RAPID FIRE CASES CDDW 2017

MARCH 6TH 2017

Laura Targownik
Associate Professor of Medicine
University of Manitoba

Case #1: Management of Post-Operative CD

- 36 y.o female
  - Diagnosed with ileocolonic Crohn's Disease 10 years ago
  - On long term AZA
  - Smokes 10 cigarettes/day
  - 6 months ago:
    - Presents with obstructive symtpoms,. Evidence of fibrotic stricture on MRI and colonoscopy
    - No response to 3 doses IFX, undergoes ileal resection and ileocecal reanastomosis
    - Now being seen 1 month post discharge

Case #1: Management of Post-Operative CD

- Question 1:
  - Should you:

A) Start Metronidazole
B) Continue IFX at maintenance dose
C) Continue AZA monotherapy
D) Observe without therapy

- Question 2:
  - You should monitor response to therapy based on:

A) Symptoms Alone
B) Endoscopy if symptoms develop
C) Endoscopy at 6-12 months if no therapy used
D) Endosopy at 6-12 months for all persons

Rutgeerts' Scoring System

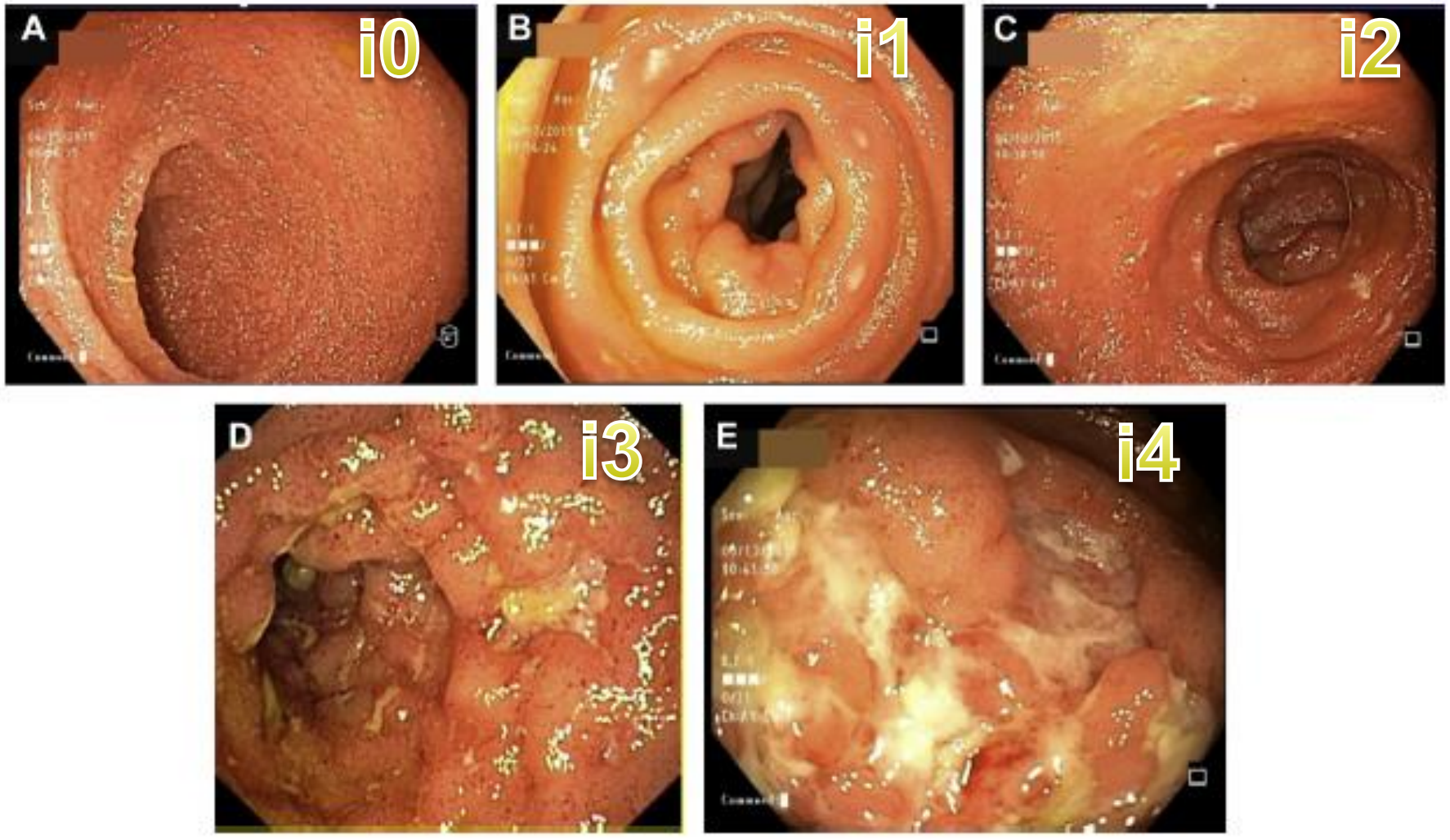


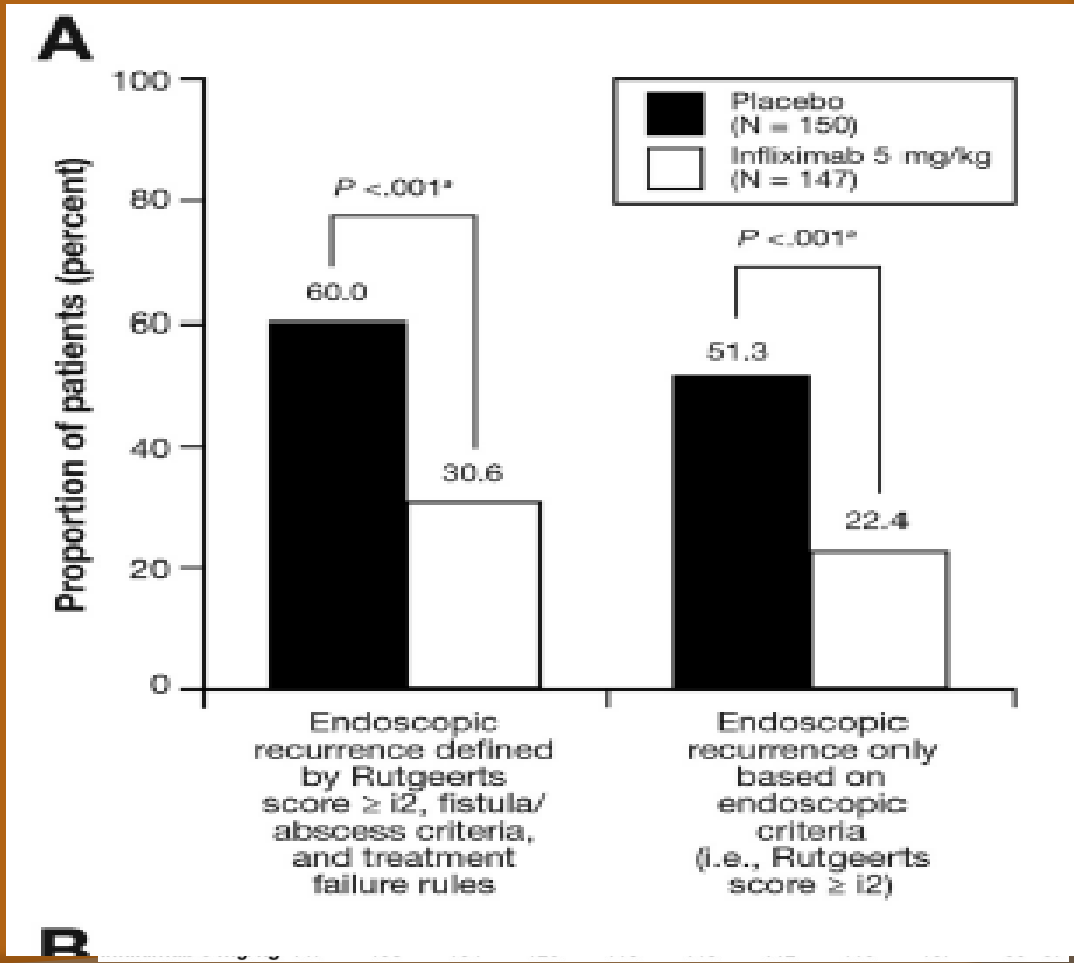
Image from Regueiro et al, Gastroenterology 2017;152:277–295

Gastroenterology 2016;150:1568–1578

Infliximab Reduces Endoscopic, but Not Clinical, Recurrence of Crohn's Disease After Ileocolonic Resection

Miguel Regueiro,[1] Brian G. Feagan,[2] Bin Zou,[3] Jewel Johanns,[3] Marion A. Blank,[4] Marc Chevrier,[3] Scott Plevy,[3] John Popp,[4] Freddy J. Cornillie,[5] Milan Lukas,[6] Silvio Danese,[7] Paolo Gionchetti,[8] Stephen B. Hanauer,[9] Walter Reinisch,[10,11] William J. Sandborn,[12] Dario Sorrentino,[13,14] and Paul Rutgeerts,[15] for the PREVENT Study Group

- RCT of IFX 5mg/kg q8w vs placebo, up to 104 weeks f/u
- Primary Outcome:
  - Clinical recurrence at w78
- Secondary Outcome
  - Endoscopic Recurrence at or prior to w78

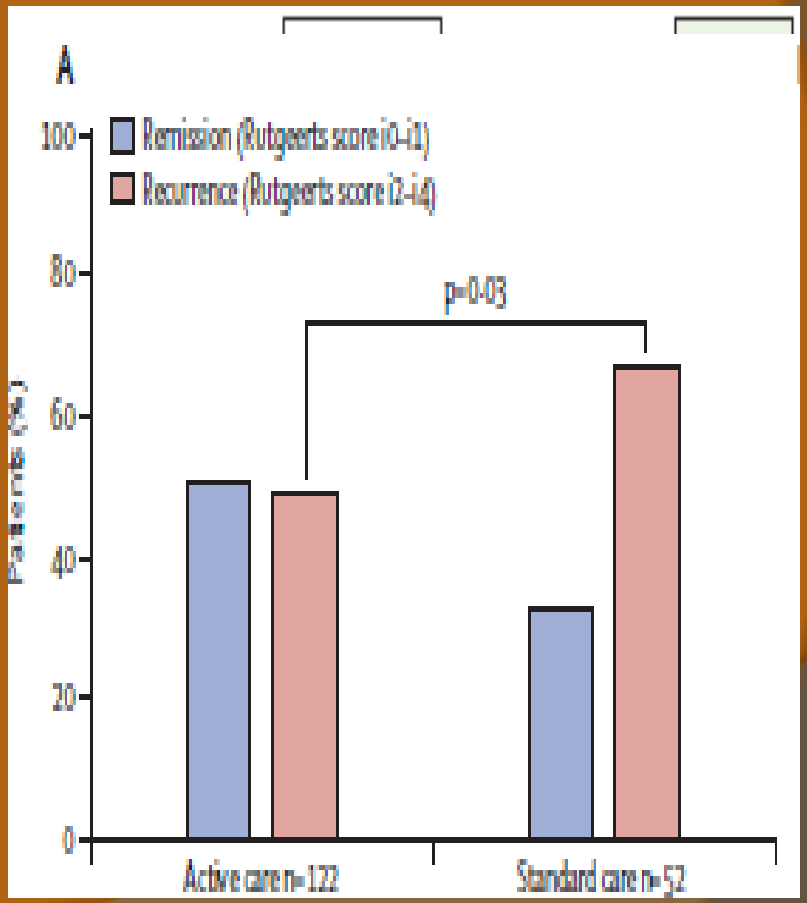


Crohn's disease management after intestinal resection: a randomised trial

Peter De Cruz, Michael A Kamm, Amy L Hamilton, Kathryn J Ritchie, Efrosinia O Krejany, Alexandra Gorelik, Danny Liew, Lani Prideaux, Ian C Lawrance, Jane M Andrews, Peter A Bampton, Peter R Gibson, Miles Sparrow, Rupert W Leong, Timothy H Florin, Richard B Gearry, Graham Radford-Smith, Finlay A Macrae, Henry Debinski, Warwick Selby, Ian Kronborg, Michael J Johnston, Rodney Woods, P Ross Elliott, Sally J Bell, Steven J Brown, William R Connell, Paul V Desmond

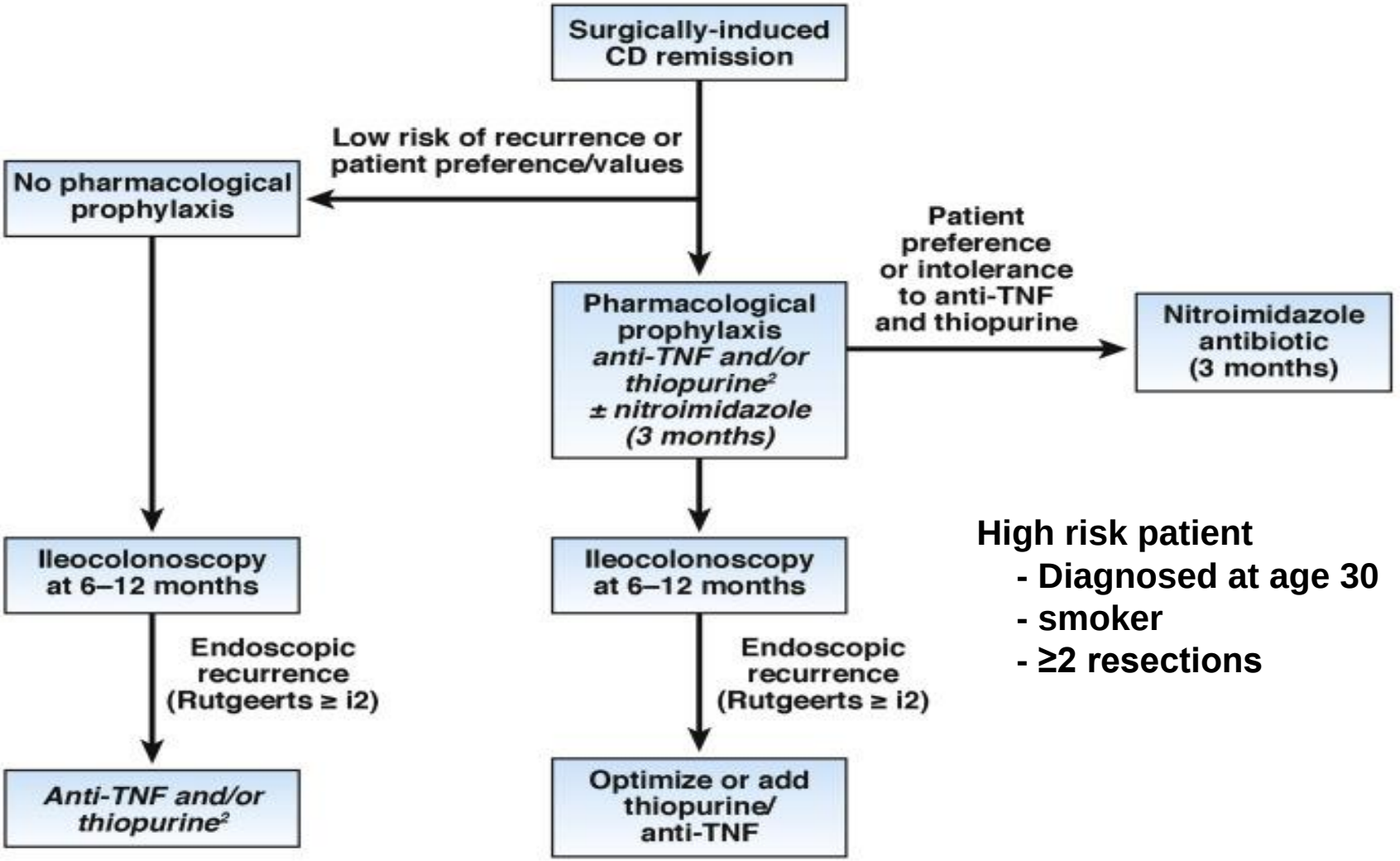
Lancet 2015; 385: 1406–17

- Post-Operative Crohn's Endoscopic Recurrence Trial (POCER)
- Assessed role for standard colonoscopy at 6 months following resection to guide therapy
- At 18 months, endosopic recurrence rate i2 or greater
  - 49% active therapy
  - 67% standard therapy
    - P= 0.03



American Gastroenterological Association Institute Guideline on the Management of Crohn's Disease After Surgical Resection

Clinical Decision Support Tool



High risk patient
- **Diagnosed at age 30**
- **smoker**
- **≥2 resections**

[1]Though most clinical trials in postoperative CD have evaluated only monotherapy, combination therapy may improve efficacy and decrease immunogenicity based on indirect evidence from trials of luminal CD.

[2]Thiopurine monotherapy may be appropriate for lower risk patients with i2 recurrence.

Case #1: Management of Post-Operative CD

- Question 1:
  - Should you:

  A) Start Metronidazole
  B) Continue IFX at maintenance dose
  C) Continue AZA monotherapy
  D) Observe without therapy

- Question 2:
  - You should monitor response to therapy based on:

  A) Symptoms Alone
  B) Endoscopy if symptoms develop
  C) Endoscopy at 6-12 months if no therapy used
  D) Endoscopy at 6-12 months for all persons

Case #2: Ustekinumab in Crohn's Disease

- 25 y.o male with ileocolonic Crohn's disease x 18 months
- Started IFX 5mg/kg + AZA 6 months ago
  - Initial response, but now once again symptomatic,
  - No response to 2 course
- Recent MRI shows active inflammation in ascending colon, cecum, and terminal ileum, Hgb 105, CRP 25
- Trough IFX level: 7.6, no response to increase in IFX to 10mg/kg q6w
- You have decided to institute Ustekinumab as a second line agent

Case #2: Ustekinumab in Crohn's Disease

- Question 3: What will you tell this patient that the likelihood of clinical remission at 8 weeks following 1 dose of UST
  - A) ~15%
  - B) ~35%
  - C) ~50%
  - D) ~65%

- Question 4: Assuming a clinical response at week 8, what is the likelihood of being in remission at the end of the year?
  - A) ~20%
  - B) ~30%
  - C) ~40%
  - D) ~50%

Case #2: Ustekinumab in CD

- Ustekinumab:
  - Monoclonal antibody to p40 subunit of IL-12 and IL-23 Leads to decrease in T_H1 and T_H-17 activity

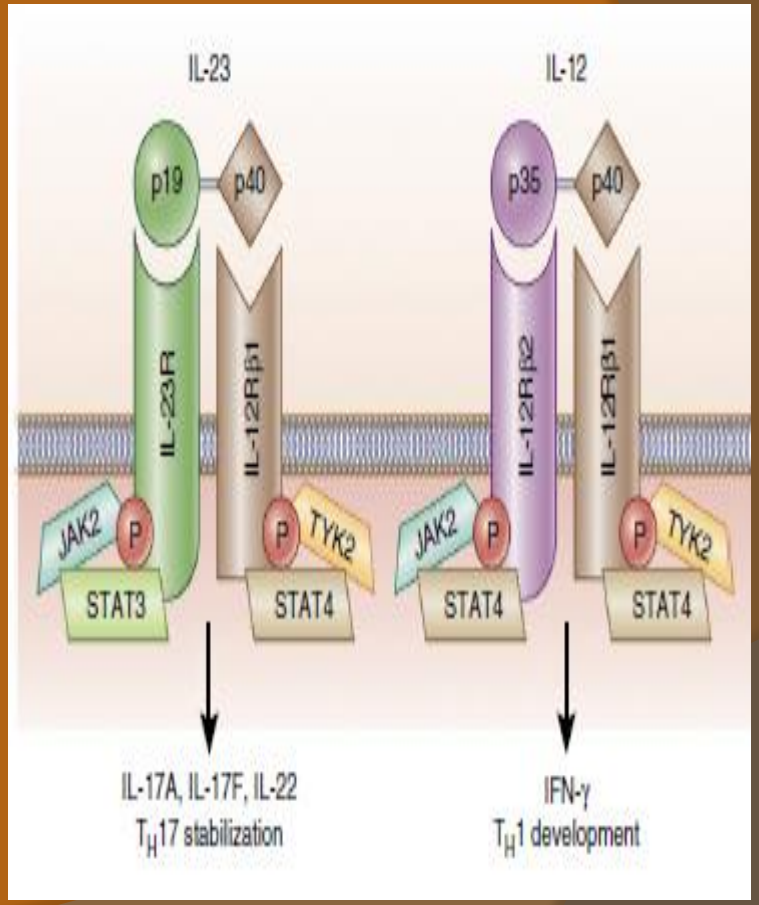


Image from Teng MW et al, Nat Med. 2015 Jul;21(7):719-29

Ustekinumab as Induction and Maintenance Therapy for Crohn's Disease

B.G. Feagan, W.J. Sandborn, C. Gasink, D. Jacobstein, Y. Lang, J.R. Friedman, M.A. Blank, J. Johanns, L.-L. Gao, Y. Miao, O.J. Adedokun, B.E. Sands, S.B. Hanauer, S. Vermeire, S. Targan, S. Ghosh, W.J. de Villiers, J.-F. Colombel, Z. Tulassay, U. Seidler, B.A. Salzberg, P. Desreumaux, S.D. Lee, E.V. Loftus, Jr., L.A. Dieleman, S. Katz, and P. Rutgeerts, for the UNITI–IM-UNITI Study Group*

N Engl J Med 2016;375:1946-60.

- Reports results of 3 linked RCTs:
  - UNITI 1: Induction of Remission in CD in Anti-TNF Failures
  - UNITI 2: Induction of Remission in CD in Anti-TNF Naïve Patients
  - UNITI-IM: Maintenance Therapy for CD up to 44 weeks

Ustekinumab as Induction and Maintenance Therapy for Crohn's Disease

B.G. Feagan, W.J. Sandborn, C. Gasink, D. Jacobstein, Y. Lang, J.R. Friedman, M.A. Blank, J. Johanns, L.-L. Gao, Y. Miao, O.J. Adedokun, B.E. Sands, S.B. Hanauer, S. Vermeire, S. Targan, S. Ghosh, W.J. de Villiers, J.-F. Colombel, Z. Tulassay, U. Seidler, B.A. Salzberg, P. Desreumaux, S.D. Lee, E.V. Loftus, Jr., L.A. Dieleman, S. Katz, and P. Rutgeerts, for the UNITI–IM-UNITI Study Group*

N Engl J Med 2016;375:1946-60.

- UNITI 1 and 2:
  - Randomized to *intravenous*
    - Placebo
    - 130mg UST
    - 260-520mg UST, dependent of weight
  - Assessed for clinical response at 8 weeks
- UNITI IM
  - Responders at 8 weeks randomized to *subcutaneous*
    - UST 90mg q8w
    - UST 90mg q12w
    - Placebo
  - Non-responders at 8 weeks given open label sc UST

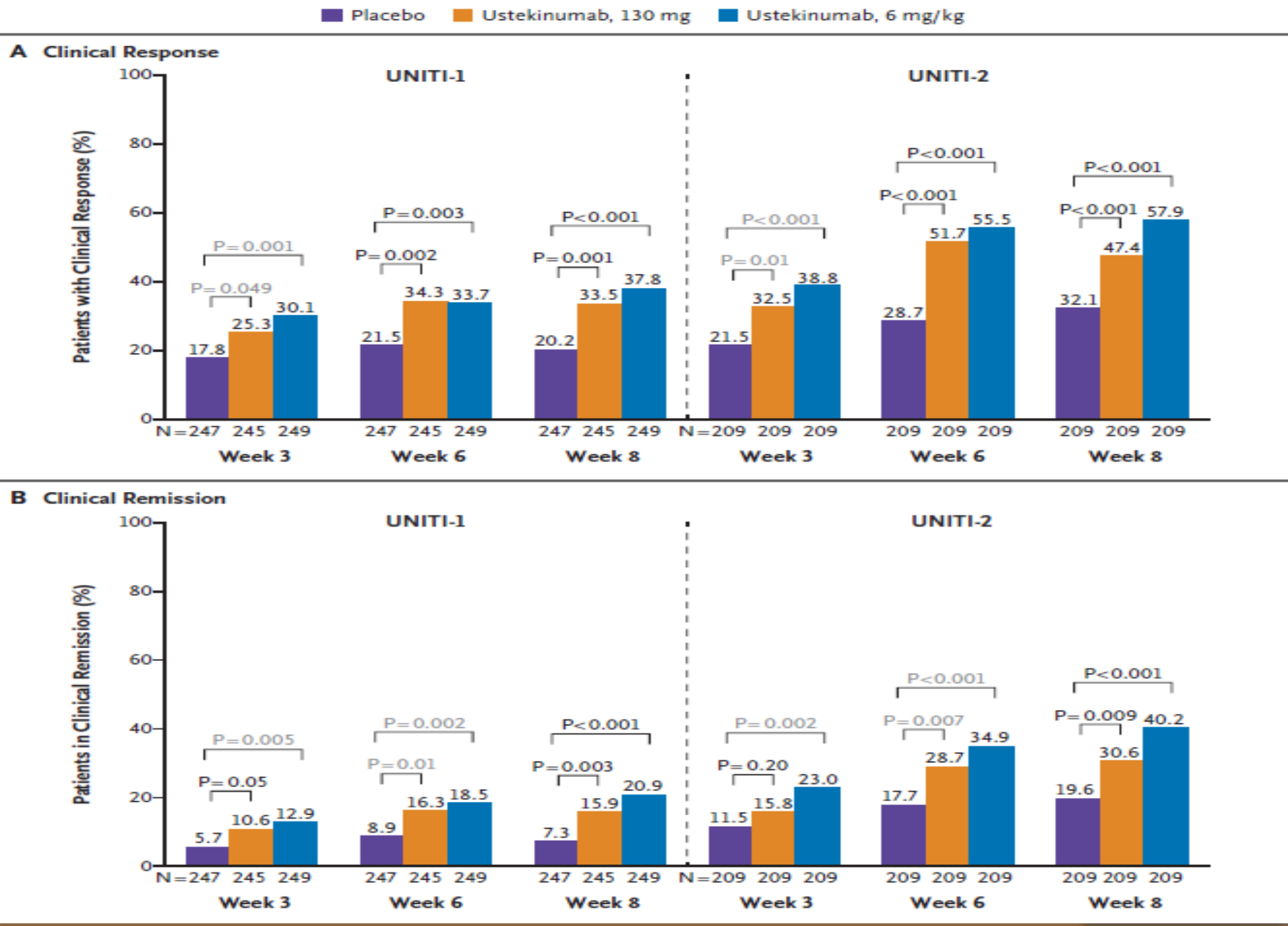


Image from Feagan B et al, N Engl J Med 2016;375:1946-60

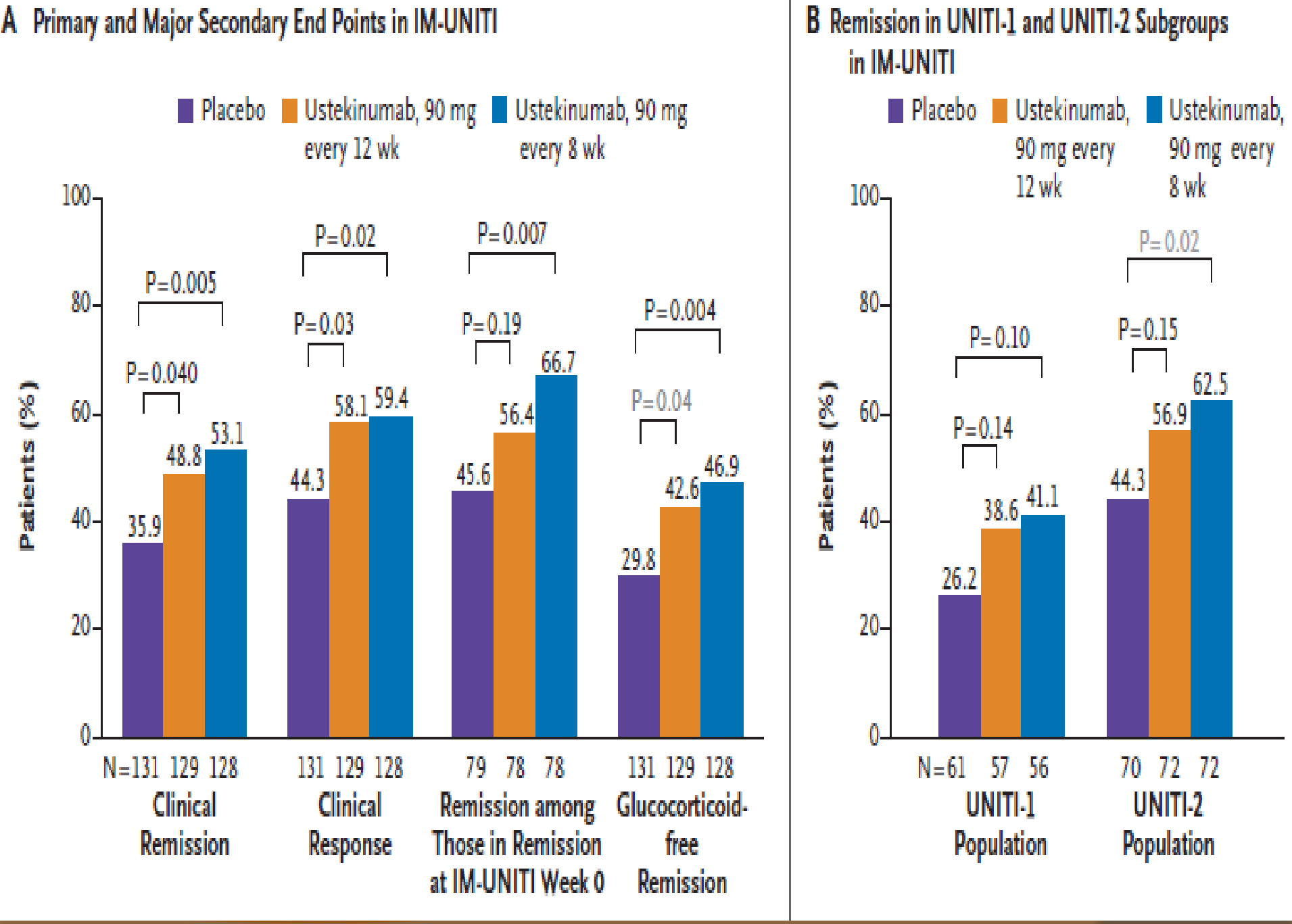


Image from Feagan B et al, N Engl J Med 2016;375:1946-60

Case #2: Ustekinumab in CD

- Among non-randomized subjects in UNITI-IM
  - ½ in clinical remission at 1 year
  - $^{2}/_{3}$ with clinical response at 1 year
- Overall
  - No endosopic outcomes
  - No differencde between IM users and non-IM users
  - Low rate of antibody development
- UST now approved in Canada
  - 6mg/kg dose for induction
  - 90mg q8w sc dosing for maintenance

Case #2: Ustekinumab in CD

- Question 3: What will you tell this patient that the likelihood of clinical response at 8 weeks following 1 dose of UST
  - A) ~15%
  - B) ~35%
  - C) ~50%
  - D) ~65%

- Question 4: Assuming a clinical response at week 8, what is the likelihood of being in remission at the end of the year?
  - A) ~20%
  - B) ~30%
  - C) ~40%
  - D) ~50%

Case #3: Dysplasia Surveillance in UC

- 41 y.o male with history of proctosigmoiditis to 20cm
- Most recent colonoscopy 3 years ago
  - Mayo 2 inflammation in rectum and distal sigmoid
  - No histologic or endoscopic inflammation proximally
- You have decided to perform endoscopic dysplasia surveillence

Case #3: Dysplasia Surveillance in UC

- Question 5: How would you survey for dysplasia in this patient?

A) Standard endoscopy with targeted biopsies + random biopsies throughout colon

B) Standard endoscopy with targeted biopsies + random biopsies from affected areas of the colon

C) Standard endoscopy with only targeted biopsies of suspicious lesions

D) Enhanced endoscopy (high definition or dye augmented), targeted biopsies + random biopsies throughout colon

E) Enhanced endoscopy (high definition or dye augmented) + targeted biopsies, random biopsies from affected areas only

F) Enhanced endoscopy (high definition or dye augmented), targeted biopsies + no random biopsies

Comparison of Targeted vs Random Biopsies for Surveillance of Ulcerative Colitis-Associated Colorectal Cancer

Toshiaki Watanabe,[1] Yoichi Ajioka,[2] Keiichi Mitsuyama,[3] Kenji Watanabe,[4] Hiroyuki Hanai,[5] Hiroshi Nakase,[6] Reiko Kunisaki,[7] Keiji Matsuda,[8] Ryuichi Iwakiri,[9] Nobuyuki Hida,[10] Shinji Tanaka,[11] Yoshiaki Takeuchi,[12] Kazuo Ohtsuka,[13] Kazunari Murakami,[14] Kiyonori Kobayashi,[15] Yasushi Iwao,[16] Masakazu Nagahori,[13] Bunei Iizuka,[17] Keisuke Hata,[1] Masahiro Igarashi,[18] Ichiro Hirata,[19] Shin-ei Kudo,[20] Takayuki Matsumoto,[21] Fumiaki Ueno,[22] Gen Watanabe,[2] Masahiro Ikegami,[23] Yoko Ito,[24] Koji Oba,[25,26] Eisuke Inoue,[27] Naoki Tomotsugu,[24] Toru Takebayashi,[28] Kenichi Sugihara,[29] Yasuo Suzuki,[30] Mamoru Watanabe,[13] and Toshifumi Hibi[31]

Gastroenterology 2016;151:1122–1130

- RCT comparing
  - HD Colonoscopy with only targeted biopsies of visible lesions
  - HD Colonoscopy with targeted and random biopsies (4 Bx q 10cm)
- All patients with UC > 7 years
- Assessed
  - Proportion with dysplasia
  - Proportion of biopsies with dysplasia
  - Relative proportions of dysplasia detected via targeted vs random biopsies
  - Procedure Time

Variable	Target group (n = 114)	Random group (n = 107)
Neoplastic lesions per colonoscopy, n	0.211	0.168
Patients with neoplasia detected, n (%)	13 (11.4)	10 (9.3)
The proportion of neoplasia per biopsy specimen		
Neoplastic lesions, n (%)	24 (6.9)	18 (0.5)
Biopsy specimens taken, n	350	3725
Neoplastic lesions detected, n	24	18
By targeted biopsy	22	4
By random biopsy	2	14
Location, n (%)		
Ascending, cecum	2 (8.3)	3 (16.7)
Transverse	2 (8.3)	3 (16.7)
Descending	3 (12.5)	0 (0)
Sigmoid	12 (50.0)	7 (38.9)
Rectum	5 (20.8)	5 (27.8)
Configuration, n (%)		
Protruded	17 (77.3)	—
Flat	1 (4.5)	—
Stricture	4 (18.2)	—
Total examination time, *min*	26.6	41.7
Low-grade dysplasia, n	23	18
High-grade dysplasia, n	1	0
Invasive cancer, n	0	0

- Random biopsies:
  - 13/2747 (0.5%) of inflamed or previous inflamed tissue
  - 0/707 in non-inflamed tissue
- RR for discovery of dysplasia: 1.25 (0.68-2.31)
- Avoiding random biopsies reduced procedure time by 50%

CONSENSUS STATEMENT

SCENIC International Consensus Statement on Surveillance and Management of Dysplasia in Inflammatory Bowel Disease

Loren Laine,[1,2] Tonya Kaltenbach,[3] Alan Barkun,[4] Kenneth R. McQuaid,[5] Venkataraman Subramanian,[6] and Roy Soetikno,[3] for the SCENIC Guideline Development Panel

Gastroenterology 2015;148:639–651

- At time of SCENIC meeting in 2014
  - 30% of panel felt unnecessary if WLE used
  - 60% felt unnecessary if chromoendoscopy was used

	# of Studies/# of patients	% with dysplasia on targeted biopsies	% with dysplasia found only on random biopsies	% of all patients with dysplasia detected only by random Bx	Rate of +ve random biopsies per all biopsies taken
Chromoendoscopy	7 / 1289	12.4%	1.2%	90.2%	0.1%
HD WLE	4/ 382	15.4%	1.6%	90.6%	0.2%
SD WLE	11 / 1785	11.8%	2.6%	80.4%	0.1%

Case #3: Dysplasia Surveillance in UC

- Question 5: How would you survey for dysplasia in this patient?

A) Standard endoscopy with targeted biopsies + random biopsies throughout colon

B) Standard endoscopy with targeted biopsies + random biopsies from affected areas of the colon

C) Standard endoscopy with only targeted biopsies of suspicious lesions

D) Enhanced endoscopy (high definition or dye augmented), targeted biopsies + random biopsies throughout colon

E) Enhanced endoscopy (high definition or dye augmented) + targeted biopsies, random biopsies from affected areas only

F) Enhanced endoscopy (high definition or dye augmented), targeted biopsies + no random biopsies

Case #4: Use of Rifaxamin in IBS-D

- 29 y.o female
  - 5 year history of IBS-D
  - Over last 3 months, has had increasing symptom burden
  - Was given rifaxamin at walk-in clinic
    - Felt better for about a month
    - Now back to usual symptoms

Case #4: Use of Rifaxamin in IBS-D

Question 6: Do you use Rifaxamin to treat symptoms of IBS-D?

A) Yes

B) No

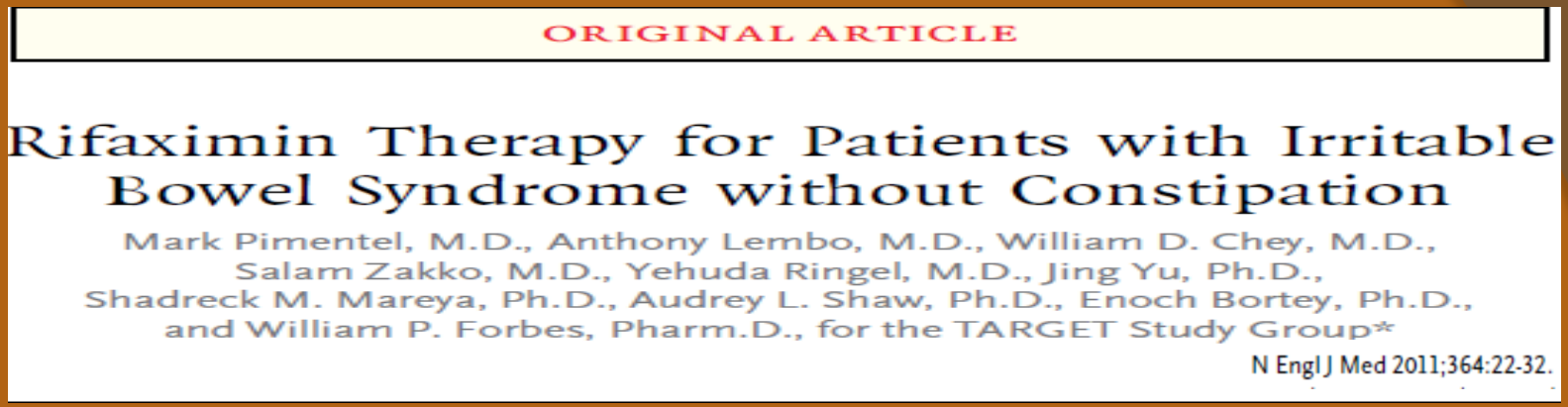
Question 7: What would be the anticipated improvement in short term response rate over placebo

A) 5-10%

B) 10-15%

C) 15-20%

D) >20%



ORIGINAL ARTICLE

Rifaximin Therapy for Patients with Irritable Bowel Syndrome without Constipation

Mark Pimentel, M.D., Anthony Lembo, M.D., William D. Chey, M.D., Salam Zakko, M.D., Yehuda Ringel, M.D., Jing Yu, Ph.D., Shadreck M. Mareya, Ph.D., Audrey L. Shaw, Ph.D., Enoch Bortey, Ph.D., and William P. Forbes, Pharm.D., for the TARGET Study Group*

N Engl J Med 2011;364:22-32.

- Original RCT evaluating Rifaxamin
- Adequate relief of IBS-D and IBS-A achieved in over 2 of next 4 weeks following treatment in:
  - RIF: 41%
  - Pla: 32%
- Approx. 1/3 of responders lose response over the next 2 months

Repeat Treatment With Rifaximin Is Safe and Effective in Patients With Diarrhea-Predominant Irritable Bowel Syndrome

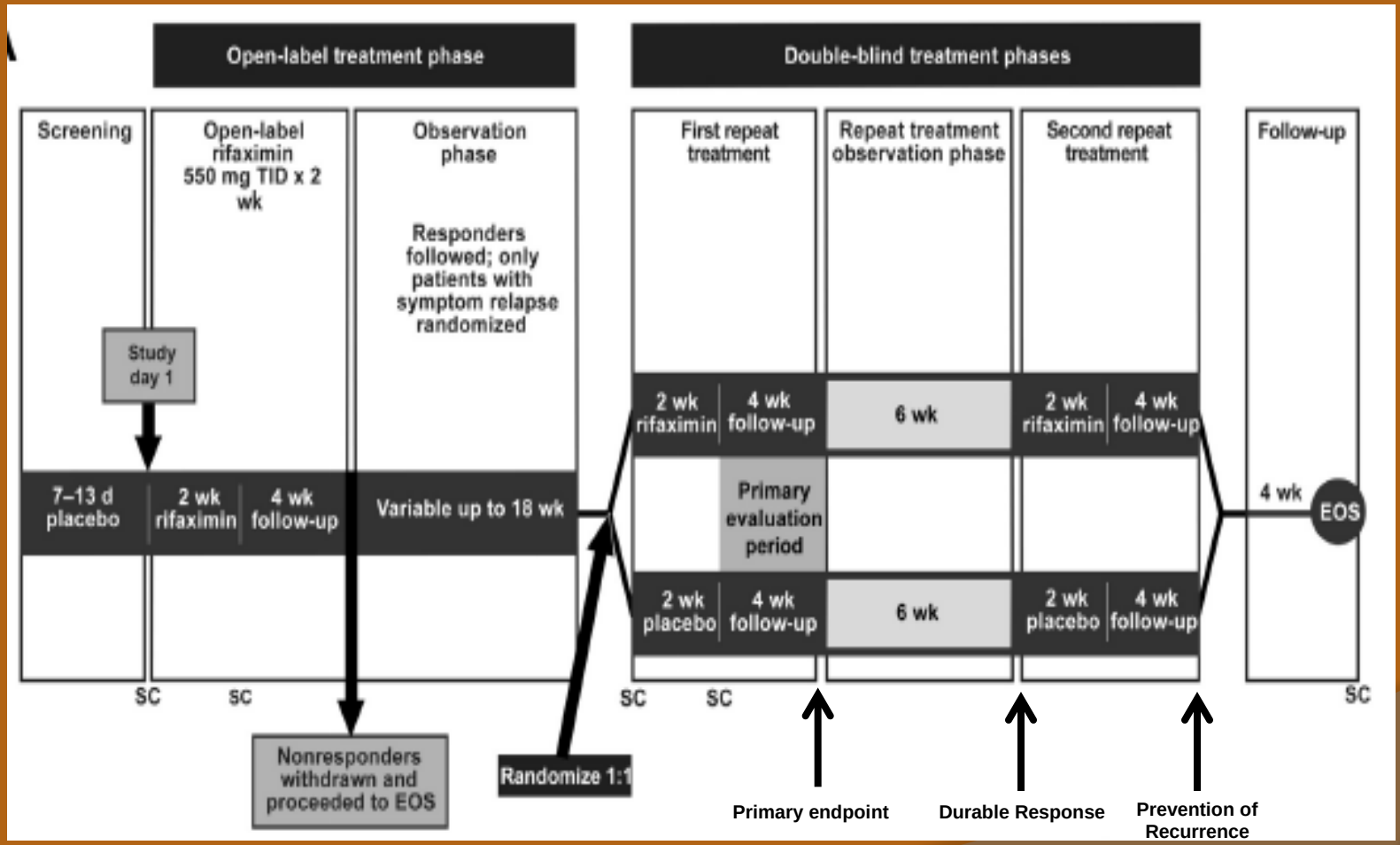
Anthony Lembo,[1] Mark Pimentel,[2] Satish S. Rao,[3] Philip Schoenfeld,[4] Brooks Cash,[5] Leonard B. Weinstock,[6] Craig Paterson,[7] Enoch Bortey,[7] and William P. Forbes[7]

Gastroenterology 2016;151:1113–1121

- RCT of retreatment with RIF for persons who
  - Had response to open label RIF
  - Relapsed within 18 weeks
- Randomized to
  - 2 weeks placebo
  - 2 weeks of RIF 550 tid
- Outcome
  - % with adequate response of IBS
    - >=2 out of 4 weeks following completion of therapy with **both**
      - 30% reduction in abd. pain score from baseline
      - 50% reduction in number of days with loose stools

Repeat Treatment With Rifaximin Is Safe and Effective in Patients With Diarrhea-Predominant Irritable Bowel Syndrome

Anthony Lembo,[1] Mark Pimentel,[2] Satish S. Rao,[3] Philip Schoenfeld,[4] Brooks Cash,[5] Leonard B. Weinstock,[6] Craig Paterson,[7] Enoch Bortey,[7] and William P. Forbes[7]



Repeat Treatment With Rifaximin Is Safe and Effective in Patients With Diarrhea-Predominant Irritable Bowel Syndrome

Anthony Lembo,[1] Mark Pimentel,[2] Satish S. Rao,[3] Philip Schoenfeld,[4] Brooks Cash,[5] Leonard B. Weinstock,[6] Craig Paterson,[7] Enoch Bortey,[7] and William P. Forbes[7]

Gastroenterology 2016;151:1113–1121

Assessment	Responders, n/total (%)		
	Rifaximin, 550 mg TID (n = 328)	Placebo (n = 308)	*P* value (95% CI)
Primary end point			
Abdominal pain and stool consistency[a,b]	125/328 (38.1)	97/308 (31.5)	.03 (0.9 to 16.9)
Key secondary end points			
Prevention of recurrence[b,c]	39/295 (13.2)	20/283 (7.1)	.007 (2.5 to 20.0)
Durable response[b,d]	56/328 (17.1)	36/308 (11.7)	.04 (1.4 to 16.6)
Bloating[b,e]	153/328 (46.6)	127/308 (41.2)	.14 (–0.9 to 15.0)

- Response rate over placebo: 6.6%
- Overall numbers of recurrence prevention is low (13.2% after 2 courses of RIF)

Case #4: Use of Rifaxamin in IBS-D

Question 6: Do you use Rifaxamin to treat symptoms of IBS-D?

A) Yes

B) No

Question 7: What would be the anticipated improvement in short term response rate over placebo

A) 5-10%

B) 10-15%

C) 15-20%

D) >20%

Rapid-Fire Case Presentations

Canadian Digestive Disease Week

Banff, AB

March 6, 2017

Philip M. Sherman, MD, FRCPC

Professor of Paediatrics, Microbiology, Nutritional Sciences, & Dentistry
Hospital for Sick Children, University of Toronto
Canada Research Chair in Gastrointestinal Disease

SickKids®

CIHR IRSC
Canadian Institutes of Health Research | Instituts de recherche en santé du Canada

FACULTY OF MEDICINE
GREAT MINDS FOR A GREAT FUTURE
University of Toronto

Disclosures

PMS has the following financial relationships to disclose:

*Lallemand Health Solutions

(research contract)

*Abbott Nutrition (honorarium)

*Mead Johnson Nutrition (honorarium)

*Nestlé Nutrition (honorarium)

*Procter & Gamble (honorarium)

Antibe Therapeutics (stockholder)

** Products or services produced by this company are relevant to my presentation.*

CanMEDS Roles Covered

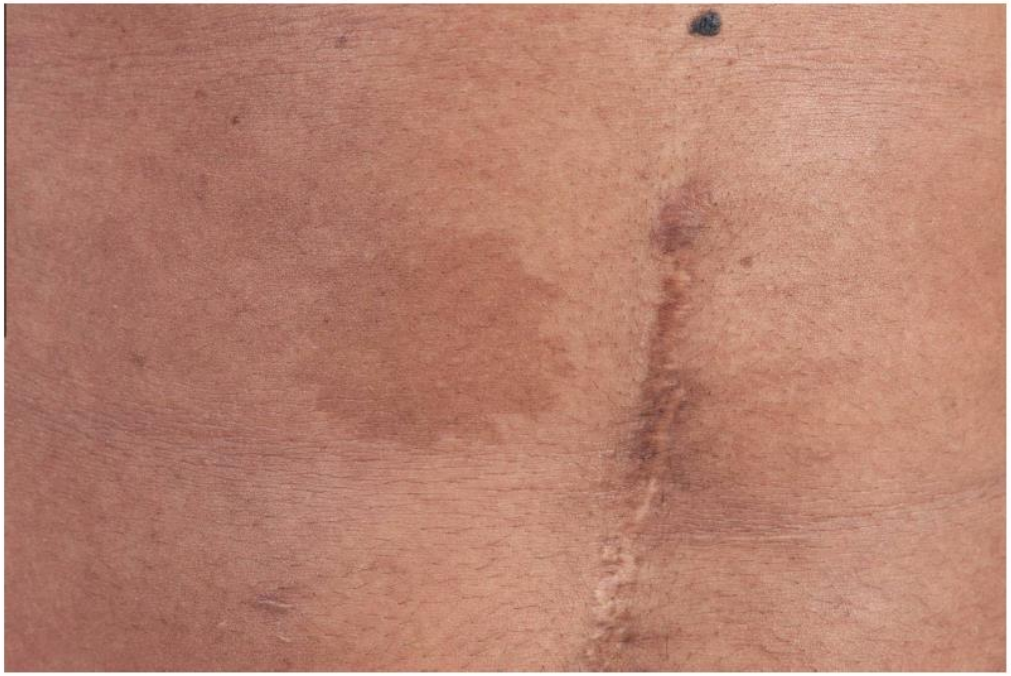
X	**Medical Expert** (as *Medical Experts*, physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional values in their provision of high-quality and safe patient-centered care. *Medical Expert* is the central physician Role in the CanMEDS Framework and defines the physician's clinical scope of practice.)
	Communicator (as Communicators, physicians form relationships with patients and their families that facilitate the gathering and sharing of essential information for effective health care.)
	Collaborator (as *Collaborators*, physicians work effectively with other health care professionals to provide safe, high-quality, patient-centred care.)
	Leader (as *Leaders*, physicians engage with others to contribute to a vision of a high-quality health care system and take responsibility for the delivery of excellent patient care through their activities as clinicians, administrators, scholars, or teachers.)
	Health Advocate (as *Health Advocates*, physicians contribute their expertise and influence as they work with communities or patient populations to improve health. They work with those they serve to determine and understand needs, speak on behalf of others when required, and support the mobilization of resources to effect change.)
X	**Scholar** (as *Scholars*, physicians demonstrate a lifelong commitment to excellence in practice through continuous learning and by teaching others, evaluating evidence, and contributing to scholarship.)
	Professional (as *Professionals,* physicians are committed to the health and well-being of individual patients and society through ethical practice, high personal standards of behaviour, accountability to the profession and society, physician-led regulation, and maintenance of personal health.)

Learning objectives:

1. Become familiar with some of the impactful papers published in GHN in 2016.
2. Decide whether these selected publications should have an impact on your clinical practice.

Case #1

30 yo F with new onset hematochezia
Brother died of brain tumour (glioma) as a teenager



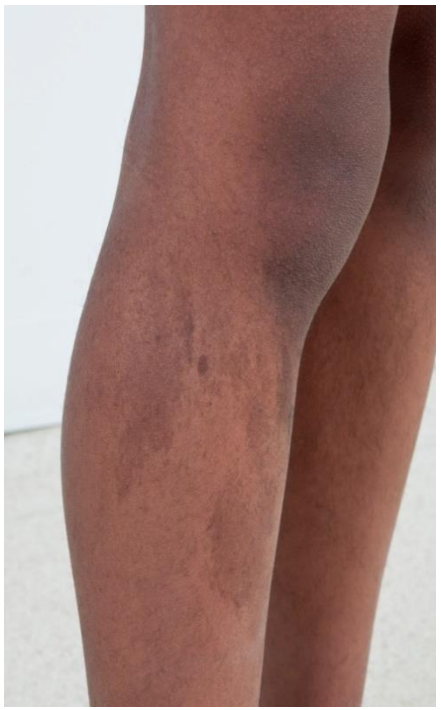
What is the diagnosis:? a) Lynch s.
b) Turcot's s.
c) Biallelic mismatch repair
d) Neurofibromatosis

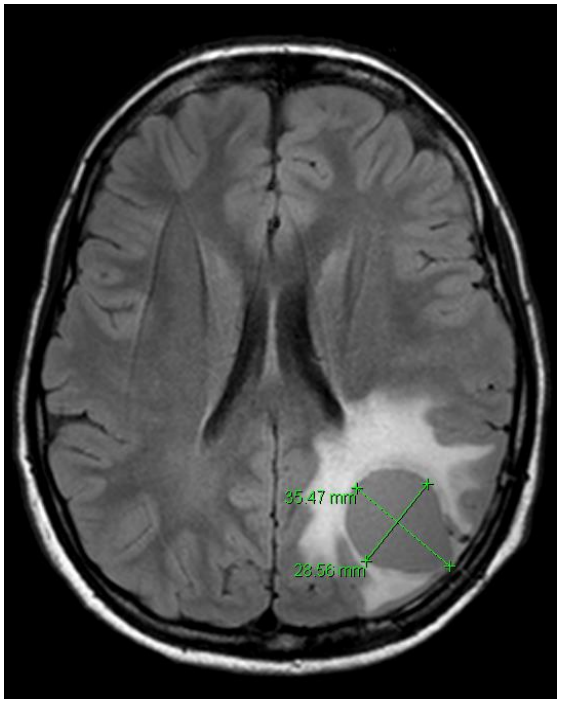
Biallelic Mismatch Repair Gene Deficiency Syndrome (BMMRD)

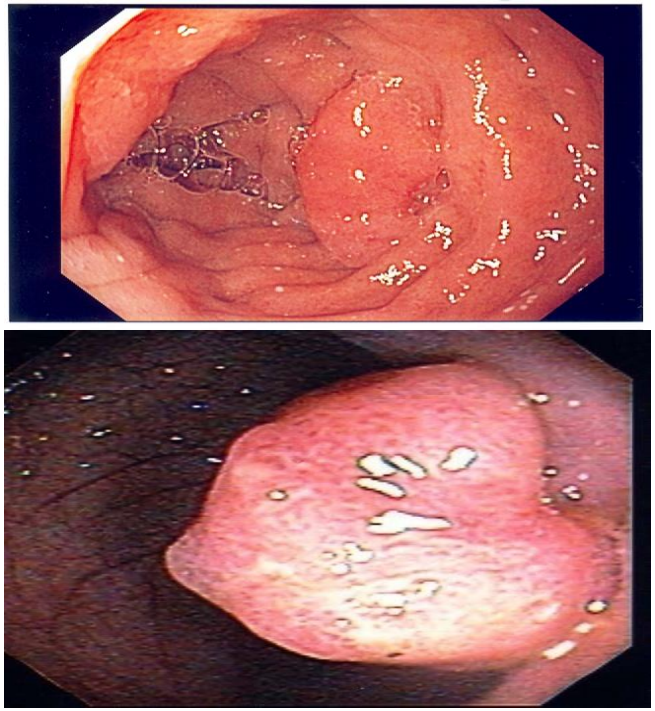
Biallelic mutations in the MMR genes:

PMS2*, *MSH6*, *MLH1*, *MSH2

Novel cancer predisposition syndrome







C Durno et al. Unifying diagnosis for adenomatous polyps, café-au-lait macules, and a brain mass? Gastroenterology 2013;145(5):e3-e4

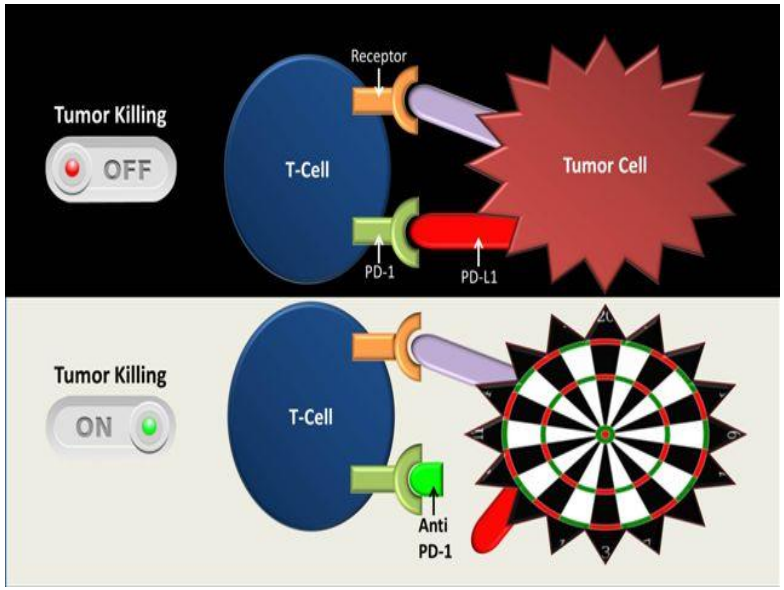
The NEW ENGLAND JOURNAL of MEDICINE

2015;372:2509-2520

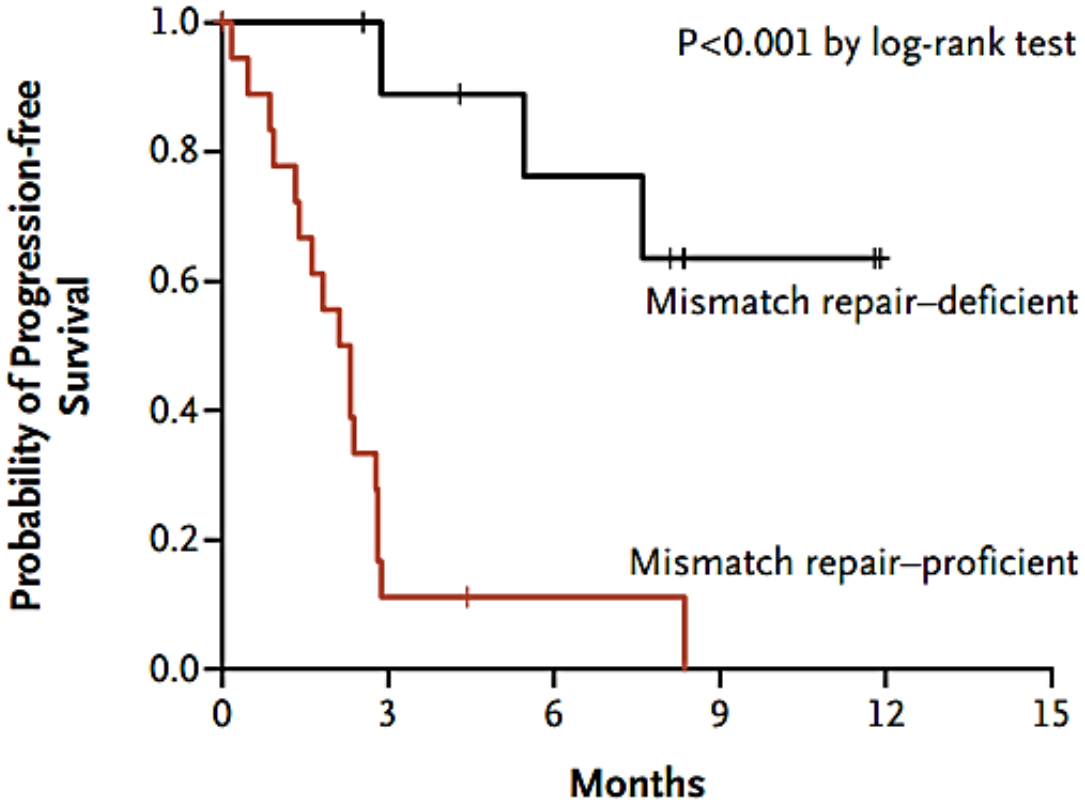
ORIGINAL ARTICLE

PD-1 Blockade in Tumors with Mismatch-Repair Deficiency

D.T. Le, J.N. Uram, H. Wang, B.R. Bartlett, H. Kemberling, A.D. Eyring, A.D. Skora, B.S. Luber, N.S. Azad, D. Laheru, B. Biedrzycki, R.C. Donehower, A. Zaheer, G.A. Fisher, T.S. Crocenzi, J.J. Lee, S.M. Duffy, R.M. Goldberg, A. de la Chapelle, M. Koshiji, F. Bhaijee, T. Huebner, R.H. Hruban, L.D. Wood, N. Cuka, D.M. Pardoll, N. Papadopoulos, K.W. Kinzler, S. Zhou, T.C. Cornish, J.M. Taube, R.A. Anders, J.R. Eshleman, B. Vogelstein, and L.A. Diaz, Jr.



Progression-free survival in cohorts with colorectal cancer



No. at Risk						
Mismatch repair–deficient	11	8	6	2	0	0
Mismatch repair–proficient	21	2	1	0	0	0

Clinical Gastroenterology and Hepatology 2016;14:836–842

Clinical, Endoscopic, and Histologic Characteristics of Ipilimumab-Associated Colitis

Eduard Cornelis Verschuren,[*] Alfonsus Johannes van den Eertwegh,[‡] Janneke Wonders,[*] Rob Michel Slangen,[§] Foke van Delft,[*] Adriaan van Bodegraven,[*,‖] Andra Neefjes-Borst,[¶,b] and Nanne Klaas de Boer[*,b]

Table 1. Patient, Clinical, and Ipilimumab-Colitis-Related Characteristics (N = 27)

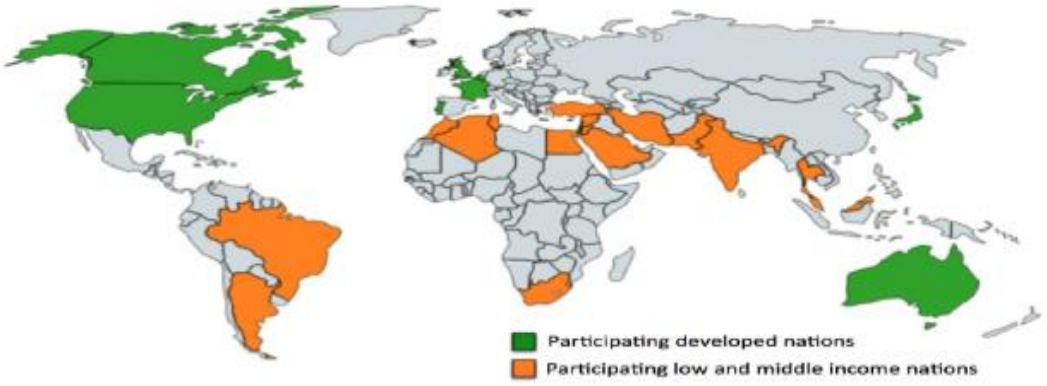
Male sex	21 (78%)
Age, *y* (mean ± standard deviation)	60 ± 12
Prostate cancer	16
Melanoma	11
Days before diarrhea onset (median)	37
Number of ipilimumab doses (median)	3
Dosage ipilimumab, 3 mg/kg	11
Dosage ipilimumab, 10 mg/kg	16
Diarrhea	27 (100%)
Abdominal pain	8 (30%)
Hematochezia	7 (26%)
Nausea/vomitus	6 (22%)
Fever	4 (15%)
Mucus in stool	1 (3%)

Review

Phenotypic and genotypic characterisation of biallelic mismatch repair deficiency (BMMR-D) syndrome

Carol A. Durno [a,b,c,*], Philip M. Sherman [c], Melyssa Aronson [a], David Malkin [d], Cynthia Hawkins [e], Doua Bakry [d], Eric Bouffet [d], Steven Gallinger [a], Aaron Pollett [c], Brittany Campbell [f], Uri Tabori [d], International BMMRD Consortium

Eur J Cancer 2015;51:977-983



Case #2

51 yo Canadian arrives for screening colonoscopy

No family history of colon cancer

Refuses fecal immunochemical testing (too “icky

Who should get the informed consent?

a) Staff person performing the procedure
b) Trainee performing the procedure
c) Trained nurse practitioner
d) Delegated administrative staff
e) Any of the above

Guideline for obtaining valid consent for gastrointestinal endoscopy procedures

Simon M Everett,[1] Helen Griffiths,[2] U Nandasoma,[3] Katie Ayres,[4] Graham Bell,[5] Mike Cohen,[6] Siwan Thomas-Gibson,[7] Mike Thomson,[8] Kevin M T Naylor[9]

Gut 2016;65:1585-1601

Patients should receive information in their own language and given an opportunity to ask questions

Consent should be obtained by the person performing the procedure (but not trainees)

Written information about the procedure should be provided

Consent should be obtained before entering the procedure room

plus 6 more key points . . .

Expert opinions and scientific evidence for colonoscopy key performance indicators

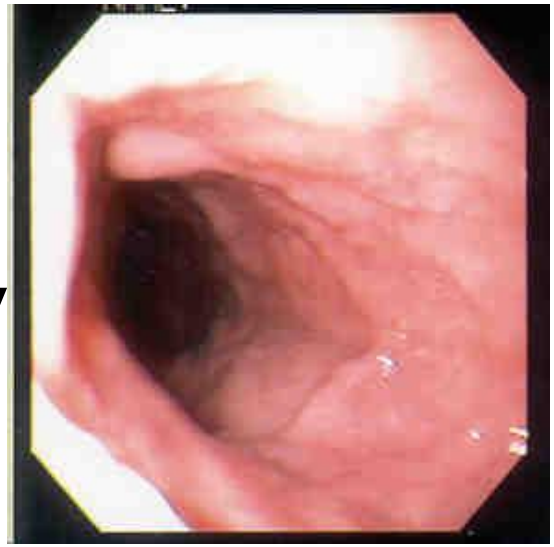
Colin J Rees,[1] Roisin Bevan,[2] Katharina Zimmermann-Fraedrich,[3] Matthew D Rutter,[2] Douglas Rex,[4] Evelien Dekker,[5] Thierry Ponchon,[6] Michael Bretthauer,[7] Jaroslaw Regula,[8] Brian Saunders,[9] Cesare Hassan,[10] Michael J Bourke,[11] Thomas Rösch[3]

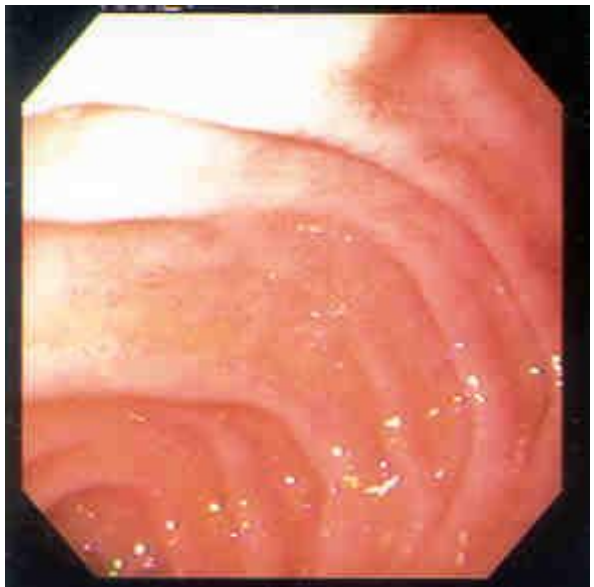
CJ Rees et al. Gut 2016;65:2045-2060

Cecal intubation rate
Adenoma detection rate
Bowel preparation
Rectal retroflexion
Withdrawal times
Sedation practices
Numbers
Polyp removal, retrieval, and histology

Case #3

33 yo F with refractory iron deficiency anemia
No GI symptoms
Family history of IBS
PE: pallor
otherwise negative
Laboratory: Hemoglobin 97 g/L; MCV
Albumin 33 g/L
anti-TTG 1 in 100

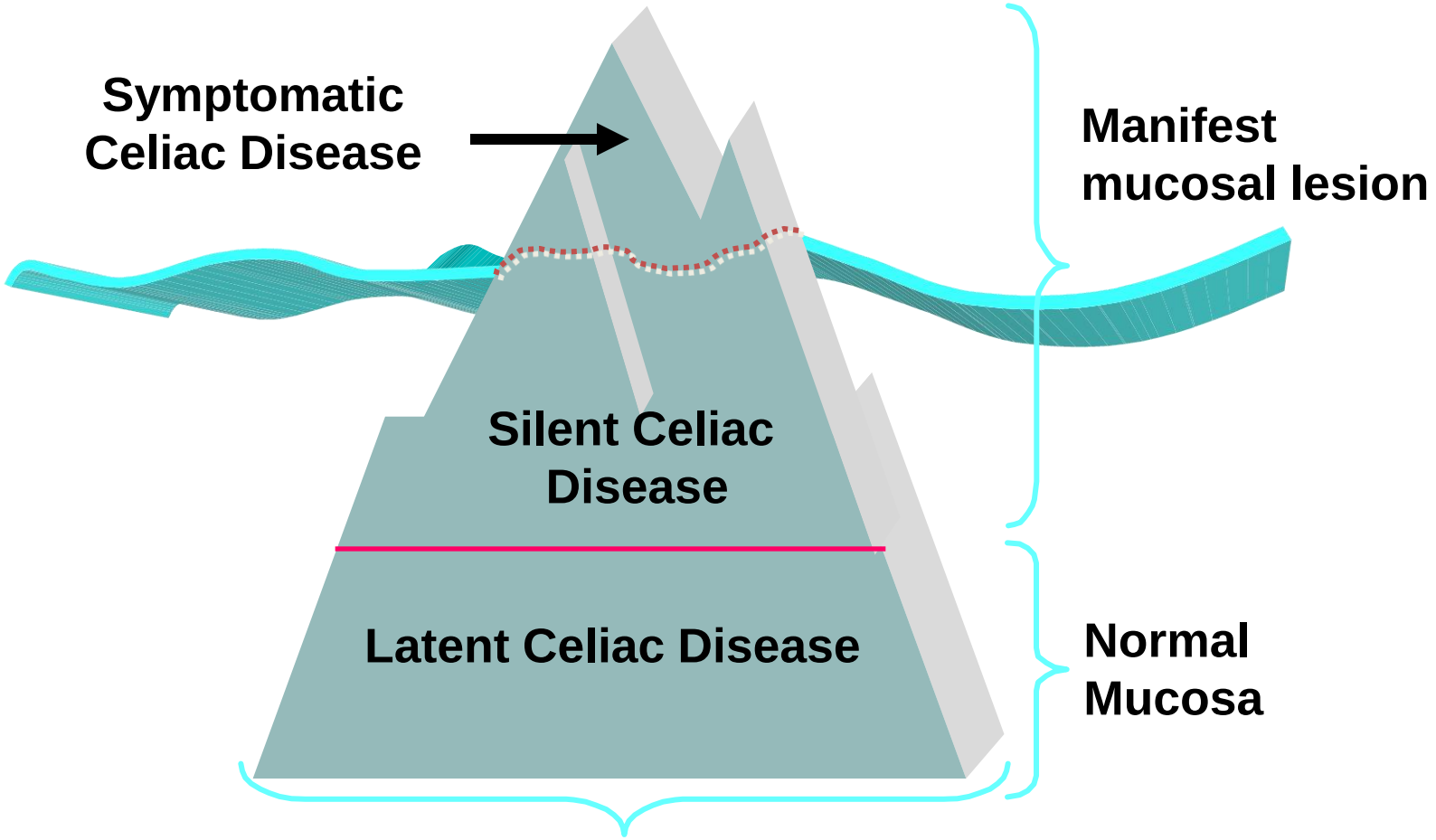




<u>Next steps?</u>:

a) Gluten free diet
b) Microbiome analysis
c) HLA DQ2/DQ8 status
d) EGD and biopsies
e) other

The Celiac Iceberg



Genetic susceptibility: - DQ2, DQ8
Positive serology

What is a normal intestinal mucosa?

M Marsh & K Rostami Gastroenterology 2016;151:744-788

Gastroenterology 2016;150:1125–1134

Clinical and Immunologic Features of Ultra-Short Celiac Disease

Peter D. Mooney,[1,2] Matthew Kurien,[1,2] Kate E. Evans,[1,2] Eleanor Rosario,[2] Simon S. Cross,[2,3] Patricia Vergani,[3] Marios Hadjivassiliou,[2,4] Joseph A. Murray,[5] and David S. Sanders[1,2]

[1]Academic Department of Gastroenterology, [3]Department of Histopathology, [4]Department of Neurology, Royal Hallamshire Hospital, Sheffield, United Kingdom; [2]University of Sheffield, Sheffield, United Kingdom; [5]Mayo Clinic, Rochester, Minnesota

Table 1. A Summary of the Available Studies Into Duodenal Bulb Biopsy Specimens for Diagnosing Celiac Disease

Year/reference	Country	Adults/pediatrics	Patients, N	Celiac disease, n (%)	USCD, n (%)
2001[10]	Austria	Adults	51	21 (41.2)	2 (9.5)
2004[30]	Italy	Pediatrics	95	95 (100)	4 (4.2)
2005[31]	Italy	Adults	1	1 (100)	1 (100)
2008[8]	United Kingdom	Adults	56	56 (100)	1 (1.8)
2008[32]	Italy	Pediatrics	1013	665 (65.6)	16 (2.4)
2009[33]	Canada	Pediatrics	35	29 (81.6)	3 (11.4)
2010[19]	United States	Pediatrics	198	198 (100)	10 (5.1)
2010[34]	Italy	Pediatrics	47	42 (89.4)	5 (11.9)
2010[9]	United States	Adults	80	40 (50)	5 (12.5)
2011[35]	Israel	Pediatrics	87	87 (100)	6 (7.0)
2011[12]	United Kingdom	Adults	376	126 (33.5)	11 (9.0)
2012[11]	United Kingdom	Adults	77	28 (36.4)	5 (17.9)
2013[36]	Australia	Pediatrics	101	101 (100)	8 (7.92)
2014[13]	Italy	Adults	42	25 (59.5)	0 (0)

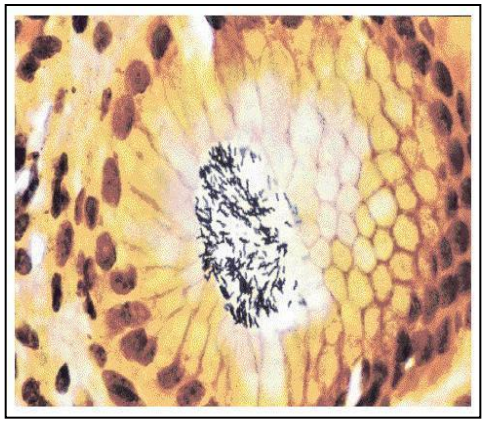
“bulb biopsies finally reaffirmed in celiac disease diagnosis”

Case #4

44 yo M from Lebanon with dyspepsia and anxiety

Family history: + gastric cancer

PEx: negative



Laboratory: positive *H. pylori* serology, positive UBT, positive silver stain:

Prior courses of treatment:, PPI alone, PMC, PAC, and PAC plus probiotics

Referred to you for treatment

A) Sequential therapy

B) Quadruple therapy

C) Triple therapy with tetracycline

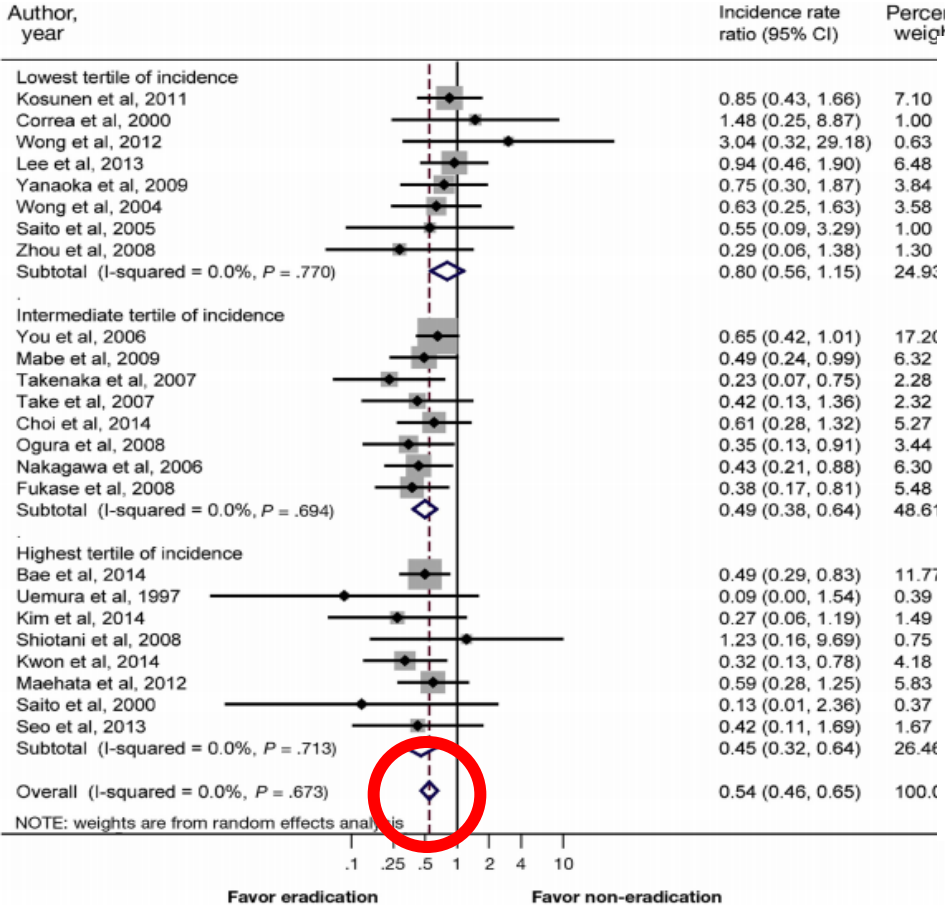
D) Monitor clinical course off treatment

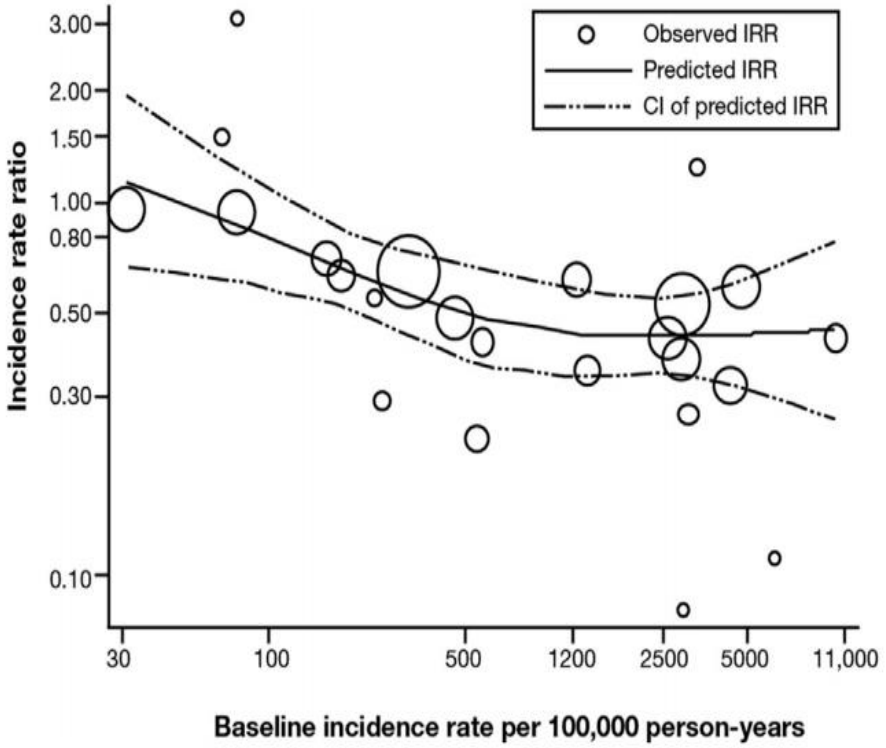
Gastroenterology 2016;150:1113–1124

CLINICAL—ALIMENTARY TRACT

Association Between *Helicobacter pylori* Eradication and Gastric Cancer Incidence: A Systematic Review and Meta-analysis

Yi-Chia Lee,[1,2,*] **Tsung-Hsien Chiang**,[1,3,4,*] Chu-Kuang Chou,[1,5] Yu-Kang Tu,[2] Wei-Chih Liao,[1,2] Ming-Shiang Wu,[1,6] and David Y. Graham[7]





CONSENSUS STATEMENT

Gastroenterology 2016;151:51–69

The Toronto Consensus for the Treatment of *Helicobacter pylori* Infection in Adults

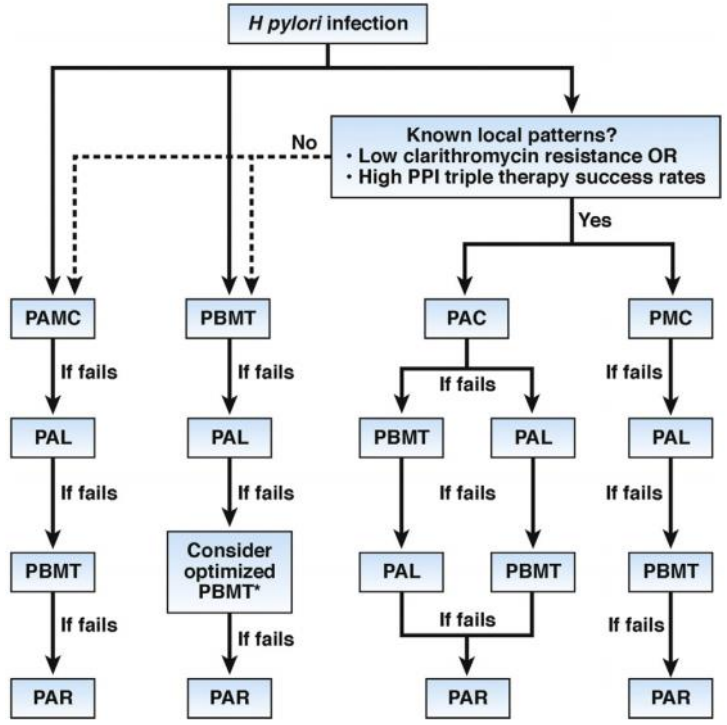
Carlo A. Fallone,[1] Naoki Chiba,[2,3] Sander Veldhuyzen van Zanten,[4] Lori Fischbach,[5] Javier P. Gisbert,[6] Richard H. Hunt,[3,7] Nicola L. Jones,[8] Craig Render,[9] Grigorios I. Leontiadis,[3,7] Paul Moayyedi,[3,7] and John K. Marshall[3,7]

Study or subgroup	Concomitant Events	Total	Sequential Events	Total	Weight	Risk difference M–H, random, 95% CI
5.3.3 10 days						
Ang TL 2015	125	153	130	154	9.4%	-0.03 [-0.11, 0.06]
Apostolopoulos P 2013	29	33	19	30	2.0%	0.25 [0.04, 0.45]
Area RD 2015	121	136	108	139	8.9%	0.11 [0.03, 0.20]
Huang YK 2012	74	84	68	85	6.2%	0.08 [-0.03, 0.19]
Kalapothakos P 2013	88	102	87	102	7.7%	0.01 [-0.09, 0.11]
Kim J 2014	52	65	49	72	3.8%	0.12 [-0.03, 0.26]
Kim SY 2014a	118	125	157	191	12.6%	0.12 [0.05, 0.19]
Kim SY 2014b	57	61	51	60	6.2%	0.08 [-0.03, 0.19]
McNicholl AG 2014a	146	168	138	170	10.4%	0.06 [-0.02, 0.14]
Ntouli V 2014	98	108	87	104	8.5%	0.07 [-0.02, 0.16]
Wu DC 2010	107	115	108	117	12.7%	0.01 [-0.06, 0.07]
Subtotal (95% CI)		1150		1224	88.4%	0.07 [0.03, 0.10]
Total events	1015		1002			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 16.41$; df = 10 ($P = .09$); $I^2 = 39\%$						
Test for overall effect: $Z = 3.53$ ($P = .0004$)						
5.3.4 14 days						
Choi C 2012	32	36	23	27	2.9%	0.04 [-0.13, 0.21]
Lee S 2012	48	58	45	58	3.8%	0.05 [-0.09, 0.20]
Lim JH 2013	63	78	65	86	4.9%	0.05 [-0.07, 0.18]
Subtotal (95% CI)		172		171	11.6%	0.05 [-0.03, 0.13]
Total events	143		133			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.02$; df = 2 ($P = .99$); $I^2 = 0\%$						
Test for overall effect: $Z = 1.14$ ($P = .25$)						
Total (95% CI)		1322		1395	100.0%	0.06 [0.03, 0.09]
Total events	1158		1135			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 16.51$; df = 13 ($P = .22$); $I^2 = 21\%$						
Test for overall effect: $Z = 4.04$ ($P < .0001$)						
Test for subgroup differences: $Chi^2 = 0.13$; df = 1 ($P = .72$); $I^2 = 0\%$						

Risk difference M–H, random, 95% CI

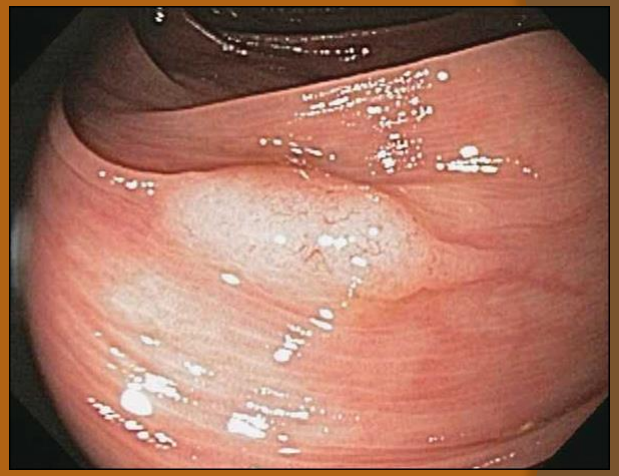
-0.2 -0.1 0 0.1 0.2

Sequential Concomitant



Case #5: Surveillance of Sessile Serrated Adenoma

- 55 y.o male undergoing colonoscopic CRC screening, otherwise asymptomatic



- Found to have a 6mm sessile adenoma in the base of the cecum
  - Histology consistent with a sessile serrated adenoma

Image from Short et al, Am Fam Physician. 2015 Jan 15;91(2):93-100

Case #5: Surveillance of Sessile Serrated Adenoma

- Question 8: When would you perform the next surveillance colonoscopy?
  - A) 1-2 years
  - B) ~ 3 years
  - C) ~ 5 years
  - D) ~ 10 years
- Question 9: What is the risk of finding a metachronous high-risk lesion in the next 5 years
  - A) 5-10%
  - B) 10-15%
  - C) 15-20%
  - D) >20%

Case #5: Surveillance of Sessile Serrated Adenoma

Baseline colonoscopy: most advanced finding(s)	Recommended surveillance interval (*y*)
No polyps	10
Small (<10 mm) hyperplastic polyps in rectum or sigmoid	10
1–2 small (<10 mm) tubular adenomas	5–10
3–10 tubular adenomas	3
>10 adenomas	<3
One or more tubular adenomas ≥10 mm	3
One or more villous adenomas	3
Adenoma with HGD	3
Serrated lesions	
Sessile serrated polyp(s) <10 mm with no dysplasia	5
Sessile serrated polyp(s) ≥10 mm	3
OR	
Sessile serrated polyp with dysplasia	
OR	
Traditional serrated adenoma	
Serrated polyposis syndrome[a]	1

Presence of small sessile serrated polyps increases rate of advanced neoplasia upon surveillance compared with isolated low-risk tubular adenomas

Joshua Melson, MD,[1] Karen Ma, MD,[1] Saba Arshad, MBBS,[1] Michael Greenspan, MD,[1] Thomas Kaminsky, MD,[1] Vinesh Melvani, MD,[1] Faraz Bishehsari, MD,[1] Brett Mahon, MD,[2] Shriram Jakate, MD[2]

Gastrointest Endosc 2016;84:307-14.

- Reviewed 2260 colonoscopies found to have SSAs and/or traditional adenomas
  - 788 with subsequent surveillance colonoscopy (mean interval: ~ 4 years)
- Assessed rates of subsquent advanced adenoma and SSPs
  - SSAs alone
  - Low-risk TA alone
  - High risk TAs alone
  - SSAs in combination with TAs

Presence of small sessile serrated polyps increases rate of advanced neoplasia upon surveillance compared with isolated low-risk tubular adenomas

Joshua Melson, MD,[1] Karen Ma, MD,[1] Saba Arshad, MBBS,[1] Michael Greenspan, MD,[1] Thomas Kaminsky, MD,[1] Vinesh Melvani, MD,[1] Faraz Bishehsari, MD,[1] Brett Mahon, MD,[2] Shriram Jakate, MD[2]

Gastrointest Endosc 2016;84:307-14.

	Rate of Subsequent Advanced Adenoma	Rate of Subsequent SSA
LRA + SSP	12/66 (18.2%)	22/66 (33/3%)
LRA, No SSP	29/370 (7.8%)	16/370 (4.3%)
Low risk SSP alone	10/56 (17.9%)	n/a
HRA no SSP	40/252 (15.9%)	15/252 (6.0%)

- "low risk" SSP alone
  - Significantly higher rate of metachronous advanced adenoma than for non-SSP low-risk adenoma (p=0.019)
  - Similar risk to
    - non-SSA high-risk adenomas
    - Low-risk traditional adenomas with low risk SSAs

Case #5: Surveillance of Sessile Serrated Adenoma

- Question 8: When would you perform the next surveillance colonoscopy?
  - A) 1-2 years
  - B) ~ 3 years
  - C) ~ 5 years
  - D) ~ 10 years
- Question 9: What is the risk of finding a metachronous high-risk lesion in the next 5 years
  - A) 5-10%
  - B) 10-15%
  - C) 15-20%
  - D) >20%

Case #6: Prevention of Post-ERCP Pancreatitis

- 63 y.o female presented with elevated bilirubin, severe RUQ pain
- Abdominal u/s shows
  - CBD dilated to 1.7cm
  - Cholelithiasis
- Otherwise healthy, no prior history of GI or biliary disease
- An ERCP is booked

Case #6: Prevention of Post-ERCP Pancreatitis

- Which is the following would you recommend?

A) Rectal indomethacin following ERCP if high-risk patient-related or procedural risk factors

B) Rectal indomethacin prior to ERCP if patient-related risk factors, PLUS following ERCP if procedure related risk factors

C) Rectal indomethacin prior to ERCP in all persons, regardless of risk factors

Case #6: Prevention of Post-ERCP Pancreatitis

- Post ERCP pancreatitis occurs following 5-10% of ERCPs

- Risk Factors include
  - Patient related
    - History of ERCP pancreatitis
    - Multiple episodes of pancreatitis
    - Young females
  - Procedural related
    - Multiple injection of pancreatic ducts
    - Acinarization
    - Pancreatic sphincterotomy
    - Precut sphincterotomy

A Randomized Trial of Rectal Indomethacin to Prevent Post-ERCP Pancreatitis

B. Joseph Elmunzer, M.D., James M. Scheiman, M.D., Glen A. Lehman, M.D., Amitabh Chak, M.D., Patrick Mosler, M.D., Ph.D., Peter D.R. Higgins, M.D., Ph.D., Rodney A. Hayward, M.D., Joseph Romagnuolo, M.D., Grace H. Elta, M.D., Stuart Sherman, M.D., Akbar K. Waljee, M.D., Aparna Repaka, M.D., Matthew R. Atkinson, M.D., Gregory A. Cote, M.D., Richard S. Kwon, M.D., Lee McHenry, M.D., Cyrus R. Piraka, M.D., Erik J. Wamsteker, M.D., James L. Watkins, M.D., Sheryl J. Korsnes, M.A., Suzette E. Schmidt, B.S.N., C.C.R.P., Sarah M. Turner, B.S., Sylvia Nicholson, C.C.R.C., and Evan L. Fogel, M.D., for the U.S. Cooperative for Outcomes Research in Endoscopy (USCORE)

- Post-procedural rectal indomethacin in high risk patients
- Significant reduction in rates of:
  - Any post ERCP pancreatitis (9.2% vs 16.9%, p=0.005
  - Severe post-ERCP pancreatitis (4.4% vs. 8.8%, p=0.03)

Case #6: Prevention of Post-ERCP Pancreatitis

- Benefits of universal pre-procedural NSAIDs
  - Don’t always know who will have procedural risk factors before hand
  - May have benefits in low-risk patients as well
- Drawbacks
  - Increased costs
  - Risks of gastrointestinal bleeding, renal failure

Routine pre-procedural rectal indometacin versus selective post-procedural rectal indometacin to prevent pancreatitis in patients undergoing endoscopic retrograde cholangiopancreatography: a multicentre, single-blinded, randomised controlled trial

Lancet 2016; 387: 2293-301

Hui Luo, Lina Zhao*, Joseph Leung*, Rongchun Zhang, Zhiguo Liu, Xiangping Wang, Biaoluo Wang, Zhanguo Nie, Ting Lei, Xun Li, Wence Zhou, Lingen Zhang, Qi Wang, Ming Li, Yi Zhou, Qian Liu, Hao Sun, Zheng Wang, Shuhui Liang, Xiaoyang Guo, Qin Tao, Kaichun Wu, Yanglin Pan, Xuegang Guo, Daiming Fan*

- Physician blinded RCT comparing
  - Universal pre-procedure rectal indomethacin
  - Selected post-procedure rectal indomethacin in high risk patients
    - 2600 subjects
    - No prior Hx of ERCP pancreatitis
    - ~80% performed for evaluation of CBD stones
- Evaluated rates of post-ERCP pancreatitis and complications

	Pre-procedural indometacin in all patients (n=1297)	Post-procedural indometacin in high-risk patients* (n=1303)	Relative risk (95% CI)	p value
Post-ERCP pancreatitis	47 (4%)	100 (8%)	0·47 (0·34–0·66)	<0·0001
Mild	36 (3%)	77 (6%)	0·47 (0·32–0·69)	<0·0001
Moderate to severe	11 (1%)	23 (2%)	0·48 (0·24–0·98)	0·040
Post-ERCP pancreatitis in high-risk patients*	18/305 (6%)	35/281 (12%)	0·47 (0·27–0·82)	0·0057
Mild	14 (5%)	29 (10%)	0·45 (0·24–0·82)	0·0079
Moderate to severe	4 (1%)	6 (2%)	0·61 (0·18–2·15)	0·44
Post-ERCP pancreatitis in average-risk patients	29/992 (3%)	65/1022 (6%)	0·46 (0·30–0·71)	0·0003
Mild	22 (2%)	48 (4%)	0·47 (0·29–0·78)	0·0024
Moderate to severe	7 (1%)	17 (2%)	0·42 (0·18–1·02)	0·048
Gastrointestinal bleeding	13 (1%)	10 (1%)	1·31 (0·57–2·97)	0·52
Mild	5 (<1%)	4 (<1%)	1·26 (0·34–4·67)	0·75
Moderate	6 (<1%)	5 (<1%)	1·21 (0·37–3·94)	0·78
Severe	2 (<1%)	1 (<1%)	2·01 (0·18–22·13)	0·62
Biliary infection	22 (2%)	33 (3%)	0·67 (0·39–1·14)	0·14
Mild	15 (1%)	24 (2%)	0·63 (0·33–1·19)	0·15
Moderate	7 (1%)	9 (1%)	0·78 (0·29–2·09)	0·62
Severe	0	0	..	..
Perforation	1 (<1%)	0	..	..
Other adverse events	5 (<1%)	5 (<1%)	..	..
Pulmonary infection	2 (<1%)	5 (<1%)	0·40 (0·08–2·07)	0·45
Incomplete bowel obstruction	3 (<1%)	0	..	..
Length of post-ERCP hospital stay (days)	2 (1–4)	3 (1–4)	..	0·17

Case #6: Prevention of Post-ERCP Pancreatitis

- Which is the following would you recommend?

A) Rectal indomethacin following ERCP if high-risk patient-related or procedural risk factors

B) Rectal indomethacin prior to ERCP if patient-related risk factors, PLUS following ERCP if procedure related risk factors

C) Rectal indomethacin prior to ERCP in all persons, regardless of risk factors

Case #7: Management of LGD in Barrett's Esophagus

- 72 y.o male with HTN, DM2, History of GERD
- 5 years ago, EGD showed nondysplastic BE, 3cm circumferential, 5cm maximal length. On chronic PPI
- f/u EGD this year
  - No visible lesions
  - 4 quadrant biopsies every 2cm
- Histology reveals
  - 1 biopsy with LGD, confirmed with second expert pathologist

Case #7: Management of LGD in Barrett's Esophagus

- Question 11: If a confirmation endoscopy with 4 quadrant biopsies is performed , what is the likelihood of **not** finding LGD again

  A) ~10%

  B) ~25%

  C) ~ 35%

  D) ~ 50%

- Question 12: If LGD is found again on a repeat EGD, what is the estimated annual rate of pregression to HGD or EAC

  A) 1% per year

  B) 3% per year

  C) 5% per year

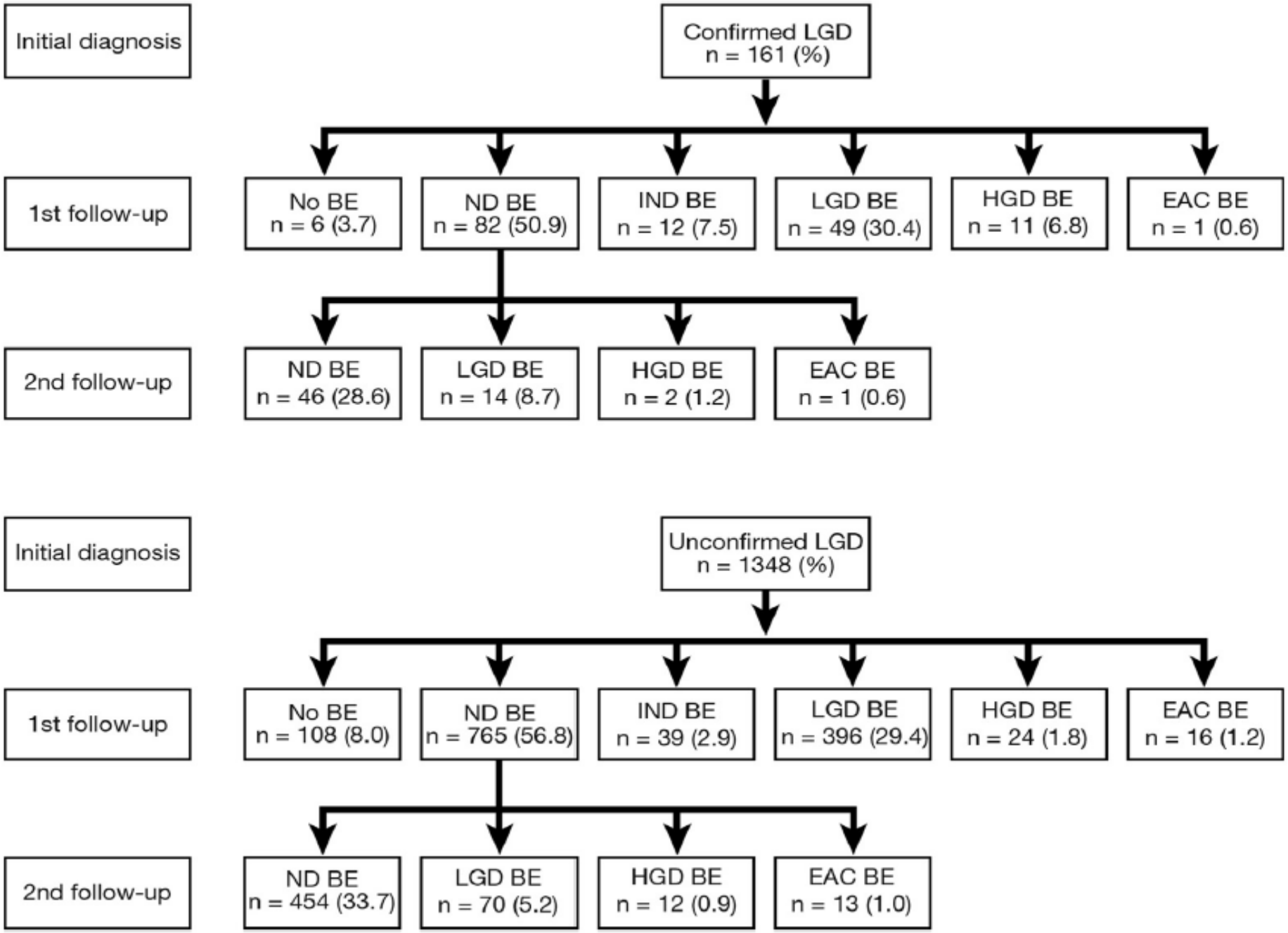
  D) 8% per year

Patients With Barrett's Esophagus and Persistent Low-grade Dysplasia Have an Increased Risk for High-grade Dysplasia and Cancer

Christine Kestens,* G. Johan A. Offerhaus,‡ Jantine W. P. M. van Baal,* and Peter D. Siersema*

Clinical Gastroenterology and Hepatology 2016;14:956–962

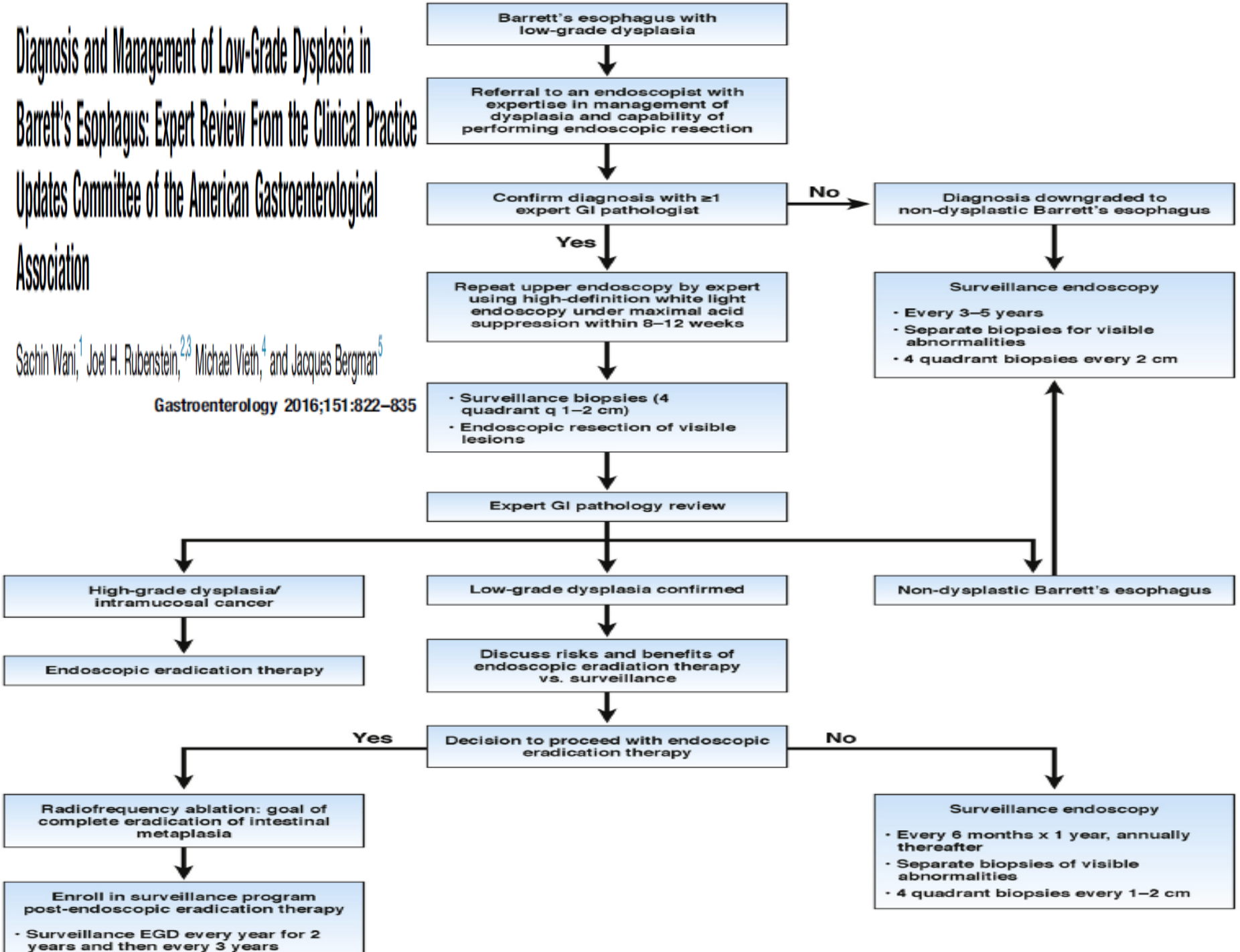
- Review of 1579 cases in a Dutch databse demonstrating LGD
  - Confirmed with second pathologist in 161 cases


Initial diagnosis
Confirmed LGD
n = 161 (%)
1st follow-up
No BE
n = 6 (3.7)
ND BE
n = 82 (50.9)
IND BE
n = 12 (7.5)
LGD BE
n = 49 (30.4)
HGD BE
n = 11 (6.8)
EAC BE
n = 1 (0.6)
2nd follow-up
ND BE
n = 46 (28.6)
LGD BE
n = 14 (8.7)
HGD BE
n = 2 (1.2)
EAC BE
n = 1 (0.6)
Initial diagnosis
Unconfirmed LGD
n = 1348 (%)
1st follow-up
No BE
n = 108 (8.0)
ND BE
n = 765 (56.8)
IND BE
n = 39 (2.9)
LGD BE
n = 396 (29.4)
HGD BE
n = 24 (1.8)
EAC BE
n = 16 (1.2)
2nd follow-up
ND BE
n = 454 (33.7)
LGD BE
n = 70 (5.2)
HGD BE
n = 12 (0.9)
EAC BE
n = 13 (1.0)

Diagnosis and Management of Low-Grade Dysplasia in Barrett's Esophagus: Expert Review From the Clinical Practice Updates Committee of the American Gastroenterological Association

Sachin Wani,[1] Joel H. Rubenstein,[2,3] Michael Vieth,[4] and Jacques Bergman[5]

Gastroenterology 2016;151:822–835



Case #7: Management of LGD in Barrett's Esophagus

- Question 11: If a confirmation endoscopy with 4 quadrant biopsies is performed , what is the likelihood of **not** finding LGD again

  A) ~10%

  B) ~25%

  C) ~ 35%

  D) ~ 50%

- Question 12: If LGD is found again on a repeat EGD, what is the estimated annual rate of pregression to HGD or EAC

  A) 1% per year

  B) 3% per year

  C) 5% per year

  D) 8% per year

Case #8: Low FODMAP diets for IBS

- 22 y.o female, new consultation for IBS-D
  - Diagnosed by Fam MD
  - Has tried increasing fibre intake and curtailing caffeine with inconsistent effects
- Has heard through friends about low FODMAP diet

Case #8: Low FODMAP diets for IBS

- Question 13:
  - Which of the following statement about the use of a low FODMAP diet is not supported by RCT evidence

A) A diet low in FODMAPs is superior to conventional dietary advice in leading to overall reduction in IBD symptoms

B) A low FODMAP diet decreased abdominal pain more than conventional dietary advice

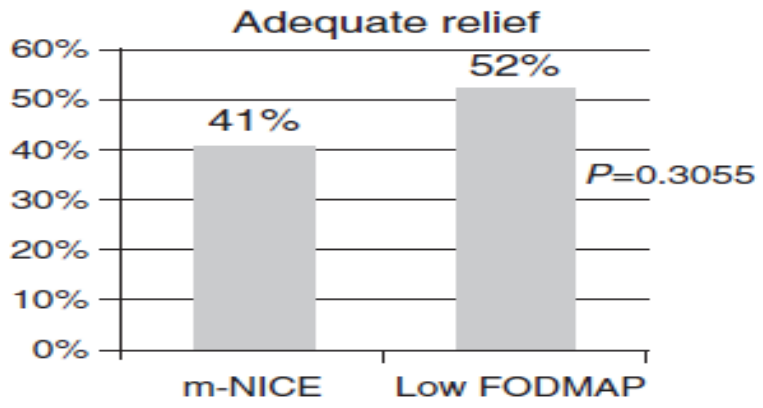
C) A low FODMAP diet decreased bloating more than conventional dietary advice

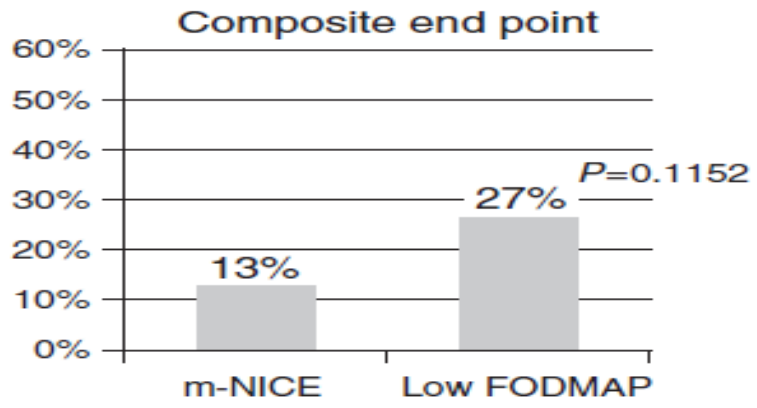
A Randomized Controlled Trial Comparing the Low FODMAP Diet vs. Modified NICE Guidelines in US Adults with IBS-D

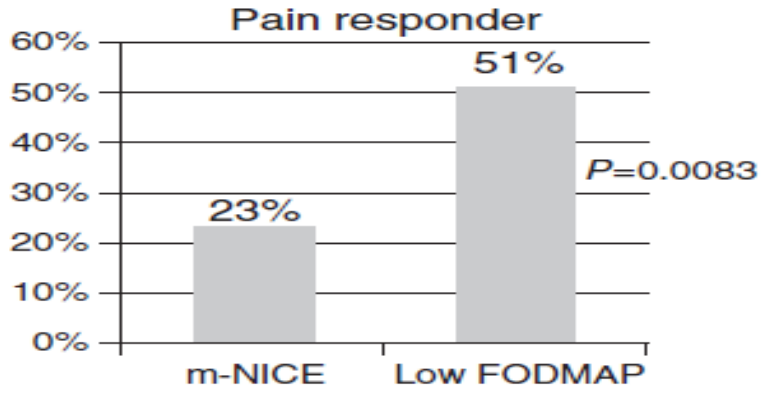
Am J Gastroenterol 2016; 111:1824–1832;

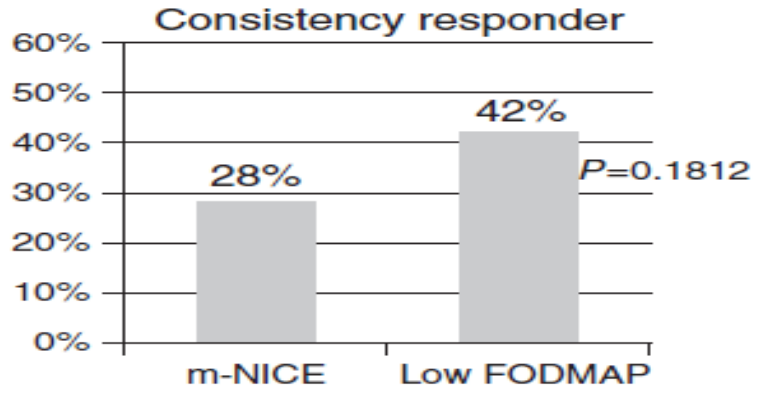
- 92 people in RCT
  - 50 randomized to low FODMAP diet
  - 42 to standard IBS diet, modified as not to advice reduction in FODMAPs
  - 4 week trial
- Primary endpoint
  - Subjective Adequate Relief of IBS symptoms in final 2 weeks os study
  - Also looked at individual rating scores for bloating, abdominal pain, consistency

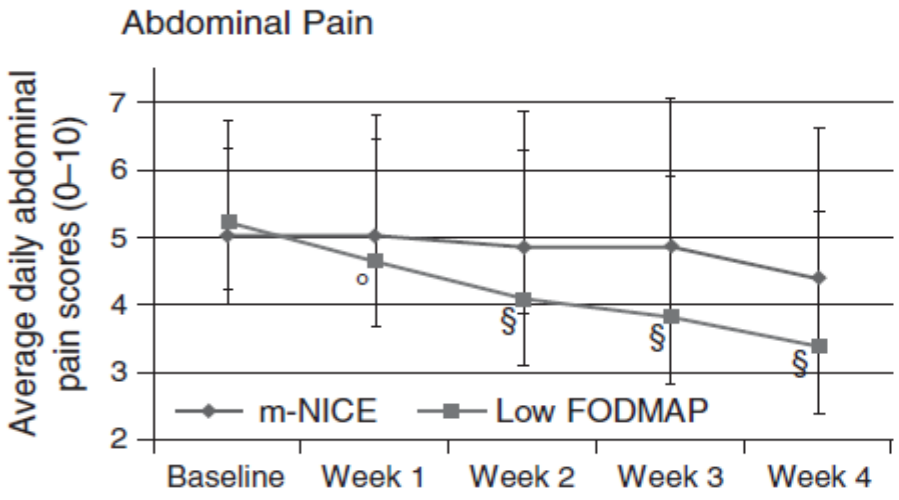
A Randomized Controlled Trial Comparing the Low FODMAP Diet vs. Modified NICE Guidelines in US Adults with IBS-D

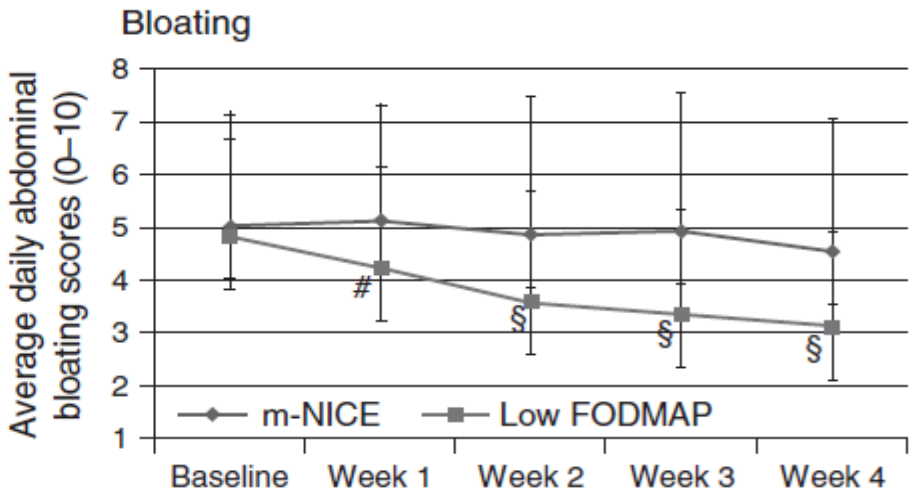


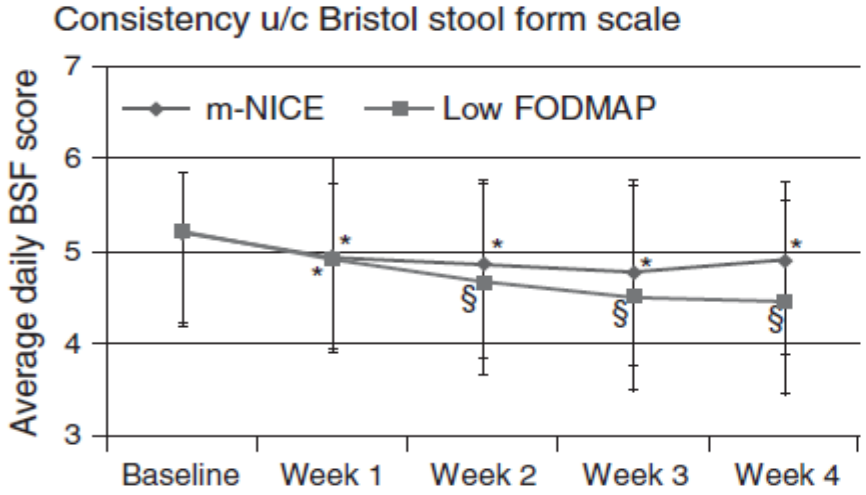


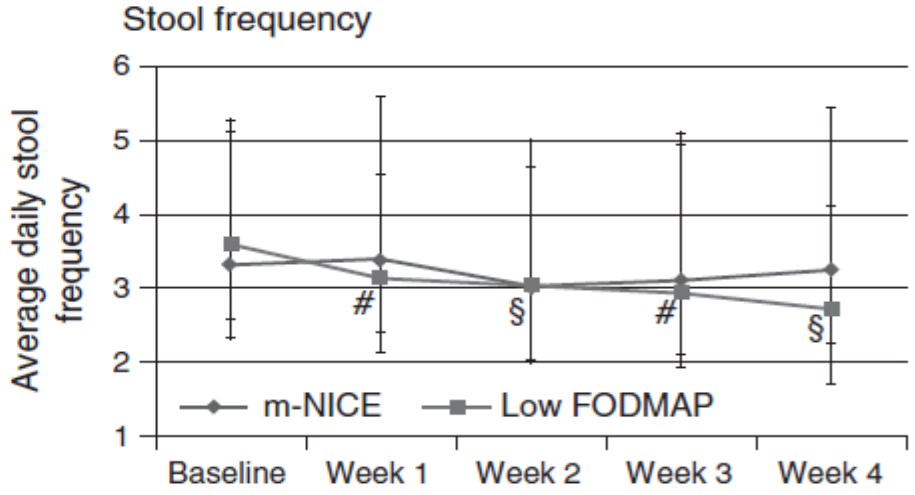


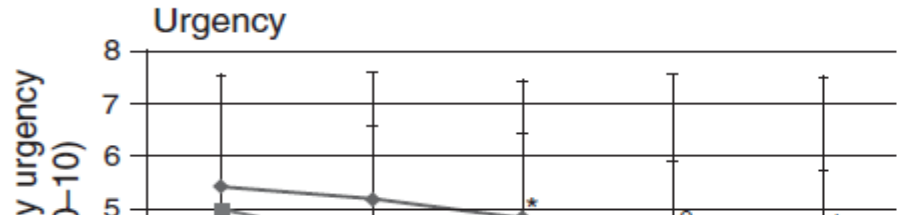












* = $P \leq 0.05$
° = $P \leq 0.01$
\# = $P \leq 0.001$

Diet Low in FODMAPs Reduces Symptoms of Irritable Bowel Syndrome as Well as Traditional Dietary Advice: A Randomized Controlled Trial

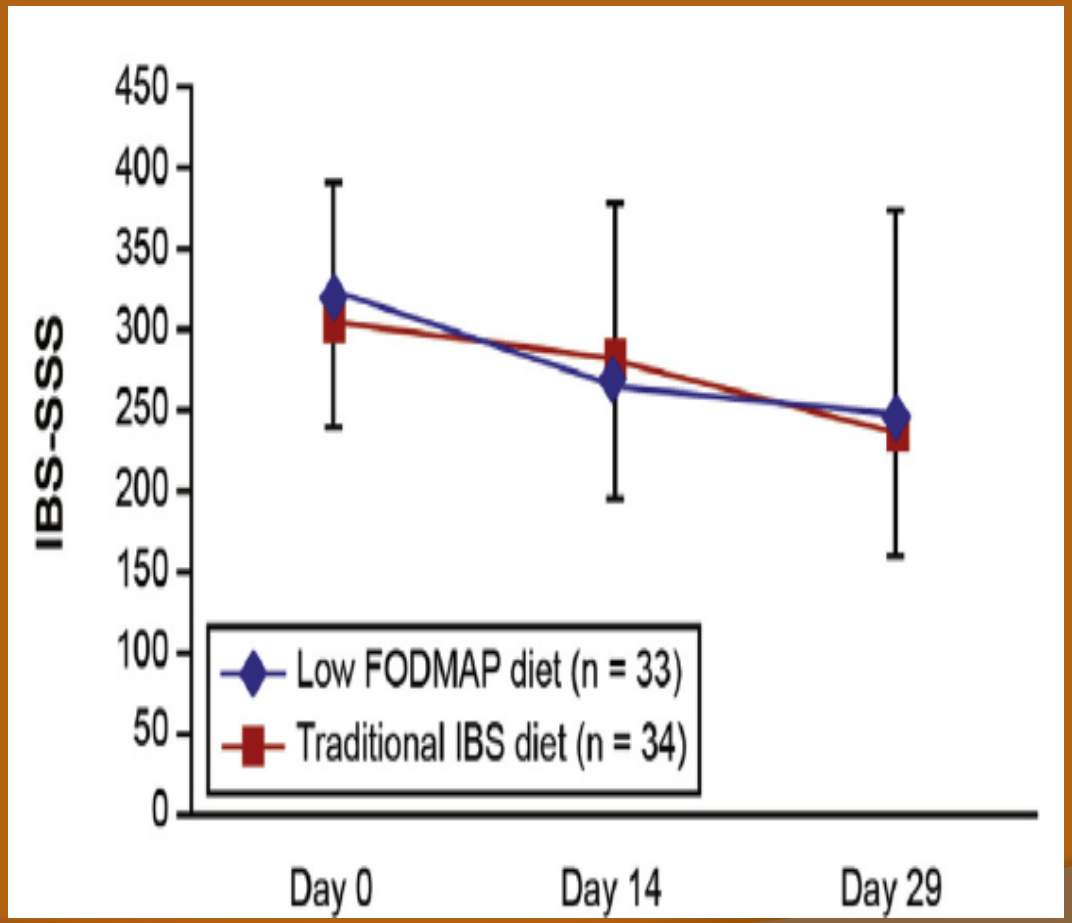
Lena Böhn,[1,2] Stine Störsrud,[1,2] Therese Liljebo,[3] Lena Collin,[4] Perjohan Lindfors,[4,5] Hans Törnblom,[1,2] and Magnus Simrén[1,2]

Gastroenterology 2015;149:1399–1407

- RCT comparing
  - Low FODMAP diet (n=38) vs non-modified IBS diet
  - 4 week trial
- Main outcome
  - Reduction in IBS Symptom Score by 50 points

Diet Low in FODMAPs Reduces Symptoms of Irritable Bowel Syndrome as Well as Traditional Dietary Advice: A Randomized Controlled Trial

Lena Böhn,[1,2] Stine Störsrud,[1,2] Therese Liljebo,[3] Lena Collin,[4] Perjohan Lindfors,[4,5] Hans Törnblom,[1,2] and Magnus Simrén[1,2]



- FODMAP intake among responder to the low FODMAP diet was 40% lower than in non-responders

Case #8: Low FODMAP diets for IBS

- Question 13:
  - Which of the following statement about the use of a low FODMAP diet is not supported by RCT evidence

A) A diet low in FODMAPs is superior to conventional dietary advice in leading to overall reduction in IBD symptoms

B) A low FODMAP diet decreased abdominal pain more than conventional dietary advice

C) A low FODMAP diet decreased bloating more than conventional dietary advice

Case #5

- 46 yo M with third visit to the ED for food impaction; self resolved twice before
- Family history of esophageal dilations
- Endoscopic disimpaction reveals white plaques, linear furrowing, feline esophagus

Should PPI be the initial Rx?

A) yes

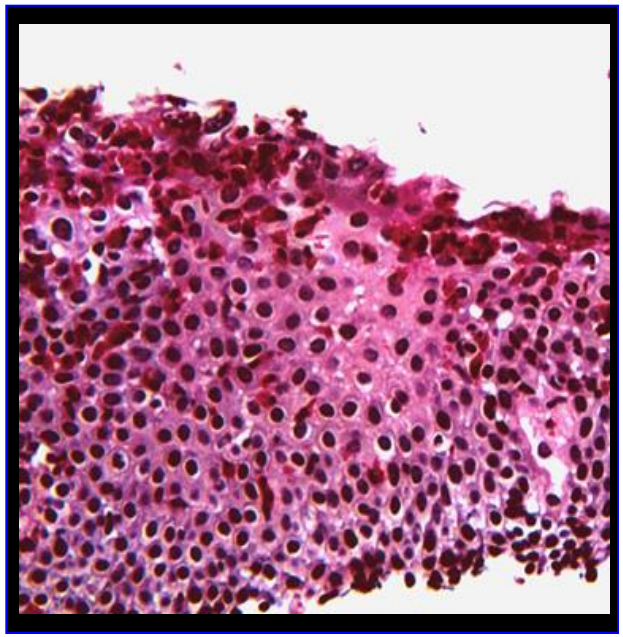
B) no – fluticasone swallowed

C) no – oral corticosteroids

D) no – elemental diet

PPIs decrease large numbers of eosinophils

- 51 subjects (>40 eos) treated with high dose PPI for 8 weeks and endoscopy performed
- 69% experienced clinico-pathological response
- Less likely if food impaction or eosinophil > 70 eos/HFP



E Gomez-Torrijos et al. APT 2016;43:745-6

PPIs have other mechanisms of action

- Abolish acid production
- Decrease eosinophil chemo-attractants and resolve esophageal eosinophilia
  - Ishimura et al AJG 2016
  - Cheng et al PLoS One 2015
- Treat Eosinophilic Esophagitis?

Should he receive PPI as treatment?

- **Yes…..**
  - **To fulfill diagnostic criteria and rule out GERD/PPIREE**
  - **It may be a treatment for esophageal eosinophilia**

EURORDIS
Rare Diseases Europe

Mar 22, 2016 **…** ”Proton-pump inhibitor-responsive esophageal eosinophilia: an entity challenging current diagnostic criteria for **eosinophilic esophagitis”**

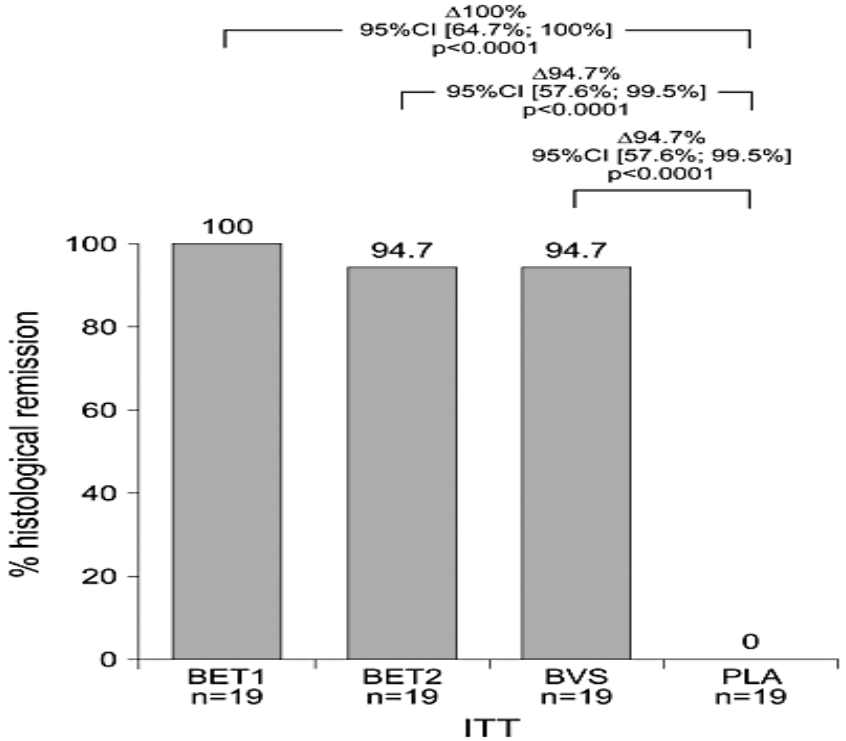
J Molina-Infante et al. Gut 2016; Sept.13:doi:10.1136
C Guitierrez-Junquera et al. JPGN 2016;62:704-710

OPEN ACCESS

ORIGINAL ARTICLE

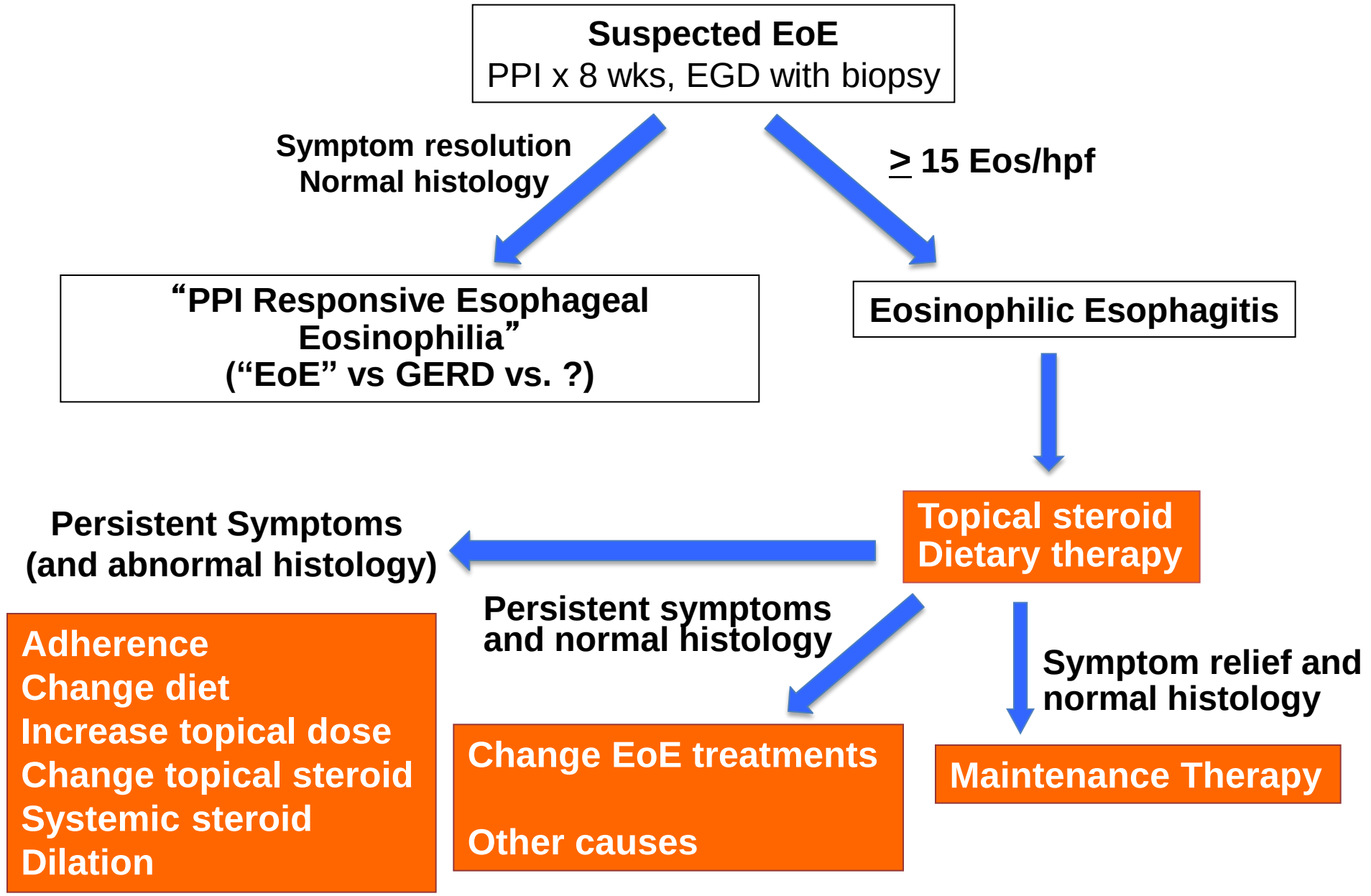
A randomised, double-blind trial comparing budesonide formulations and dosages for short-term treatment of eosinophilic oesophagitis

Stephan Miehlke,[1] Petr Hruz,[2] Michael Vieth,[3] Christian Bussmann,[4] Ulrike von Arnim,[5] Monther Bajbouj,[6] Christoph Schlag,[6] Ahmed Madisch,[7] Christiane Fibbe,[8] Henning Wittenburg,[9] Hans Dieter Allescher,[10] Max Reinshagen,[11] Stefan Schubert,[12] Jan Tack,[13] Michaela Müller,[14] Patrick Krummenerl,[15] Joris Arts,[16] Ralph Mueller,[17] Karin Dilger,[17] Roland Greinwald,[17] Alex Straumann[18]



Gut 2016;65:390-399

Management of Eosinophilic Esophagitis in 2017



Case #6: Global health in Canada

Parents of three healthy pre-schoolers who attend daycare both develop 3 days of non-bloody watery diarrhea a/w fever, but no vomiting. You advise ORT, but parents ask about alternatives . . .

a) Ondansetron
b) Probiotics
c) Racecadotril
d) Lactose restriction
e) Loperamide

Parents don't have alternative care plans. How can one reduce the risk of acute enteric infections?

a) Hand washing
b) Smectite
c) Oral antibiotics
d) Prebiotics
e) Rotavirus vaccination

REHYDRATION

Mild

Moderate

ORS

COMPOSITION	Hypotonic-osmolarity ESPGHAN
Sodium (mmol/L)	60
Potassium (mmol/L)	20
Chloride (mmol/L)	60
Base (mmol/L)	10 (citrate)
Glucose (mmol/L)	74-111
Osmolarity (mOsm/L)	225-260

Families should be encouraged to have a supply of oral rehydration solution (ORS) at home

Level of evidence supporting recommendations

Recommendation	Australia NSW Ministry of Health 2014	ESPGHAN 2014	Latin America 2014	Kenya 2013	WGO 2012	Botswana 2012	South Africa 2012	CCHMC 2011	Malaysia 2011	Canada: Leung 2006 + Cheng 2011	NICE 2009	China 2009	Australia Harris 2008	India 2007	WHO 2005
Dehydration signs	–	+	+	+	–	–	+	+	+	–	+	–	+++	–	+
Severity Score	NR	+	NR	NR	NR	–	NR	NR	NR	–	NR	–	+/–	NR	NR
Breast-feeding	–	+	NR	NR	–	–	+	NR	+	+++	+	–	+++	NR	++
Modified formula	–	+	NR	NR	–	–	NR	+	+	–	+	–	+/–	NR	NR
Early refeeding	–	+	+	NR	–	–	+	+	+	+++	+	–	+	NR	+
Restrictive diet	–	+	+	NR	–	–	+	+	+	–	+	–	+	NR	+
Sport drinks	–	+	+	NR	–	–	+	+	+	–	+	–	+	NR	NR
ORS	–	++	++	++	–	–	+	++	++	+++	++	–	+++	++	++
NGT rehydration	–	++	+	+/–	–	–	NR	++	NR	–	++	–	+/–	NR	+
IV rehydration	–	+	+	+/–	–	–	+	++	+	–	++	–	+/–	NR	+
Antiemetics	–	+	++	+	–	–	++	++	+	+++	++	–	+++	NR	++
Loperamide	–	+/–	+	+	–	–	+	+/–	+/–	NR	+/–	–	+++	NR	+
Smectite	–	++	++	+	–	–	+	NR	++	NR	NR	–	+/–	NR	+
Racecadotril	–	++	+++	+	–	–	+	NR	++	NR	NR	–	+/–	+/–	+
Zinc	–	++	+++	+	–	–	+	NR	++	+++	–	–	NR	+	+
Probiotics	–	++	+++	+	–	–	+	++	+	NR	++	–	+++	NR	NR
Antibiotics	–	+	NR	+	–	–	+	++	+	NR	++	–	NR	NR	+

Strong evidence classified as "High level" in GRADE system and "I" in Muir–Gray & Cook. Data coming from metanalysis and more than 1 RCT

Moderate evidence classified as "Moderate level" in GRADE system and "II" in Muir –Gray & Cook. Data coming from RCT

Low evidence classified as "Low level" in GRADE system and "III" in Muir –Gray & Cook. Data coming from cohort and observational studies

Poor evidence classified as "Very low level" in GRADE system and "IV or V" in Muir–Gray & cook. Data coming from case series, case report and expert opinion

No reference supporting the guidelines' recommendations or level of evidence not reported

Recommendation not reported in the guidelines

A Lo Vecchio et al. JPGN 2016;63:226-235

Emerging therapies for acute diarrhea

Racecadotril (acetorphan):

- **Thiorphan is the active metabolite**
- **Encephalinase inhibitor**
- **Acts as an anti-secretory agent**
- **Licensed in many countries, but not USA**
- **3 RCT's of 1.5 mg/kg po tid**

  642 subjects, 540 >1 mo & <6 yr age

  diarrhea -53.5 hr (95% CI: -65.6, -41.3)

M Gordon & A Akobeng. Arch Dis Childh 2016;101:234-240

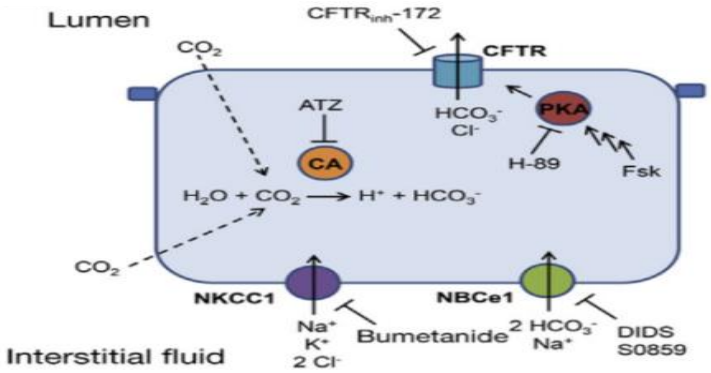
M Piescik-Lech et al. APT 2013;37:289-303

Other novel therapies for acute diarrhea

Serotonin-3 receptor antagonists (in IBS-D)

ramosetron S Fukudo et al. Gastroenterology 2016;150:358-66

Na+/HCO3- co-transporter target (in enteroids)



J Foulke-Abel et al.
Gastroenteroogyl 2016;150:638-49

Smectite (diosmectite): absorbent clay

Relative effectiveness analysis of ORT adjuncts

Systematic review and network meta-analysis underway . . .

ID Florez et al. Systematic Reviews 2016;5:14

RCT of hand-washing with soap and chlorine treatment of water

Dhaka, Bangladesh

47% reduction in *Vibrio cholerae* infections!

C George et al. Emerg Infect Dis 2016;22:233-241

Rotavirus vaccine impacts health:

Table 5. Estimated Reductions in the Number and Cost of Diarrhea-Associated Hospitalizations among Children under 5 Years of Age, after the Introduction of Rotavirus Vaccine.

Variable*	Number and Cost			Reduction		
	2001–2006	2007–2008	2008–2009	2007–2008	2008–2009	2007–2009
No. of hospitalizations	110,688	73,778	82,703	36,890	27,965	64,855
Cost of hospitalizations ($)	473,770,195	315,842,541	354,051,300	157,927,653	119,718,894	277,646,547

USA: JE Cortes et al. NEJM 2011;365:1108-117

Global: LM Lamberti et al. Pediatr Infect Dis J, 2016;35:992-998

Case #7

35 yo F with jaundice and pruritus

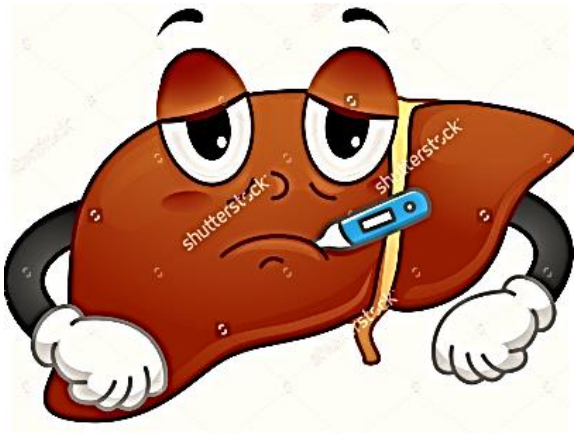
PEx: hepatomegaly

- no stigmata of chronic liver disease

Laboratory:

- increased LET's
- elevated conjugated bilirubin
- normal LFT's

No response to empiric trial of UDCA



<u>Next steps?</u>:

A) IgG4 level

B) Colonoscopy

C) MRCP

D) Liver biopsy

Any new therapies to consider . . .

The NEW ENGLAND JOURNAL of MEDICINE

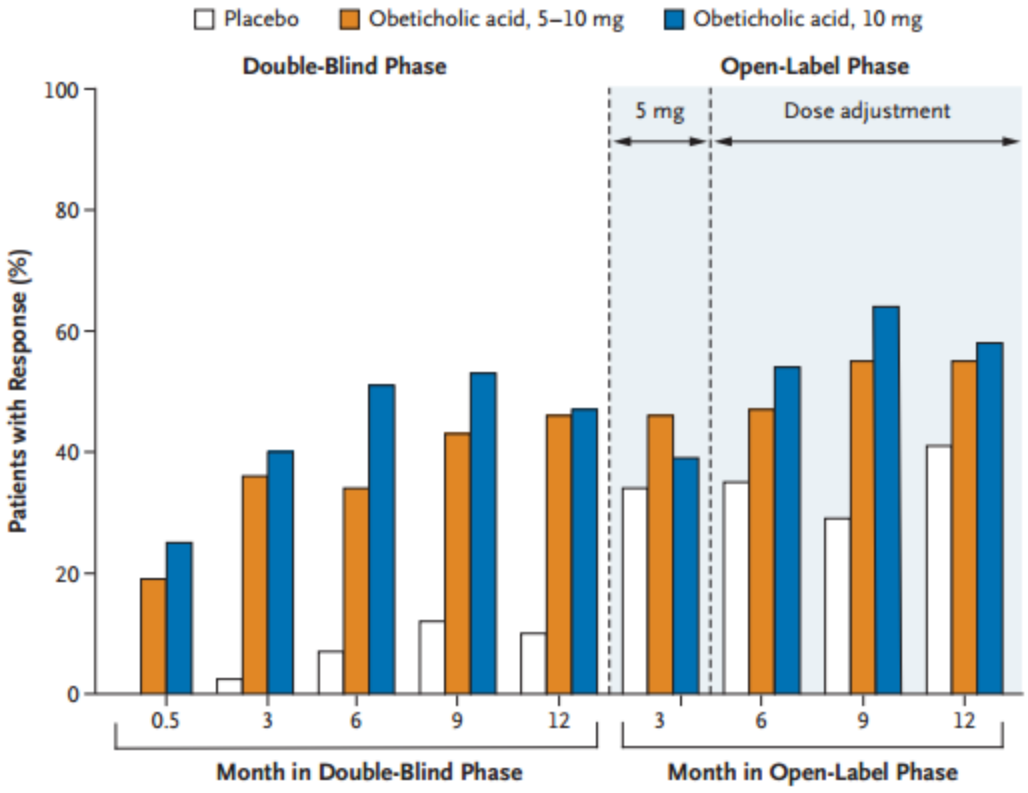
ORIGINAL ARTICLE

A Placebo-Controlled Trial of Obeticholic Acid in Primary Biliary Cholangitis

F. Nevens, P. Andreone, G. Mazzella, S.I. Strasser, C. Bowlus, P. Invernizzi, J.P.H. Drenth, P.J. Pockros, J. Regula, U. Beuers, M. Trauner, D.E. Jones, A. Floreani, S. Hohenester, V. Luketic, M. Shiffman, K.J. van Erpecum, V. Vargas, C. Vincent, G.M. Hirschfield, H. Shah, B. Hansen, K.D. Lindor, H.-U. Marschall, K.V. Kowdley, R. Hooshmand-Rad, T. Marmon, S. Sheeron, R. Pencek, L. MacConell, M. Pruzanski, and D. Shapiro, for the POISE Study Group*

2016;375:631-643

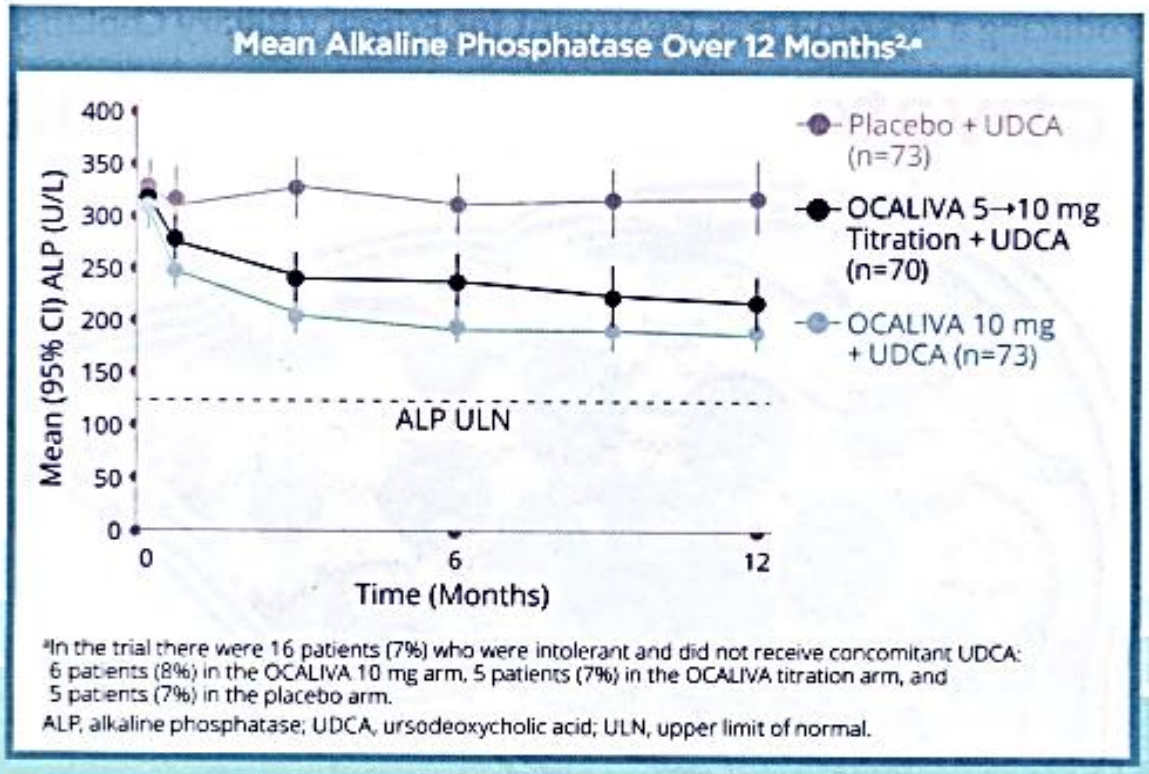
Phase 3, 12-month RCT
Farsenoid X receptor agonist
US 70,000. per year



No. of Patients									
Placebo	73	73	73	73	73	64	60	59	59
Obeticholic acid, 5–10 mg	70	70	70	70	70	63	62	62	60
Obeticholic acid, 10 mg	73	73	73	73	73	64	59	61	59

OCALIVA™
obeticholic acid

Delivered Significant, Sustained Reductions in Alkaline Phosphatase[2]



[a]In the trial there were 16 patients (7%) who were intolerant and did not receive concomitant UDCA: 6 patients (8%) in the OCALIVA 10 mg arm, 5 patients (7%) in the OCALIVA titration arm, and 5 patients (7%) in the placebo arm.

ALP, alkaline phosphatase; UDCA, ursodeoxycholic acid; ULN, upper limit of normal.

Case #8

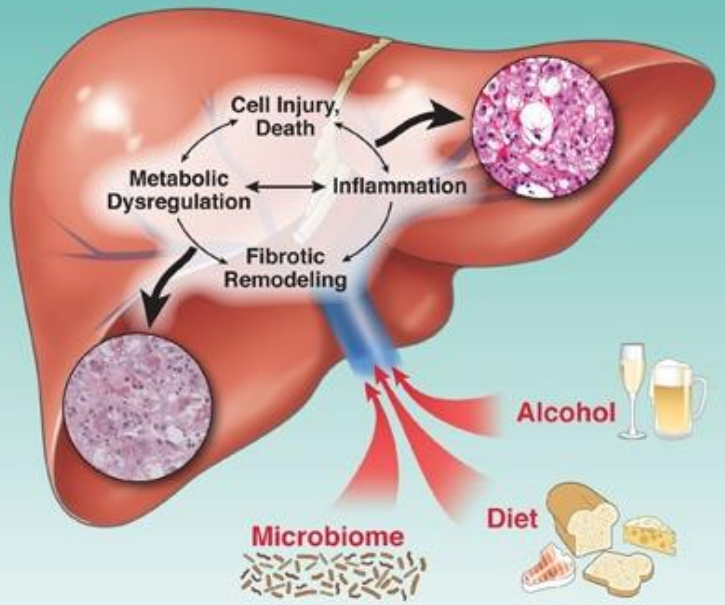
35 yo M with sleep apnea
PEx: hypertensive
BMI 45
Laboratory:
elevated AST, ALT
normal bilirubin
normal LFT's
raised TG and cholesterol
hepatomegaly on AUS
elastography normal
MRE normal

<u>What therapies should one offer?</u>:

A) Non-pharmacological
B) Surgical intervention
C) Antioxidant cocktail
D) GLP-1 analogue

Special Issue
Gastroenterology
www.gastrojournal.org Volume 150 Number 8 June 2016

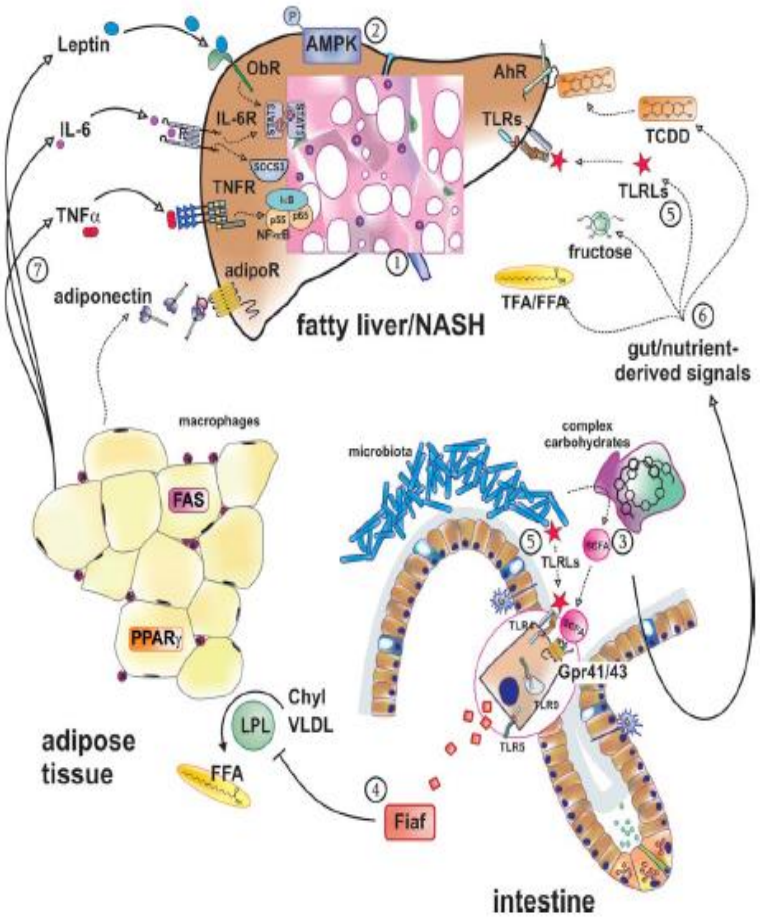
Alcoholic & Nonalcoholic Fatty Liver Disease



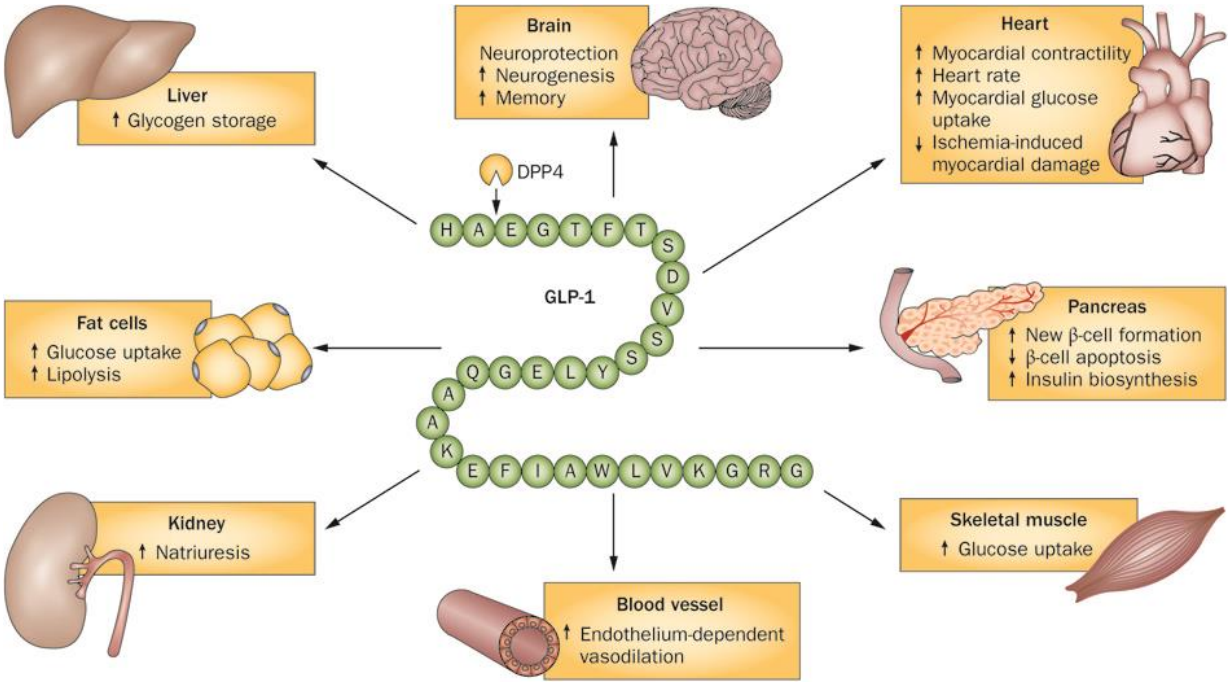
Commentaries | Basic Aspects | Clinical Aspects | Management

OFFICIAL JOURNAL OF THE AGA INSTITUTE

Multiple hit hypothesis



GLP (glucagon-like peptide)-1



- **Glucose-induced GLP-1 secretion is diminished in adults with NAFLD**
- **Liraglutide is a long acting GLP-1 analogue licensed for the treatment of type 2 diabetes**

Reviewed in: Y Rotman & A Sanyal. Gut 2017;66:180-190

Liraglutide safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): a multicentre, double-blind, randomised, placebo-controlled phase 2 study

Matthew James Armstrong, Piers Gaunt, Guruprasad P Aithal, Darren Barton, Diana Hull, Richard Parker, Jonathan M Hazlehurst, Kathy Guo, LEAN trial team*, George Abouda, Mark A Aldersley, Deborah Stocken, Stephen C Gough, Jeremy W Tomlinson, Rachel M Brown, Stefan G Hübscher, Philip N Newsome

Lancet 2016;387:679-690

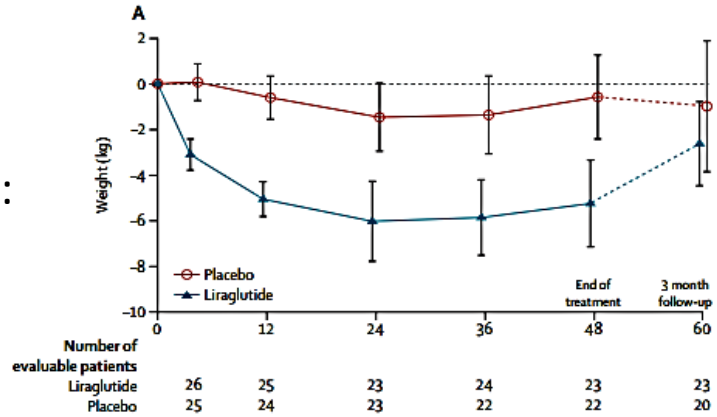
- **Phase 2, double-blinded, RCT**
  - **4 medical centers in UK**
- **Overweight patients with NASH**
- **SQ liraglutide (1.8 mg daily) x 48 weeks**
  - **vs. placebo; n=26 in each group**
- **Primary outcome: resolution of definite NASH without fibrosis progression**

Liraglutide safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): a multicentre, double-blind, randomised, placebo-controlled phase 2 study

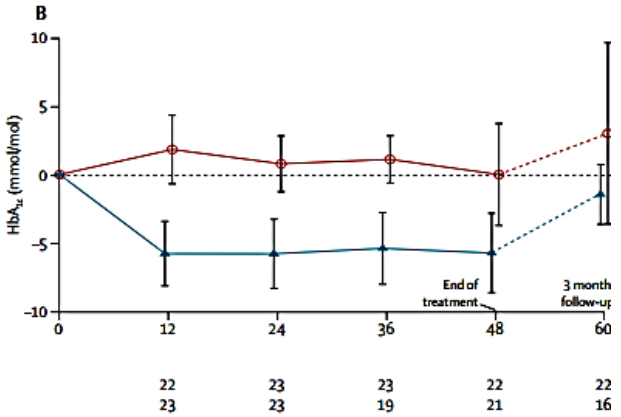
Matthew James Armstrong, Piers Gaunt, Guruprasad P Aithal, Darren Barton, Diana Hull, Richard Parker, Jonathan M Hazlehurst, Kathy Guo, LEAN trial team, George Abouda, Mark A Aldersley, Deborah Stocken, Stephen C Gough, Jeremy W Tomlinson, Rachel M Brown, Stefan G Hübscher, Philip N Newsome*

Lancet 2016:387:679-690

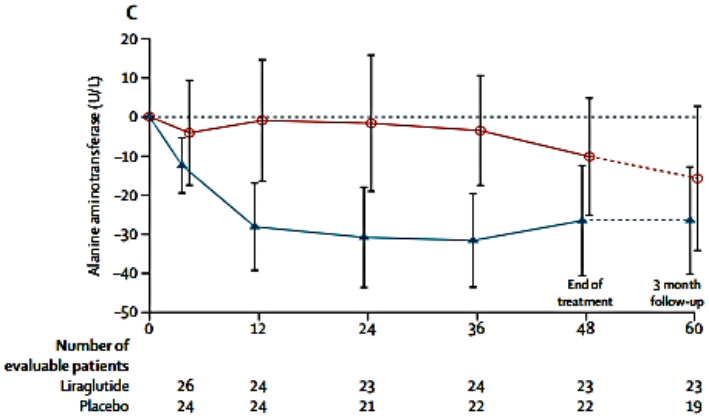
Weight:



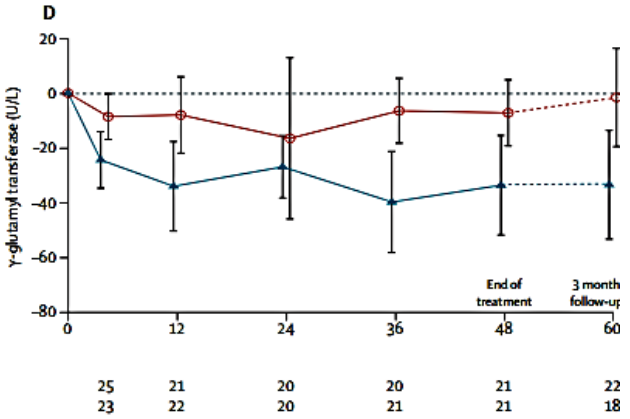
:HbA1c



AST:



:GGTP



Case #9: Prevention of Recurrent ASA-Related UGI Bleeding

- 77 y.o male with past Hx of MI, HTN, on ASA 81mg/d
- Presented 8 weeks ago with UGIB, endoscopy revealed multiple gastric erosions
- HP –ve on biopsy and serology
- Treated with PPI for past 8 weeks
- Today, expressed concern about recent news linking PPI use to dementia

Case #9: Prevention of Recurrent ASA-Related UGI Bleeding

- Question 14:
  - Would you consider using an H2RA to prevent recurrent upper gastrointestinal bleeding

A) Insist on PPI Therapy

B) Consider Use of H2RAs if PPIs will not be used

C) Discontinue ASA therapy, as risk of recurrent bleeding is too great if PPIs not used

Case #9: Prevention of Recurrent ASA-Related UGI Bleeding

- ACCF/AHA/ACG 2008 consensus recommends PPIs as gastroprotection for persons using ASA at high risk of UGIB
  - History of PUD/UGIB
  - Age > 65
  - Use of multiple anti-platelets/anticoagulants
  - Severe medical comorbidity
  - Systemic corticosteroid use
- Increased concerns about PPIs and serious medical complications
  - CDAD
  - Hip fracture
  - Dementia
  - CVA
  - Pneumonia
- No proven direct causal relationship, but clinicians and patients are jittery

Famotidine Is Inferior to Pantoprazole in Preventing Recurrence of Aspirin-Related Peptic Ulcers or Erosions

GASTROENTEROLOGY 2010;138:82–88

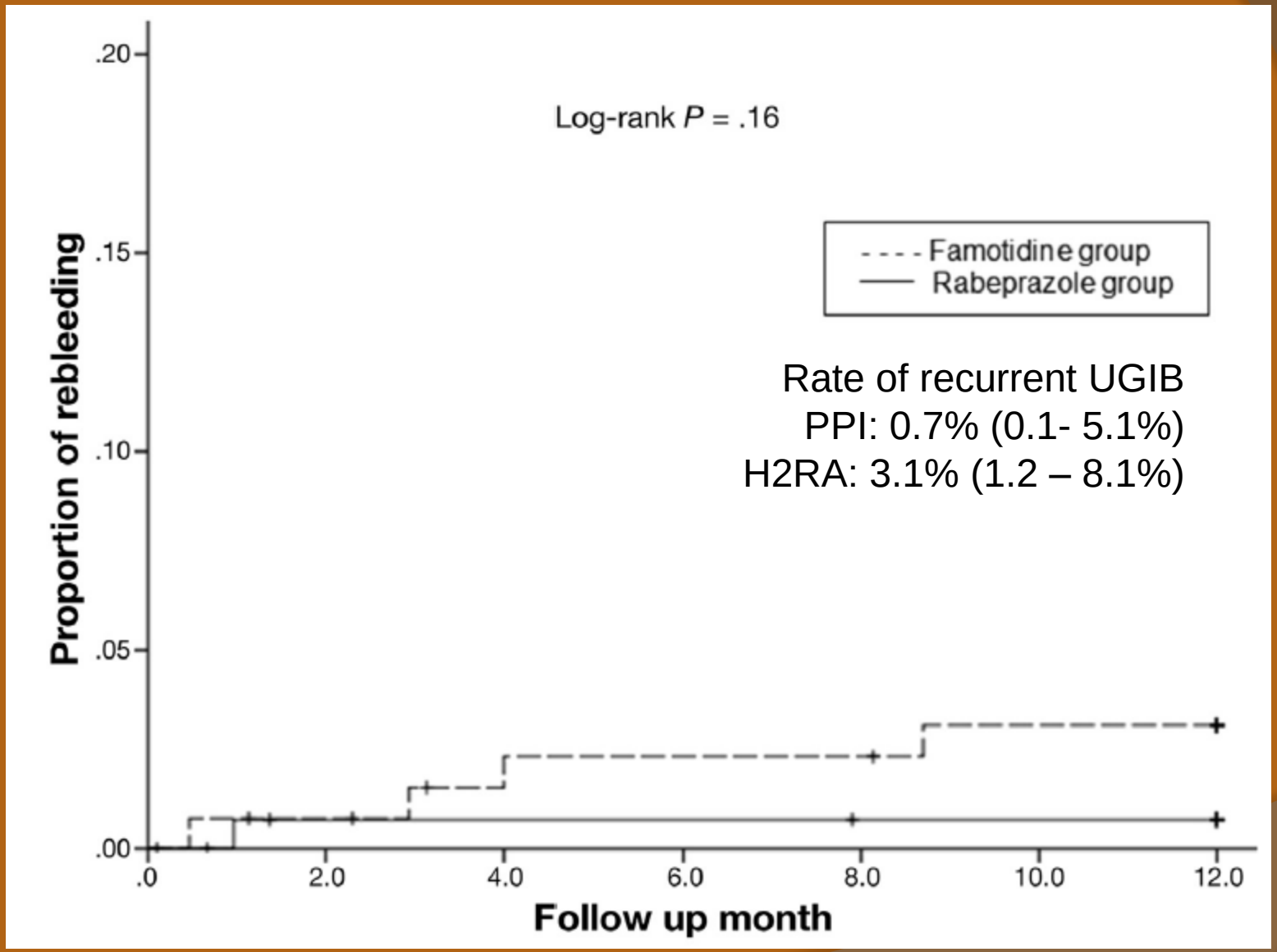
FOOK–HONG NG,* SIU–YIN WONG,‡ KWOK–FAI LAM,§ WAI–MING CHU,* PIERRE CHAN,‡ YUK–HEI LING,‖ CAROLYN KNG,* WAI–CHEUNG YUEN,‖ YUK–KONG LAU,* AMBROSE KWAN,¶ and BENJAMIN C. Y. WONG‡

- Compared ESO 20 bid to Famotidine 20mg bid, n=130
- Trend towards lower rates of UGIB with PPI vs H2RA
  - 0% vs. 7.5%
    - P=0.058

Similar Efficacy of Proton-Pump Inhibitors vs H2-Receptor Antagonists in Reducing Risk of Upper Gastrointestinal Bleeding or Ulcers in High-Risk Users of Low-Dose Aspirin

Gastroenterology 2017;152:105–110

- RCT of 270 people randomized with endoscopically confirmed PUD bleeding
  - On ASA <-325mg/d
  - HP –ve
- Randomized to
  - Rabeprazole 20mg/d
  - Famotidine 40mg/d
- Followed every 2 months for symptoms up to 12 months
- Endoscopy repeated for UGI symptoms or evidence of recurrent UGIB



Rate of recurrent UGIB
PPI: 0.7% (0.1- 5.1%)
H2RA: 3.1% (1.2 – 8.1%)

Case #9: Prevention of Recurrent ASA-Related UGI Bleeding

- Question 14:
  - Would you consider using an H2RA to prevent recurrent upper gastrointestinal bleeding

A) Insist on PPI Therapy

B) Consider Use of H2RAs if PPIs will not be used

C) Discontinue ASA therapy, as risk of recurrent bleeding is too great if PPIs not used

Case #10: Management of Achalasia

- 67 y.o male with 5 year history of progressive dysphagia
  - First to solids, now to all foods
- Diagnosed with Type 1 Achalsia on the basis of esophageal manometry
- Wants definitive therapy

Case #10: Management of Achalasia

- Question 15:
  - According to a recent RCT, which is the preferred strategy for definitive management of achalasia?

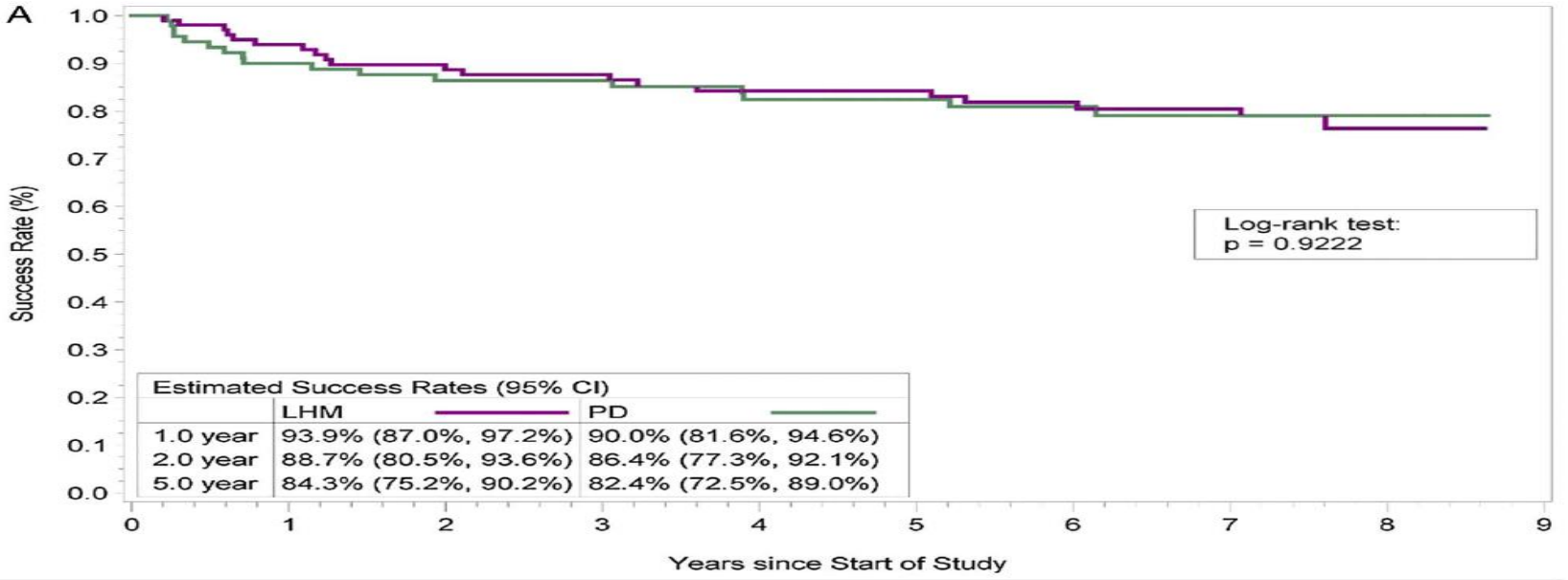
A) Laparoscopic Heller Myotomy (LHM)
B) Pneumatic Dialation (PD)
C) No difference between LHM and PD

Long-term results of the European achalasia trial: a multicentre randomised controlled trial comparing pneumatic dilation versus laparoscopic Heller myotomy

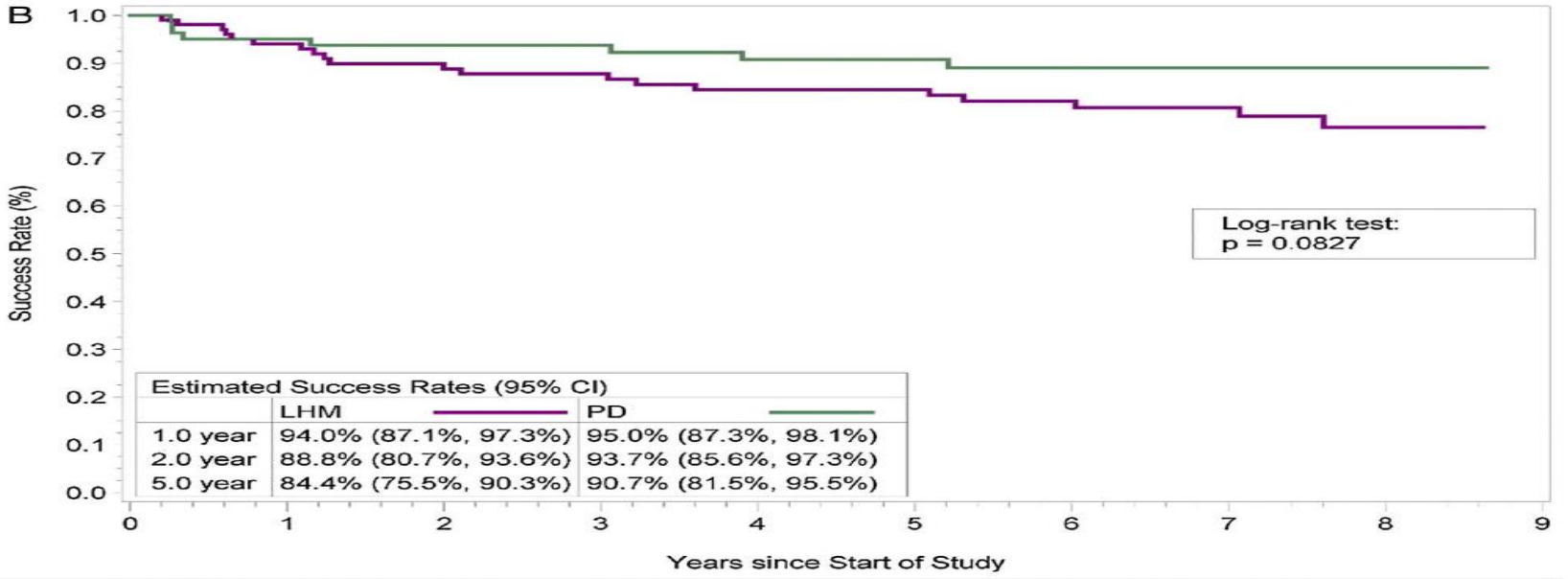
Gut 2016;**65**:732–739.

An Moonen,[1] Vito Annese,[2] Ann Belmans,[3] Albert J Bredenoord,[4] Stanislas Bruley des Varannes,[5] Mario Costantini,[6] Bertrand Dousset,[7] J I Elizalde,[8] Uberto Fumagalli,[9] Marianne Gaudric,[10] Antonio Merla,[11] Andre J Smout,[4] Jan Tack,[1] Giovanni Zaninotto,[12] Olivier R Busch,[13] Guy E Boeckxstaens[1]

- RCT comparing PD and LHM
  - 105 in LHM, 98 to PD
- In PD arm,
  - Allowed to have 2 redilations in first 24 months, one additional in 60 months
  - 2 analysis
    - Redilations allowed
    - Redilations considered as treatment failure



Number at risk										
LHM	104	91	84	79	74	71	60	47	27	16
PD	96	79	71	67	61	57	49	35	17	6



Number at risk										
LHM	106	92	85	80	75	72	60	47	27	16
PD	85	74	68	64	59	55	48	35	17	6

Long-term results of the European achalasia trial: a multicentre randomised controlled trial comparing pneumatic dilation versus laparoscopic Heller myotomy

An Moonen,[1] Vito Annese,[2] Ann Belmans,[3] Albert J Bredenoord,[4] Stanislas Bruley des Varannes,[5] Mario Costantini,[6] Bertrand Dousset,[7] J I Elizalde,[8] Uberto Fumagalli,[9] Marianne Gaudric,[10] Antonio Merla,[11] Andre J Smout,[4] Jan Tack,[1] Giovanni Zaninotto,[12] Olivier R Busch,[13] Guy E Boeckxstaens[1]

- In subgroup analysis
  - Type 1: LHM 75%, PD 69%
  - Type 2: LHM 88%, PD 96% (p=0.03)
  - Type 3: LHM 86%, PD 44% (p=0.10)
- Younger age, chest pain and esophageal dilation > 4cm associated with treatment failure

Case #10: Management of Achalasia

- Question 15: According to a recent RCT, which is the preferred strategy for definitive management of achalasia?

A) Laparoscopic Heller Myotomy (LHM)
B) Pneumatic Dialation (PD)
C) No difference between LHM and PD

Liraglutide safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): a multicentre, double-blind, randomised, placebo-controlled phase 2 study

Matthew James Armstrong, Piers Gaunt, Guruprasad P Aithal, Darren Barton, Diana Hull, Richard Parker, Jonathan M Hazlehurst, Kathy Guo, LEAN trial team, George Abouda, Mark A Aldersley, Deborah Stocken, Stephen C Gough, Jeremy W Tomlinson, Rachel M Brown, Stefan G Hübscher, Philip N Newsome*

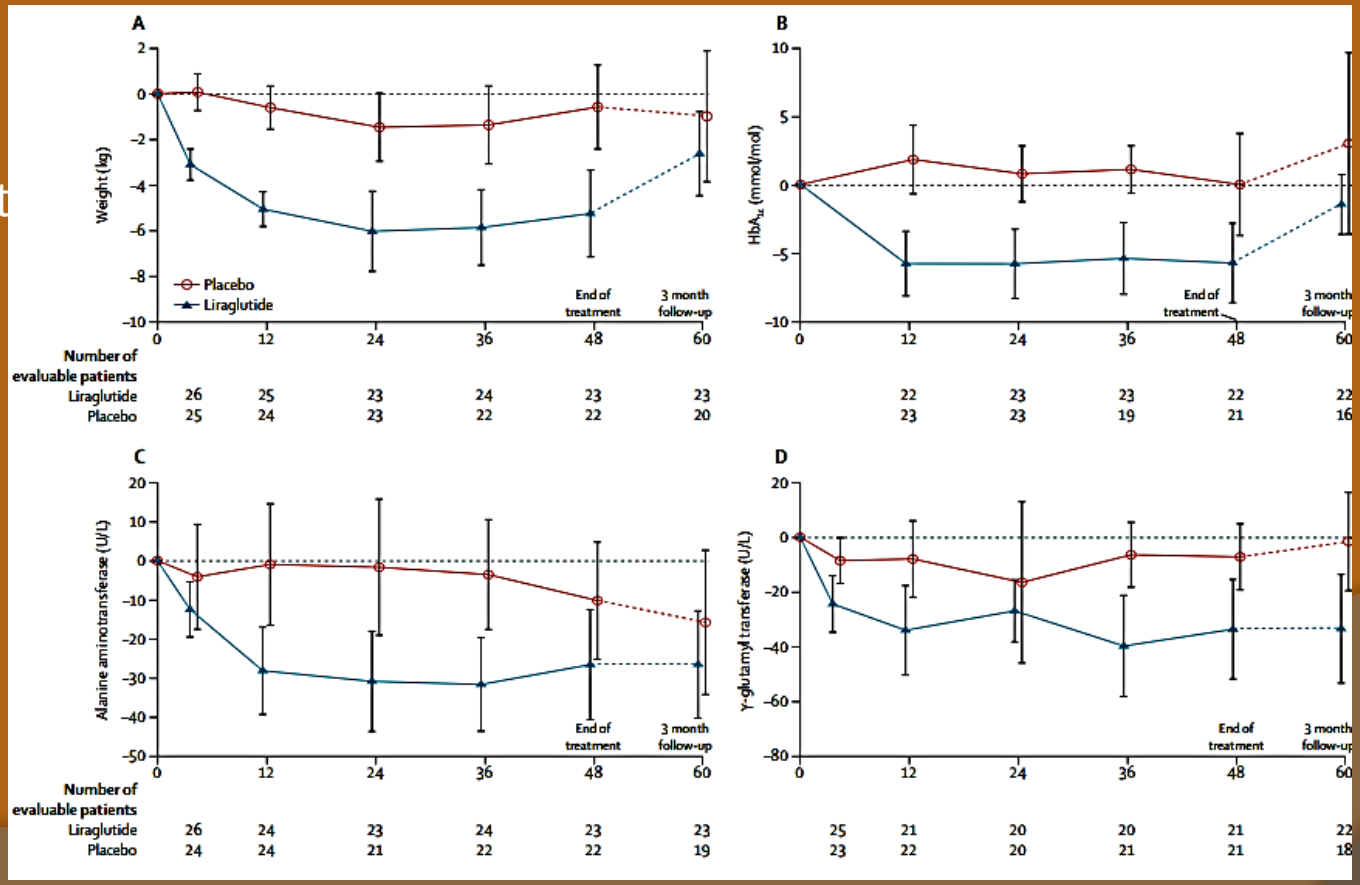
Lancet 2016:387:679-690

Weight

:HbA1c

AST:

:GGTP



Case #9

25-year-old F with 3 year history of IBS-diarrhea predominant (Rome IV) that began after an acute episode of bloody diarrhea affecting the entire family.

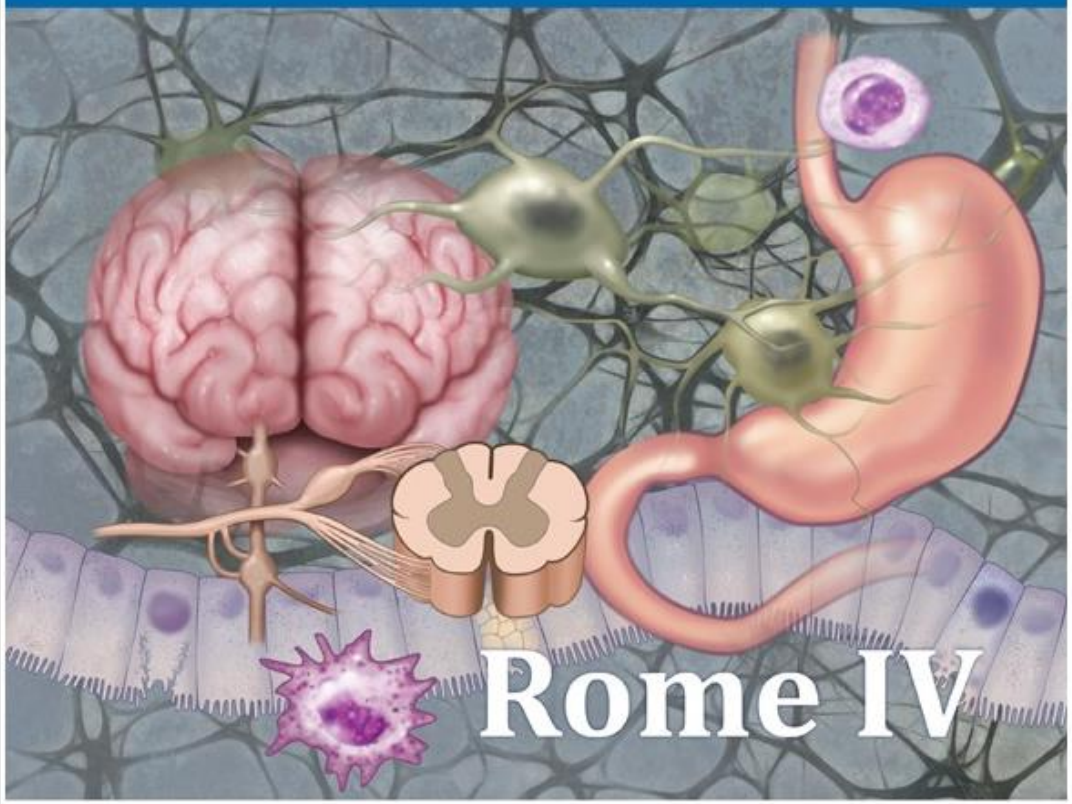
What intervention has a NNT of just 7?

a) **Cognitive behavioral therapy**
b) **Probiotics**
c) **Low Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols (FODMAPs) diet**
d) **Tricyclic antidepressants**
e) **SSRIs**

Special Issue

Gastroenterology

www.gastrojournal.org Volume 150 Number 6 May 2016

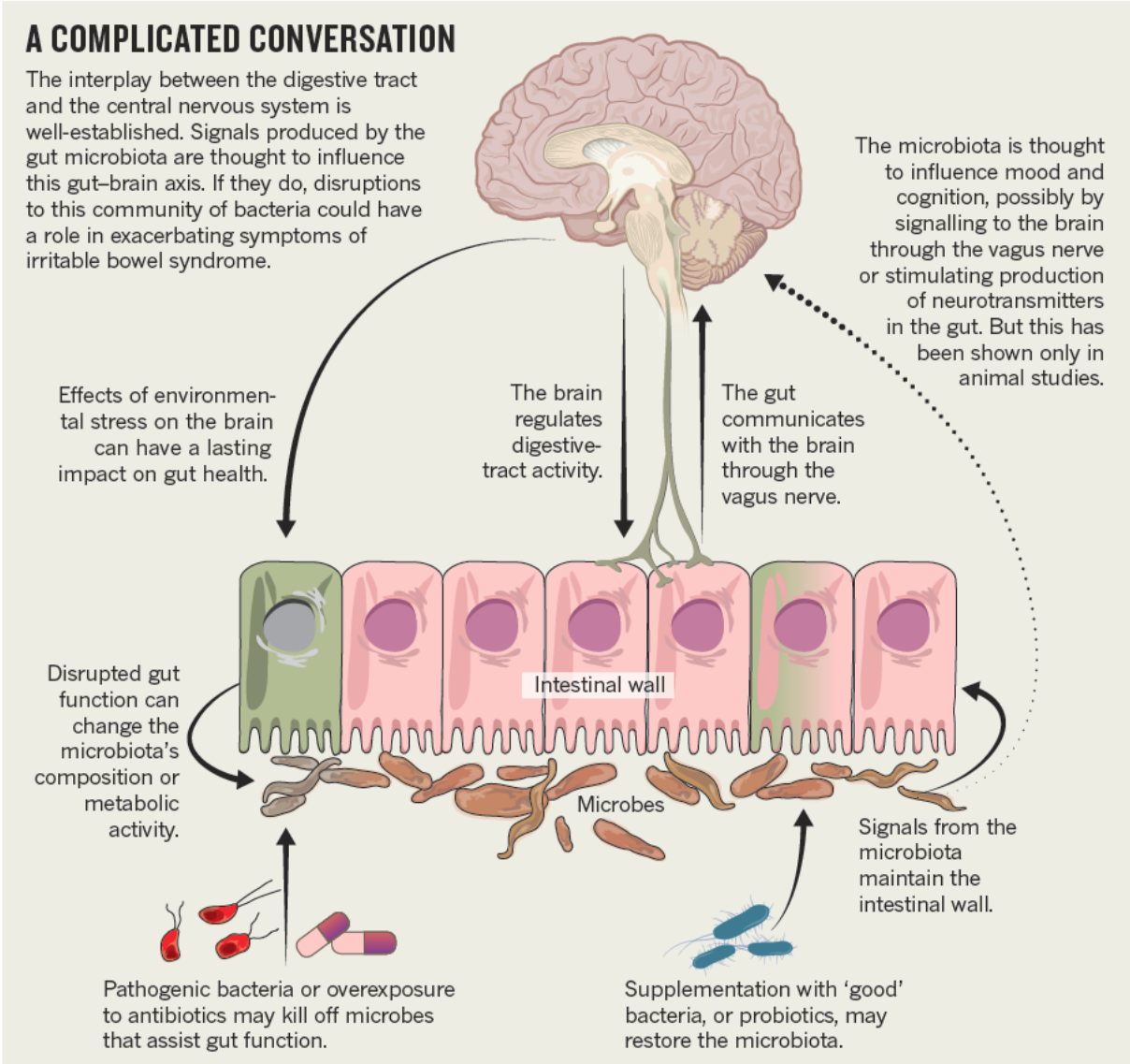


Functional Gastrointestinal Disorders:
Disorders of Gut-Brain Interaction

OFFICIAL JOURNAL OF THE AGA INSTITUTE

May 2016
Volume 150, Issue 6

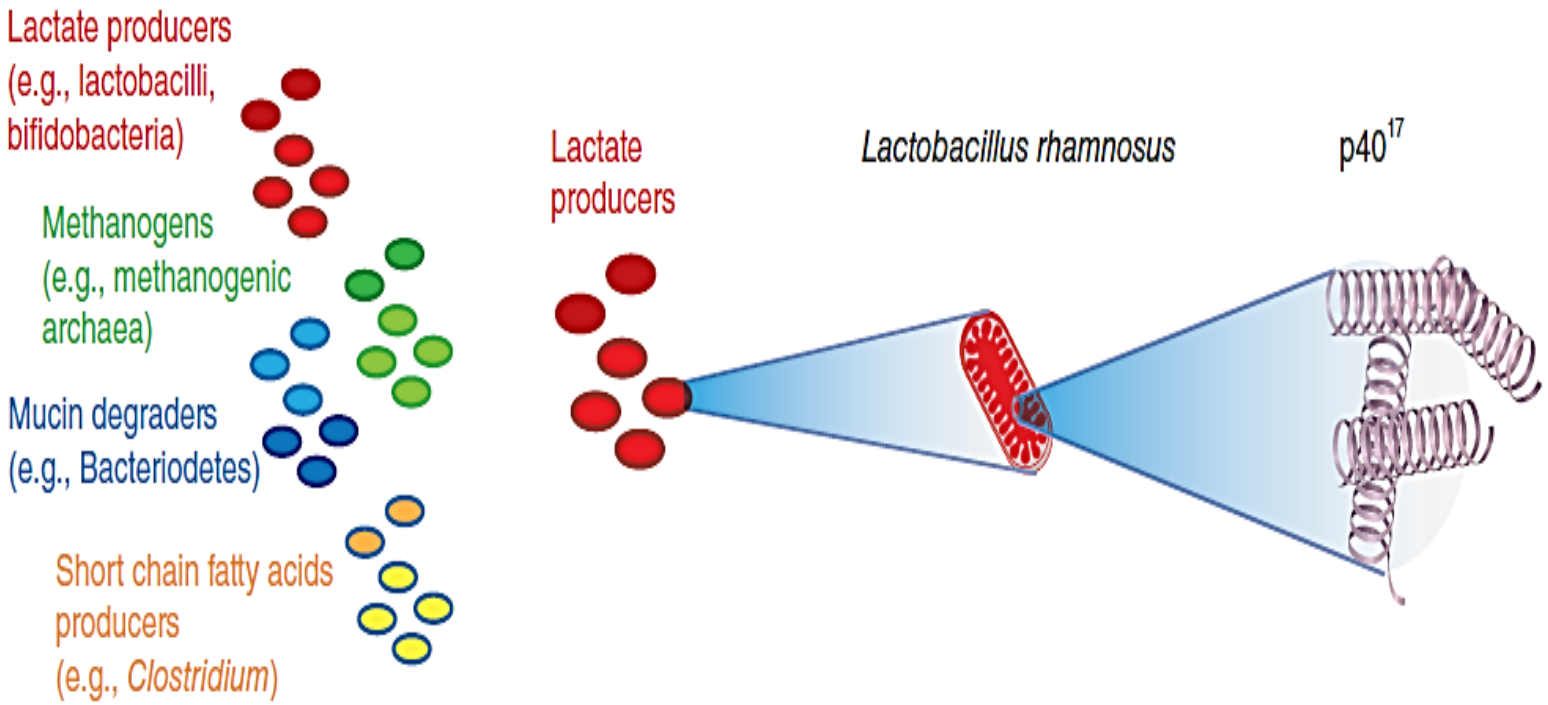
Microbiome-gut-brain communication



Nature 2016;533:S104-S106

Reviewed in: KC Bauer et al. Cell Microbiol 2016;18:632-644

How does one increase diversity?



Fecal transplant
(100s of strains, undefined composition)

Consortium
(defined composition of more than one strain, which together, perform a function of interest)

Single strain
(one strain, pure isolate)

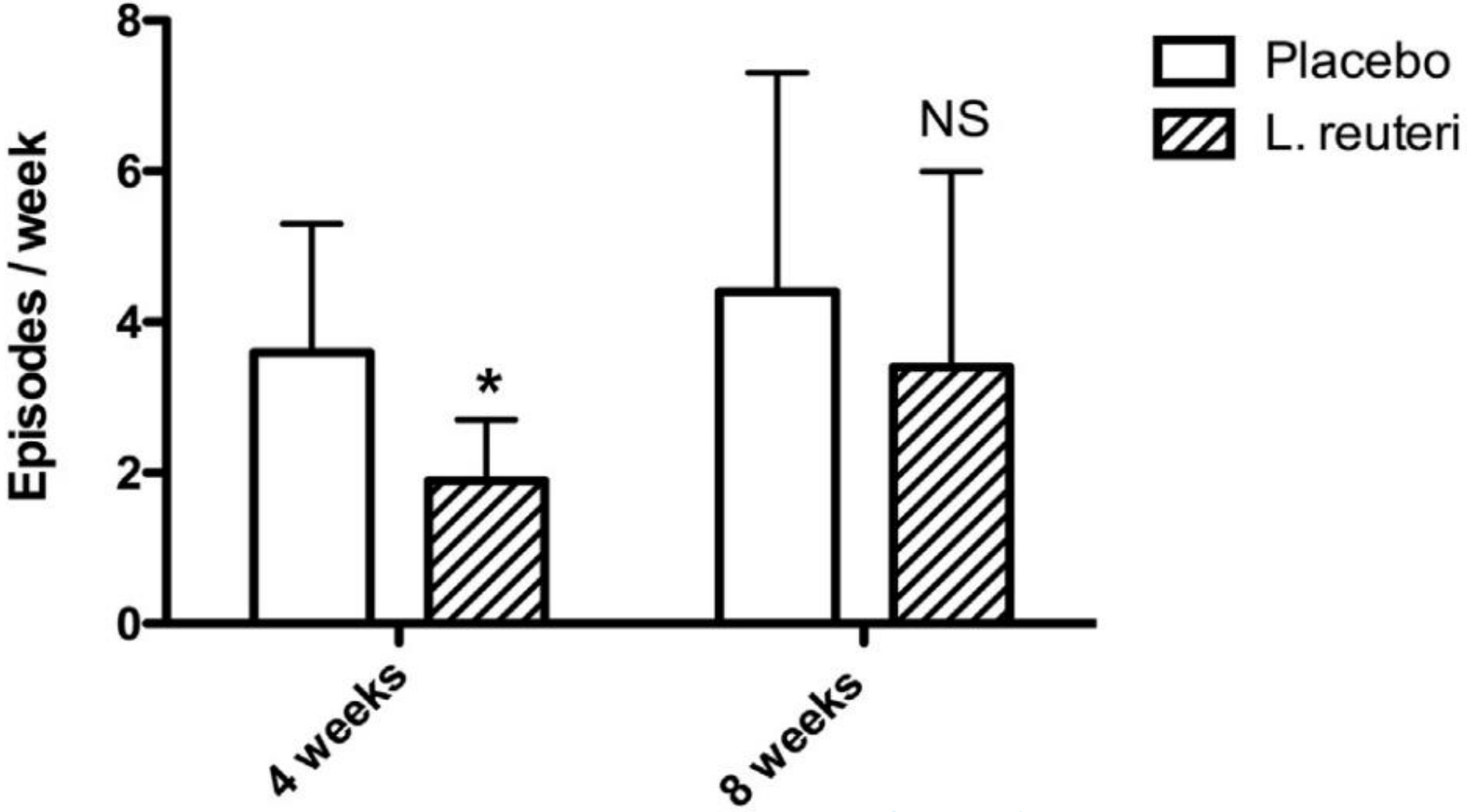
Bioactive
(molecule produced by strain that mediates effect on host)

B Olle. Nat Biotechnol 2013;31:309-315

"Precision microbiome reconstitution"

C Buffie et al. Nature 2015;517:205-208

Probiotics reduce symptoms of functional abdominal pain in childhood

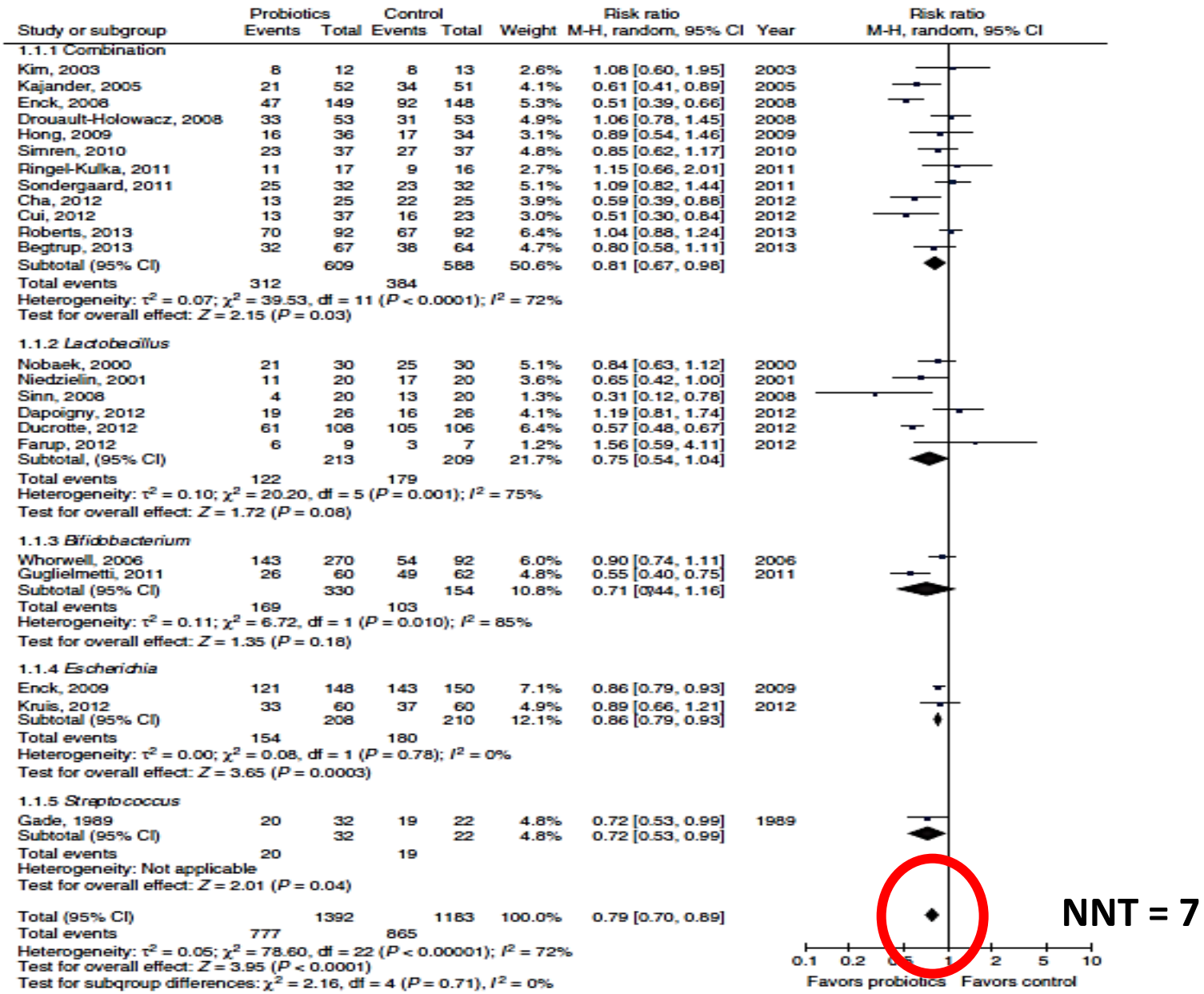


Z. Weizman et al. J Pediatr 2016;174:160-164

S Guandalini et al. JPGN 2010;51:24-30 (VSL#3)

A Gawronska et al. APT 2007;25:177-184 (LGG)

Probiotics vs. placebo in adults with IBS



Study or subgroup	Probiotics Events	Total	Control Events	Total	Weight	Risk ratio M-H, random, 95% CI	Year
1.1.1 Combination							
Kim, 2003	8	12	8	13	2.6%	1.06 [0.60, 1.95]	2003
Kajander, 2005	21	52	34	51	4.1%	0.61 [0.41, 0.89]	2005
Enck, 2008	47	149	92	148	5.3%	0.51 [0.39, 0.66]	2008
Drouault-Holowacz, 2008	33	53	31	53	4.9%	1.06 [0.78, 1.45]	2008
Hong, 2009	16	36	17	34	3.1%	0.89 [0.54, 1.46]	2009
Simren, 2010	23	37	27	37	4.8%	0.85 [0.62, 1.17]	2010
Ringel-Kulka, 2011	11	17	9	16	2.7%	1.15 [0.66, 2.01]	2011
Sondergaard, 2011	25	32	23	32	5.1%	1.09 [0.82, 1.44]	2011
Cha, 2012	13	25	22	25	3.9%	0.59 [0.39, 0.88]	2012
Cui, 2012	13	37	16	23	3.0%	0.51 [0.30, 0.84]	2012
Roberts, 2013	70	92	67	92	6.4%	1.04 [0.88, 1.24]	2013
Begtrup, 2013	32	67	38	64	4.7%	0.80 [0.58, 1.11]	2013
Subtotal (95% CI)		609		588	50.6%	0.81 [0.67, 0.98]	
Total events	312		384				
Heterogeneity: $\tau^2 = 0.07$; $\chi^2 = 39.53$, df = 11 ($P < 0.0001$); $I^2 = 72\%$							
Test for overall effect: $Z = 2.15$ ($P = 0.03$)							
1.1.2 *Lactobacillus*							
Nobaek, 2000	21	30	25	30	5.1%	0.84 [0.63, 1.12]	2000
Niedzielin, 2001	11	20	17	20	3.6%	0.65 [0.42, 1.00]	2001
Sinn, 2008	4	20	13	20	1.3%	0.31 [0.12, 0.78]	2008
Dapoigny, 2012	19	26	16	26	4.1%	1.19 [0.81, 1.74]	2012
Ducrotte, 2012	61	108	105	106	6.4%	0.57 [0.48, 0.67]	2012
Farup, 2012	6	9	3	7	1.2%	1.56 [0.59, 4.11]	2012
Subtotal, (95% CI)		213		209	21.7%	0.75 [0.54, 1.04]	
Total events	122		179				
Heterogeneity: $\tau^2 = 0.10$; $\chi^2 = 20.20$, df = 5 ($P = 0.001$); $I^2 = 75\%$							
Test for overall effect: $Z = 1.72$ ($P = 0.08$)							
1.1.3 *Bifidobacterium*							
Whorwell, 2006	143	270	54	92	6.0%	0.90 [0.74, 1.11]	2006
Guglielmetti, 2011	26	60	49	62	4.8%	0.55 [0.40, 0.75]	2011
Subtotal (95% CI)		330		154	10.8%	0.71 [0.44, 1.16]	
Total events	169		103				
Heterogeneity: $\tau^2 = 0.11$; $\chi^2 = 6.72$, df = 1 ($P = 0.010$); $I^2 = 85\%$							
Test for overall effect: $Z = 1.35$ ($P = 0.18$)							
1.1.4 *Escherichia*							
Enck, 2009	121	148	143	150	7.1%	0.86 [0.79, 0.93]	2009
Kruis, 2012	33	60	37	60	4.9%	0.89 [0.66, 1.21]	2012
Subtotal (95% CI)		208		210	12.1%	0.86 [0.79, 0.93]	
Total events	154		180				
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.08$, df = 1 ($P = 0.78$); $I^2 = 0\%$							
Test for overall effect: $Z = 3.65$ ($P = 0.0003$)							
1.1.5 *Streptococcus*							
Gade, 1989	20	32	19	22	4.8%	0.72 [0.53, 0.99]	1989
Subtotal (95% CI)		32		22	4.8%	0.72 [0.53, 0.99]	
Total events	20		19				
Heterogeneity: Not applicable							
Test for overall effect: $Z = 2.01$ ($P = 0.04$)							
Total (95% CI)		1392		1183	100.0%	0.79 [0.70, 0.89]	
Total events	777		865				
Heterogeneity: $\tau^2 = 0.05$; $\chi^2 = 78.60$, df = 22 ($P < 0.00001$); $I^2 = 72\%$							
Test for overall effect: $Z = 3.95$ ($P < 0.0001$)							
Test for subgroup differences: $\chi^2 = 2.16$, df = 4 ($P = 0.71$), $I^2 = 0\%$							

AC Ford et al. Am J Gastroenterol 2014;109:1547-1561

Comparison of Profiles of *L. plantarum* and *B. infantis*

Bacterial Strain	Product Name	IBS Indication Approved by Health Canada	Allergen Safety	Dose and Cost	Storage
Lactobacillus plantarum 299v	TuZen	Helps to reduce flatulence and abdominal pain associated with flatulence in individuals with IBS	No lactose or milk protein but has contact with soy	1 cap bid x1wk and then 1/day for maintenance Cost: 30 capsules: $36.99* Average Monthly Maintenance Cost:$36.99/ month (as of May, 2011)*	Room temperature in a dry place (hot months may need to refrigerate) until labelled expiry date
Bifidobacterium longum subsp. *infantis* 35624 (Bifantis™)	Align	For relief and management of IBS symptoms. Relieves symptoms of Irritable Bowel Syndrome (IBS) such as abdominal discomfort, gas, and bloating. With daily use, provides ongoing relief of IBS symptoms such as abdominal discomfort, gas, and bloating.	No lactose or soy but there is milk protein in the ingredients	1 cap once daily Cost: 28 capsules: $36.00* Average Monthly Maintenance Cost:$38.57/ month (as of May, 2011)*	Room temperature until labelled expiry date. Recommended to keep in original blister packaging for best shelf life

* Based on an average retail cost range of $32–40 per package and a 30-day month.

CME Approval Provided by the Can Assoc Gastroenterol

Case #10

90 yo F in nursing home with repeated bouts of diarrhea, incontinence, quality of life: nil

PEx: withdrawn, sarcopenic, BMI 15

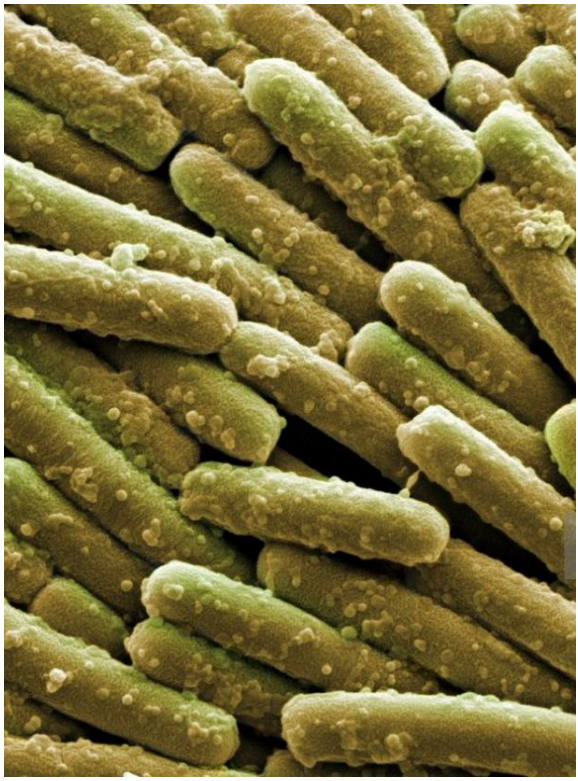
Laboratory:

Hypokalemia

hypocalcemia, but free ionized Ca normal

low alkaline phosphatase, and low zinc

C. difficile toxin + on 5 separate tests



<u>What therapies could be considered?</u>:

a) Antibiotics (combination, repeated, newish)

b) Monoclonal antibodies

c) Probiotics

d) Zinc

e) FMT (what if she has a history of IBD?)

http://www.gettyimages.ca/detail/photo/clostridium-difficile-bacteria-coloured

Annals of Internal Medicine

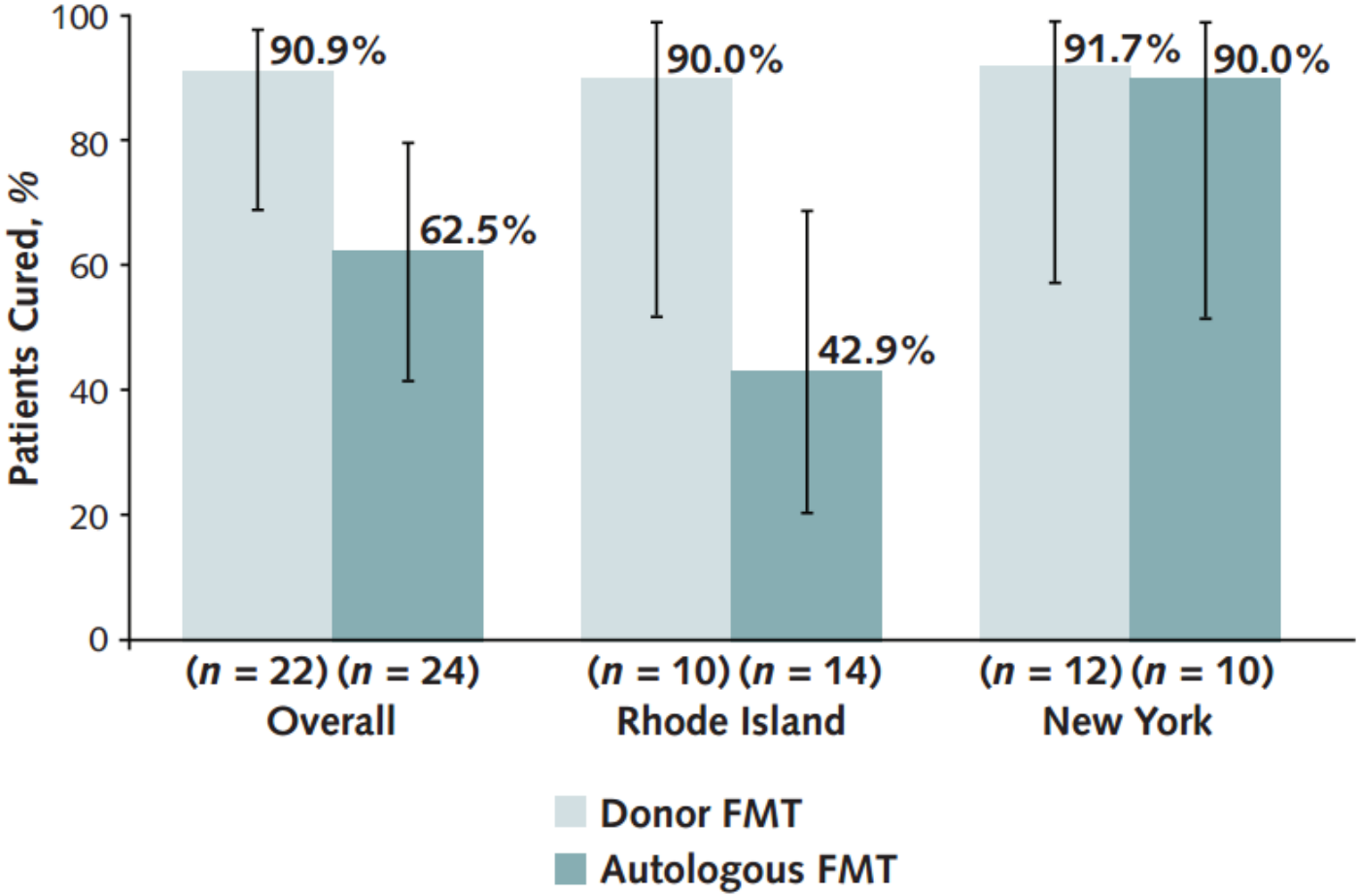
ORIGINAL RESEARCH

Effect of Fecal Microbiota Transplantation on Recurrence in Multiply Recurrent *Clostridium difficile* Infection

2016;165:609-616

A Randomized Trial

Colleen R. Kelly, MD; Alexander Khoruts, MD; Christopher Staley, PhD; Michael J. Sadowsky, PhD; Mortadha Abd, MD; Mustafa Alani, MD; Brianna Bakow, BA; Patrizia Curran, MD; Joyce McKenney, MS; Allison Tisch, NP; Steven E. Reinert, MS; Jason T. Machan, PhD; and Lawrence J. Brandt, MD



Gastroenterology
www.gastrojournal.org Volume 149 Number 1 July 2015

Fecal Microbiota Transplantation Induces Remission in Patients With Active Ulcerative Colitis in a Randomized Controlled Trial

Paul Moayyedi,[1] Michael G. Surette,[1] Peter T. Kim,[2,3] Josie Libertucci,[1] Melanie Wolfe,[1] Catherine Onischi,[3] David Armstrong,[1] John K. Marshall,[1] Zain Kassam,[4] Walter Reinisch,[1] and Christine H. Lee[3]

Findings From a Randomized Controlled Trial of Fecal Transplantation for Patients With Ulcerative Colitis

Noortje G. Rossen,[1] Susana Fuentes,[2] Mirjam J. van der Spek,[1] Jan G. Tijssen,[3] Jorn H. A. Hartman,[2] Ann Duflou,[1] Mark Löwenberg,[1] Gijs R. van den Brink,[1] Elisabeth M. H. Mathus-Vliegen,[1] Willem M. de Vos,[2,4] Erwin G. Zoetendal,[2] Geert R. D'Haens,[1] and Cyriel Y. Ponsioen[1]

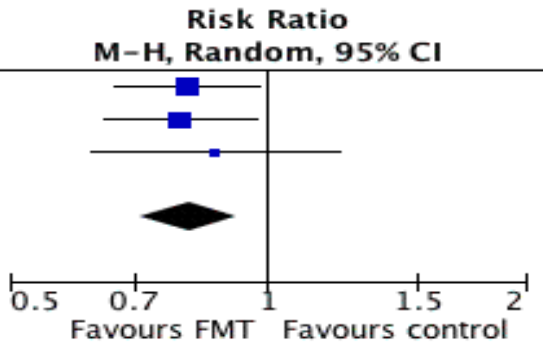
OFFICIAL JOURNAL OF THE AGA INSTITUTE

Meta-analysis of RCTs of FMT in UC: remission rates

- 3 RCTs, 204 patients
- NNT = 6 (95% CI = 4 to 14)
- RR = 0.81 (95% CI = 0.71-0.92), p=0.001
- I^2 = 0%
- GRADE = moderate quality evidence

Study or Subgroup	FMT Events	FMT Total	placebo Events	placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Moayyedi 2015	29	38	35	37	45.0%	0.81 [0.67, 0.98]
Paramsothy 2016	30	41	37	40	39.9%	0.79 [0.64, 0.97]
Rossen 2015	16	23	20	25	15.1%	0.87 [0.62, 1.21]
Total (95% CI)		**102**		**102**	**100.0%**	**0.81 [0.71, 0.92]**
Total events	75		92			

Heterogeneity: Tau² = 0.00; Chi² = 0.23, df = 2 (P = 0.89); I² = 0%
Test for overall effect: Z = 3.19 (P = 0.001)



Slide courtesy of P. Moayyedi, CCC Future Directions in IBD Toronto, November, 2016

CIHR SPOR IMAGINE Network Leadership

Aida Fernandes
Executive Director

Paul Moayyedi
Principal Investigator

Glenda MacQueen
Co-PI and Psychiatry Lead

Charles Bernstein
IBD Lead

Stephen Vanner
IBS Co-lead

Premsyl Bercik
IBS Co-lead

Anthony Otley
Pediatric Lead

Case #11

17.5 yo M with autism spectrum disorder, and

- generalized irritability (possible pain)
- chronic constipation
- abdominal bloating

PEx: BMI 35

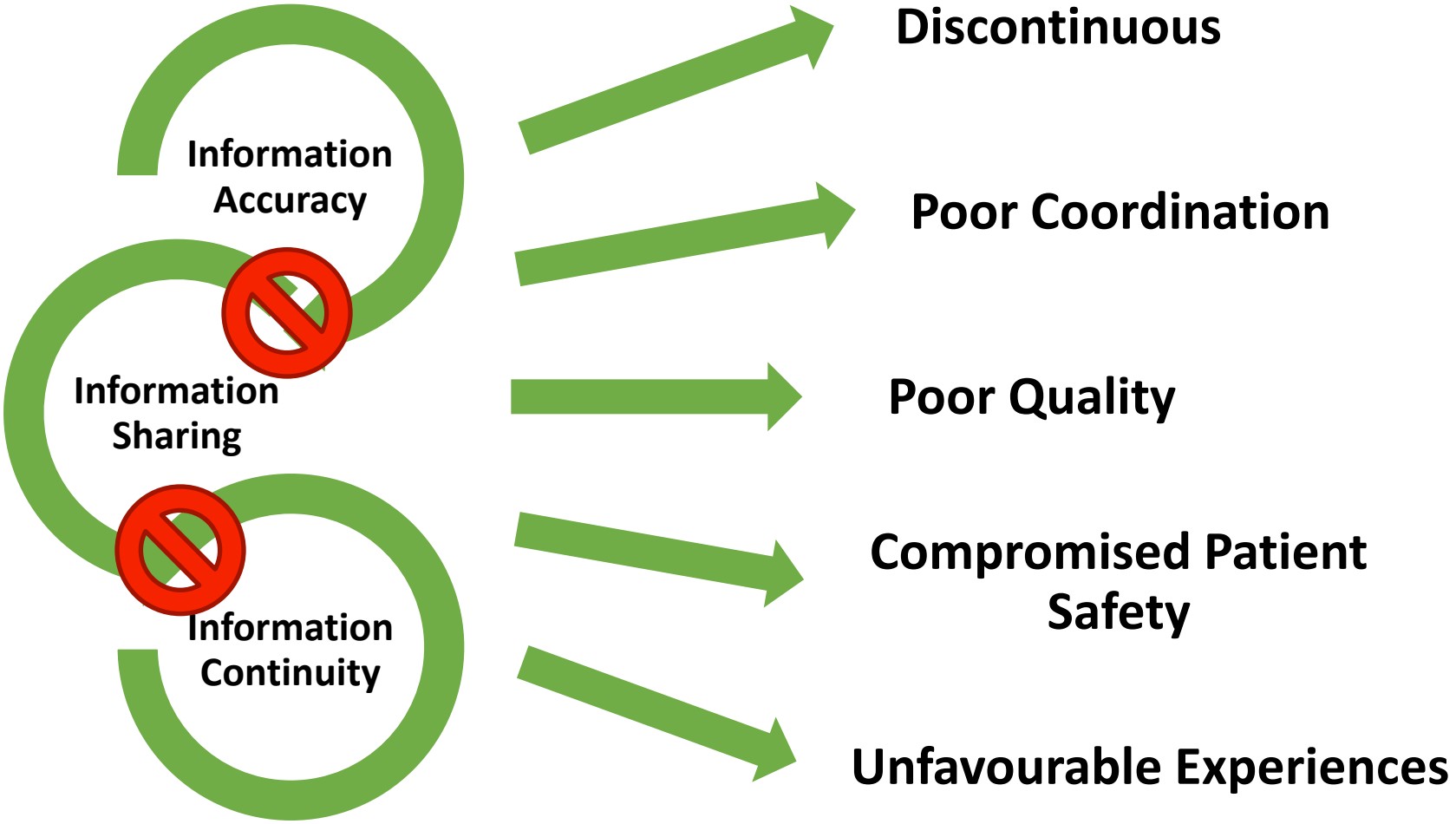
- developmental delay

Laboratory:

- elevated acute phase reactants
- normal fecal calprotectin
- colonic impaction on AXR
- peptic esophagitis on 3 upper endoscopies
- nodular lymphoid hyperplasia at ileoscopy

How (well) are you going to handle taking over his long-term care?

Risks in Transitions in Care



Slide courtesy of: Dr. Brian Rowe, Univ. Alberta

JPGN 2016;63:488-493

Transitions in Pediatric Gastroenterology: Results of a National Provider Survey

*†Rachel Bensen, *Rebecca B. McKenzie, *‡Susan M. Fernandes, and §||Laurie N. Fishman

TABLE 2. Importance of transitioning patient skills to ADULT providers

Aspect of transition care	Pediatric GI providers, N = 150 mean (±SD)	Adult GI providers,* N = 363 mean (±SD)
Knowledge of name, dose, and major adverse effects of medication (medical condition)	4.4 ± 0.6	4.6 ± 0.6
Knowledge of own medical history (medical condition)	4.4 ± 0.6	4.5 ± 0.6
Conception of disease and its basic nature (medical condition)	4.7 ± 0.5	4.7 ± 0.5
Filling prescriptions (medical condition)	4.5 ± 0.6	4.3 ± 0.9
Active participation during office visits (independence)	4.5 ± 0.6	4.4 ± 0.7
Attending office visits alone (independence)	4.0 ± 0.7	3.2 ± 1.1
Identification of people involved in their health care (both family and professionals) (medical condition)	4.3 ± 0.6	4.4 ± 0.7
Initiate contact (by telephone or e-mail) if a problem arises between visits (independence)	4.4 ± 0.6	4.3 ± 0.9

GI = gastrointestinal. Responses provided on a Likert scale from 1 to 5, in which 1 represented "not important at all" and 5 represented "very important."
*Responses from adult gastroenterology providers taken from Hait et al (13).

Bridging the cultures of pediatric and adult medicine:

Pediatric Health Care providers:

- may be reluctant to transfer care
- may communicate anxiety to parents/families
- used to allied health support resources
- don't always transfer requisite information

Internal Medicine Health Care practitioners:

- may want to reassess ("baseline")
- may want to change management
- change timing of interval follow-ups
- more limited access to allied health care
- parental involvement adds another dimension

TABLE 4. Barriers to successful transfer

What are some of the barriers that you perceive of in your current health care system to the transfer of care of a patient to adult care providers? (check all that apply)	%
Parent's/guardian's attachment to pediatric health care providers	81
Patient's attachment to pediatric health care providers	74
Patient emotional/cognitive delay	64
Provider's attachment to patient or family	56
Parent's/guardian's attachment to institution or practice	54
Patient's on-going active medical issues not amenable to transfer	47
Patient's attachment to institution or practice	46
Patient noncompliance with transfer	40
Patient's unstable social situation	38
Perceived resistance of other involved pediatric practitioners to transition	32
Lack of qualified adult providers familiar with disease process	31
Health insurance issues	29

Rapid-fire 2016 papers for CDDW-2017

ANSWERS to Questions

Colon cancer	BMMRD syndrome	Slide# 5: C
Endoscopy	consent, performance indicators	#11: A, C
Celiac	cap biopsy	#14: D
H. pylori	cancer prevention	#17: B, C
Eosin. esophagitis	front line therapies	#20: A
Acute diarrhea	beyond ORT	#26: A, E
PBC	obeticholic acid	#32: D
NASH	liraglutide	#35: A, ?D
IBS	FODMAPs or probiotics	#40: A, B
Dysbiosis	fecal microbial transplantation	#47: all
Life trajectory	transitions in care	#52: n/a