and primary anastomosis was performed in 49/57 patients (86%). Major post-operative complications (Clavien-Dindo 3-4) occurred in 4 patients (6.6%) . We observed 0% anastomotic leakages and 0% post-operative mortality.
Conclusion: Our study shows that patients with obstructive bowel disease can be safely treated with this feeding protocol and thereby converting the operation from an emergency to an elective setting. It results in good surgical outcome with majority of patients receiving elective laparoscopic resection with primary anastomosis and little severe postoperative complications.

**Hartmann's procedure or sigmoidectomy with primary anastomosis for perforated diverticulitis with purulent or fecal peritonitis: results of the international, multicenter, parallel-group, randomised, open-label LADIES trial**

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Background: Perforated diverticulitis with purulent or faecal peritonitis (Hinchey classification III or IV) requires emergency surgery. Hartmann's procedure (HP) remains the favoured option for most surgeons. However, previous cohort studies suggested postoperative mortality and morbidity of primary anastomosis (PA) (±loop ileostomy [LI]) compared equally to HP. The likelihood of LI reversal is reported to be higher than that of HP reversal (85% vs. 50-60%). Moreover, LI reversal reportedly has a lower risk for morbidity and mortality. Therefore, the aim was to assess outcomes after HP vs. PA in patients with perforated diverticulitis in a prospective, randomised trial.
Methods: A multicenter, parallel-group, randomised, open-label trial was conducted in eight academic and 34 teaching hospitals in Belgium, Italy, and the Netherlands. Patients with purulent or faecal peritonitis were randomly assigned (1:1; age-stratified [<60 vs. ≥60 years]) to HP or PA (±LI), excluding patients older than 85 years, with high-dose steroid use (≥20 mg daily), or with haemodynamic instability. Patients were followed up for 12 months and were seen in outpatient setting after index operation and stoma reversal. The primary endpoint was 12-month stoma-free survival. Secondary endpoints were short-term (30-day) and long-term (12-month) morbidity, mortality, and quality of life (QoL) during follow-up. Patients were analysed following the intention-to-treat principle.
Results: Overall, 130 patients (92 Hinchey III, 38 Hinchey IV) were randomised to HP (n=66) and PA (n=64), of which in 17 PA patients (27%) no LI was constructed. Long-term results were not available for one patient. No significant baseline differences were found between Hinchey III and IV patients, except for Mannheim Peritonitis Index (21 vs. 27.5, p<0.001). Primary endpoint differed significantly in favour of PA (log-rank p=0.001), with no difference in short- and long-term overall morbidity and mortality. Short-term overall morbidity after stoma reversal was lower in PA patients (3 [8.1%] vs. 13 [30.2%] patients, p=0.023). No differences in QoL were found.
Conclusion: PA is superior to HP as treatment for patients with perforated diverticulitis (Hinchey III and IV) with regards to 12-month stoma-free survival, without significant differences in short- and long-term morbidity and mortality. Therefore, PA should be preferred over HP.

**Achievements in colorectal cancer care during 8 years of auditing in the Netherlands**

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Background: Auditing has been suggested to be an important tool for quality improvement, with potential impact on outcomes parameters like mortality and morbidity. However, the efficacy of auditing is still a subject of debate and concerns exist if auditing promotes favorable patient selection. The purpose of this population-based analysis was to study outcomes of CRC treatment for different risk-stratified subgroups of patients and to assess potential risk averse behavior since the start of the Dutch ColoRectal Audit (DCRA).
Methods: Data of the DCRA between 2009 and 2016 were extracted. To evaluate overall trends in outcomes over time, uni- and multivariable analyses were used. Patients were stratified according to operative risk based on tumor stage (T1-3N0-2M0, T4N0-2M0 and M1), age (≤60years, 61-70years, 71-80years and ≥81years) and ASA group (ASAI-II and ASAIII-IV) and compared over time using absolute (ARR) and relative risk reduction (RRR). The following outcomes were evaluated for the different subgroups: 30-day or in-hospital mortality, surgical complications, non-surgical complications, complicated postoperative course (postoperative complication resulting in a hospital stay >14 days and/or a reintervention and/or mortality), reinterventions, readmissions, length of stay (LOS), stoma construction rate in (low) anterior resections ((L)AR) and in low (≤5cm from anal verge) rectal cancer.
Results: 40,004 colon cancer and 19,853 rectal cancer patients were included. Overall postoperative mortality decreased from 3.3% to 1.8% in colon cancer and from 2.3% to 1% in rectal cancer. Surgical and non-surgical complications slightly increased, but with less reinterventions over time. For colon cancer, the high-risk elderly patients seem to have benefitted the most, with an ARR of 6.4% on a complicated postoperative course and an ARR of 5.9% on mortality. The proportion of patients receiving a diverting stoma or end colostomy after a (L)AR decreased 11% and 7%, respectively. In low rectal cancer, patients increasingly received a non-diverted primary anastomosis (5.4% in 2011 and 14.4% in 2016). Overall, postoperative length of stay decreased from 7 to 5 days for colon cancer ($p<0.001$) and from 8 to 6 days for rectal cancer ($p<0.001$).
Conclusion: No signs of risk averse behavior was found since the start of the audit. Especially the high-risk elderly patients seem to have benefitted from improvements made in colon cancer treatment in the past 8 years. For rectal cancer, trends towards the construction of more primary anastomoses are seen. Future quality improvement measures should focus on reducing surgical and non-surgical complications.

**Population based comparative study of postoperative outcomes of screen-detected colorectal cancer.**

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Background: In the Netherlands, a national colorectal cancer (CRC) screening program was introduced in 2014. However, little is known about the surgical outcomes of CRC patients referred through a nationwide FIT-based screening program, thereby impeding a comprehensive appreciation of screening. The aim of our study was to determine whether surgical outcomes of FIT screen-detected CRC patients are different from non-screen-detected CRC patients.
Methods: Data were extracted from the Dutch ColoRectal Audit (2011-2016). To evaluate the influence of screen-detected CRC on overall outcomes in CRC surgery, patients registered since 2014 were categorized in screen-detected and non-screen-detected. A risk-stratified comparison was made based on tumor stage (I-IV) and, for tumor stage I-III, also on age (≤70 years vs. >70 years) and ASA score (I-II vs. III-IV) between screen-detected and non-screen-detected CRC patients for different postoperative outcomes: 30-day or in hospital mortality, surgical complications, non-surgical complications and complicated postoperative course (postoperative complication resulting in a hospital stay >14 days and/or a reintervention and/or mortality). Uni- and multivariable analyses were used to determine any casemix-adjusted differences in outcomes of screen-detected versus non-screen-detected CRC patients.
Results: Stratified comparison showed a significant lower rate of complicated postoperative course and mortality-rate for patients with screen-detected colon cancer stage I-III. For patients with screen- detected rectal cancer, only a significant higher mortality for stage IV was found. Screen-detected colon cancer was independently associated with lower odds ratio on non-surgical postoperative complications (AOR 0.813, 95%CI 0.729-0.907), surgical postoperative complications (AOR 0.799, 95%CI 0.716-0.89) and complicated postoperative course (AOR 0.797, 95%CI 0.706-0.9) compared to non-screen detected colon cancer. For rectal cancer, a higher odds ratio on mortality for screen-detected CRC patients was found.
Conclusion: Patients referred for surgery through the FIT-based screening program had better outcomes in colon cancer compared to non-screen-detected patients, which was not observed in rectal cancer. Even with extensive casemix-correction, screen-detected patients with colon cancer still had better outcomes, suggesting additional underlying factors favoring screen-detected colon cancer patients.

**Postoperative Risks after Surgical Treatment for Submucosal Invasive Colorectal Cancer: a National Cohort Study**

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Background: With the introduction of population based colorectal screening programs, the detection of earlier stage colorectal cancer as compared to more advances cancers has been rising. In patients with submucosal invasive colorectal cancer (T1 CRC), harms and benefits of surgery must be weighted when secondary surgery is considered after polypectomy. The aim of this study was to assess morbidity and mortality rates of surgery for T1 CRC, and to compare these with outcomes for more advanced CRC (T2-T3 CRC). Secondary aim was to develop a risk stratification table with the estimated morbidity and mortality risk for T1 CRC surgery, in order to help clinicians to estimate the risk for individual patients, hereby enhancing shared decision-making.
Methods: This was a population-based study of patients surgically treated for pT1-pT3 CRC between 2009 and 2016 in the Netherlands, using data from the Dutch ColoRectal Audit (DCRA). The risks for complications, both surgical and non-surgical, and mortality were compared between T1 CRC and T2-3 CRC surgery using multivariate logistic regression. A risk stratification table was developed based on factors independently associated with major complications after elective surgery for pT1 CRC. Bootstrapping was performed to calculate 95%CI.
Results: Among 39,813 patients with CRC, 5,170 patients (13%) had T1 CRC. Overall complication rate was lower for T1 CRC surgery as compared to T2-3 CRC surgery (23.6 vs 27.7%, adjusted OR 0.90, 95%CI: 0.84 – 0.97, p=0.008). There was no difference in surgical complication rate (12.6 vs 13.5%, adjusted OR: 0.93, 95%CI: 0.84-1.02, p=0.12), major complication rate (8.3 vs 9.5%, adjusted OR: 0.89, 95%CI: 0.80-1.01, p=0.06) or mortality rate (1.7 vs 2.5%, adjusted OR: 0.94, 95%CI: 0.74-1.19, p=0.60) between T1 CRC and T2-3 CRC patients. Male gender, high ASA-score, previous abdominal surgery, open approach and the type of procedure (subtotal colectomy vs right colectomy) were associated with a higher major complication rate in T1 CRC patients.
Conclusions: Elective bowel resection for pT1 CRC holds a comparable risk on surgical complications, mortality or major postoperative complications as compared to elective bowel resections for pT2-3 CRC. These risks should be considered when deciding on additional surgery for T1 CRC. We provide a risk table that might help clinicians to estimate the risk for major complications for T1 CRC surgery. Women with ASA 1-2 that underwent sigmoid resection or right colectomy had the lowest risk on major complications (<5%), whereas men with ASA 3-4 that were treated with right or left colectomy had the highest risk on major complications (>19%).

**Therapy refractory ulcerative colitis patients may benefit from appendectomy; long-term clinical results from a multicenter prospective cohort series**

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Background: Appendectomy may reduce relapses and need for medication in patients with ulcerative colitis (UC). However, the possibility of a placebo effect is still debated, as long-term prospective data are lacking. The aim of this study was to analyse the effect of an appendectomy on the clinical course of refractory UC patients.
Methods: In this observational prospective cohort study, a consecutive series of refractory UC patients referred for proctocolectomy between 2012 and 2015 were counseled to undergo laparoscopic appendectomy first. Primary endpoint was clinical response at 12 months and long-term follow-up (>2 years), defined as a decrease of ≥3 points in the partial Mayo ranging from 0–9. Secondary endpoints were failure (colectomy or start of new, mostly experimental medication), endoscopic remission (endoscopic Mayo score ≤1), changes in IBDQ, and a patient rated 'global change' question ("Since your operation, have your UC symptoms improved overall?"). The minimal clinically important difference (MID) in IBDQ was calculated from the difference in IBDQ change scores of the patients answering "yes" and "no" to the global change question. Statistical differences were analysed using mixed-models analysis for repeated measures applying a random-effects model.
Results: In total, 28 patients (46% female, 10 using steroids) with a median age of 41 (IQR, 33-48) underwent appendectomy with a median preoperative partial Mayo score of 7 (IQR, 6-8). The mean baseline IBDQ was 127 (95%CI 113-141).
After 12 months, 12/26 (46%) patients had a clinical response, none using steroids. Of those with a response, 5/12 refused endoscopy and 5/12 were in endoscopic remission. A total of 9 patients failed (7x colectomy, 2x trial medication). For the remaining patients, the IBDQ significantly improved to mean 161 (95%CI 144-177; p<0.001).
Long-term data were available for 27/28 patients. After median follow-up of 4 years (range 2-5) another 4 patients failed (in total 9x colectomy, 4x trial medication). Thirteen of the remaining 14 patients had clinical response (4 on steroids) of whom 6 were in endoscopic remission (endoscopy data of 3 patients is pending). The IBDQ was further improved to mean 171 (95%CI 153-189; p<0.001). Overall, 77% of the patients answered "yes" to the global change question, the MID for the IBDQ was 27 points resulting in a clinical benefit for 75% of the patients.
Conclusion: After long-term follow-up, appendectomy resulted in a clinical response in at least 48% of refractory UC patients of whom 46% were in endoscopic remission. Appendectomy could be beneficial in this patient group, as a long-term (endoscopic) placebo effect seems unlikely.

**Interobserver variability in the classification of appendicitis during laparoscopy**

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Background: The intraoperative classification of appendicitis dictates the patient's postoperative management: prolonged antibiotic prophylaxis is recommended for complex appendicitis (gangrenous, perforated, abscess), whilst preoperative prophylaxis suffices for simple appendicitis. Distinguishing these two conditions can be challenging. The aim of this study was to assess the interobserver variability in the classification of appendicitis during laparoscopy.
Methods: Short video-recordings taken during laparoscopy for suspected appendicitis were shown to surgeons and surgical residents. They were to 1) classify the appendix as no, simple or complex appendicitis, 2) categorize it as normal, phlegmonous, gangrenous, perforated and/or abscess, and 3) decide whether they would prescribe postoperative antibiotics. Answers to the second question were recategorised into complex appendicitis and not complex appendicitis according to the definition by Bhangu et al. (Lancet 2015). Interrater reliability was evaluated using Fleiss' kappa (K) score and the S* statistic.
Results: Eighty assessors participated in the study. Video-recordings of twenty patients were used. Interobserver agreement was minimal for both the classification of appendicitis (K 0.398, 95% CI 0.385 – 0.410) and the choice for postoperative antibiotic treatment (K 0.378, 95% CI 0.362 – 0.393). Agreement was slightly higher when Bhangu's definition of complex appendicitis was applied (K 0.552, 95% CI 0.537 – 0.568).
Conclusion: The present study indicates that there is considerable variability in the intraoperative classification of appendicitis and the decision to prescribe postoperative antibiotic treatment.

**Influence of conversion and anastomotic leakage on survival in rectal cancer surgery; a large retrospective cross-sectional study**

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Background: Conversion and anastomotic leakage in colorectal cancer surgery have been suggested to have a negative impact on long-term oncologic outcomes. However, small and heterogeneous patient populations were included in those studies. The aim of the current study in a large national cohort was to analyze the influence of conversion and anastomotic leakage on long-term oncologic outcome in rectal cancer surgery.
Methods: Patients were selected from a retrospective cross-sectional database. Patients with a benign lesion, distant metastasis or unknown tumor or metastasis status were excluded. Overall and disease-free survival was compared between laparoscopic, converted and open surgery as well as between patients with and without anastomotic leakage.
Results: Out of a database of 2095 patients, 638 patients were eligible for inclusion in the laparoscopic, 752 in the open and 107 in the conversion group. A total of 746 patients underwent low anterior resection with primary anastomosis, including 106 (14.2%) with anastomotic leakage. Overall and disease-free survival were significantly shorter in the conversion compared to the laparoscopic group (P=0.025 and P=0.001, respectively) as well as in the anastomotic leakage group compared to patients without anastomotic leakage (P=0.002 and P=0.024, respectively). In the primary open group, only disease-free survival (P=0.016) was significantly better compared to the conversion group. In multivariable analysis, anastomotic leakage was an independent predictor of overall (hazard ratio 2.167, 95%-confidence interval 1.322-3.551) and disease-free survival (1.592, 1077-2.353). Conversion was an independent predictor of disease-free (1.525, 1.071-2.172), but not of overall survival.
Conclusion: Technical difficulties during laparoscopic rectal cancer surgery, as reflected by conversion as well as anastomotic leakage, have a negative prognostic impact.

**Patient blood management in colorectal cancer patients: a survey among Dutch gastroenterologists, surgeons and anesthesiologists**

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Introduction: There is an increasing awareness of the need to integrate patient blood management (PBM) within routine surgical care to improve patient outcome. However, to date, and despite the high prevalence of preoperative anemia associated with increased morbidity and mortality, virtually nothing is known about the use and implementation of PBM strategies in colorectal cancer surgery, in contrast to orthopedic and cardiac surgery. Present study aimed to assess the current preoperative blood management strategies in the Netherlands, and to identify preferences of different physicians in the treatment of preoperative anemia.
Methods: An online electronic survey was developed and was sent to all surgeons of the Dutch Taskforce Coloproctology (i.e. 177 in total). In addition, for each hospital in which surgery for colorectal cancer surgery is performed (i.e. 75 in total), the survey was sent to one gastroenterologist and one anesthesiologist. Analyses were performed using descriptive statistics
Results: A total of 192 physicians responded to the survey (response rate 58.7%). In 73 hospitals (97.3%) the survey was conducted by at least one physician, while in 21 hospitals (28.0%) the survey was conducted by both surgeon, anesthesiologist and gastroenterologist. Interestingly, in case of more than one respondent per hospital, often a high variety in responses was found. 45.3% and 17.8% of responding hospitals indicated that iron status was measured during screening for colorectal cancer and during preoperative assessment, respectively. Regarding management of preoperative anemia, there is no clear and ambiguous policy in the vast majority of hospitals (49.3%). As objective for treatment of preoperative anemia, 'prevention of blood transfusions because of its association with impaired long-term tumor prognosis' was ranked first. Most physicians (98.0%) considered severity of anemia as variable in their decision-making to treat anemia.
Conclusion: The present study shows a distinct variability in preoperative blood management practices in colorectal cancer care, indicated by varied responses from gastroenterologists, surgeons and anesthesiologists. Strikingly, this variability was not only seen between, but also within Dutch hospitals. As a result, the present study clearly demonstrates the lack of consensus between gastroenterologists, surgeons and anesthesiologists, resulting in a suboptimal preoperative blood management strategy.

**Endoscopic features of response to chemoradiation for rectal cancer**

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Background: Rectal cancer patients with a clinical complete response (CR) to neoadjuvant treatment can be treated with a watch-and-wait (W&W) approach. The aim of this study was to assess the diagnostic performance of restaging endoscopy for the selection of luminal CR after neoadjuvant treatment.
Methods: This study was performed in a single center where restaging endoscopy was routinely done after neoadjuvant treatment for rectal cancer to assess the luminal response. All patients underwent flexible sigmoidoscopy between 6-12 weeks after the end of neoadjuvant treatment, followed by rectal surgery or a W&W approach with minimum follow-up of 2 years. All white light endoscopic images were scored by one experienced endoscopist. The presence of a white scar, flat ulcer, ulcer with irregular border, adenomatous tissue or tumour tissue were evaluated and likelihood for a CR was scored at a 5-point scale (1=definite CR, 5=definite residual tumour). Histology after surgery represented the reference standard (ypT0 = CR). In patients undergoing watch-and-wait, a regrowth free period of >2 years was considered a CR. Area under the ROC curve (AUC), sensitivity and specificity were calculated, considering a likelihood score 1 or 2 as complete response. A second reader scored a subset of patients, to calculate the interobserver agreement.
Results: Sixty-five patients were included (71% male, mean age: 65 years). Forty-two patients had surgery (ypT0: 12, ypT1-4: 30) and 23 patients underwent W&W (2 year regrowth free: 20, regrowth: 3).Median time to restaging endoscopy was 9 weeks (IQR 8-12). Median time from endoscopy to surgery was 22 days (IQR 15-45). AUC for prediction of a CR with endoscopy was 0.74. Sensitivity and specificity were 68.8% and 78.8%, respectively. In a subset of 25 patients, the interobserver agreement was good (quadratic weighted $\kappa$=0.77). In case of a white scar, the positive predictive value (PPV) for a CR was 81.0%. For adenomatous tissue or a flat ulcer the PPV for a CR were 42.9% and 37.5%, respectively. For an ulcer with irregular border and clinical residual tumor, this was 20.0% and 36.4%.
Conclusion: Endoscopy predicts complete response after a median time of 9 weeks with a sensitivity of 68.8% and specificity of 78.8%. At 9 weeks, only two-third of the patients with a complete responses are detected by endoscopy. An extended observation period in selected patients may potentially lead to a higher detection rate, especially in patients with a flat ulcer. Endoscopy should be used in combination with MRI to provide more detailed information on the response in the deeper layers of the bowel wall and the mesorectum.

## The effect of intestinal manipulation on healing of the intestinal anastomosis

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Background: Postoperative ileus (POI) is an inevitable complication following colorectal resection which is known to develop after manipulation of the intestine during surgery. This results in a rapid inflammatory response causing hypomotility of the intestine. Furthermore, anastomotic leakage (AL) is the most feared complication with unknown etiology. We hypothesize that the inflammatory response caused by intestinal manipulation (IM) also affects healing of the anastomosis after colorectal resection.
Methods: Twenty-eight male C57BL/6 mice underwent transection of the proximal colon. IM was applied in 14 animals prior to the transection. Anastomoses were made with 6 interrupted sutures in all animals. Mice were sacrificed after 5 days to macroscopically evaluate the healing of the anastomosis using the Anastomotic Complication Score (ACS), ranging from 0 (no adhesions or abnormalities) to 6 (fecal peritonitis/death due to peritonitis). A score of ≥3 was considered AL. Anastomoses were collected and assessed by histologic examination and gene expression. Furthermore, a cohort of a human trial was used in which patients underwent colorectal surgery with primary anastomosis to compare AL between patients with and without POI.
Results: Mice that underwent IM had significantly more AL than mice without IM (13/14 vs. 6/14 respectively, $p=0.013$). Consequently, these mice had a significant higher ACS (4 vs. 2, $p=0.0014$). Results from the histologic examination and array are imminent. In the human trial, the incidence of AL was higher in patients with POI (21 vs. 5%, $p<0.001$).
Conclusion: This study shows that rodents develop AL more often when IM is applied before the creation of an anastomosis. In patients, POI is associated with AL. Interventions aiming at reducing POI could reduce the incidence of AL as well.

## Durability of radiofrequency ablation for treatment of esophageal squamous cell neoplasia: 5 year follow-up of a prospective study in China

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Background: Radiofrequency ablation (RFA) is an accepted treatment modality for early Barrett's neoplasia. Less is known about RFA for esophageal squamous cell neoplasia (ESCN), and RFA has not been registrated for this purpose. Our group has reported several prospective studies of RFA for ESCN in high-risk areas in China. Complete remission (CR) of ESCN was achieved in 87% of patients, but follow-up (FU) was restricted to 12 months. We aimed to evaluate long-term 5 year outcomes after RFA for ESCN.
Methods: Patients with flat type (Paris 0-IIb) unstained lesions (USL) on Lugol's endoscopy, 3-12cm in length and with moderate or high grade intraepithelial neoplasia (MGIN/HGIN) or mucosal squamous cell cancer (ESCC-m) were treated with RFA every 3 months until CR (absence of MGIN or worse). All patients with CR at 12 months (CR12) were included in the current study extension, and underwent annual FU endoscopy with Lugol and biopsies. Flat type USLs were treated with RFA; other lesions were treated per investigator's discretion. We also describe the clinical course of patients with persistent ESCN at 12 months (non-CR12), with treatment and FU per investigator's discretion.
Results: The 78 patients with CR12 were included in this extension. During a median FU of 48 months (IQR 48-48) and 5 endoscopies (IQR 4-6), 67/78 patients (86%) sustained CR. Recurrence occurred in 7 pts (9%; MGIN:6, HGIN:1) and all were managed with RFA. CR was re-established in 4, and the other 3 were treated at the last FU. Four other pts (5%) had progression (HGIN:1; ESCC-sm:3) and were managed endoscopically with ESD. During FU, protocol violations (prolonged intervals, USLs left untreated, no adequate FU) occurred in 46/78 patients (59%). Of the 12 non-CR12 patients, progression of ESCN occurred in 6 (50%), managed by endoscopic (1) or non-endoscopic (5) treatment. Overall, 2 patients developed subepithelial disease that was not clearly visible with Lugol. Post-hoc analysis on the 'pink-color sign' at baseline, showed that this reddish to pink color change after Lugol staining significantly predicted recurrence or progression during FU (HR 4.0, 95% CI 1.8-9.2).
Conclusion: RFA is relatively easy to apply and can efficiently treat large areas with ESCN. Despite protocol violations that may have interfered with the efficacy of RFA, the great majority with CR12 had sustained CR during FU. However, some patients progressed to advanced disease and 2 patients developed subepithelial disease that was not visible with Lugol's. Based on currently available data, we advise to restrict the use of RFA for flat type MGIN and HGIN without pink-color sign on Lugol's chromoscopy.

**Clinical and endoscopic predictors of neoplastic progression in Barrett's esophagus surveillance: a multi-center community based prospective cohort study**

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Introduction: The incidence of esophageal adenocarcinoma (EAC) is increasing and overall 5-yr survival is poor. Barrett's esophagus (BE) is the most important risk factor for EAC. BE Patients are thus endoscopically surveyed to detect EAC at a curable stage. Aim was to assess risk of neoplastic progression in BE and to identify endoscopic and clinical factors associated with increased risk of neoplastic progression.
Methods: This is a prospective multicenter cohort study initiated in 2003, in six community-based hospitals. Patients with BE and any newly diagnosed BE patients, were asked consent to enter a prospective surveillance program. Patients were excluded if they did not have confirmed intestinal metaplasia, if they had a history of EAC or prevalence of EAC or high-grade dysplasia (HGD) This study was coordinated by a tertiary referral center, with two research nurses who scheduled and attended surveillance endoscopies to ensure adherence to guidelines. At each center, all endoscopies were performed by a dedicated endoscopist. Patients completed questionnaires with demographic and clinical data at each endoscopy. If patients had surveillance prior to inclusion, endoscopic and histological data were collected retrospectively. Endpoint of the study was histological progression to HGD/EAC during follow-up. Univariate regression was used to identify predictors of progression.
Results: Follow-up was closed July 2017. In total 986 eligible patients were included for analysis (727 men, median age 58 years, median BE length C1M3). During a total follow-up of 8643 patient years, 68/986 (6.9%) patients developed HGD (n=27) or EAC (n=41) during surveillance, leading to an annual risk of neoplastic progression of 0.79% per patient year. Median surveillance time was 7.9 yrs for non-progressors and 7.7 yrs for progressors. In univariate analyses, increasing age at baseline endoscopy (yrs) (HR 1.07, 95% CI 1.04-1.10), longer BE length (cm) (HR 1.17, 95% CI 1.12-1.24) and low-grade dysplasia at baseline (HR 2.33, 95% CI 1.27-4.29) were statistically significant predictors. No increased progression risk was found for sex, BMI and smoking.
Conclusion: During median follow-up of more than 7 years, we found an annual risk of progression to HGD/EAC of 0.79% per patient year. With its long-term follow-up, prospective, multicenter, community-based design without referral bias, strict adherence to guidelines and optimal surveillance context, this study is unique in its kind. Barrett length and low-grade dysplasia at baseline were associated with increased risk of neoplastic progression. These factors may be used to tailor surveillance in BE patients.

## Development of an Updated Score Chart to Predict the Risk of Chronic Mesenteric Ischemia based on a Multicenter Cohort of 666 Patients

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Background: Chronic mesenteric ischemia (CMI) is the result of insufficient mucosal perfusion of the gastrointestinal tract. CMI is mostly caused by atherosclerotic mesenteric artery stenosis. Other causes are vasculitis, median arcuate ligament syndrome (MALS) or non-occlusive ischemia (NOMI). Harki et al. designed a score chart to predict the risk of CMI consisting of patient characteristics (gender, weight loss, cardio-vascular disease) and radiologic evaluation (degree of celiac artery (CA) stenosis and superior mesenteric artery stenosis). We aimed to update this score chart based on its performance in an extended multicenter cohort of CMI suspected patients including the etiology of CA stenosis (vascular disease versus MALS) since these etiologies differ in patient presentation and characteristics.

Methods: We included all patients suspected of CMI that were referred to 2 Dutch specialized CMI centers from November 2006 to January 2016. All patients underwent a standard diagnostic work-up of medical history taking, mesenteric CTA or MRA and measurement of mucosal ischemia with visible light spectroscopy or tonometry. Multidisciplinary consultation resulted in an expert based consensus diagnosis. All patients with a CMI consensus diagnosis were planned for treatment (revascularization for occlusive disease and vasodilatory medication for NOMI). A definitive diagnosis of CMI was made if successful treatment resulted in durable symptom relief.

Results: We included 666 patients (definitive diagnosis of CMI: 289 patients (43%)). Multivariable logistic regression analysis was performed using the 5 original predictors combined with CA stenosis etiology. In contrast to the original model, gender was not a significant predictor for CMI (female OR=1.01, 95% CI: 0.68-1.52). The original score chart was updated by estimating new multivariable logistic regression coefficients. The total score of the updated score chart ranged from 0 to 28 points: 0-5 points indicating a low-risk of CMI of 19%, 6-18 points indicating an intermediate-risk of CMI of 45%, and 19 points or more indicating a high-risk of CMI of 92%. The discriminative ability of the updated score chart was strong (C-Statistic 0.8).

Conclusions: We developed an updated version of a score chart to predict the risk of CMI based on the performance in an extended cohort and with inclusion of CA stenosis etiology. This score chart is useful in clinical decision-making, for example to adopt a wait-and-see policy in low-risk patients or to perform immediate vascular intervention in high-risk patients. This may result in less diagnostics, prompt treatment, decreased patient-burden and reduced health costs.

## Incidence of colorectal cancer in young adults in europe

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Introduction: While colorectal cancer (CRC) incidence for individuals older than 50 years steadily declines, an opposite trend has been suggested among young adults in the North American population. Data on trends in CRC incidence among younger subjects in the European population are lacking. Therefore, the aim of this study was to analyze the trends in incidence rates of young adults with CRC in the European Union over the last years.
Methods: Data on age-related incidence of CRC were retrieved from national European cancer registries with a data time-frame of at least 10 years. Young adults, defined as people between the ages of 15 to 50 years old with confirmed colon and rectal cancer, were included. Five-year incidence- and mortality rates were collected, expressed per 100.000 person-years. Trends were calculated using a Joinpoint regression analysis of the timeframe available for each country, and expressed as annual percent change (APC) with their 95% confidence.
Results: Data from fourteen European countries were included. Time frames varied with a range of 10 to 63 years of data available, until very recent. An increasing trend in CRC incidence was shown over almost all age groups in nine European countries (64%): Norway, The Netherlands, Sweden, Germany, Iceland, Ireland, Finland, Belgium and France. The largest increase in incidence rate was found in Germany in age group 15-19 ($APC_{female}$ 45.7; CI:19.4-77.9) and the smallest in Finland in age group 35-39 ($APC_{female}$ 0.7; CI:0.0-1.4). Denmark revealed a significant decrease in CRC incidence in age group 20-24 and 30-44, ranging from an APC of -0.42 (CI:-0.7– -0.2) to -8.18 (CI:-13.2– -2.8). Overall mortality rates decreased in age groups 20-49 in Switzerland, Denmark, Germany, The Netherlands, Finland, Italy, Sweden and Switzerland. The largest decrease in mortality was seen in Switzerland ($APC_{female}$ -14.27; CI: -23.4−-4.1) and the smallest in Finland and The Netherlands ($APC_{female}$ -0.95; CI:-1.7−-0.2). Norway revealed an increasing trend in mortality rates over all age groups, ranging from an APC of 0.99 (CI:0.4-1.6) to 9.2 (CI:4.9-13.6).
Conclusion: There is an increased incidence in CRC in young adults in most European countries. The cause for this trend is still unknown. Awareness and future studies to elucidate causes for this trend are needed and may help to set up screening strategies to prevent and detect these cancers at an early and curable stage.

**Aberrant intra-epithelial lymphocytes in refractory celiac disease type II cause villous atrophy by granzyme-B mediated apoptosis of enterocytes via CD103-E-cadherin-interaction**

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Background: Refractory celiac disease type II (RCDII) is an indolent intestinal tumor of aberrant intraepithelial T-lymphocytes (IEL). The severe enteropathy found in RCDII is caused by aberrant IEL that exert cytotoxicity against the enterocytes. In this study, we investigated the cell death mechanisms that are responsible for villous atrophy in RCDII.
Methods: mRNA and protein expression of granzyme-B were determined using RT-MLPA analysis and flowcytometry, respectively. Enterocyte killing and degranulation by aberrant IEL were measured in the presence of a transwell or specific inhibitors, with flowcytometry. Secretion of granzyme-B was detected by ELISA.
Results: mRNA and protein expression of granzyme-B were significantly upregulated in aberrant IEL of patients with RCDII compared to levels of granzyme-B expression in patients with CD on a gluten-free diet (GFD). The level of granzyme-B expression in RCDII patients correlated with the severity of villous atrophy. RCDII cell lines also demonstrated increased levels of granzyme-B expression. Furthermore, in RCDII patients and cell lines degranulation of granzyme-B was observed in the presence of epithelial cells. Incubation of RCDII cell lines with epithelial cell line Caco2 showed that aberrant IEL induced apoptosis of Caco2. Treatment with a granzyme-B inhibitor demonstrated that killing of enterocytes was granzyme-B dependent and that degranulation by IEL was imperative. In addition, we found that the aberrant IEL induced cell death through triggering of the intrinsic apoptosis pathway via mitochondrial membrane depolarization and caspase-3 and -9 activation. For degranulation of granzyme-B and killing of the enterocytes, binding of the epithelial cell to the aberrant IEL was necessary. Functional studies revealed that CD103-E-cadherin interaction was essential for release of granzyme-B and loss of enterocytes.
Conclusion: Killing of enterocytes is dependent on upregulated expression and degranulation of granzyme-B and on interaction with the aberrant IEL through CD103-E-cadherin binding. These data contribute to understanding of the pathogenesis of villous atrophy in RCDII and therefore are important for diagnostic purposes and for identification of new treatment options.

**Mast cell activation syndrome (mcas) in patients with rapid onset of food induced symptoms of dyspepsia, ibs, diarrhea, nausea or vomiting reacts favorably on histamine 1 or 2 blockers or cromoglycate. An observational study.**

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Background: Many patients with functional dyspepsia or IBS indicate that their symptoms are being provoked by specific food or food components. This may be due to the mast cell activation syndrome. MCAS of the digestive tract is characterized by 2 major criteria: 1. Multifocal or disseminated infiltrates in mucosal biopsies of >20 CD 117 stained mast cells (MC) per high power field (hpf 400x). 2. Presence of symptoms attributable to pathologically increased MC activity. An additional minor criterion is symptomatic response to inhibitors of MC activation or mediator production. The awareness of MCAS is limited. This milder form of MC hyperreactivity must be distinguished from the more severe and systemic mast cell activation disease (MCAD) or mastocytosis where often skin and bone marrow are infiltrated with abundant MC. In regular HE stained slides MC are overlooked. Special staining with CD 117 displays the cells in characteristic brown color followed by cell count per hpf. We investigated the efficacy of histamine receptor antagonists and MC stabilizers in patients with distinct food induced MCAS.
Patients and methods: Fifty-two patients (45 female, age 41.3±23.3 yrs) with one or more rapid onset (<60 min), food induced symptoms of diarrhea (n=23), functional dyspepsia (n=15), IBS (n=14), nausea (n=12), pain (n=11), bloating (n=6), vomiting (n=5) and cyclic vomiting syndrome (n=3) were included. Biopsies of duodenum (n=47) and colon or ileum (n=6) showed an increase of CD 117 stained MC (30,0±13.1) per hpf. Many patients had long standing and persistent complaints with an average of 10.5±18.4 yrs. Therapy was initiated for four weeks, first with H1 receptor antagonist and MC stabilizer ketotifen 1-4 mg bid or fexofenadine 120-180 mg bid and subsequently H2 receptor antagonist ranitidine 150 mg bid or cromoglycate nalcrom 100 or 200 mg qid.
Results: Medication was tried and changed until the desired clinical response was achieved with one of the drugs. Ultimately 12 patients responded to ketotifen, 15 to fexofenadine, 2 to ranitidine and 14 to nalcrom. The therapeutic efficacy varied from excellent (no to minimal residual symptoms) in 17 (33%), substantial improvement in 15 (29%), modest amelioration in 10 (19%) or no effect in 10 (19%). Three patients used a combination of 2 or 3 drugs.
Conclusion:This observational study shows that when rapid onset, food induced symptoms are present and an increased number of MC (>20 per hpf) is found in mucosal biopsies trial and error treatment of MCAS with H1 or H2 receptor blockers or cromoglycate may substantially improve or remedy often longstanding and frequently debilitating symptoms of the GI tract.

## Development of a core outcome set for infant gastroesophageal reflux disease

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Background: Gastroesophageal reflux disease (GERD) is a common problem in infancy. Ways to define GERD and to measure and report study outcomes vary widely in therapeutic trials for infant GERD, which limits successful uniform evidence-based clinical management. To improve comparison between future therapeutic trials, the aim of this study was to develop a core outcome set (COS) for infant GERD.

Methods: The COS was developed using the Delphi technique and by adhering to the recommendations as provided by the OMERACT 2.0 filter. HCPs visiting the ESPGHAN annual meeting in Athens, Greece 2016, were invited between sessions to participate in the survey. Parents from infants with GERD (age 0 – 12 months) from Europe (Belgium, France, Italy, The Netherlands and the United Kingdom), Australia and the USA were invited to participate in the survey by their infant's treating physician during their scheduled appointment. An English-written questionnaire was handed out on paper and HCPs and parents were asked to list up to five harmful and/or beneficial outcomes which they considered important in the treatment of GERD. Outcomes mentioned by > 10% of participants were included in two shortlists. Outcomes on these shortlists will be rated and prioritized and the five outcomes with the highest rank will be put forward to form a draft core domain set. Regardless of their ranking, adverse events will be added to this draft set. The final COS will be defined in a face-to-face international meeting of pediatric gastroenterologists and representatives of GERD patient associations (May 2018).

Results: In total, 125 HCPs from 33 different countries of origin and 139 parents completed the questionnaires. Sixteen outcome measures were included in the HCP shortlist; seven for the outpatient setting (top 5 listed: 'weight gain', 'feeding problems', 'general symptom improvement', 'parental stress/anxiety', 'failure to thrive') and nine for the inpatient setting (top 5 listed: 'weight gain', 'feeding problems', 'GERD related complications', 'general symptom improvement', 'hematemesis'). The parental shortlist included thirteen outcome measures (top 5 listed: 'parental reassurance', 'feeding problems', 'parental satisfaction', 'use of anti-reflux medication', 'general symptom improvement').

Conclusions: The created shortlists will facilitate the development of the final COS, that will define a minimum set of outcomes that should ideally always be measured and reported in future therapeutic trials in infant GERD. Embedding the COS in these trials may potentially advance the usefulness of research to inform clinical practice, enhance patient care and improve clinical outcomes.

**Detection of Gastrointestinal Ischemia by Means of Endoscopic Visible Light Spectroscopy after Luminal Feeding**

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Background: Endoscopic Visible Light Spectroscopy (VLS) enables targeted catheter-based measurement of mucosal oxygen saturation of the upper gastro-intestinal tract during upper endoscopy. VLS is currently used in the diagnostic work-up of chronic mesenteric ischemia (CMI). Mucosal saturation is significant lower in CMI patients than in patients without CMI. Measurements are typically done during upper endoscopy during fasting. Since CMI is provoked by a meal, VLS during fasting could potentially underdiagnose CMI. We therefore determined the effect of a food challenge on VLS in patients suspected of CMI and in healthy controls.

Methods: We included patients suspected of CMI referred to a specialized CMI center and healthy controls from September 2014–March 2017. All patients underwent a standard diagnostic work-up of medical history taking, mesenteric CTA or MRA and upper endoscocopy with VLS. After VLS measurements in antrum, duodenal bulb and descending duodenum in fasting state, a feeding tube was placed in the stomach. Forty-five minutes after 450 kcal luminal feeding VLS measurements were performed at the same locations. All patients were discussed in a multidisciplinary meeting for an expert view consensus diagnosis of CMI. Patients with a consensus diagnosis of CMI were planned for revascularization therapy. A definitive diagnosis of CMI was established if successful treatment resulted in durable symptom relief. Patients were classified as no-CMI if a consensus diagnosis of no-CMI was established or if successful treatment did not resulted in symptom relief. Healthy controls underwent preprandial and postprandial VLS measurements after abdominal duplex ultrasound confirmed patent mesenteric arteries.

Results: We included 67 patients suspected of CMI and 16 healthy controls. Significantly higher postprandial (post) versus preprandial (pre) VLS-values were seen in the duodenum in healthy controls (post 56% IQR 53-58 versus pre 54% IQR 49-56, p=0.01), no-CMI patients (post 57% IQR 53-59 versus pre 55% IQR 50-57, p<0.01) as well as CMI patients (post 55% IQR 51-57 versus pre 51% IQR 48-53, p<0.01). The relative differences in pre and post VLS values were also calculated per patient. No significant relative differences were observed between CMI patients, no-CMI patients and healthy controls.

Conclusions: Duodenal VLS-values after food administration are significantly higher in healthy controls, no-CMI patients, as well as CMI patients. Postprandial VLS measurements nor the relative difference (pre versus post) provide additional discriminative ability. Therefore postprandial VLS measurements have no clinical applicability for the diagnosis of CMI.

**Differentiation between paediatric irritable bowel syndrome and inflammatory bowel disease based on faecal scent: proof of principle study**

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Background: The diagnostic work-up of paediatric irritable bowel syndrome (IBS) and functional abdominal pain – not otherwise specified (FAP-NOS), commonly includes invasive tests for discrimination from inflammatory bowel disease (IBD). Since this carries a high burden on patients, an ongoing need exists for development of non-invasive diagnostic biomarkers for IBS and FAP-NOS. Several studies have shown microbiota alterations in IBS/FAP, which are considered to be reflected by faecal volatile organic compounds (VOC). The aim of this study was to evaluate whether paediatric IBS/FAP-NOS could be discriminated from IBD and healthy controls by faecal VOC analysis.
Methods: IBS/FAP-NOS was diagnosed according to the ROME IV criteria, and de novo IBD patients and healthy controls (HC) aged 4 to 17 years were matched on age- and sex. Faecal VOCs were analysed by means of field asymmetric ion mobility spectrometry (FAIMS).
Results: Faecal VOCs of 15 IBS/FAP-NOS, 30 IBD (15 ulcerative colitis, 15 Crohn's disease) patients and 30 HC were analysed and compared. Differentiation between IBS/FAP-NOS and IBD was feasible with high accuracy (AUC (95%CI), P-values; 0.94 (0.88-1), <0.00001). IBS/FAP-NOS profiles could not be differentiated from HC (0.59 (0.41-0.77), 0.167), whereas IBD profiles could with high accuracy (0.96 (0.93 – 1), <0.00001).
Conclusion: Paediatric IBS/FAP-NOS could be differentiated from IBD by faecal VOC analysis with high accuracy, but not from healthy controls. The latter finding limits the potential of faecal VOCs to serve as diagnostic biomarker for IBS/FAP-NOS. However, VOC could possibly serve as additional non-invasive biomarker to differentiate IBS/FAP-NOS from IBD.

**Improved barrett's neoplasia detection using computer assisted multi-frame analysis of volumetric laser endomicroscopy images**

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Background and aims: Volumetric laser endomicroscopy (VLE) provides a circumferential near-microscopic scan of the superficial esophageal wall layers, and has potential to improve the detection of early Barrett's neoplasia. However, the interpretation of numerous grey-shaded VLE images is complex and time-consuming. Computer-aided detection (CAD) may aid in this process. Recent CAD studies have focused on neoplasia detection algorithms based on single VLE frames, yet valuable information is then lost because multiple adjacent VLE frames are not used in the analysis. Our study aims to investigate if multi-frame analysis increases the reliability and performance level of CAD assisted Barrett's neoplasia detection.
Patients and Methods: A database consisting of 52 endoscopic resection specimens from 29 Barrett's patients with and without early neoplasia, containing high quality ex-vivo VLE-histology correlations, was used. Sixty VLE images with appointed regions of interest (30 non-dysplastic vs. 30 neoplastic) were assessed using several machine learning methods. We evaluated multiple neighboring VLE frames (± 25 frames), corresponding to 1.25 mm proximal and distal to each region of interest. Therefore, a total of 3060 VLE frames were interpreted via multi-frame analysis in combination with various voting methods, using multiple predictions per region of interest resulting in a weighted score per frame, for the differentiation between non-dysplastic and neoplastic tissue. Results of the multi-frame analysis were compared to the outcomes of previous reported studies by our group using VLE-experts and CAD single-frame analysis.
Results: Multi-frame analysis combined with the best performing voting methods resulted in an AUC of 0.91 (IQR: 0.88 - 0.92) compared to single-frame analysis with an AUC of 0.83 (IQR: 0.78-0.86). Performance of VLE experts demonstrated an AUC of 0.81, with a sensitivity and specificity of 83% and 71%, respectively. The best overall outcome was achieved by including 15-22 adjacent VLE frames, after which an adverse effect was seen. Average time for the CAD algorithm to analyze 60 VLE images was 78 milliseconds, and 3.9 seconds for 3060 VLE images.
Conclusions: Multi-frame VLE image analysis for the computer assisted detection of Barrett's neoplasia, outperforms clinical VLE assessment by experts using the VLE prediction score. Multi-frame analysis shows improved neoplasia detection compared to single-frame analysis. In addition, computer aided detection allows for objective VLE analysis in a split second, bringing future full VLE scan interpretation one step closer.

## The argos project: first results of the development of a computer aided detection system for barrett`s neoplasia

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Background: Early neoplasia in Barrett's esophagus (BE) is difficult to detect during surveillance endoscopies. This is partly because of its subtle appearance and partly because most endoscopists rarely encounter early BE neoplasia and therefore are unfamiliar with its endoscopic appearance . A computer aided detection (CAD) system might assist endoscopists in recognition of early BE neoplasia, thereby improving efficacy of BE surveillance.
Aim: To develop a CAD algorithm using high quality endoscopic images of BE neoplasia.
Methods: Endoscopic images of 40 early neoplastic BE lesions and 20 non-dysplastic BE patients were prospectively collected in 3 tertiary referral centers. Images were obtained using white light endoscopy (WLE) and Blue Light Imaging (BLI) in overview. Six international BE experts annotated all neoplastic images using a proprietary online delineation module specifically designed for this project. The area with ≥1 expert delineations was labelled as the soft spot. This area served as gold standard for detection by the algorithm. The overlap area of ≥4 expert delineations was considered to have the highest suspicion of visible neoplasia and was labeled as the sweet spot. This area served as the gold standard for delineation by the algorithm. The algorithm was trained on local color and texture features (using Gabor filters) of the original neoplastic images, where positive features were taken from the soft- and sweet spot of neoplastic images and negative features from the non-dysplastic images. No pre-processing of the expert delineations prior to input into the algorithm was performed at this stage. Detection performance was investigated based on per-image analyses.
Outcome parameters: 1) Detection scores for WLE and BLI in terms of accuracy, sensitivity, specificity, NPV and PPV; 2) Delineation scores for WLE and BLI: Percentage of sweet spot delineated by the algorithm.
Results: Accuracy, sensitivity, specificity, NPV and PPV for detection on WLE images were 82%, 95%, 55%, 85% and 81% resp., and on BLI images 68%, 100%, 5%, 100% and 68% resp. Mean percentage of the sweet spot delineated by the algorithm on WLE and BLI was 68% and 61%, resp.
Conclusions: This first version of our CAD algorithm detected early neoplastic BE lesions on both WLE and BLI images with high sensitivity and NPV, thereby suggesting feasibility of automated detection of early BE neoplasia. Further work will include additional pre-processing of the expert delineations for probabilistic training of the algorithm to further improve its performance and to relate the performance of the algorithm to the individual performance of the participating experts.

## Safety, tolerability and dosimetry of a novel Swipe Cryoballoon device (90°-SCBA) for ablation of dysplastic Barrett's esophagus

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Background: Cryotherapy has been used for years to eradicate flat dysplastic Barrett's esophagus (BE). It preserves the extracellular matrix and may be better tolerated and result in lower stricture rates when compared to other ablation techniques. Cryoballoon ablation (CBA) comprises a through-the-scope catheter with a conformable balloon that is simultaneously inflated and cooled using nitrous oxide. Thus far, focal CBA has been promising for limited BE. When the cryogen is applied in this novel 90°-swipe-CBA (90°-SCBA), it covers 90° of the esophageal circumference over 3cm in a single step. The controller software allows adjustment of the dose. Dose is the rate at which the diffuser traverses the 3cm long axis of the balloon catheter while emitting cryogen. The 90°-SCBA has been feasible and safe in animal and pre-esophagectomy studies.
Aim: To assess the feasibility, safety and efficacy of 90°-SCBA at increasing doses in patients with dysplastic BE
Methods: Patients with flat BE (circumferential extent ≤3cm) and low or high-grade dysplasia (LGD/HGD) or residual BE after endoscopic resection, were enrolled in 5 Dutch centers. We started with 0.8mm/sec (dose 1). The dose was escalated with 0.1mm/sec until the optimal dose (OD) was found. OD was defined as the lowest dose resulting in median BE regression ≥80% in absence of dose-related serious adverse events (DR-SAEs). DR-SAEs included severe pain (VAS>6 ≥7 days), stenosis requiring dilation. Pain (VAS 0-10) and dysphagia (0-4) and adverse events were evaluated at days 0, 1, 7 and 30. Outcomes were technical success, BE regression (at 8 weeks follow-up (FU) endoscopy assessed by 2 independent endoscopists by systematic comparison of baseline and FU videos), and safety.
Results: We studied 13 patients with median BE length C0M3 with LGD (85%) or HGD (15%). The procedure was technically successful in 12 patients (92%) and 1 procedure partially failed (balloon slid into the hiatal hernia). Device malfunction occurred in 2 other patients (16%) and was resolved with device replacement. No SAEs occurred. BE regression at FU was 78% (IQR 68-86) with 0.8mm/sec (dose 1) and 85% (75-95) with 0.7mm/sec (dose 2), which was in turn defined as OD. Median pain scores were 4 (IQR 3-6), 1(0-2), 0(0-1) and 0(0-0) at days 0, 1, 7 and 30 respectively. Median dysphagia score was 0 at all days.
Conclusion: Our open, pilot, multicenter study shows that 90°-SCBA is feasible, safe and well tolerated in patients with flat dysplastic BE. At the dose of 0.7mm/sec, it results in median BE regression of 85% and is a promising new modality for endoscopic eradication. The latter will be confirmed in a consecutive study.

## Self-sizing radiofrequency ablation balloon for eradication of Barrett's esophagus: results of an international multicenter randomized trial comparing three different treatment regimens.

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Introduction: The 360 Express RFA balloon catheter ("360 Express") has the ability to self-adjust to the esophageal lumen ensuring optimal tissue contact during ablation. Aim of this randomized clinical trial was to compare 3 different ablation regimens for radiofrequency ablation (RFA) treatment of Barrett's esophagus (BE) using the 360 Express.
Methods: Patients with a 2-15 cm BE with low-grade dysplasia (LGD), high-grade dysplasia (HGD) or early cancer (EC) were included. Visible lesions were removed by endoscopic resection (ER) prior to RFA. 36 patients were randomly assigned to each arm: the standard (1x10J/cm2-clean-1x10J/cm2), simple-double (2x10J/cm2-no clean), or simple-single ablation regimen arm (1x10J/cm2-no clean). Primary outcome: % of endoscopically visual BE regression at 3 months (scored by two independent blinded endoscopists). Secondary outcomes: adverse events and procedure time.
Results: Inclusion started September 2015 and was completed by October 2017. A total of 103 patients (81 male, median 66 yrs, median C4M7 BE) were included. 43 patients underwent ER prior to RFA (EC n=22, HGD: n=13, LGD: n=6, non-dysplastic IM: n=2). Worst histology prior RFA: HGD: n=42; LGD: n=51; non-dysplastic IM: n=10. In February 2017, after 28 patients were included in the simple-double arm, this arm was closed early because of an unexpected high risk of severe stenosis (n=6, 21%, 95% CI:10-39%, requiring median 6 dilations). The study was continued with the standard and simple-single arm. To date, a total of 90/103 patients have completed the study (standard, n=31/37; simple-single, n=31/38, simple-double, n=28/28). Median BE regression was higher in the standard arm compared to the simple-single arm: 85% (IQR 75-94), 95% CI:78-92% versus 73% (IQR 48-90), 95% CI:59-85%( p0.009). A poor response (defined as ≤50% regression) was found in 3/31 and in 9/31 patients in respectively the standard and simple-single arm (p 0.05). The standard ablation procedure was significantly longer: median 31mins (IQR 26-36) versus 17mins (IQR 13-20), p<0.001. Adverse events: 5/37 patients in the standard arm (minor laceration n=4, unrelated death n=1) and 5/38 patients in the simple-single arm (minor laceration n=3, minor bleeding n=1, pain and fever n=1).
Conclusions: Results of this randomized controlled trial suggest that RFA with the 360 Express using the standard regimen results in significant better regression after 1 treatment session compared with the simple-single regimen. However, the procedure is longer when using the standard regimen. The simple-double ablation regimen is not advised given the unacceptable risk of severe stenosis.

## Long-term follow-up results of a randomized trial comparing radiofrequency ablation versus endoscopic surveillance in Barrett's esophagus patients with low-grade dysplasia

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Background: In 2014, a randomized clinical trial (SURF trial) comparing radiofrequency ablation (RFA) with endoscopic surveillance in Barrett's esophagus (BE) patients with low-grade dysplasia (LGD) showed a reduction of 25% for progression to high-grade dysplasia (HGD) and cancer in the RFA arm. Based on this study, current international guidelines advise RFA for BE with confirmed LGD. Our aim was to describe the 6 year follow-up results of the SURF-trial.
Methods: The SURF trial was conducted in five countries and included 68 BE patients in the RFA-arm and 68 in the surveillance arm, with LGD confirmed by an expert pathologist. We retrieved all endoscopy and histology reports, performed after study closure in May 2013. Primary endpoint was development of HGD or cancer. Secondary outcomes were number of patients in the surveillance arm treated with RFA for LGD, recurrence of IM with LGD after successful RFA in all treated patients, and regression of LGD during follow-up in the surveillance group.
Results: By the end of the SURF-study, 1 patient (1%) in the RFA group showed progression, compared to 18 patients (26%) in the surveillance arm. During additional median follow-up of 48 (IQR 35-55) months, resulting in a total median follow-up of 77 (IQR 64-91) months, no additional patients in the RFA arm progressed. Of the 50 patients without progression in the surveillance arm, 16 patients were treated with RFA after closure of the study. In the 34 patients kept under surveillance for BE with LGD, progression to HGD/cancer during follow-up was diagnosed in five patients leading to 23/68 (34%) patients in the surveillance arm with neoplastic progression. In 13 of the patients kept under endoscopic surveillance, LGD was not reproduced during follow-up. Looking at all 84 patients treated with RFA for BE with LGD during or after closure of the SURF study, recurrence of small non-circumferential areas of columnar mucosa with focal LGD was found in two cases.
Conclusion: Long-term follow-up results of the SURF-trial comparing RFA versus surveillance for BE with confirmed LGD, show that after RFA progression to HGD/cancer is extremely rare (1%) and recurrence of LGD is very low. In the remaining surveillance group, the progression rate to HGD/cancer increased further to 34%, whereas on the other hand no more LGD was found in 13 patients. This suggests that some patients may have been over-treated for a single finding of LGD. However, this also suggests that if RFA is applied in patients with a repeated diagnosis of LGD overtime, the effect of RFA in reducing neoplastic progression compared to endoscopic surveillance would become even more significant.

## Cryoballoon ablation of dysplastic Barrett's esophagus causes shorter duration and less severe post-procedural pain as compared to radiofrequency ablation

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Introduction: Radiofrequency ablation (RFA) is safe and effective for eradication of Barrett's Esophagus (BE), but is associated with significant post-procedural pain. As an alternative, cryoablation using focal cryoballoon ablation (CRYO) has recently been developed, which freezes BE using nitrous oxide. Cryoablation preserves the extracellular matrix and might therefore result in less pain while maintaining sufficient Dept.h of ablation. Early uncontrolled studies suggest comparable safety and efficacy for focal CRYO and RFA in eradication of short segment BE. Therefore, secondary endpoints such as pain might become decisive for treatment selection. We aimed to compare post-procedural pain between focal CRYO and RFA.

Methods: We included patients with focal ablation of BE (either CRYO or RFA) in two Dutch referral centers from January 2016 to March 2017. All patients were treated in a similar fashion with ablation of all visible BE. Thereafter patients completed a 14 days digital diary to assess chest pain (range 0-10), dysphagia (range 0-4) and use of analgesics. A follow-up (FU) endoscopy was scheduled after 3 months to assess the BE surface regression (blindly assessed by 2 independent BE expert endoscopists by comparing baseline and FU images). Outcomes included cumulative scores over the course of 14 days (assessed by area-under-the-curves (AUCs)) for pain, dysphagia and analgesic use; peak pain; and BE surface regression.

Results: We included 46 patients (20 CRYO, 26 RFA). All baseline characteristics were similar (CRYO vs RFA): worst histologic diagnosis (low grade dysplasia 50% vs 54%, high grade dysplasia or early cancer 50% vs 46%, p0.52), prior endoscopic resection (50% vs 46%, p0.80), prior ablation (50% vs 69%, p0.19) and maximum BE length (2 vs 1cm, p0.52) (. Median AUCs over the course of 14 days for pain (4 vs 22), dysphagia (0 vs 8) and use of analgesics (0 vs 2) were significantly smaller after CRYO versus RFA (all $p<0.01$). Peak pain was lower after CRYO (median VAS 2 vs 4, $P<0.01$). The duration of pain was shorter after CRYO (median 2 vs 4 days, $p<0.01$). CRYO patients used analgesics for a median of 2 days, versus 4 days for RFA patients ($p<0.01$). Median BE regression at FU was comparable (88% versus 90%, p0.65).

Conclusion: In this multicenter, non-randomized cohort study, patients reported less pain after CRYO as compared to RFA; moreover, CRYO patients used less analgesics. Although a randomized trial should provide definitive evidence for differences in post-procedural tolerability, our results strongly suggest a differences favoring CRYO over RFA.

**EUS-guided keyhole biopsies for diagnosis of sub-endothelial tumors: technique description, histological diagnostic yield and safety**

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Incidental subepithelial tumors (SETs) are found in 0.36% of all gastroscopies with a differential diagnosis that ranges from benign leiomyoma or lipoma to (pre)malignant gastro intestinal stromal tumors and neuro endocrine tumors. Endoscopic ultrasound is the first diagnostic step with an accuracy rate of 45.5% - 49% with an interobserver kappa of 0.6 . The currently most used tissue acquisition techniques are fine needle aspiration with a diagnostic yield of 68-89%, bite on bite biopsy 17-59%, fine needle biopsy 63-86% and unroofing >90%. A recently published Dutch study with data from 6 large teaching hospitals showed surprisingly poor real-life data with a diagnostic yield of all procedures of 19%. Therefore, cost effective and safe tissue acquisition with high diagnostic yield is required and for this purpose we developed the EUS guided biopsy procedure. By using a colon biopsy forceps, a channel is made into the SET followed by tissue acquisition from within the lesion all under endo-sonographic guidance.
Objective: To assess the diagnostic yield and safety of the new EUS-guided keyhole biopsy technique in SET tissue acquisition.
Design: A prospectively gathered case series
Setting: A single operator, single center study in a Dutch teaching hospital.
Patients: 23 patients that underwent EUS examinations of a SET in which EUS guided keyhole biopsy was used for tissue acquisition.
Main outcome measurements: The diagnostic yield of EUS guided keyhole biopsy and complication rates.
Results: 20 out 24 of the biopsies resulted adequate histology as 3 were non-diagnostic (including both Schwannomas). In 2 patients, repeat procedures were performed, in which a non-diagnostic procedure and a Leiomyoma turned out to be GIST's in the second procedure and later confirmed surgically. 8 of the 22 SETS were smaller than 2.0 cm and all of these except 2 duodenal lesions were Leiomyoma's. When excluding repeat biopsies 18 out of 22 procedures were diagnostic, resulting in a diagnostic yield of 81%, which increases to 83% if all procedures are included. No complications occurred.
Limitations: A single-center analysis with small sample size with all procedures performed by 1 gastroenterologist.
Conclusion: EUS-guided keyhole biopsy appears to be a simple, safe and effective technique for acquiring tissue of gastrointestinal SET's including lesions smaller then 2cm.

**Endosonographic measurements of tumor thickness and surface area to evaluate tumor response after neoadjuvant chemoradiotherapy in patients with esophageal cancer; a multicenter prospective cohort study**

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Introduction: Endosonography (EUS) is an accurate method for initial staging in esophageal cancer, but does not accurately assess T stage after neoadjuvant chemoradiotherapy (nCRT). EUS maximum tumor thickness (MTT) and maximum tumor area (MTA) have been shown to correlate well with histopathologic residual tumor volume. This study assessed the predictive value of EUS-based measurement by using both MTT and MTA for detection of residual disease after completion of nCRT.
Method: This was a multicenter prospective cohort study within the preSANO study. Patients with esophageal cancer were treated according to the CROSS-regimen. In all patients a radial EUS was performed with measurement of MTT and MTA pre-treatment and at 6 weeks after completion of nCRT. When patients had no tumor in biopsies at 6 weeks post-treatment, a third EUS was performed at 12 weeks. The primary aim of this study was to assess the accuracy to detect Tumor Regression Grade (TRG) 3-4 residual tumors by EUS-based measurements. For this study, a TRG1 was considered a complete response. It was presumed that TRG2 residual tumors were allowed to be missed as these tumors would be detectable during active surveillance when having outgrown from TRG2 to TRG3-4, and were therefore categorized as undetermined. A univariate logistic regression model and a receiver-operating characteristic curve were used to determine the association between EUS-based measurements and residual tumor.
Results: Out of 207 patients included in the preSANO trial a total of 156 underwent surgery. After revision of all EUS measurements, a total of 138 patients were included for analysis. MTT and MTA were significantly associated with residual tumor at 12 weeks (odds ratio 1.36, $p<0.01$ and 1.64, $p=0.02$, resp.). A cut-off of 4.5mm for MTT had a sensitivity of 87%, a specificity of 52%, a positive predictive value of 72%, and a negative predictive value of 74%. For MTA, a cut-off of 0.92cm$^2$ was optimal, with a sensitivity of 89%, a specificity of 40%, a positive predictive value of 68%, and a negative predictive value of 71%.
Conclusion: In this multicenter prospective study we found that MTT and MTA adequately predict TRG3 and TRG4 residual tumor with a sensitivity of almost 90% at 12 weeks after completion of nCRT.

**Long-term outcome of dilatation and stenting of anastomotic and non-anastomotic biliary strictures after liver transplantation**

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Background: Anastomotic (AS) and non-anastomotic (NAS) biliary strictures after orthotopic liver transplantation (OLT) cause morbidity and graft failure. Strictures can be dilated and stented with endoscopy (ERCP), percutaneously (PTC) or treated surgically.
Methods: Risk factors and long-term outcome of dilatation and stenting were analysed for consecutive OLTs 1/2005-1/2015, follow-up till 1/2017, in a single center.
Results: Out of 285 OLTs (31% with donation after circulatory death, DCD), incidence after DCD vs donation after brain death (DBD) was 25.8% vs 21.9% for AS (p=0.47) and 33.3% (n=30) vs. 11.9% (n=24) for NAS (p<0.01). For AS 183 and for NAS 154 intervention ERCPs were performed, with success (no further treatment >1 year) for only AS in 60.5%, for only NAS in 34.6%, for combined NAS and AS in 32.1%. AS required ongoing treatment (interval <1 year) in 27.3%, surgical revision in 7.8%, 1.5% died from cholangiosepsis. In NAS 22.2% required retransplantation, 3.7% died from cholangiosepsis and 31.5% required continued dilatation/stenting. Surgery or death from cholangiosepsis was avoided in 82% of AS and 74% of NAS cases. Normalisation of liver biochemistry after successful dilatation and stenting occurred in 55.5% of NAS and 78.1% of AS cases. Graft- and patient survival were not different for DCD and DBD.
Conclusion: After stenting and dilatation no further treatment was required for more than a year in twothirds of AS and onethird of NAS cases, but many could be managed with shorter treatment intervals, with reduced cholestasis and low rates of retransplantation.

## AP1 components ATF2 and ATF7 are dispensable for the intestinal epithelium during homeostasis

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Background: Transcriptional complex activating protein 1 (AP-1) transcription family is importantly involved in maintaining and restoring intestinal homeostasis. Activating transcription factor 2 (ATF2), a member of the AP-1 family, is exclusively activated in the epithelial crypt, where stemcells and Paneth cells reside, as judged by its phosphorylation status. However, ATF2 contribution to intestinal homeostasis is largely unknown. We generated intestinal specific double ATF2/ATF7 knockout mice and set out to investigate the role of ATF2 and take into account its potential redundancy with another member of AP-1 family ATF7.

Methods: We used germline ATF7$^{-/-}$ knockout animals to generate ATF7$^{-/-}$ATF2$^{fl/fl}$ compound mutants in which injections with tamoxifen resulted in homozygous deletion of ATF2 specifically in intestinal epithelial cells (IEC, ATF2$^{fl/fl(IEC)}$). To monitor ATF2 recombination efficacy, we crossed LacZ reporter alleles into mice.

Results We analyzed the phenotype of ATF7$^{-/-}$ knockout animals and compound ATF7$^{-/-}$ ATF2 $^{fl/fl(IEC)}$ mutants compared to wild type controls during homeostasis. We observed no changes in body weight and no gross morphological changes of the small intestine, as judged by crypt and villi length measurements. Compared to controls, proliferation, assessed by BrdU incorporation in ATF7 $^{-/-}$ and ATF7$^{-/-}$ ATF2 $^{fl/fl(IEC)}$ animals was unaltered and expression of markers of stemness Lgr5, Ascl2 and Olfm4 were not affected. However, we found an altered distribution of Paneth cells. Immunofluorescent staining showed increased lysozyme positive cells per crypt. Altered expression of a set of genes associated with Paneth cell function (e.g. lysozyme, defensins, DLL1 and EGF) in compound ATF2/ATF7 mutant mice corroborate this finding.

Conclusion: Single ATF7 deficiency has no discernible effects during homeostatic conditions. Double ATF2/ATF7 compound mutant, without changing the intestinal epithelial proliferation and expression of stem cell markers, displays an alteration in Paneth cell compartment. The number of lysozyme-expressing Paneth cells is increased, suggesting the involvement of altered antimicrobial function.

**An unbiased proteomic screen identifies CtBP2 as an ER stress dependent regulator of intestinal epithelial stemness**

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Background: In the intestinal epithelium, stem cells are located at the crypt base and their maintenance and differentiation is essential for sufficient organ function. ER-stress, the accumulation of mis- or unfolded proteins in the endoplasmic reticulum, leads to an unfolded protein response (UPR) which can force intestinal epithelial stem cells into differentiation. However, the molecular mechanism remains largely unknown. Differentiation upon ER-stress is dependent on PERK-eIF2a phosphorylation, a prominent feature of the UPR. We hypothesize that loss of transcription factors (TFs), through translational attenuation via PERK-eIF2a phosphorylation, effects stem cell fate. So far, investigating alterations of TFs has been technically challenging. Here we successfully set out to identify TF changes upon ER stress using an unbiased proteomic screen and investigated their role on stem cell fate maintenance.
Methods: LS174T-cells, which resemble the transcriptional profile of intestinal stem cells, were treated with thapisigargin for two hours to induce ER stress. Cells were lysed in a hypotonic buffer. In a TF DNA-binding assay (CatTFRE), TFs present in cellular lysate are bound to plasmid DNA, co-extracted and quantified using mass-spectrometry.
Results: CatTFRE assay quantified the binding activity for >1000 TFs. Approximately 40 TFs showed downregulated binding to template DNA upon thapsigargin treatment compared to control. TFs that were also downregulated on protein level by immunoblot, suggested that these TFs were lost due to translational attenuation. We identified transcriptional corepressor CtBP2 as the most significantly downregulated protein. In mouse small intestine, immunohistochemistry showed CtBP2 expression in the proliferative compartment where stem cells reside. In situ hybridization and mRNA expression analysis on epithelial FACS sorted cells confirmed this finding. We next investigated the effect of CtBP2 knockdown on stemness in LS174T colon cancer cells. Knockdown of CtBP2 using transient transfection of shRNA directed against CtBP2 resulted in significant decrease of stem cell markers LGR5 and OLFM4 compared to control cells. Conversely, we observed increase in differentiation markers VIL and P21.
Conclusion: ER stress results in differentiation of intestinal epithelial stem cells through attenuation of protein translation. Using a proteomic screen we identified TFs with decreased DNA binding activity upon ER stress, pinpointing the transcriptional regulator CtBP2 as a target that is lost through translation attenuation. Our data suggests that the loss of CtBP2 contributes to intestinal epithelial stem cell differentiation.

**Aberrant lipid metabolism in patients with DGAT1 deficiency**

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Background and aims: Congenital diarrhoeal disorders (CDD) are rare disorders of the gastrointestinal system that can be attributed to numerous monogenic aetiologies. Recently, mutations in DGAT1 have been identified in patients with a form of CDD that involved early-onset protein-losing enteropathy (EO-PLE), but the underlying molecular pathomechanism of DGAT1 deficiency has remained largely elusive.
Methods: We studied 9 patients from 6 unrelated pedigrees suffering from intestinal failure, including early-onset severe diarrhoea, hypoalbuminemia, and sometimes fatal PLE that segregates perfectly with the disease in an autosomal recessive fashion. We performed whole exome sequencing to identify genetic disease aetiologies. We analysed DGAT1 variants in patient-derived fibroblasts and intestinal organoids. We confirmed the phenotype through rescue by exogenous expression of DGAT1 in patients' fibroblasts and CRISPR/Cas9-guided deletion of DGAT1 in healthy control intestinal organoids.
Results: We identified 5 novel bi-allelic loss-of-function mutations in the gene DGAT1 encoding diacylglycerol-acyltransferase 1. DGAT1 catalyses the formation of triglyceride from diacylglycerol and acyl-CoA. The mutations led to severely reduced or absent protein expression, resulting in lack of lipid droplet formation after treatment with oleic acid in patient derived fibroblasts and intestinal organoids. Using lipid chromatography, we show that DGAT1 deficiency specifically altered triglyceride metabolism. Exogenous DGAT1 reconstitution, and intriguingly exogenous DGAT2 expression rescued lipid droplet formation in fibroblasts.
Conclusion: We here identified the largest cohort of DGAT1-deficient patients thus far, linking DGAT1 deficiency to altered lipid metabolism and fat intolerance. For the first time, we show the importance of DGAT1 in gut epithelium, and that exogenous DGAT1 and DGAT2 expression could rescue aberrant lipid metabolism in patient cells.

**Intestinal fetal organoids as a model of intrinsic postnatal epithelial maturation**

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Objective: One of the most important features of postnatal gut maturation in rodents is the change in intestinal brush border enzyme expression, allowing the epithelium to adapt from milk to solid food. Transplantation experiments of fetal epithelium into subcutaneous tissue of adult animals suggest that at least part of this transition is intrinsically programmed. In this context, we used mouse fetal intestinal organoids as a model and aimed to determine whether fetal intestinal organoids in vitro mimic the in vivo gut epithelial maturation process that takes place from birth till weaning.
Methods: Mouse intestinal organoids were cultured from primary fetal intestinal epithelial cells (E19) for one month, with adult intestinal organoids cultured in parallel. Global gene expression profiles of fetal organoids at day 3 and day 28 of culture were identified by micro-array and compared to fetal and adult intestinal tissue. Subsequently, expression of specific maturation markers was evaluated weekly in fetal organoids by qPCR, enzyme activity assay and immunohistochemistry. To investigate whether gut maturation in fetal intestinal organoids can be modulated, organoids were treated with dexamethasone.
Results: Global gene expression profiles showed an overall shift from fetal towards adult epithelium in fetal organoids cultured for 28 days, compared to day 3 of culture. Markers of neonatal intestinal epithelium (Argininosuccinate synthase 1, Blimp-1, Cnx43 and FcRn) could be detected in fetal organoids at day 3, but were progressively lost and completely absent at day 28 of culture. In contrast, characteristics for adult intestinal epithelium, such as sucrase-isomaltase, trehalase, arginase 2 and Paneth cell markers, were absent in the fetal organoids during the first two weeks of culture and gradually increased to adult levels after 4 weeks. Results were confirmed on protein and enzyme activity level, indicating that fetal organoids develop a functional adult brush border over time. Finally, dexamethasone accelerated certain aspects of in vitro maturation in fetal intestinal organoids.
Conclusion: Our data show that mouse fetal intestinal organoids mature into adult epithelium in vitro, recapitulating the hallmarks of in vivo intestinal epithelial maturation. Fetal organoids can therefore be used to elucidate the mechanisms of postnatal epithelial development and identify novel factors that influence the timing of epithelial maturation. Such insights are essential for a better understanding of (nutritional) factors that promote gut maturation, especially for infants with delayed or compromised gut maturation such as preterm and undernourished infants.

**UPR transcription factors ATF6 and XBP1s reduce colorectal cancer cell proliferation and stemness through interaction with PERK**

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Background: The unfolded protein response (UPR) is a cellular stress response activated upon accumulation of misfolded proteins in the lumen of the endoplasmic reticulum (ER). Activation of the UPR results in differentiation of intestinal epithelial stem cells and colon cancer stem cells via UPR kinase PERK, which results in increased chemosensitivity.
Activation of PERK and downstream phosphorylation of eIF2α attenuates translation. Transcriptional activity of XBP1 and ATF6 in contrast result in expansion of the ER. Previously, it was shown that knockout of XBP1 increases proliferation and tumor formation in mice. Therefore, we hypothesize that XBP1 signaling results in reduction of stemness and cellular proliferation in colon cancer cells. Since XBP1 and ATF6 have overlapping transcriptional targets, we additionally examine colorectal cancer cell proliferation upon ATF6 activation.
Methods: We generated LS174T colorectal cancer cell lines that stably carry transcripts enabling doxycycline inducible expression of the active form of XBP1 (XBP1s) or ATF6 (ATF6-373 truncated protein). In these cell lines, we measured downstream activation of UPR signaling or intestinal stem cell markers using quantitative RT-PCR or protein immunoblot. We determined proliferation using crystal violet and EdU incorporation. Global translation was measured with $^{35}S$ methionine incorporation.
Results: Enforced expression of transcription factor XBP1s or $ATF6^{373}$ resulted in marked increase of downstream UPR target genes GRP78 and CHOP. Cellular proliferation was decreased significantly. We additionally found reduced expression of intestinal epithelial stem cell markers OLFM4 and LGR5. Interestingly, we found that XBP1s or ATF6 increased activation of PERK-eIF2α signaling, with decreased cellular translation as a result. Inhibition of eIF2α phosphorylation via constitutive expression of phosphatase GADD34 rescued XBP1 or ATF6 induced growth retardation.
Conclusion: Activation of UPR signaling in the intestinal epithelium, adenomas and colorectal cancer cells results in differentiation of stem cells. We observe that activation of transcription factors XBP1s and ATF6 inhibit proliferation and reduce translation in LS174T colon cancer cells. XBP1s and ATF6 induced proliferation inhibition exposed a novel interaction with PERK-eIF2α signaling. We identify inhibition eIF2α phosphorylation as responsible for XBP1s and ATF6 induced differentiation. Targeting PERK-eIF2α in colon cancer may thus be utilized for colorectal cancer cell differentiation and increase in chemosensitivity.

**Colonic CD90+ crypt-based fibroblasts secrete semaphorins to support epithelial growth**

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Background and aim: The intestinal epithelium renews every 3-5 days and this process is fully dependent on stem cells. Stem cell potential is strictly defined by its microenvironment – the stem cell niche – which provide all signals required for stem cell maintenance and differentiation. Cell cultures developed from a single stem cell – organoids – still requires addition of growth factors such as EGF, R-spondin1 and Noggin. Local fibroblasts may help to support stem cells by producing these missing factors. We aimed to find a specific fibroblast subpopulation in mouse colon that is able to support stem cell growth and can be visualised by a membrane staining.
Methods: Different fibroblast subpopulations were isolated by flow sorting technique. Sorted cells were further characterized by microarray analysis and results were confirmed by qPCR. Based on microarray results few membrane markers were chosen and an expression pattern of these markers was studied by immunofluorescent and in situ hybridisation tissue staining. To access the ability of fibroblasts to support organoid growth perimeter of organoids was measured.
Results: We identified several new membrane markers expressed by all colon fibroblasts (such as Itga9, Sdc2 and Sdc3) and two markers that showed a differential expression (Itga8 and CD90). Itga8 stained mostly smooth muscle cell layer in a colon and does not contribute to the stem cell niche. CD90+ cells located in close proximity to stem cells, supported stem cell growth and express crucial stem cell growth factors such as Grem1, Wnt2b and R-spondin3. We also identified semaphorins class 3 (Sema3) members expressed by CD90+ fibroblasts. Treatment of organoids with recombinant Sema3a increased organoid growth. Alternatively, blocking of Sema3 binding to its receptor Nrp2 by using recombinant Nrp2 reduced organoid growth in co-cultures with CD90+ fibroblasts.
Conclusion: We identified CD90 as a marker for mouse colon fibroblasts located in close proximity to stem cells. This subpopulation supported stem cell growth and expressed crucial stem cell growth factors such as Grem1, Wnt2b and R-spondin3. Moreover we found an additional protein family, class 3 semaphorins (Sema3), which is expressed by CD90+ fibroblasts and able to increase organoid growth.

**Preoperative biliary drainage reverses cholestasis-associated inflammatory and fibrotic gene signatures in patients with perihilar cholangiocarcinoma**

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Background and Aims: Perihilar cholangiocarcinoma (PHCC) can only be cured by major liver surgery. Preoperative biliary drainage (PBD) alleviates cholestasis in PHCC patients, but postoperative mortality rates remain high. PBD-related complications contribute substantially to perioperative morbidity. There is currently no agreement on the timing, technique, or extent of PBD for PHCC. The aims of this study were to investigate the mechanisms through which cholestasis impairs the hepatic resilience to partial liver resection and to assess the extent to which PBD reverses these changes.
Method: Eight patients with resectable PHCC underwent unilateral PBD, meaning that only the future remnant liver received biliary decompression. During surgery, paired cholestatic and post-cholestatic (after PBD) liver biopsies were collected. Control ('healty') liver biopsies were collected from 8 patients with a non-PHCC hepatic malignancy or a benign liver lesion. Patients with pre-existent parenchymal pathology, patients who received preoperative chemotherapy, or patients who underwent preoperative portal vein embolization were excluded. Gene expression profiles of the 24 collected liver biopsies were generated by microarray according to standard bioinformatics methods/protocols.
Results: The median(±IQR) duration of cholestasis in the PBD group was 87 (67-91) days. Total bilirubin levels peaked at 270 (193–304) µmol/L and dropped to 20 (12–33) µmol/L prior to surgery. The incidence of cholangitis and pancreatitis prior to surgery was 3 out of 8 and 1 out of 8, respectively. The control group comprised patients with (cyst)adenoma, giant haemangioma, hepatocellular carcinoma, intrahepatic cholangiocarcinoma, or angiosarcoma. Cholestasis triggered the expression of extracellular matrix-related genes (e.g., collagens), pro-fibrotic (transforming growth factor beta pathway) gene sets, and pro-inflammatory (tumor necrosis factor alpha and inflammasome pathway) gene sets. In addition, gene sets reflecting hepatocyte-specific function were suppressed by cholestasis. Following unilateral PBD, the expression of hepatocyte-specific genes normalized. In addition, the aforementioned pro-fibrotic and inflammatory changes in gene expression were largely alleviated.
Conclusion: Unilateral preoperative biliary drainage reverses cholestasis-associated pro-fibrotic and inflammatory hepatic gene signatures in the future remnant liver of patients with perihilar cholangiocarcinoma.

**Autologous neoantigen-specific T cell responses in low mutation burden colorectal cancers**

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Background: Innovative treatment options are required to improve cure rates in advanced colorectal cancer patients. Immune checkpoint blockade therapy (anti-PD-1) was shown to be effective in colorectal cancers with high mutation burden (e.g. mismatch repair deficient) as anti-tumour reactivity is largely explained by the recognition of somatically mutated antigens (neo-antigens). No immunotherapeutic strategies are currently available for patients diagnosed with CRC with low mutation burden while they could greatly benefit from the induction of immune responses. We hypothesized that if autologous neo-antigen-reactive T cells are present in such patients, they might benefit from specific immunotherapeutic interventions that stimulate neo-antigen recognition.
Methods: In order to detect neo-antigens, exome and RNA next-generation sequencing were performed in cancer and healthy tissues from colorectal cancer patients. Corresponding peptides were synthesized and tested for their ability to induce immune cell activation in lymphocytes isolated from the tumor tissue and from peripheral blood. Reactivity of the obtained tumour-reactive T cells was assessed after co-incubation with synthetic peptides containing the neoantigen-epitopes identified based on whole-exome and RNA sequencing.
Results: Neoantigen-specific T cell responses were identified against 5 out of 39 neo-antigens corresponding to 35 somatic mutations that were expressed in the tumor tissue from a CRC patient. Strikingly, one of the recognized peptides corresponds to a mutation in a cancer driver gene, essential for CRC development and progression and therefore, an ideal therapeutic target.
Conclusion: We developed a neo-antigen screening pipeline to unlock the immunogenic potential of colorectal cancers with low mutation burden. We have detected a relatively high number of neo-antigens that are recognized by autologous T cells in a mismatch repair proficient, low mutation burden CRC patient. This finding supports the widespread evaluation of the potential to employ neo-antigen-targeted therapies to improve the treatment of colorectal cancer patients.

**TRAIL produced by SMAD4 deficient tumors stimulates BMP2 production by fibroblasts and enhances colorectal cancer invasiveness**

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Although it is widely accepted that carcinomas arise as a consequence of accumulation of somatic mutations in epithelial cells, there is increasing evidence that the tumor stroma plays a significant role in colorectal cancer (CRC) progression and metastasis. Previously, it was shown that CRC patients with a SMAD4 mutation (a central component of the Bone Morphogenetic Protein (BMP) signaling pathway) with a high stromal content have a worse prognosis compared to SMAD4$^+$ CRCs. This suggests the existence of metastasis enhancing tumor-stroma crosstalk specifically in SMAD4$^-$ CRCs. We set out to investigate whether this is the case and if so, by which molecular mechanisms. Transwell invasion assays showed that SMAD4$^-$ negative HT29 CRC cells invade more when fibroblasts are used as a chemoattractant, compared to isogenic SMAD4$^+$ HT29 cells. Gene expression analysis revealed that upon stimulation with conditioned medium (CM) from SMAD4$^-$ HT29 cells, BMP2 is strongly upregulated in fibroblasts but not by the isogenic SMAD4$^+$ cells. More importantly, when fibroblasts were replaced by BMP2 invasion of SMAD4$^-$ HT29 cells was equally stimulated. To investigate which secreted factors SMAD4$^-$ cell lines produce that could activate fibroblasts and stimulate BMP2 expression, in silico analysis of mRNA expression data of 26 human CRC cell lines was performed. TNF-Related Apoptosis-Inducing Ligand (TRAIL) was increased 3-fold in SMAD4$^-$ lines compared to SMAD4$^+$ lines. Indeed, stimulation of fibroblasts with recombinant human TRAIL increased BMP2 expression. To further study the role of SMAD4$^-$ tumor-stroma interactions in vivo, we co-injected fibroblasts and either HT29 SMAD4$^+$ or SMAD4$^-$ cells in a mouse model of metastasis. A significant increase in liver metastasis was found in mice that were co-injected with fibroblasts and SMAD4$^-$ HT29 cells compared to mice that received co-injections with SMAD4$^+$ HT29 or SMAD4$^-$ HT29 cells only. To investigate the clinical relevance in human CRC, immunohistochemical analysis was performed. Results showed a significant reduced overall survival in CRC patients with the combination of high stromal BMP2 expression, and loss of tumor SMAD4 expression.
In conclusion, we propose a model in which SMAD4$^-$ tumor cells drive upregulation of fibroblast BMP2 expression via TRAIL secretion, resulting in increased invasive behavior and metastases. This might explain the observed reduced overall survival found exclusively in patients with SMAD4$^-$ CRC and high stromal BMP2 expression.

**Synergistic inhibition of tumor growth by combined endoglin and PD1 targeting in colorectal cancer**

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Colorectal Cancer (CRC) is one of the most common cancers in the western world. Although tumors arise from mutations in epithelial cells, the tumor micro environment (TME) plays an important role in the progression of CRC. The TME consists of a heterogeneous group of cells; the inflammatory cells, endothelial cells forming the tumor vasculature and cancer associated fibroblasts (CAFs). These cells also express the Transforming Growth Factor - beta (TGF-b) co-receptor endoglin, as we could previously show. TRC105 is an endoglin neutralising antibody, which is currently under clinical development. In preclinical models we have shown that TRC105 can directly inhibit tumor metastases by targeting both endothelial cells and CAFs in the TME, at least partly by immune dependent mechanisms. To enhance the therapeutic efficacy of TRC105 in the current study we have combined TRC105 with anti-programmed cell death-1 (PD-1) therapy. PD-1 is found on activated T-cells and when interacting with its ligand PD-L1 suppresses T-cell function.
In three different mouse models, representative for different stages of CRC, we have investigated the effects of TR105 anti-endoglin therapy in combination with anti-PD-1. In the azoxymethane (AOM) dextran sodium sulphate (DSS) model for early tumor development model we observed significantly less lesions in the colon upon combination therapy (14 vs 8 lesion respectively, $P<0.05$). This was accompanied by a decrease in the amount of blood vessels within the tumor ($P<0.05$). In a subcutaneous syngeneic MC38 model we found significant delay in tumor growth and a significant increase in tumor-free mice in the group who received TRC105/PD1 combination therapy. To investigate the potential therapeutic efficiency in advanced cancer, we tested TRC105/PD1 therapy in a orthotopic syngeneic MC38 tumor model. A small piece of donor tumor was transplanted to the caecum of recipient mice and after engraftment and randomisation, therapy was commenced. Nine days after the start of therapy a significant increase in tumor-specific T-cells was seen ($P<0,05$) in the blood in the combination group. At the end of the experiment significantly smaller tumors were detected in the combination group. Flow cytometric analyses revealed a decrease in the tumor associated neutrophils (TANs) ($P<0,05$) and increase in NK cells, capable of inducing cellular cytoxicity responses. Taken together we have shown that TRC105 combined with anti-PD-1 increases therapeutic efficacy in three CRC models. Currently, we are investigating the underling mechanism, including ADCC responses.

**Altered arginine metabolism in hyperproliferative intestinal epithelium: a potential role in tumorigenesis and wound healing**

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Background: The semi-essential amino acid arginine is important for intestinal epithelial cell proliferation and is delivered by solid food. Homeostatic adult intestinal enterocytes catabolize arginine, by expressing arginase 2. During embryonic development, the demand for arginine increases, due to rapid growth. Neonatal enterocytes are capable of de novo synthesis of arginine, by expressing argininosuccinate synthetase 1 (ASS1), the rate-limiting enzyme in arginine biosynthesis. A hallmark of postnatal intestinal epithelial development is increased epithelial cell proliferation. Similarly, a hyperproliferative intestinal epithelium marks onset of tumorigenesis and wound healing. The aim of this study is, to investigate, whether de novo arginine synthesis via ASS1 occurs and contributes to these processes.
Methods: We performed immunohistochemistry and RT-qPCR for ASS1 on intestines from mice in various damage/repair and tumorigenesis models. RNA and protein expression were also assessed in two separate cohorts of Stage I/III colorectal adenocarcinoma patients (n=70 and n=112 patients). Stable isotope labelling was measured in urea-cycle metabolites after addition of [13C;3,3,4-D3]citrulline by means of liquid chromatography mass spectrometry. Intestinal organoids from $APC^{fl/fl}$ mice were transduced with a shRNA for ASS1. Growth and proliferation were assessed upon knockdown, and protein synthesis was measured by [35S]-methionine labeling.
Results: ASS1 highly expressed in murine intestinal adenomas and hyperpoliferative crypts from wounds, as well as after irradiation, compared to homeostasis. ASS1 expression is increased in human adenomas and stage III adenocarcinomas. In organoids generated from the $APC^{fl/fl}$ genotype, ASS1 RNA and protein are highly expressed, with concomitant increase of intracellular arginine. A similar metabolic shift is observed in arginine metabolism between $APC^{fl/fl}$ organoids and regenerating intestine after irradiation. After incubation with labelled citrulline, we found that the urea cycle does not flux in $APC^{fl/fl}$ organoids resulting in intracellular arginine accumulation. Upon knockdown of ASS1 in $APC^{fl/fl}$ organoids, organoid size and protein synthesis are compromised.
Conclusion: In a hyperproliferative state, arginine metabolism undergoes a metabolic shift: intestinal epithelial cells synthesize arginine via ASS1 and the urea cycle no longer fluxes. The upregulation of ASS1 plays a functional role to support growth and protein synthesis of these cells.

**Mutations of the adenoma to carcinoma sequence control an increased cellular capacity of global translation in the intestine**

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Background: The adenoma to carcinoma sequence (ACS) consists of a number of defined recurrent driver mutations that govern formation of intestinal adenomas and subsequently development of colorectal cancer (CRC). It remains unclear how these mutations alter the cellular identity to enable oncogenic transformation. Pathways associated with cancer development are known to impinge on global translational control, but whether this occurs in CRC remains unknown. The purpose of this study was to assess the effect of the most commonly mutated CRC genes - Apc, Kras, and Smad4 – on the global translational capacity.
Methods: To mimic CRC development on a mutational level, we introduced homozygous Apc deletion ($Apc^{-/-}$) and heterozygous transgenic $Kras^{G12D}$ ($Kras^{G12D/wt}$), into small intestinal organoids from previously used mouse models, using tamoxifen-induced cre-lox recombination in vitro. We further generated stable lines of lentivirally transduced shSmad4 in wildtype and $Apc^{-/-}$/$Kras^{G12D}$ organoids. Mutational presence was enforced by selection with growthfactor withdrawal (R-spondin/Apc, Egf/Kras, Noggin/Smad4) or treatment with recombinant TGF-β (Apc-Kras-Smad4 triple mutants). Global translation rates were measured by $^{35}$S-methionine incorporation followed by TCA precipitation and quantification by liquid scintillation.
Results: Already 48 hours after tamoxifen-inducted Apc loss, global translation rates were increased by 26% compared to unfloxed control organoids (P=0.0009). Interestingly, although $Kras^{G12D}$ expression alone did not alter translation, in addition to Apc loss it led to further increased global translation of 156% (P<0.001), compared to Apc mutations alone. shSmad4 organoids showed increased translation between 30-40% (P=0.04) when compared to wildtype organoids, while the combination of Apc, Kras, and Smad4 mutations resulted in the highest rate of translation. Furthermore, 24 hour withdrawal of Egf and R-spondin (Ras/MAPK and Wnt signaling) significantly decreased global translation rates by 28% and 24% respectively (P=0.0002). qPCR analysis showed increased mRNA levels of the key translation initiation factors – eIF2B5, eIF3, eIF4E – in both $Apc^{-/-}$ and $Apc^{-/-}$/$Kras^{G12D}$ organoids, whilst these factors were decreased in $Kras^{G12D}$ organoids.
Conclusion: We conclude that the most commonly mutated genes in CRC - Apc, Kras, and Smad4 – enhance the rate of global translation, indicating that the global translation capacity is strongly affected throughout the adenoma to carcinoma sequence. In light of the emerging role of deregulated translational control in many cancers, increased global translation may be a crucial component of CRC development.

**Anti-BMP2/4 lama-derived antibodies promote neo-squamous re-epithelization at the squamo-columnar junction in a novel cryo-ablation mouse model**

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The best current endoscopic treatment options for Barrett Esophagus (BE), are ablative therapies. Endoscopic cryo-ablation is a minimal invasive thermo-ablative method that can be to erradicate BE. After ablation, the damaged columnar metaplastic BE epithelium is replaced by neo-squamous epithelium. One problem is that in 10-20% of the BE patients still have remnant BE mucosa after undergoing ablative therapies, being resistant to the treatment. Therefore, additional targeted therapies to prevent recurrence of the columnar metaplastic epithelium are desired. In previous studies we demonstrated that bone morphogenetic proteins (BMPs) play an important role in the development of columnar metaplasia or BE. Recently, we developed anti-BMP llama-derived antibodies that specifically inhibit for BMP2/4.

AIM: To test the effect of the anti BMP2/4 inhibitor for its effect of epithelial healing in an cryo-ablation model. Additionally, to perform lineage tracing using K5-cre-Tomato-GFP lineage tracing mice to investigate the site of origin of the neo-squamous epithelium.

Method: Cryoablation of the stomach epithelium in wild-type and CK5 lineage tracing mice was performed just distal of the squamo-columnar junction and mice were treated with intraperitoneal injections of saline or BMP inhibitor for 0, 7, 14 and 21 days. The healing process of the ablated area was investigated by histology and immunohistochemistry, (IHC) using a panel of both squamous (CK5 and p63) and columnar markers (Villin, CK19).

Results: At 21 days post ablation, we observed that the inhibition of BMP4 promoted the re-generation of neo-sqaumous epithelium in the ablated area, while the control group showed re-generation of normal stomach epithelium. IHC showed that the neo-squamous epithelium was positive for the CK5 and p63 squamous markers. Lineage tracing indicated that the squamous cells originated for multilayered glands at the squamo-columnar junction and from the adjacent squamous epithelium.

Conclusion: Our results demonstrate that inhibition of BMP2/4 after ablation of columnar epithelium at the squamo-columnar junction, promotes development of neo-squamous epithelium from submucosal multi-layered glands residing at the SCJ and adjacent squamous epithelium, at the same time the regeneration of columnar epithelium is inhibited. These pre-clinical findings can be translated to a clinical setting in order to optimize ablative therapies for treatment of BE patients.

**Increased levels of the systemic immune-inflammation index and risk of incident cancer: results from a population-based cohort study**

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Background: It is commonly accepted that there is an association between inflammation and cancer, however there are multiple theories on how the two are related. It is thought that chronic inflammation increases the risk of cancer, but another theory is that the body has an inflammatory response to the cancer. The systemic immune inflammation index (SII) is a novel inflammatory marker with a prognostic value in solid tumors, such as colorectal and pancreatic cancer. However it is unknown whether higher levels are also associated with a higher risk of incident cancers. Therefore we assessed the relationship between the SII and incident cancers in the general population.
Methods: Data were obtained between 2002 and 2013 from the Rotterdam study, a population-based prospective cohort study among the elderly. Absolute granulocyte (N), lymphocyte (L) and platelet (P) counts were used to calculate the SII at baseline (N/L*P). Cox proportional hazard models were used to assess the risk of a solid tumor over time. All analyses were adjusted for important cancer risk factors such as age, gender, smoking status, diabetes status and BMI. To assess a dose-effect relationship, we performed an into quartiles stratified analysis. We additionally assessed the effect over time and lastly we explored whether the effects could be attributed to any specific cancer.
Results: In total 8,024 individuals were included, of which 57.3% female with a mean age of 65.6 years (SD 10.5 years). During a mean follow-up period of 6.7 years (IQR 5.2 - 8.3 years) 733 individuals developed a solid cancer. Higher inflammatory markers at baseline were associated with a significantly higher risk of developing a solid tumor; HR of 1.30 (95% CI; 1.11 – 1.53). A dose-effect relationship was present; for each subsequent quartile the risk was higher, with a significantly higher risk in the 4$^{th}$ quartile compared to the reference (1$^{st}$ quartile): HR 1.39 (95% CI; 1.12 – 1.72 and $P_{trend}$ = 0.002). Effects were similar for prostate, colorectal and lung cancer, however there was a null-effect for breast cancer. Cancer risk was highest in the first 6 months after measurement, but also significantly increased five or more years later.
Conclusion: Higher values of the SII are associated with a higher risk of a solid incident tumor on the short- as well as the long-term. The increased risk of incident cancer diagnosis within 6 months after measurement might reflect a systemic immune response to a subclinical cancer. In contrast, the association between longstanding chronic inflammation over time and cancer risk might indicate that inflammation plays a role in the initiation of cancer.

## Features of incident CRC in Lynch syndrome

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Purpose: Despite intensive colonoscopic surveillance, many Lynch syndrome (LS) patients develop colorectal cancer (CRC). Incomplete surveillance colonoscopies and irradical polypectomies can explain some of the cases. Whether adenoma and tumor morphology could also play a role has not been investigated in detail. The aim of this study was to characterize incident CRC in LS patients.

Methods: All patients diagnosed with incident CRC after start of colonoscopic surveillance were identified in the Dutch Lynch Syndrome registry. A retrospective analysis of patient records was carried out for patient characteristics, survival, CRC characteristics and findings of previous colonoscopy.

Results: Seventy-one patients (7.8% of the LS cohort) were diagnosed with incident CRC. The median colonoscopy interval was 23.8 (range 6.7 – 45.6) months. Median tumor diameter was 2.5cm (range 0.8-8.0cm). Most tumors (60%) were polypoid or exophytic in appearance, and sessile or flat morphology was described for 17% of the tumors. Most patients (83%) had no lymph node metastases. Tumor size was not associated with positive lymph node status. CRC was discovered in previously unvisualized colon in 4% of the patients, and ten patients (14%) developed CRC at the site of previous polypectomy. Most patients (65%) had no adenomas during previous colonoscopy. Two patients (2.8%) eventually died from metastatic CRC.

Conclusion: The high rate of incident CRC in LS can in part be explained by the fast conversion of adenomas to CRC, supported by our finding of a high frequency of small tumors in combination with 65% of patients having no adenomas during the previous exam. Non-polypoid appearance of tumors makes colonoscopic detection more difficult. Furthermore, incomplete colonoscopy and irradical polypectomy could explain at least 18% of the incident CRC. Early detection and indolent growth of CRC, as demonstrated by the lack of lymph node metastases, contribute to the excellent survival observed.

## Comparison of two brands of fecal immunochemical tests within the Dutch nationwide CRC screening program

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Background: Colorectal cancer (CRC) screening is gradually being implemented worldwide. Although different brands of fecal immunochemical tests (FITs) are currently used for CRC screening, studies in large screening settings comparing the accuracy of different FITs in detecting advanced neoplasia (AN) are lacking. We compared the accuracy of two different FIT brands to detect AN within a population CRC screening program.
Methods: A large prospective equivalence study was conducted in the Dutch CRC screening program. Of all screening-naïve subjects aged 55-75 years living in the South-Western region of the Netherlands, 42,179 were randomly selected and invited to perform two FITs simultaneously on the same stool sample: one OC-Sensor (Eiken, Japan) and one FOB-Gold (Sentinel, Italy). Colonoscopy was performed in case of at least one positive FIT(s), using a cut-off of 15µg hemoglobin/gram feces. Primary outcome was detected AN in invitees. Equivalence in diagnostic yield was evaluated, with a predefined margin of 0.15%. We also calculated the relative true-positive and false-positive rate of both brands.
Results: Of 42,179 individuals invited, 22,111 (52%) participated. Of these, 21,078 (95.3%) completed both FITs, 694 (3.1%) completed one FIT, and 339 (1.5%) gave informed consent for the study but completed none. A total of 2,112 participants (9.6%) had at least one positive FIT, of whom 1,778 (84%) had a colonoscopy. Overall diagnostic yield of AN in invitees was 1.45% for FOB-Gold and 1.44% for OC-Sensor, with an absolute difference of 0.01% (95% CI: -0.06% to 0.08%). Of those who completed both FITs (n=21,078), 1,582 (7.5%) had a positive FOB-Gold and 1,627 (7.7%) a positive OC-Sensor.AN was detected in 583 of the FOB-Gold positives (36.9%) and in 604 of the OC-Sensor positives (37.1%). For CRC, these numbers were 73 (4.6%) versus 77 (4.7%). Relative true-positive rate (sensitivity) of FOB-Gold to OC-Sensor in detecting AN was 0.97 (CI 0.92 to 1.01) and 0.95 (CI 0.87-to 1.03) in detecting CRC. Likewise, the relative false-positivity rate for AN was 0.99 (CI 0.93 to 1.05) and 0.98 (CI 0.94 to 1.02) for CRC.
Conclusion: Based on this large trial we can exclude meaningful accuracy differences between FOB-Gold and OC-Sensor in detecting AN and CRC in population-based CRC screening. This study and its results can enable informed decision making about the implementation of future FIT-based screening programs.

**Effect of oral anticoagulants and NSAIDs on the accuracy of a fecal immunochemical test (FIT) within a colorectal cancer screening program - A systematic review and meta-analysis -**

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Background: Most colorectal cancer (CRC) screening programs globally are now based on fecal immunochemical testing (FIT). The positive predictive value for advanced neoplasia ($PPV_{AN}$) of FIT has been reported to range between 35 and 55%. The $PPV_{AN}$ is known to depend on gender, FIT cut-off, and screening round. A significant proportion of subjects in the screening age range use oral anticoagulants (OACs) or non-steroidal anti-inflammatory drugs (NSAIDs). These may in theory increase the tendency of neoplastic lesions to bleed, and thus increase $PPV_{AN}$. In contrast, these drugs could increase the tendency of non-neoplastic lesions to bleed too, and cause a decrease in $PPV_{AN.}$ Previous studies into the effect of OAC and NSAID use on FIT performance were inconclusive. Screening guidelines thus lack recommendations on FIT screening in NSAID / OAC users. The aim of this meta-analysis was to study the effect of OAC and NSAID use on FIT performance.
Methods: A systematic search was conducted until June 2017 to retrieve studies from Pubmed, Embase, Medline, Web of science, Cochrane central and Google Scholar. Studies were included when reporting on FIT results in users versus non-users of OAC and/or NSAID in average risk FIT-based CRC screening populations. Primary outcome was $PPV_{AN}$ of FIT in relation to NSAID / OAC use. Values were obtained by conducting separate analyses for the use of OAC and for NSAIDs (including acetylsalicylic acid) by random-effect forest plots.
Results: Our literature search identified 2022 records, of which 8 studies were included in total. Four studies provided data on OAC use and 6 studies on NSAID use. A total of 1510 FIT positive screening participants were included for OAC analysis and a total of 2901 for NSAID analysis. Pooled $PPV_{AN}$ of FIT in OAC users vs. non-users was 42.3% (95%CI 36.5-48.3) vs. 45.6% (95%CI 42.9-48.4) (p=0.69). Pooled $PPV_{AN}$ in NSAID users vs. non-users was 38.2% (95%CI 33.8-42.9) vs. 36.9% (95%CI 35.0-38.9) (p=0.42). Subgroup analysis of one included study showed that the detection rate of advanced neoplasia significantly decreased with long-term acetylsalicylic acid use (over 5 years) compared to short-term use (less than 5 years); 38.5% vs. 61.2%, respectively (p=0.03).
Conclusion: Accuracy of FIT is not affected by OAC and NSAID use at time of sampling. Based on the current literature, withdrawal of OACs or NSAIDs before FIT screening is not recommended. Future studies should focus on duration of use and drug specifics in association with accuracy of FIT to conduct specific guideline recommendations.

## Endoscopic resection of large non-pedunculated colorectal neoplasms (LNPCPs): outcomes in the Dutch colorectal cancer (CRC) screening program

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Introduction: Large non-pedunculated colorectal polyps (LNPCPs) have been recognized as complex colorectal neoplasms that are technically difficult to resect at endoscopy. Optimal diagnosis, endoscopic treatment and follow up of LNPCPs further increases the burden on colonoscopy capacity. We examined the prevalence and outcomes of endoscopic resection of LNPCPs in the fecal immunochemical test-based colorectal cancer (CRC) screening program in the Netherlands.
Methods: We conducted a prospective, observational cohort study, in which we included all participants of the national CRC screening program who underwent colonoscopy at an academic and non-academic center from January 2014 to August 2015. We defined LNPCPs as large (≥20mm) flat or sessile colorectal neoplasms. Clinical, endoscopy and pathology data at index colonoscopy were collected including 12 months follow-up data.
Results: In total, 1610 participants with 3748 colorectal neoplasms were included. 192 LNPCPs were found in 164 patients (10.2% of all patients). The mean age of patients with a LNPCP was 71.4 years (SD 5.41) and 39.9% were female. 24% of all LNPCPs contained high grade dysplasia (HGD) or T1 CRC. Logistic regression analysis adjusted for age, location, size and endoscopic shape revealed that location (OR 3.21 for distal vs proximal) was an independent predictor for HGD and T1 CRC in LNPCPs. 91% of the LNPCP lesions were treated endoscopically. Of these 6.9% needed additional surgery. En-bloc and piecemeal endoscopic resection were performed in 42% and 58% of cases, respectively. Of note, sessile LNPCPs were more likely to be resected en-bloc compared to flat LNPCPs after correction for location and size (OR 2.69, P=0.047).
In 6 cases of piecemeal resection (5.9%) and 3 cases of en-bloc resection (4.1%), indirect surgery was performed because of T1 CRC. Endoscopic follow-up was chosen after piecemeal resection in 5 LNPCPs with T1 CRC because of pathological proven complete resection (n=2) and patient's wish (n=3). Residue or recurrence occurred in 3% after en-bloc resection and 8% after piecemeal resection. Of all residue/recurrent lesions only one required surgery because a carcinoma was found. Residue occurred only in polyps with low grade dysplasia, while recurrence only after resection of polyps with HGD or CRC.
Conclusion: Approximately 10% of the patients undergoing colonoscopy in our CRC screening program have a LNPCP. The vast majority (91%) of LNPCPs are treated endoscopically with low rates of residual tissue/recurrence. Monitoring of the quality of endoscopic resection of LNPCPs is crucial to optimize the outcomes of our nationwide colorectal cancer screening program.

## Optical diagnosis of diminutive polyps in the Dutch CRC screening program: Are we ready to start?

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Background: Implementation of optical diagnosis of diminutive polyps increases the efficacy and reduces the economic burden of a colorectal cancer (CRC) screening program. To adopt such strategy in clinical practice, the ASGE PIVI thresholds should be met: ≥90% negative predictive value (NPV) for diagnosis of adenomatous histology and ≥90% agreement between optical diagnosis and histological diagnosis in determining the post-polypectomy surveillance intervals. We evaluated these performance parameters in the Dutch nationwide CRC screening program.

Methods: We collected endoscopic and histopathologic data from participants of the FIT based Dutch CRC screening program from February 2014 to August 2015 at 1 academic and 3 peripheral endoscopy units. All endoscopists were familiarized with optical diagnosis of colorectal polyps and in current daily practice all lesions are sent in for histological evaluation. High definition white light colonoscopy was used, and if necessary (virtual) chromoendoscopy was used. The classification options were: adenomatous polyp, hyperplastic polyp, sessile serrated polyp, carcinoma and other. The 'diagnose and leave' strategy was applied to hyperplastic polyps ≤5mm in the rectosigmoid while the 'resect and discard' strategy was applied to polyps ≤5mm in the entire colon. We measured the agreement between optical diagnosis and histological diagnosis in determining the post-polypectomy surveillance intervals. For this, the percentage of congruent pairs was calculated.

Results: A total 2738 diminutive polyps were included and 14 certified endoscopists participated in this study. Optical diagnosis of diminutive adenomatous polyps was accurate in 72% (95% CI 70-74) with a NPV of 59% (56-63). Optical diagnosis of diminutive hyperplastic polyps in the rectosigmoid (n=1084) show accuracy of 69% (67-72), a NPV of 72% (69-76) and a PPV of 62% (57-67). In 2085 patients with neoplasms both optical diagnosis and histopathological data for index colonoscopy were available. Applying the 'diagnose and leave' strategy resulted in 97% (95% CI 96-97) agreement on surveillance intervals, while applying the 'resect and discard' strategy resulted in 91% (95% CI 93-95) agreement on surveillance intervals. The latter strategy will result in 2% of patients receive surveillance later than recommended based on histopathological evaluation.

Conclusion: In the Dutch nationwide CRC screening program the optical diagnosis of diminutive polyps remains difficult, but the ASGE PIVI thresholds for determining surveillance intervals are met. Systematic training in optical diagnosis can optimize the efficacy of our nationwide CRC screening program.

## Histological model to improve the assessment of the indication for surgery in pedunculated T1 colorectal carcinomas: a multicenter cohort-nested matched case control study

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Background and Aims: Most patients with pedunculated T1 colorectal cancer (CRC) referred for surgery do not have lymph node metastasis (LNM), and are – in hindsight – unnecessarily exposed to surgery-associated complications. We aimed to develop a prediction model to improve the assessment of the indication for surgery in pedunculated T1 CRC.
Methods: We collected data from 2253 patients with T1 CRC, diagnosed between January 1, 2000, through December 31, 2014, from 13 Dutch hospitals. Eligible patients with pedunculated T1 CRC were selected (N=708). Among these, 37 patients (5.2%) with an indication for surgery (i.e., LNM, intramural or distant metastasis) were identified, and these were matched 1:3 with controls. Hematoxylin-eosin stained slides were reviewed by expert pathologists blinded to the outcome. A multivariable penalized logistic regression model was developed considering 6 histologic factors. The model's performance was compared with conventional models (i.e., high-risk in the presence of poor differentiation, lymphovascular invasion, or Haggitt level 4 [model 1], or the aforementioned factors combined with tumor budding [model 2]).
Results: The optimal prediction model included 4 histological factors (i.e., lymphovascular invasion, Haggitt level, budding and status of the muscularis mucosa), with a cross-validation area under the curve (AUC) of 0.80 (95%CI 0.74 – 0.88). At a ≥4.0% threshold, 67.5% of patients tested negative (i.e., no need for surgery in 478 of 708 patients), with 83.8% (95%CI 68.0 – 93.8) sensitivity and 70.3% (95%CI 60.9 – 78.6) specificity. Conventional model 1 and 2 yielded significant lower AUCs (0.67 [95%CI 0.60 – 0.74], p=0.002 and 0.64 [95%CI 0.58 – 0.70], p<0.001, respectively). When using our model at a ≥4.0% threshold, the percentage of missed cases (i.e., low-risk T1 CRC with the outcome) was comparable (1.3%; 6/478) to conventional model 1 (1.3%; 4/307) or conventional model 2 (1.2%; 3/244). However, the percentage of patients referred for surgery (i.e., high-risk T1 CRC) was much lower (32.5%; N=230) than when using conventional model 1 (56.6%; N=401) or conventional model 2 (65.5%; N=464).
Conclusion: This multicenter study is the first to develop a prediction model to estimate the indication for surgery in pedunculated T1 CRC. This model might support clinicians in the difficult selection of candidates who will benefit from adjuvant surgery.

**Magnetic resonance imaging for response assessment after neoadjuvant chemoradiotherapy in oesophageal cancer: can we select complete responders?**

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Purpose: In order to select oesophageal cancer patients after neoadjuvant chemoradiation (nCRT) for organ-preserving treatment instead of surgery, complete response (CR) assessment must be highly accurate. Our aim is to assess the performance of T2-weighted MRI (T2W-MRI) combined with diffusion-weighted MRI (DW-MRI) to select oesophageal cancer patients with CR after nCRT.
Methods: Thirty-two patients with locally advanced oesophageal cancer were assessed. All patients underwent MRI (1.5T) before and after nCRT with a maximum of 21 days between MRI and surgery. MRI consisted of T2W- and DW-MRI (b-values=0,200,800 s/mm$^2$). Three independent experienced radiologists scored the MRI's using a 5-point score (1=definite CR, 2=probably CR, 3=inconclusive, 4=probably residual tumour, 5=definite residual tumour). Histology after surgery represented the reference standard (tumour regression grade 1=CR, 2-5=residual tumour). Area under the ROC (AUC), sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) were calculated considering MRI scores 3-5 as tumour-positive. Interobserver agreement was calculated.
Results: Two patients were excluded due to poor image quality. Seven (23%) of the remaining 30 patients had CR. AUC for prediction of residual tumour with MRI was 0.76, 0.69 and 0.72. Sensitivity was 96%, 96% and 87%, whereas specificity was 57%, 43% and 57%. Interobserver agreement was moderate to good (quadratic weighted kappa = 0.49; 0.73 and 0.65). Four out of seven complete responders were correctly assessed by two or more radiologists and three were false-positive. Using consensus of radiologists' scores led to a sensitivity and negative predictive value of both 100%.
Conclusion: MRI is a promising modality for predicting complete response after nCRT in oesophageal cancer. Sensitivity is high and even 100% with consensus of radiologists, indicating that the risk of missing residual tumour is limited. Specificity is lacking, indicating that the degree of residual tumour is overestimated and complete responders are often missed. A multimodality approach with endoscopy, endosonography and PET may further improve response assessment.

**Prediction in surveillance of Barrett's esophagus: The effect of multiple measurements of biomarkers on the estimated neoplastic progression risk**

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Introduction: Barrett's esophagus (BE) is a premalignant condition, where surveillance is carried out to reduce morbidity and mortality related to esophageal adenocarcinoma (EAC). The harm-benefit ratio of this strategy is questionable, because identification of high-risk patients is difficult. To improve risk stratification, additional biomarkers, and their variations between and -in particular- within patients should be taken into account. To date, no more than 2 time points have been included when studying the risk of neoplastic progression. We aimed to develop a model incorporating all follow-up (FU) measurements of low-grade dysplasia (LGD), p53, and SOX2 to study their predictive performance.
Methods: In this multicenter prospective cohort study, we included consecutive BE patients from 15 hospitals in the Netherlands with histologically confirmed BE, a segment of ≥2 cm, and a FU time of at least 0.5 year. The study endpoint was identification of high-grade dysplasia (HGD) or EAC. The surveillance guidelines of the American College of Gastroenterology were followed. Data were collected during every FU. Two BE expert pathologists independently reviewed all H&E slides and immunohistochemistry of p53 and SOX2. We incorporated the dynamic values of LGD, p53, and SOX2 as registered at each endoscopy in a multivariate joint model, adjusted for age, sex, length of BE, and esophagitis.
Results: The median FU time was 7.2 years (IQR 5.4-9.9) of 628 patients included (69% male, median age 60 years, 76% length of BE ≥3 cm); 48 developed HGD or EAC. If a patient would have only 2 FU moments, one with normal (0) expression of the biomarker, one with aberrant (1), the hazard ratio (HR) of neoplastic progression was 1.2 for LGD (p=0.61), 1.5 for p53 (p=0.004), and 5.0 for SOX2 (p=0.004), annually. With more FU endoscopies, these multiple observations will set the probability of aberrant expression to a value between 0 and 1, with a ditto proportion of the previously mentioned hazard ratios. Dynamic risk profiles of neoplastic progression could be estimated for individual patients during their FU, based on these biomarker patterns.
Conclusion: The risk of neoplastic progression can be estimated better by p53 and SOX2 than LGD if measurements of all FU endoscopies are taken into account. In the future, this prediction model will provide an updated prediction of neoplastic progression based on new observations in ongoing FU. The combination of dynamic observations of biomarkers such as p53 and SOX2 merits further study to improve the identification of high-risk patients in a personalized surveillance program, eventually reducing the burden of surveillance.

## Safety and efficacy of using lumen apposing metal stents in the management of post-operative fluid collections (POFC): a large, international, multicenter study

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Although multiple studies have examined the use of lumen-apposing metal stents (LAMS) for the drainage of pancreatic fluid collections, data on the use of LAMS for post-operative fluid collections (POFC) are scarce. These POFCs may lead to intraperitoneal abscess formation, sepsis, pseudo-aneurysm formation and even fatal hemorrhage without appropriate treatment. Aims: To study the outcomes (technical and clinical success, rate/severity of adverse events, length of stay, recurrence) of the use of LAMS for the drainage of POFC. Methods: International, multicenter retrospective study in 21 centers between 2012-2017. Consecutive patients who underwent EUS-guided LAMS placement for POFC were included. Primary outcome was clinical success (radiologic resolution). Secondary outcomes included technical success and rate/severity of adverse events (AEs). Results: 61 patients (59.2±13.7 years, female 45.69%) were included. Etiologies of POFCs were distal pancreatectomy 44.3% (27/61), cholecystectomy 16.4% (10/61), Whipple 9.8% (6/61), and colon resection 8.2% (5/61). POFCs were located intraperitoneal 41% (25/61), retroperitoneal 37.7% (23/61), pelvic 8.2% (5/61), intrathoracic 4.9% (3/61), and others 8.2% (5/61). The mean diameter was 84.2 ± 30.9mm. Most common indication for drainage was infection (49.2%). Technical success rate was 96.7% with a mean procedure time of 30.2 ± 14.3 min. Nasocystic drain was placed in 8 patients while 10 patients underwent placement of a double pigtail stent within the LAMS. Endoscopic approaches were: 82% (50/61) transgastric, 8.2% (5/61) transduodenal, 8.2% (5/61) transrectal and 1.6% (1/61) others. Mean length of stay post LAMS insertion was 7.6 days ± 2.1 days. All stents were successfully removed following POFC resolution. Overall, clinical success was achieved in 91.8% (56/61) patients during a median follow-up of 183 (84-267) days. Clinical success rate based on POFC location: 100% (3/3) intrathoracic, 92% (23/25) intraperitoneal, 91.3% (21/23) retroperitoneal, 80% (4/5) pelvic, and 100% (5/5) others. Mean number of endoscopic procedures needed to achieve clinical success was 1.2 ± .07. Percutaneous drainage was needed in 9.8% (6/61) of patients. A total of 11.5% (7/61) AEs (3 mild, 3 moderate, 1 severe) occurred: 3 bleeding (none due to pseudoaneurysms), 2 abdominal pain, 1 stent dislodgement, and 1 infection. AEs occurred intraoperatively in 1 patient (mild bleeding) and post-operatively in 6 at a mean of 6.7±4.1 days after LAMS insertion. There were no POFC recurrences at 3-month follow-up. Conclusion: This is the largest study on the use of LAMS for POFC and suggests high clinical efficacy and safety of this approach.

## Comprehensive Analysis of Adverse Events Associated with Endoscopic Ultrasound drainage of Pancreatic Fluid Collection using lumen-apposing metal stents: An International Multicenter Study

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Background: Recently, the use of lumen-apposing metal stents (LAMS) for management of pancreatic fluid collections (PFCs) has increased significantly. While there has been significant focus on the clinical outcomes of the use of LAMS for a variety of indications, there is concern that the incidence of adverse events (AEs) and associated factors with LAMS placement may not be adequately understood. The aim of this study was to evaluate the incidence, severity, and management of AEs for the drainage of PFCs. Methods: This is a multicenter, international, retrospective survey, involving 15 centers, of patients in which LAMS were used for management of pancreatic pseudocyst (PP) or walled off necrosis (WON). AE's in these patients were recorded and categorized using the ASGE system grading. Consecutive patients who underwent EUS-drainage for PFCs using electrocautery-enhanced LAMS between 03/2013 and 10/2017 were included. Results: A total of 333 patients (female 35.1%) with a mean age (56yr ± 15.84) were identified, with 167 WON, and 166 (PP). A total of 335 LAMS were used, with 2 (0.6%) patients being treated with 2 LAMS. PFCs were most commonly located in pancreatic body (54.95%) with a mean diameter of 113.11± 58.98 mm. Demographic data are listed in Table 1. The procedure was technically successful in 324/335(96.7 %), with a mean procedural time of 32.45 min ± 22.95. A 15mm diameter stent was placed in 225/335(67.2%). EC-LAMS was used in 303/335(90.4%). Clinical success (resolution of PFC) was achieved in 286/333(85.9%) of patients with LAMS removal after a mean of 59 days (95% CI:52.9-65.2). AE's associated with stent placement occurred in 89/333(26.6%, 95% CI: 18.9-36.1%) of cases. A total of 98 AEs occurred with 2 complications occurring in 9(2.7%) patients. Characteristics and management of AE's are listed in Table 2. Death occurred in 9 cases. The mean time between stent placement and occurrence of complication was 22.8 (95% CI:16.6-29.9; range 0-146) days. Conclusion: Data from this survey confirms that the use of AXIOS stent for management of PFCs has excellent technical and clinical success rates. The rate of complications including fatal events, however, is not negligible and should be carefully considered before using the stent in this clinical setting. Further studies are needed to determine the optimal algorithm for follow-up of LAMS placement to attempt to minimize AEs.

**Safety and efficacy of the new 20 mm lumen apposing metal stent (lams) for endoscopic treatment of pancreatic and peripancreatic fluid collectios (ppfcs): a large, international, multicenter study**

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Lumen apposing metal stents(LAMS) have been utilized for the access and drainage of (peri)pancreatic fluid collections (PPFCs). To date, a variety of LAMS sizes have been commercially available and widely used. Recently, a new LAMS with a larger (20mm) lumen diameter was released for a limited commercial launch, with the idea that a larger diameter would allow a faster drainage of PPFCs and facilitate endoscopic necrosectomy. Aim of our study was to evaluate the safety and efficacy of the new 20mm LAMS placement.
Methods: This is an international, multicenter retrospective study involving 18 centers. Between 1-10/2017, consecutive patients who underwent EUS-guided 20mm Hot Axios stent placement for PPFCs were included. Primary outcome was technical and clinical success (defined as correct deployment of the stent and resolution of PPFCs respectively). Secondary outcomes was rate/severity of adverse events (AEs) (ASGE lexicon).
Results: A total of 78 patients(female 28.2%) with a mean age of 57yr(± 16.37) were identified. 79 LAMS were placed overall, with 1(1.3%) patient being treated with 2 stent. WON were 75(96%), with a mean diameter of 111.12(± 49.57)mmx69.3(±68.91). Major etiology of pancreatitis were gallstones(44.9%) and alcohol (29.5%). Mean necrosis on EUS imaging was 39.93%(range 15-90%). 77(97.5%) of LAMS were placed in a transgastric manner. Procedure was technically successful in all cases79/79 (100 %). Stent dilation was performed in 44(55.7%) cases with 15(18.9%) pigtails placement across the LAMS. Endoscopic necrosectomy was performed in 53.2% of the cases, with a mean of 2 sessions(range 1-8). Clinical success was achieved in 66/78(84.6%) of patients with stent removal after a mean of 50.6 (±36.09) days. AEs occurred in 10 (12.8%) cases with spontaneous migration in 5(6.4%), bleeding in 3(3.8%) others in 2(2.6%). WON recurrence rate after stent removal was 2.9%.
Discussion: This study represents the first published data regarding the use of the new 20mm diameter LAMS and shows its efficacy and safety for EUS-guided transluminal drainage of PPFCs. The technical and clinical success rates for resolving PPFCs were 100% and 84.6%, respectively. These are similar to previous published data on LAMS use for PPFCs. AEs occurred in 10 (12.8%) cases; other studies including smaller diameter LAMS have shown similar or even higher adverse event rates. Overall, our study suggests that a 20mm LAMS is comparable in terms of safety, efficacy, and adverse events to smaller LAMS when used to drain PPFCs. Larger studies are needed to determine the ideal size for a LAMS going forward to achieve maximal clinical benefit with minimal patient risk.

**Long term evaluation of Endoscopic Transpapillary Pigtail Gallbladder Stenting in patients with symptomatic gallbladder disease: a singlecenter retrospective study**

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Background: In patients with serious underlying comorbidity the treatment of first choice of symptomatic gallbladder disease – a laparoscopic cholecystectomy – comes with complication rate up to 41% and mortality rate up to 4,5%, particularly due to anesthetic complications. For those considered as poor surgical candidates, percutaneous cholecystostomy is a widely used temporarily alternative. However, recurrent cholecystitis is reported 29.6%-33,3% after drain removal. A new alternative treatment for symptomatic gallbladder disease in patients with underlying comorbidities is an endoscopic placed transpapillair pigtail gallbladder stent, with good technical success rates, but less is known about the long term efficacy.
The aim of this study is the evaluation of long-term treatment by endoscopic placed transpapillar pigtail gallbladder stent.
Methods: Data from all patients receiving endoscopic transpapillar pigtail gallbladder stenting in the HMC Westeinde Hospital were collected between 2013 and 2017, and patients were excluded in case of unsuccessful pigtail placement. Symptomatic gallbladder disease was diagnosed by ultrasound and/or computer tomography in combination with clinical presentation and all 7Fr double pigtail stent were placed through endoscopic retrograde cholangiopancreaticography by one gastroenterologist. Main outcomes were recurrence of gallbladder disease and complications in patients with serious underlying comorbidity.
Results: In total, 38 patients were included who received a pigtail stent, from which 42.1% had an ASA classification of 3 or higher as reason not to receive surgery, 13.2% old age, 7,9% extensive abdominal surgery in the past, 7.9% recent trombo-embolic event requiring anticoagulation and 3 (7.9%) patients received transpapillar stenting on own request. Most common indication to receive transpapillar stenting was recurrent calculus cholecystitis (44.7%). Mean stent patency at end of study period was 551,7 days (interquartile range 206,75-827,75 days) and remained successful with no recurrence of cholecystitis in 94.7% (N=36). Adverse event occurred in 23,7%, with 13.1% within 4 weeks after stent placement i.a. post-ERCP pancreatitis (5,3%) and stent migration (2,6%), 5.3% suffered delayed adverse events (4 weeks - 6 months) and late adverse events happened in 2 patients (5.3%).
Conclusion: Endoscopic transpapillar pigtail gallbladder stenting for patients with serious underlying co-morbidities, and thereby unfit to receive surgery, is an alternative with long term low recurrence rate for symptomatic gallbladder disease and thus seems effective.

**A novel tool for fast and effective endoscopic removal of pancreatic necrosis**

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Introduction: Acute pancreatitis may run a severe course when pancreatic necrosis becomes infected. Invasive treatment of these patients is virtually always necessary and over the last decade the treatment has changed dramatically towards less invasive treatments. Endoscopic drainage and ensuing necrosectomy have been shown to be effective in the management of pancreatic necrosis. One of the main limitations during endoscopic management is the lack of suitable instruments to remove necrotic tissue, resulting in time consuming procedures with marginal results and often necessitating multiple procedures. We aimed to evaluate the technical feasibility, safety and clinical outcome of the EndoRotor®, a novel automated mechanical endoscopic resection system to suck, cut and remove small pieces of tissue in patients with necrotizing pancreatitis.
Methods: Subjects with infected walled-off pancreatic necrosis were endoscopically treated using the EndoRotor® device. Procedures were performed under conscious or propofol sedation by four endoscopists with a broad experience in advanced endoscopic procedures including conventional endoscopic necrosectomy. Endoscopists were additionally asked to fill out a short questionnaire about their experience using the EndoRotor®.
Results: Six patients have been endoscopically treated for pancreatic necrosis, five patients were men and the median age was 61.7 years (range 43-71). Imaging data of the pancreas revealed a mean necrotic collection size of 114.7mm diameter (range 50-180mm). Transgastric drainage was performed in all patients, four patients received plastic stents and two a fully covered lumen apposing stent. Three patients were previously treated unsuccessfully with conventional tools with a median of two procedures (range 1-3). Additionally, the EndoRotor® was used in six patients with a total of 16 procedures, the average procedure length was 46.5 minutes (range 32-80). To achieve complete removal of pancreatic necrosis, the median number of required procedures was two per patient (range 1-7). No procedure-related adverse events occurred. Endoscopists agree on the ease of use and effective removal of necrotic tissue with the EndoRotor®, rating both 8.3 on a 10-point scale. They are especially satisfied by the ability to manage the removal of necrotic tissue in a controlled way (8.6 on a 10-point scale). Moreover, they are convinced that this device is of additional value in the management of pancreatic necrosis (8.6) and are willing to use it again (9.3 on a 10-point scale).
Conclusion: Initial experience with the EndoRotor® suggests that this device can safely, quickly and effectively remove pancreatic necrosis.

**Technical feasibility and safety of suck-and-snare EMR for treatment of difficult colorectal polyps**

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Background: Endoscopic mucosal resection (EMR) is a well-established technique for removal of colorectal polyps. However, complete resection cannot be achieved in all cases, for instance due to non-lifting areas. It is often difficult or even impossible to grasp non-lifting tissue in the snare. Often APC or cold avulsion is used, which increases recurrent polyp rate. Suck-and-snare (SAS) is a modified EMR technique using suction to grasp and snare the target area. Our aim was to describe our experience of the SAS technique for difficult colorectal polyps not amenable to standard EMR.
Methods: We prospectively registered all consecutive patients in whom the SAS technique was used in the endoscopic treatment of colorectal polyps. Brief description: target area is suctioned into a cap (Olympus soft straight 4mm) mounted on the scope. A prepositioned snare strangulates the lesion after maximum aspiration. Clinical and endoscopic data on target area, indication, technical success, adverse events and follow-up were collected.
Results: From May 2016 until November 2017 44 patients (mean age 69 yrs (SD±9.9), male 59%) were included. Main indication for using SAS was a non-lifting area (n=37), followed by flat morphology (n=4) and location on ileocecal valve or appendix (n=3). Non-lifting was caused by fibrosis due to prior incomplete resection (n=20), IBD (n=4), both (n=2), mechanical forces (n=8) or malignant infiltration (n=3). The target areas were remaining island(s) (n=30) or the entire lesion (n=14), with a median size of 15 mm (range 2-45). Technical success with complete removal of polyp tissue with SAS alone was achieved in 29 patients (66%). In 13 patients (30%) at least 75% of the target area could be resected, needing additional cold avulsion and/or ablative therapy. In 2 patients no polyp tissue could be removed. Reason for incomplete removal was inadequate grasp with the snare, together with insufficient suction into the cap in 2 cases. Kato III/IV non-lifting was associated with incomplete removal (p=0.03, $X^2$-test). Muscle layer injury related to SAS occurred in 5 patients (11%), all successfully treated with clips. Benign histology was reported in 40 cases (91%). Unexpectedly, invasive cancer was found in 4 patients, of whom 3 were referred for surgery and 1 preferred surveillance. Absence of recurrence was seen in 15/20 patients (75%) of whom follow-up of the scar was performed (median follow-up time 6 months (range 2-11)).
Conclusions: Suck-and-snare EMR is a promising technique with an acceptable safety profile, and seems attractive in finishing endoscopic resection in case non-lifting fibrotic parts of a colorectal polyp are encountered.

## The therapeutic yield of repeated colonoscopy for delayed bleeding after endoscopic mucosal resection of large colorectal polyps

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Background: Clinically significant post-endoscopic bleeding (CSPEB) is the most frequent complication of colorectal endoscopic mucosal resection (EMR). Identification of patients likely to benefit from additional hemostatic therapy is often difficult, frequently resulting in a repeated (re)-colonoscopy without intervention. In this study, we aimed to identify patients with CSPEB with active bleeding and in whom hemostatic therapy is used.
Methods: In this retrospective observational cohort study, patients with CSPEB after EMR of a ≥20 mm non-pedunculated colorectal polyp were identified in the endoscopy database of 7 regional (2015-17) and 1 academic center (2012-17). CSPEB was defined as any bleeding occurring after completion of the procedure, necessitating emergency Dept. presentation, hospitalization or re-intervention. Patient characteristics, endoscopic features and data on clinical presentation and management were collected. Variables associated with active bleeding during re-colonoscopy or use of hemostatic therapy were analyzed using logistic regression.
Results: EMR was performed on 536 polyps in 466 patients. CSPEB occurred in 41 patients (8.7%), mean age 69.4 yrs, range 58-87, 73% male, 87.8% ASA≥2, 58.5% antithrombotic therapy. Mean polyp size was 41mm (SD±18mm) (proximal colon 68.2% / rectum 28.8%, 95.1% benign histology). CSPEB occurred after a median of 3 days (range 0-38), including 18 events within the first 24h. Hemodynamic instability (syst. RR <100mmHg or heart rate ≥100/min) was observed in 10 patients and 11 received blood transfusion. 11 patients (26.8%) were treated conservatively without re-colonoscopy. In 30 patients (73.2%) re-colonoscopy was performed. In 6 patients (14.6%) active bleeding was seen, all treated endoscopically. 8 patients were left untreated, although 1 received hemostatic therapy in a next colonoscopy because of re-bleeding. Overall, endoscopic hemostatic therapy was performed in 23 patients (56.1%) and clips were most frequently used. Re-bleeding occurred in 3 patients after hemostatic therapy, managed by endoscopy, embolization and conservatively. No variables (e.g. antithrombotic therapy, location, hemodynamic instability, blood transfusion) were significantly associated with an actively bleeding post-EMR ulcer or use of hemostatic therapy.
Conclusions: Re-colonoscopy was deemed necessary in 73% of CSPEBs. Active bleeding was found in a minority and hemostatic therapy was also used for non-bleeding stigmata. No risk factors could be identified for active bleeding or use of hemostatic therapy.

**Deep mural injury after colorectal endoscopic mucosal resection (EMR): occurrence, risk factors and outcome of endoscopic clip placement**

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Background: Perforation is the most feared adverse event after EMR for colorectal polyps, with potential life-threatening consequences. Early recognition of deep mural injury (DMI) during the procedure is crucial, as this allows immediate endoscopic treatment. Detailed data on DMI and outcome of treatment are scarce. We aimed to assess the occurrence and risk factors for DMI after EMR in a multi-center registry, and also to determine the clinical outcome after endoscopic clip placement.

Methods: Patients with DMI after EMR for ≥20 mm non-pedunculated colorectal polyps were identified in the endoscopy registries of 7 regional (2015-17) and one academic center (2012-17). DMI was defined as (potential) injury to the proper muscle layer by endoscopic assessment, and graded according to the severity of injury: I, muscle layer visible; II, possible injury to the muscle layer; IIIa, superficial injury; IIIb target sign, IV transmural perforation. Patient characteristics, endoscopic and histological features, image analysis, and data on clinical outcome were collected. Variables associated with DMI were analyzed using multivariable logistic regression analysis.

Results: EMR was performed on 536 polyps in 466 patients. Mean polyp size was 3.6 cm (SD± 1.6), 65% were right-sided, 17.9% had suboptimal lifting, and 95.1% showed benign histology. DMI was recognized in 35/536 resections (6.5%). No delayed perforations were observed. DMI was considered type I in 5 (14.3%), II in 11 (31.4%), IIIa in 4 (11.4%), IIIb in 7 (20%) and IV in 8 (22.9%) cases. Presence of adenocarcinoma (OR 5.04, p=0.002) and increasing polyp size (OR 1.22 per 10 mm increase, p=0.03) were independently associated with the occurrence of DMI. All DMIs were closed using clips, one with the over-the-scope-clip. Clinical outcome was favorable in 34 of 35 (97.1%) patients, without the need for surgery. Only in 1 patient prolonged hospitalization was required (4 days) after the regular observational period. In 1/35 (2.9%) patient (DMI type IIIb after EMR 35 mm serrated lesion in the cecum) surgical suturing was required because of ongoing peritonitis.

Conclusion: Larger polyp size and malignant infiltration increase the risk of DMI during EMR for non-pedunculated colorectal polyps. Immediate endoscopic clip placement is effective in almost all patients, in general without the need for prolonged hospitalization.

**Antibiotic Prophylaxis in Percutaneous Transhepatic Cholangiography and Biliary Drainage (PTCD), a retrospective multicenter study**

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Aims: Yearly, over 2500 percutaneous transhepatic cholangiography (PTC) and biliary drainages (PTCD) are performed in the Netherlands. These interventions are mainly used as a treatment for biliary obstruction in case of failed endoscopic biliary cannulation. The 2010 CIRSE and the SIR guidelines advocate antibiotic prophylaxis (ABp) in PTCD procedures (evidence level 4-5), because transient bacteremia commonly occurs. In many centers, including ours, no standard protocol for ABp in PTCD is applied. Patients receive ABp at the physician's discretion. The effect of ABp has only been studied in case series with no controls included. Therefore, the crucial question unanswered today is whether ABp indeed reduces the risk of severe infectious complications in patients undergoing PTCD.
Methods: We performed a retrospective study to assess the effect of ABp in adult patients who underwent PTCD. A systematic search in the hospital electronic patient records from one academic and four teaching hospitals from 2011-2016 was performed. Primary objective was the occurrence of severe infectious complications (e.g. sepsis, cholangitis, abscess or cholecystitis) within 30 days of the procedure. Secondary objectives and characteristics were: mortality, mechanical complications (bile leakage/biloma, catheter blockage, peritonitis, acute pancreatitis, severe hemorrhage, pneumothorax), age, gender and BMI.
Results: Of the 224 patients included, 127 (56,7%) were treated with ABp. In univariate analysis, no significant difference in severe infectious complications between the ABp and control group was observed: 35.4% vs. 47.4%, respectively (p=0.076). Correction for confounders via a log binomial regression analysis did not affect the outcome. The relative risk on infectious complications without ABp remained 1,34 (0,98-1,83). Overall occurrence of infectious complications was 40.6%; cholangitis 26.3% (p=0.066); sepsis 24.6% (p=0.212); abscess 2.7% (p =1.000); cholecystitis 1.3% (p=0.580). Mortality was 4.7% vs. 10.3%, respectively (p=0.123).
Conclusion: This retrospective multicenter study shows a non-significant reduction of severe infectious complications by ABp in PTCD-patients. The overall complication rate of PTCD is considerable. The efficacy of antibiotic prophylaxis prior to PTCD should therefore be re-evaluated, preferably in a multicenter RCT.

## Pancreatic cyst surveillance imposes low psychological burden: preliminary results of the pacyfic study

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Background: Neoplastic pancreatic cysts are identified with increasing frequency, mainly as incidental findings. Because some have a malignant potential, yearly lifelong surveillance is globally recommended and executed, even though evidence on effectiveness is lacking. A prerequisite for any surveillance program to be feasible is adherence, in which psychosocial aspects play an important role. However, the impact of such intensive surveillance on participants and their willingness to participate has never been studied.

Objective: To evaluate the perception and psychological burden of pancreatic cyst surveillance from a participant's perspective.

Methods: The present patient survey is part of an international cohort study (PACYFIC study, http://www.pacyfic.net), which prospectively records the outcome of pancreatic cyst surveillance. Participants with a newly diagnosed pancreatic cyst (<6 months) are invited to complete questionnaires after diagnosis (baseline) and each subsequent control visit (follow-up). The questionnaires contain the Hospital Anxiety and Depression Scale (HADS, with both subscale scores ranging from 0-21 and a score <7 indicating a low level of anxiety or depression) and questions concerning patients' perception of surveillance and wishes regarding follow-up frequency and duration.

Results: 103 patients with a newly diagnosed cyst returned the baseline questionnaire (median age 69 years (IQR 62-76), 35% male). 86 participants (84%) agreed or strongly agreed that surveillance reduces their concerns about pancreatic cancer and 81 (80%) confirmed that it contributes to their sense of security. Although 26 participants (25%) reported that it leads to worries and 23 (22%) found it burdensome, almost all (99 respondents, 96%) agreed that the advantages outweigh the disadvantages 'somewhat', 'rather' or 'very much'. The majority (77 participants, 75%) wanted surveillance to continue for the rest of their lives, with a yearly or even 6-monthly frequency.

In the 20 patients who already completed a second questionnaire, median HADS scores (2 for anxiety (IQR 1-6.75) and 2 for depression (IQR 0-5.75)) were unaffected by the follow-up visit (p=0.551 for anxiety and p=0.487 for depression, paired T-test).

Conclusions: The majority of respondents reported a highly positive attitude towards pancreatic cyst surveillance. HADS scores were low to begin with and appear unaffected by subsequent follow-up, presuming a low psychological burden. Based on these preliminary results, the adherence in a pancreatic cyst surveillance program is predicted to be high, and annual surveillance such as currently recommended in the guidelines seems feasible.

**The Dutch national ERCP quality registration with RAF-E does not correlate with clinical ERCP outcome.**

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Background and study aim: Since January 1. 2016 endoscopists in the Netherlands are obligated to register their Endoscopic Retrograde Cholangiopancreatography (ERCP) in a national ERCP quality registration (NEQR). This evaluates ERCP quality and volume per center and endoscopist. NEQR is based on the Rotterdam Assessment Form for ERCP (RAF-E), a self-assessment, which does not score complications. This study examines whether NEQR correlates with objective post-ERCP clinical outcomes such as complications and mortality in a tertiary referral center.
Patients and methods: A retrospective cohort study of all ERCPs performed at the Gastroenterology Dept. of a tertiary referral center, between January 1. 2016 and January 1. 2017, examining the registered data in the NEQR and individual patient data including ERCP outcomes in the local electronic medical records.The Spearman's rank correlation coefficient was performed to measure correlations between NEQR self-assessments and post-ERCP complications and mortality.
Results: 333 procedures were performed, of which 254 were registered in the NEQR (76.3%). Registered and non-registered patients showed equal characteristics and results. No significant correlations were found between the subjective self-assessment and objective post-ERCP outcomes, except a weak negative correlation between stent placement self-assessment and post-ERCP total complications (r=-0.315; p=0.018) and post-ERCP cholangitis (r=-0.308; p=0.021). Of all 333 procedures the total post-ERCP complication rate was 13.5%, including 4.8% cholangitis, 4.2% pancreatitis, 1.8% bleeding and 1.5% perforation. Cardiopulmonary complications occurred in 2.1%. ERCP-related 30-day mortality rate was 0.6% (2 patients).
Conclusion: The currently used national quality registration for ERCP (NEQR) does not correlate with post-procedural clinical outcomes. We believe that objective and harder clinical outcome measures will enhance representativeness of the mostly subjective NEQR results. Therefore NEQR should be combined with the already existing national complication database.

**Reducing pancreatic cyst surveillance: development of the dutch american risk stratification tool (dart-i) to identify ipmn with low risk to progress and fulfill resection criteria**

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Background: Neoplastic pancreatic cystic lesions are discovered with increasing frequency, with the most prevalent being the intraductal papillary mucinous neoplasm (IPMN). Most IPMNs will never evolve into malignancy, but because risk stratifying tools are lacking, the majority of cysts currently undergo redundant lifelong surveillance.
Objective To develop a score chart to identify IPMN with low risk to progress and fulfill the resection criteria according to the 2012 international Fukuoka guidelines.
Methods: We retrospectively reviewed the prospectively-maintained databases of three international academic institutions, containing patients with a pancreatic cystic lesion identified in the period 2003-2013. Patients were included if they had a presumed IPMN on imaging, without worrisome features or high-risk stigmata at baseline, as defined by the 2012 international Fukuoka guidelines, and were followed ≥12 months. Fulfilling resection criteria was defined as any of the following: jaundice, an enhancing solid component, main pancreatic duct ≥5 mm, cyst size ≥3 cm, non-enhancing mural nodule, abrupt change in caliber of pancreatic duct with distal pancreatic atrophy, and cytology suspect or positive for malignancy. A multivariable prediction model was developed with Cox proportional hazard regression analysis using stepwise backward selection. The prediction model was internally validated with bootstrap resampling. The Dutch American Risk stratification Tool (DART-I) was developed to identify patients with low risk to progress and fulfill the resection criteria.
Results: A total of 559 patients with presumed IPMN were included (mean age 65 years, 38% male, 72% Caucasian). After a mean follow-up of 48 months (range 12-157) and a total follow-up of 2,254 person-years, 71 patients progressed to fulfill resection criteria. Age, history of diabetes, BMI, smoking, cyst size, and cyst multifocality were analyzed as predictors. The final model included cyst size (HR 1.11, 95% CI 1.08-1.16), cyst multifocality (HR 2.26, 95% CI 1.39-3.65), and smoking (1.53, 95% CI 0.94-2.50) and had a moderate discriminative ability (C-statistic 0.705, corrected for optimism). When using the DART-I, a patient with unifocal IPMN <10 mm and without a history of smoking has a predicted 3-year risk of 1-2% and 5-year risk of 2-5% to progress and fulfill resection criteria.
Conclusion: In presumed IPMNs without worrisome features or high-risk stigmata, the DART-I score chart successfully identifies lesions with low risk to progress and fulfill resection criteria. When validated, this model may be used to explore strategies that will reduce unnecessary surveillance.

**Influence of antibiotic duration in cholangitis after successful drainage by ERCP**

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Background: The cornerstone of treatment in cholangitis exist of adequate drainage of the biliary tract by means of an ERCP in combination with antibiotics. Recommendations in current international guidelines regarding the duration of antibiotic treatment after adequate drainage vary from 3 days or less up to 10 days. The Dutch (SWAB) guideline recommends antibiotics for 3 days or less. However, high level of evidence to justify this recommendation is lacking. Our aim was to assess the incidence of infectious complications after adequate drainage of ascending cholangitis and to evaluate the potential influence of the antibiotic duration.

Methods: We performed a retrospective multicenter study in 7 medical centers in the Amsterdam region. Patients with cholangitis due to choledocholithiasis between January 2012 and January 2017 were extracted from local prospective endoscopy databases. Adequate drainage by means of ERCP was required. The primary outcome was number of infectious complications within 3 months after the initial ERCP. An infectious complication was defined as the need for antibiotics within 3 months after ERCP. Secondary outcomes included duration of hospital stay and guideline adherence.

Results: 426 patients with cholangitis due to choledocholithiasis were identified of which 303 patients met all the inclusion criteria. During follow-up 68 infectious complications occurred in 64 patients (21%). The median duration of antibiotics given after adequate drainage was 4 days (IQR 2-6 days). In 141 patients (47%) the Dutch guideline was adhered, and antibiotics were given for 3 days or less. 39 of 68 complications (24%) occurred in patients receiving antibiotics more than 3 days versus 29 (21%) in the patients treated less than 3 days (P=0.615). Severity of cholangitis (according to Tokyo guideline) did not differ between patients receiving antibiotics for 3 days or less or longer. The median duration of hospital stay was 6 days (IQR 4-9 days). Hospital stay in patients receiving antibiotics for 3 days or less was shorter in comparison with patients receiving antibiotics for more than 3 days; 6 days (IQR 4-8.5 days) and 7 days (IQR 5-9.5 days) respectively (P=0.026).

Conclusion: The Dutch guideline regarding duration of antibiotics in cholangitic patients after successful ERCP is not consistently followed. Our data confirms that antibiotics for less than 3 days after adequate drainage does not lead to an increase in infectious complications in comparison with longer treatment. Moreover, treating for more than 3 days increases, likely unnecessary, hospital stay. We therefore recommend stricter adherence to the Dutch guideline.

**Durable Response in Markers of Cholestasis Through 24 Months of Open-Label Extension with Obeticholic Acid in Patients in the Benelux with Primary Biliary Cholangitis**

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Obeticholic acid (OCA) is a potent and selective farnesoid X receptor (FXR) agonist indicated for treatment of primary biliary cholangitis (PBC) in patients with an inadequate response or intolerability to ursodeoxycholic acid (UDCA). This analysis evaluated efficacy and safety of OCA in patients with PBC in the Benelux.

POISE was a Phase 3, 12-month, double-blind (DB), placebo-controlled study. Patients on stable or no UDCA with alkaline phosphatase (ALP) ≥1.67x ULN or total bilirubin >ULN to <2x ULN were randomized to daily Placebo (PBO), OCA 5-10 mg, or OCA 10 mg. After completion of the DB phase, patients had the option to enroll in an ongoing open-label extension (OLE). Upon initiation of the OLE, all patients received OCA 5 mg with the option to up-titrate after 3 months based on response and tolerability. The primary endpoint was defined as ALP <1.67x ULN with ≥15% reduction in ALP and a total bilirubin ≤ULN.

Thirty-two of 216 patients randomized and dosed in POISE were treated at Benelux sites (PBO, n=11; OCA 5-10 mg, n=5; OCA 10 mg, n=16) and 30 patients continued into the OLE. Similar to the overall POISE population, more OCA-treated patients achieved the primary endpoint in the DB phase compared to PBO (0% PBO; 25% OCA 5-10 mg; 60% OCA 10 mg). After 24 months of OLE, 45% of PBO patients, 50% of OCA 5-10 mg patients, and 64% of OCA 10 mg patients met the primary endpoint. Compared to PBO, OCA 10 mg demonstrated significant reductions in ALP (U/L) after 12 months of DB treatment (mean change from baseline [SD]: PBO -20.4 [72.8]; OCA 5-10 mg -30.6 [51.8]; OCA 10 mg -132.4 [92.5], p<0.01). The reduction in ALP was durable through an additional 24 months of treatment during the OLE (PBO -48.1 [79.6]; OCA 5-10 mg -66.4 [85.3]; OCA 10 mg – 99.1 [101.0], p<0.01). Total bilirubin (mg/dL) remained within the normal limits after 12 months of DB treatment and 24 months in the OLE. Pruritus was the most common adverse event (AE). Patients on OCA had an incidence of pruritus between 81-100% in the DB phase and 21-40% in the OLE. In comparison, 36% of PBO patients experienced pruritus in the DB phase.

Conclusions: OCA treatment in patients with PBC in the Benelux resulted in improvements in ALP and a greater percentage of patients achieving the primary endpoint compared to placebo-treated patients. Consistent with the overall POISE cohort, the improvements were durable through an additional 24 months of OCA treatment in the OLE. Pruritus was the most common AE. No new safety signals were observed with longer term treatment.

## Increased risk of death and liver transplantation in autoimmune hepatitis, results from a national cohort study

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Introduction: Autoimmune hepatitis (AIH) is a chronic immune-mediated inflammation of the liver. Studies on survival show conflicting results. This study aims to assess the mortality rate in AIH patients in the Netherlands.

Methods: A total of 449 patients (77% female) with established AIH were included in six academic and ten non-academic hospitals. AIH variants with primary biliary cholangitis (AIH-PBC) or primary sclerosing cholangitis (AIH-PSC) were present in 29 and 35 patients, respectively. Mortality and liver transplantation were assessed during ten years, from August 1st 2006 until July 31st 2016. The median age at inclusion was 51 years (range 14-88). Standardized mortality ratios (SMR) were calculated using age, gender and calendar-year matched mortality rates.

Results: During the ten year follow-up, 60 (13%) patients died at a mean age of 71 years (range 33-94). Causes of death were liver related n=26 (43.3%), circulatory system disease n=13 (21.6%), respiratory system disease n=2 (3.3%), non-liver malignancies n=12 (20.0%), other n=5 (8.3%) and unknown causes n=2 (3.3%). The patients that died due to liver disease cumulatively encountered 47 complications of liver failure, cirrhosis or treatment. Survival was impaired in patients with AIH (SMR 1.4, 95%C.I. 1.1-1.8) and AIH-PSC (SMR 4.7,C.I. 1.5-14.6), but not in AIH-PBC (SMR 1.2, 95%C.I. 0.3-4.9). Liver transplantation was performed in 9 patients. In addition, 9 patients were placed on the transplantation waiting list, of whom four died before receiving a donor liver.

Conclusion: Patients with AIH of all ages have an relatively small increased risk of death and liver transplantation. Patients with the AIH-PSC variant syndrome have the poorest prognosis. Excess death in patients with AIH can be attributed to liver disease.

**Drug utilization in patients with cirrhosis in ambulatory care: a retrospective cohort study, MLDS voordracht, projectnr. CDG 12-10**

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Background: Patients with cirrhosis are susceptible for adverse drug reactions due to changes in pharmacokinetics and pharmacodynamics. Certain drugs have known safety risks in these patients, such as NSAIDs and benzodiazepines. Not much is known about drug use in patient with cirrhosis in ambulatory care, where the risks may be higher due to less monitoring of the patient. In this retrospective cohort study, we aim to explore which drugs patients with cirrhosis use in ambulatory care.
Methods: Data were used from an out-patient pharmacy database combined with hospitalization data from the PHARMO Database Network. Patients with a diagnosis of cirrhosis (ICD-9 code 571.2 or 571.5) between January 1998 and December 2015 were included. The index date was the day of discharge from hospital with a diagnosis of cirrhosis. Data on drug dispensions were analyzed during the total follow-up of a patient and the period prevalence of drug use was determined.
Results: In total 5,618 patients were included of which 59.4% was male and the mean age at the index date was 60.7 (standard deviation 12.5) years. Patients were followed for a median of 3 years after the index date (interquartile range (IQR) 3). Follow-up ended due to a liver transplantation in 3.2% of patients. During the total follow-up, 102,297 drugs were prescribed. General practitioners prescribed most of these drugs (61.5%), specialists about a third (36.4%) and the prescriber was unknown in 2.2%. Per year, a median of 6.8 drugs were used per patient (IQR 8.4). During the total follow-up, proton pump inhibitors were the most often used drug class (prevalence 68.2%), followed by the high-ceiling sulfonamide diuretics (49.8%) and the osmotically acting laxatives (49.7%). Spironolactone (48.7%), furosemide (44.0%) and pantoprazole (34.9%) were the most frequently used drugs. The most frequently used drugs for non-liver related comorbidities were temazepam (23.2%), diclofenac (22.2%) and paracetamol (21.3%). The prevalence of use of NSAIDs and benzodiazepines was respectively 37.1% and 46.2% during the total follow-up.
Conclusion: Patients with cirrhosis frequently use drugs in ambulatory care. This includes also drugs with known safety risks in cirrhosis, such as NSAIDs and benzodiazepines. Pharmacotherapy in patients with cirrhosis is complex and requires attention by both specialists and general practitioners to prevent adverse drug reactions.

**Drug survival and immunogenicity after switching from Remicade® to biosimilar CT-P13 in inflammatory bowel disease patients: Two year follow-up of a prospective observational cohort study**

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Background: The infliximab biosimilar CT-P13 is widely implemented in current daily IBD practice in most European countries. Several studies showed reassuring data on switching from Remicade® to CT-P13 in IBD patients. However, long-term outcomes beyond 1 year are scarce, especially pharmacokinetic and immunogenicity data are lacking. We previously reported 1-year data from our cohort of IBD patients who switched to CT-P13. Our current aim was to investigate the long-term drug survival, pharmacokinetics and immunogenicity two years after switching to CT-P13.
Methods: We performed a single-center prospective observational cohort study in all Remicade®-treated IBD patients who switched to CT-P13 in 2015. Primary endpoint was drug survival at week 104 and reasons for discontinuation. We systematically documented trough levels and anti-drug antibodies to infliximab (ADA) at baseline, week 52 and week 104. Furthermore, biochemical and clinical disease activity were registered by measuring C-reactive protein (CRP), fecal calprotectin (FCP), Harvey-Bradshaw Index (HBI) for Crohn's disease (CD) and Simple Clinical Colitis Activity Index (SCCAI) for ulcerative colitis (UC) and IBD unclassified (IBD-U).
Results: Eighty-three patients were enrolled, 57 with CD, 24 with UC and 2 with IBD-U (28 male, median age 36, IQR 27-51). At week 104, 53/78 (68%) patients remained on CT-P13 while 5 were lost to follow-up. Reasons for discontinuation during year 1 and 2 were disease remission (n=2 and 5), loss of response (n=5 and 5) and adverse events (n=6 and 2). Median trough levels at baseline, week 52 and week 104 were 3.6 ug/ml [IQR 1.7-5.5], 3.7 ug/ml [IQR 2.1-5.8] and 3.9 ug/ml [IQR 2.2-5.7] (p=0.664). During year 2, dosing was increased in 14/53 (26%) patients, due to low trough levels (n=5), disease activity (n=4) or both (n=5). Dosing was decreased in 5/53 (9%) patients, due to supra-therapeutic trough levels (n=2), remission (n=2) or both (n=1). ADA were present in 5/83 patients at baseline (prior to switching), in 2 patients before week 52, and no subsequent ADA were detected until week 104. HBI, SCCAI, FCP and CRP levels did not significantly change during the 104 week follow-up.
Conclusion: In a prospective cohort with >2 year follow-up, 68% of IBD patients continued CT-P13 beyond 2 years after switching from Remicade®. Main reasons for discontinuation were loss of response, adverse events and stable disease remission. Two new cases with ADA were observed in year one, but no immunogenicity was detected beyond week 52.

**Latent cytomegalovirus infection does not influence disease course in Inflammatory Bowel Disease**

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Background: Cytomegalovirus (CMV) infection is common in the general population. Patients with inflammatory bowel disease (IBD) are at risk for CMV reactivation, most likely mediated by both the inflammatory state of the mucosa and use of immunosuppressive drugs. A CMV infection affects the disease course in transplant recipients and HIV patients. However, it is unclear if latent CMV infection has influence on the long-term disease course in IBD. In this study, we investigated if latent CMV infection has an impact on IBD disease outcome.
Methods: A nested case-only cross-sectional study was performed in the IBD cohort of a large tertiary university medical center in the Netherlands. Data were prospectively collected relating patients' clinical characteristics, disease course and medication use. Patients were screened for the availability of CMV serology tests performed as part of standard clinical care. When multiple tests were available, most recent test results were used for further analysis. Patients were considered seropositive when anti-CMV IgG antibodies were detected (>4 AU/mL). Logistic regression models were used to estimate multivariable-adjusted odds ratios for disease outcomes, adjusting for confounding factors.
Results: CMV serology was available for 412 of 1215 (33.9%) patients, of whom 186 (45.1%) patients were seropositive, which is comparable to seroprevalence in the general Dutch population.
Seropositive patients were significantly older and had a longer disease duration (both p-values≤0.01). No difference was found for CMV IgG seroprevalence between types of IBD (p-value=0.86). CMV IgG seroprevalence was associated with patients of non-Western origin, birth outside the Netherlands, and a lower educational level (all p-values≤0.02).
CMV IgG seroprevalence was not associated with a more complicated disease course evaluated by the Montreal classification, need for surgical resection or the use of steroids, immunosuppressive drugs and biologicals (all p-values>0.05).
Discussion: In this study, we show that latent CMV infection is not associated with a more complicated disease course, the need for surgery or treatment regimens in IBD. While testing for CMV IgG/IgM antibodies and viremia as part of the diagnostic work-up for acute enteritis remains important, standard CMV IgG testing is unnecessary for clinical decision making in IBD.

**Gallstone disease necessitating cholecystectomy after ileal or ileocecal resection in Crohn's disease: a nationwide cohort study in the Netherlands**

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Backgrounds: Crohn's disease (CD) patients are at twofold risk of developing gallstones. Resection of the ileum may play an important pathogenic role in the development of gallstones. Data on the risk of gallstones necessitating cholecystectomy in CD are necessary to interpret the clinical relevance of this observation. We aimed to assess the absolute risk of cholecystectomy in CD patients after ileal resection in a large nationwide cohort.
Methods: A cohort of adult CD patients after ileal or ileocolonic resection between 1991 and 2015 was identified in PALGA, a nationwide pathology database. Details on subsequent bowel resections and cholecystectomies were recorded. Cholecystectomy rates of the general Dutch population were selected as reference group.
Results: The identified cohort comprised 8302 CD patients after ileal resection, 3466(42%) male, median follow-up 12.0 (IQR 6.3-18.1)years. The cumulative incidence of a cholecystectomy after ileal resection was 0.5%, 2.4%, 4.6% and 10.3% after 1, 5, 10 and 20 years of follow-up, respectively. In multivariate analysis female sex (HR 1.9, CI: 1.5-2.3; P<0.001), year of ileal resection (HR/5 year increase 1.27 CI: 1.18-1.35; p<0.001) and re-resection (time-dependent HR 1.37 CI 1.06-1.77; p=0.016) were associated with an increased risk of cholecystectomy. Cholecystectomy rates per calendar year showed a higher incidence rate of cholecystectomy in our population as compared to the general Dutch population. Furthermore, an increase in the probability of cholecystectomy over calendar time in our postoperative CD population was observed. Although the number of cholecystectomy cases in the first years of our cohort was too low to assess a trend, in the general Dutch population a significant increase in incidence of cholecystectomy was also observed.
Conclusion: This large nationwide long-term cohort study shows that, although yearly cholecystectomy rates are higher in CD patients after ileal resection as compared to the general population, the absolute risk of gallstones necessitating cholecystectomy is low. Overall this risk does not warrant routine synchronous prophylactic cholecystectomy during bowel resection for CD. Finally, our data suggests an increasing probability of cholecystectomy after ileal resection in accord with increased cholecystectomy incidence rates in the general population.

## The gut microbiome can distinguish inflammatory bowel disease from healthy controls and irritable bowel syndrome

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Background: Inflammatory Bowel Disease (IBD) and Irritable Bowel Syndrome (IBS) are widespread disorders of the gut, with a total prevalence exceeding 10% in the European population. In clinical practice, diagnosis of IBS and IBD is frequently performed by excluding other gastrointestinal diseases and involves multiple, often invasive, diagnostic procedures. Our previous research indicates that the composition and function of the gut microbiota is associated with IBS and IBD. As the gut microbiome is increasingly being recognized to have diagnostic potential, the goal of this study was to utilise features of the gut microbiome to build predictive models for the diagnosis of IBD and IBS.

Methods: We performed whole metagenome sequencing of the faecal microbiome, and recorded clinical phenotypes, for 181 IBS patient, 380 IBD patients and 859 healthy controls. The microbiome composition and phenotypes were utilised to train an ensemble of machine-learning classifiers, including random forests (RFs), support vector machines (SVMs) and neural networks (ANNs), for the prediction of IBD and IBS compared to healthy controls. The predictive power of these models was then compared to similar models trained on an independent dataset of publicly available faecal metagenomes (1228 IBD patients and 441 healthy controls), generated utilising different DNA isolation methods, to assess the reproducibility and the impact of DNA isolation on the predictive power of the gut microbiome.

Results: RF and ANN based classifiers, trained on phenotype-corrected species- and genera-level composition of faecal metagenomes, successfully classified IBD samples versus controls with accuracy over 90%, and sensitivity and specificity over 85%. The predictive power of these models was consistent with equivalent classifiers trained using the publicly available faecal metagenomes.

Comparison of models showed that the quantification of metagenome composition at genera or species level is necessary to achieve the high accuracy of prediction, illustrating that the high resolution obtained by whole metagenome sequencing is required for precise prediction of IBD. The models trained for prediction of IBS showed high sensitivity (higher than 95%), but low specificity (35%), indicating that the inclusion of covariates other than gut microbiota composition is necessary for accurate prediction of IBS.

Conclusion: We demonstrate that faecal metagenome composition is a strong predictor for IBD and to a lesser extent for IBS, and that metagenome-based diagnostics has a potential to reduce the diagnostic costs and patient inconvenience for patients with gastrointestinal complains.

**The 1000IBD project: multi-omics data of 1000 inflammatory bowel disease patients; Data release 1**

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Background: Inflammatory bowel disease (IBD) is a chronic complex disease of the gastrointestinal (GI) tract. Patients with IBD can experience a wide range of symptoms, but the pathophysiological mechanisms that cause these individual differences in clinical presentation remain largely unknown. In consequence, IBD is currently classified into subtypes using clinical characteristics. If we are to develop a more targeted treatment approach, molecular subtypes of IBD need to be discovered that can be used as new drug targets. To achieve this, we need multiple layers of molecular data generated from the same IBD patients.
Methods: We initiated the 1000IBD project to prospectively follow more than 1000 IBD patients from the Northern provinces of the Netherlands. For these patients, we have collected a uniquely large number of phenotypes and generated multi-omics profiles. To date, 1,215 participants have been enrolled in the project and enrolment is on-going. Phenotype data collected for these participants includes information on dietary and environmental factors, drug responses, and adverse drug events. Genome information has been generated using genotyping (ImmunoChip, Global Screening Array and HumanExomeChip) and sequencing (whole exome sequencing and targeted resequencing of IBD susceptibility loci). Transcriptome information was generated using RNA-sequencing of intestinal biopsies and microbiome information from stool samples and intestinal biopsies was generated using both sequencing of the 16S rRNA gene and whole genome shotgun metagenomic sequencing. We uploaded and shared these 1000IBD data.
Results: All molecular data generated within the 1000IBD project is shared on the European Genome-Phenome Archive: www.ega-archive.org, accession number EGAB00000001286. The first data release, detailed in this abstract, contains basic phenotypes for /*-1,215 IBD patients, genotypes of 473 IBD patients, and gut microbiome data from stool samples of 313 patients and from intestinal biopsies of 152 generated by tag sequencing the 16S gene of 1,215 participants of 1000IBD.
Conclusions: We report on the establishment, the available data and the future development of the 1000IBD project: the first comprehensive multi-omics dataset aimed at discovering IBD biomarker profiles and treatment targets. 1000IBD data can freely be used by other IBD researchers as a replication cohort, a dataset to test new software tools, or a dataset for applying new statistical models. Future releases will comprise many more additional phenotypes and -omics data layers.

**Increased abundance of gut microbial virulence genes and pro-inflammatory pathways during Crohn's disease exacerbations**

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Background: Crohn's Disease (CD) is a chronic inflammatory disorder of the gastrointestinal tract characterized by alternating periods of exacerbation and remission. The pathophysiological mechanisms that trigger an exacerbation remain largely unknown, but accumulating evidence suggests that pro-inflammatory changes in the gut microbiome play an important role. The aim of this study was to identify microbial features associated with the onset and progression of a CD exacerbation.
Methods: We collected 196 stool samples of CD patients (one stool sample per patient) in 2013-2014. Microbial profiles were generated using whole genome shotgun metagenomic sequencing on the Illumina HiSeq platform. Microbial taxonomy, pathways and abundances of virulence factor genes were determined using the software tools KraKen/Bracken, HuMann2 and the Virulence Factor Database. To relate microbiome profiles to disease activity, the clinical records of all patients were analyzed two years later, and the date of the prior and/or next exacerbation, as calculated from the date of sampling, were determined. Microbiome profiles were correlated to disease activity using logistic regressions and linear models using the software tool MaAsLin. An FDR<0.1 was considered statistically significant.
Results: Of the 196 CD patients, 24 patients were having an exacerbation, while 172 were in remission. We found that during an exacerbation, as compared to remission, 160 pathways were differentially abundant, including a decrease in the production of vitamin B2 (RIBOSYN2_PWY FDR=0.03), butanoate (PWY_5676 FDR=0.03) and sulfate (SULFATE_CYS_PWY FDR=0.01). Furthermore, pathways involved in the biosynthesis of vitamin B2 and sulfate were increased in pre- and post- flare condition, as compared to active disease (FDR<0.1). Finally, we found that 6 months prior to and after a flare, 22 species, 18 pathways and 40 virulence factors linearly shifted inversely before as compared to after a flare, including the virulence factors flaA Flagella, flhB Flagellar Biosynthesis Protein, flhF Flagellar GTP binding Protein and bcrD, which linearly increased before and decreased after a flare (FDR<0.01).
Conclusion: In this study, we found that gut microbiome genes encoding the biosynthesis of vitamin B2 and sulfate are decreased during exacerbations and increased in remission, moreover, genes encoding virulence factors FlaA, flhB, flhF and bcrD, all associated to cellular adhesion and invasion, increase during the onset of and decrease in the recovery from a flare.

**How to measure environmental exposures (the exposome) in Inflammatory Bowel Disease?**

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Background: The etiology of inflammatory bowel disease (IBD) is complexly shaped with a major contribution of the exposome. Though many environmental exposures shaping the exposome have been identified, either in early childhood (i.e. breastfeeding), adulthood (i.e. cigarette smoking) or lifelong (i.e. vitamin D), their corresponding level of evidence varies greatly and overall evidence for the exposome is therefore insufficient and inconclusive. A universal, precise and reproducible measurement tool combining previously described exposures is therefore needed to study the exposome in IBD.
Methods: As a first step, we built the web-based Groningen IBD Environmental Questionnaire (GIEQ), an extensive and structured questionnaire measuring so far described possibly involved environmental exposures. For validation, readability and repeatability, a subset of 75 patients of the IBD cohort (n=1215) of a large tertiary referral center in the Netherlands, were asked to complete the questionnaire twice with an interval of two months. Baseline characteristics of the validation cohort were compared to the full IBD cohort. Cohen's kappa and correlation coefficients, were used to compare both fills in order to validate the GIEQ. Internal consistency was evaluated using Cronbach's alpha tests.
Results: Compared to our full IBD cohort, patients of the validation cohort were significantly older, accompanied by an increased mean disease duration (both $p<0.01$). Furthermore, no significant differences were observed. A mean kappa coefficient of 0.78 (standard deviation 0.17) was shown for categorical questions, ranging across the 15 different categories of the GIEQ from 0.68 (0.16) for questions concerning medication use, to 0.92 (0.13) for questions addressing birth and development. For numeric questions, a mean correlation of 0.85 (0.16) was shown. Correlation was highest for questions concerning family health (0.97, 0.09) and lowest in physical activity scores (0.62,0.11). Cronbach's alpha ranged from 0.64 to 1.0 across categories with a mean of 0.79 (0.14).
Discussion: The GIEQ is shown to be a reliable tool to measure environmental factors in IBD and can be used to study the role of the exposome and novel environmental factors in IBD. Due to simultaneous measurement of exposome elements, interactions between possibly involved environmental exposures can also be examined. Large scale studies using this measurement tool will lead to more generalized and comparable results, needed for further understanding of IBD etiology.

**Evaluation of Quality of life and caregiver burden in home parenteral nutrition patients: a cross sectional study**

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Rationale: Home total parenteral nutrition (HPN) is indicated in long-term intestinal failure (IF) to maintain or improve the nutritional status, guarantee patient survival and improve quality of life (Qol). The patients "caregiver" is often an essential partner to help perform daily activities. The aim of this study was to compare Qol, experienced distress and (if present) caregiver burden for relatives in two distinct categories of IF patients, i.e. those with short bowel syndrome as compared to those suffering from intestinal dysmotility.
Methods: All HPN patients and their caregivers of our HPN population were invited for this study. Qol and distress were assessed using the validated HPN-Qol and the "Lastmeter" (distress thermometer) questionnaire (for HPN patients) or the Caregiver Strain Index (CSI)(for caregivers) for the short bowel and dysmotility groups as well as for the combination.
Results: Fifty-six patients (37%) reported not to have a caregiver. Overall, 147 patients (76%) and 91 caregivers (63%) completed the questionnaires. The most common underlying conditions leading to IF were short bowel syndrome (SBS, 48%) and intestinal dysmotility disorders (42%). Both the SBS and the dysmotility group had a reasonable Qol (SBS 6 vs. dysmotility 5.8) but the experienced distress was significantly higher in the latter group. The distress of the dysmotility group was mainly determined by fatigue, abdominal pain, immobility, inability to work/go to school, limited contact with friends, nausea and vomiting, bloating, abdominal pain, troubles with sleeping, dizziness, inability to eat, being cold, fatigue and decreased taste. The Qol of patients with SBS was not significantly affected by neither aspects associated with HPN. The caregiver of dysmotility patients experienced a higher burden when compared with caregiver in the SBS group (average 7), due to increased demands on time and perceived strain.
Conclusion: Our results suggest that Qol of IF patients differs depending on the underlying disease, with the dysmotility group experiencing a higher burden when compared to short bowel patients. Also, in particular the burden that dysmotility patients experience with regard to eating, presence of fatigue and abdominal pain significantly impacts their Qol.
This study provides the first evaluation of perceived caregiver burden for relatives of patients with HPN. Here also the caregiver of dysmotility patients experienced a higher burden compared to caregivers of patients with SBS. These findings suggest that more focused care with attention to specific items within various groups (SBS, dysmotility) of the IF population is needed.

**Anti-inflammatory dietary recommendations based on the relation between food and the gut microbiome composition in 1424 individuals**

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Background: The gut microbiome plays an essential role in maintaining intestinal health. As microbes thrive on nutrients, the question arises whether we can nourish a protective gut flora. While there is increasing interest in the anti-inflammatory capacity of dietary factors, little is known on the correlation between food clusters or individual foods and gut microbial features. In this study, we investigated the effect of 176 dietary factors on the gut microbiome of 1424 individuals across four cohorts comprising the general population, and patients with Crohn's disease, ulcerative colitis, and irritable bowel syndrome.
Methods: For every participant one stool sample was collected and microbial DNA was isolated. Dietary intake data was derived from Food Frequency Questionnaires filled out on the day of faecal sampling. To reconstruct the microbiome composition of stool samples, shotgun metagenomic sequencing was performed. A cluster analysis was conducted to identify which dietary patterns were associated with particular microbial clusters. In addition, association analyses of individual food categories with individual microbial species and pathways were performed, using linear models. Analyses were conducted separately for each cohort, followed by a weighted meta-analysis and heterogeneity estimation.
Results: We identified 74 food items associated with 98 taxa and 194 pathways (FDR<5%). Overall, the consumption of a plant-based diet was associated with an increase in short chain fatty acid (SCFA) producing bacteria. A pattern comprising plant proteins, vegetables, fruits, muesli, nuts, and fish was associated with increased Roseburia hominis and Faecalibacterium prausnitzii abundance, and increased levels of bacterial carbohydrate fermenting pathways. This dietary pattern was also associated with an increased level of the L-ornithine biosynthesis pathway. This amino acid is known to stimulate the excretion of ammonium, a toxic by-product of protein metabolism. Moreover, fruit consumption was positively correlated with the bacterial pathway of folate biosynthesis, an attribute of Bifidobacteria.
Conclusion: We show that specific food groups are associated with the abundance of gut bacteria capable of the biosynthesis of vitamins and fermentation of carbohydrates to SCFAs, inferring that certain foods can exert mucosal protection by inducing bacteria with anti-inflammatory effects. A decrease in these bacteria has already been associated with both IBS and IBD. Based on these identified diet-microbiome relations, we can construct dietary recommendations to treat and prevent gastrointestinal disease through modulation of the gut microbiome.

## Lijst van standhouders, Digestive Disease Days NVGE, 15 en 16 maart 2018 te Veldhoven

| *G = Genderzaal, D = Diezezaal, K = Kempenzaal* | *Standnummer* |
|---|---|
| AbbVie BV | K3 |
| apDia-R-Biopharm | D 5 |
| B. Braun Medical BV | K 13 |
| Bayer BV | K 11 |
| Boston Scientific Nederland BV | D 1 |
| Cablon Medical BV | K 15 |
| Cobra Medical BV | G 7 |
| Crohn en Colitis Ulcerosa Vereniging Nederland | D 9 |
| Dr. Falk Pharma Benelux BV | G 1 |
| Erbe Nederland BV | K 5 |
| Ferring BV | K 1 |
| FMH Medical BV | G 2 |
| Fresenius Kabi BV | D 3 |
| Gilead Sciences Netherlands BV | K 4 |
| Halyard Nederland BV | D 6 |
| Intercept Pharma Nederland BV | D 12 |
| Jansen Medicars | G 10 |
| Janssen-Cilag BV | G 14 |
| Laborie | D 7 |
| Lamepro BV | G 8 |
| Mediplast | K 10 |
| Medivators BV | G 5 |
| Medix Publishers BV | G 9 |
| Medtronic Trading NL BV | D 2 |
| Merck Sharp & Dohme BV | K 6 |
| Mermaid Medical | K 9 |
| Mylan BV | G 11 |
| Norgine BV | K 7 |
| Olympus Nederland BV & Olympus Surgical | K 12 |
| Pentax Nederland BV & Hitachi Medical systems Nederland BV | G 12 |
| Pfizer BV | G 13 |
| Prion Medical BV | D 11 |
| RVC BV | K 8 |
| Sananet Care BV | G 3 |
| Sandoz | K 16 |
| Selinion Medical | D 13 |
| Stichting Opsporing Erfelijke Tumoren | D 10 |
| Takeda Nederland BV | K 2 |
| Teva Nederland BV | D 4 |
| Tramedico BV | G 6 |
| Uniphar Europe | K 14 |
| V&VN MDL | D 8 |
| Zambon Nederland BV | G 4 |

Plattegrond expo

Plattegrond Koningshof