



La transplantation de microbiote fécal

Passé, présent, futur ...

Alexis Mosca
Hôpital Robert Debré (Paris)

16ème rencontre de la FAMP, 02/02/2019, Paris





Ge Hong
4th century

A bit of history ..

卷之三

治寒热诸症方第十六

治症病方

1. 鼠妇、豆豉二七枚。合捣令相和，未发时服二丸，欲发时服一丸。
- 2 又方，青蒿一握，以水二升渍，绞取汁，尽服之。
- 3 又方，用独父蒜，于白炭上烧之，未，服方寸匕。
- 4 又方，五月五日蒜一片去皮，中破之，刀割令容巴豆一枚，去心皮，内蒜中令合，以竹挟以火炙之，取可热，捣为三丸。未发前服一丸，不止，复与一丸。
- 5 又方，取蜘蛛一枚，芦管中密塞管中，以绾颈，过发时，乃解去也。
- 6 又方，日始出时，东向日再拜，毕，正长跪，向日叉手，当闭气，以书墨注其管两耳中，各七注，又丹书舌上，言子日死，毕，复再拜，还去勿顾，安卧勿食，过发时断，即差。
- 7 又方，多煮豉汤，饮数升，令得大吐，便差。
- 8 又方，取蜘蛛一枚，著饭中，合丸吞之。
- 9 又方，临发时，捣大附子下筛，以苦酒和之，涂背上。
- 10 又方，鼠妇虫子四枚，各一以饴糖裹之，丸服便断，即差。
- 11 又方，常山(捣下筛成末)三两，真丹一两。白蜜和，捣百

- The indications for the fecal therapy included

- food poisoning with the risk of death
- high level of fever with neuropsychic symptoms
- cold pathogenic febrile disease
- seasonal febrile disease with high fever

Chinese medical book

Zhou Hou Bei Ji Fang (Handy Therapy for Emergencies)

The NEW ENGLAND JOURNAL of MEDICINE

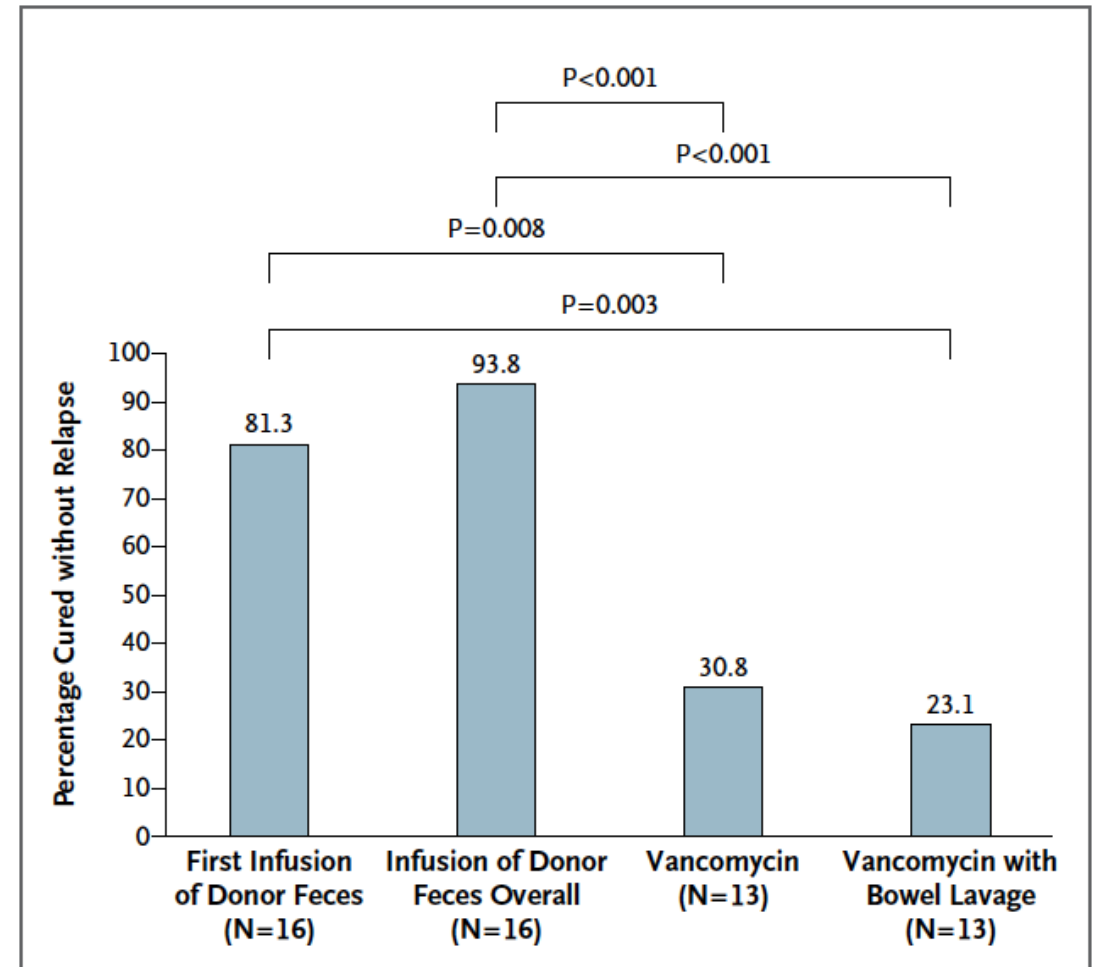
ESTABLISHED IN 1812

JANUARY 31, 2013

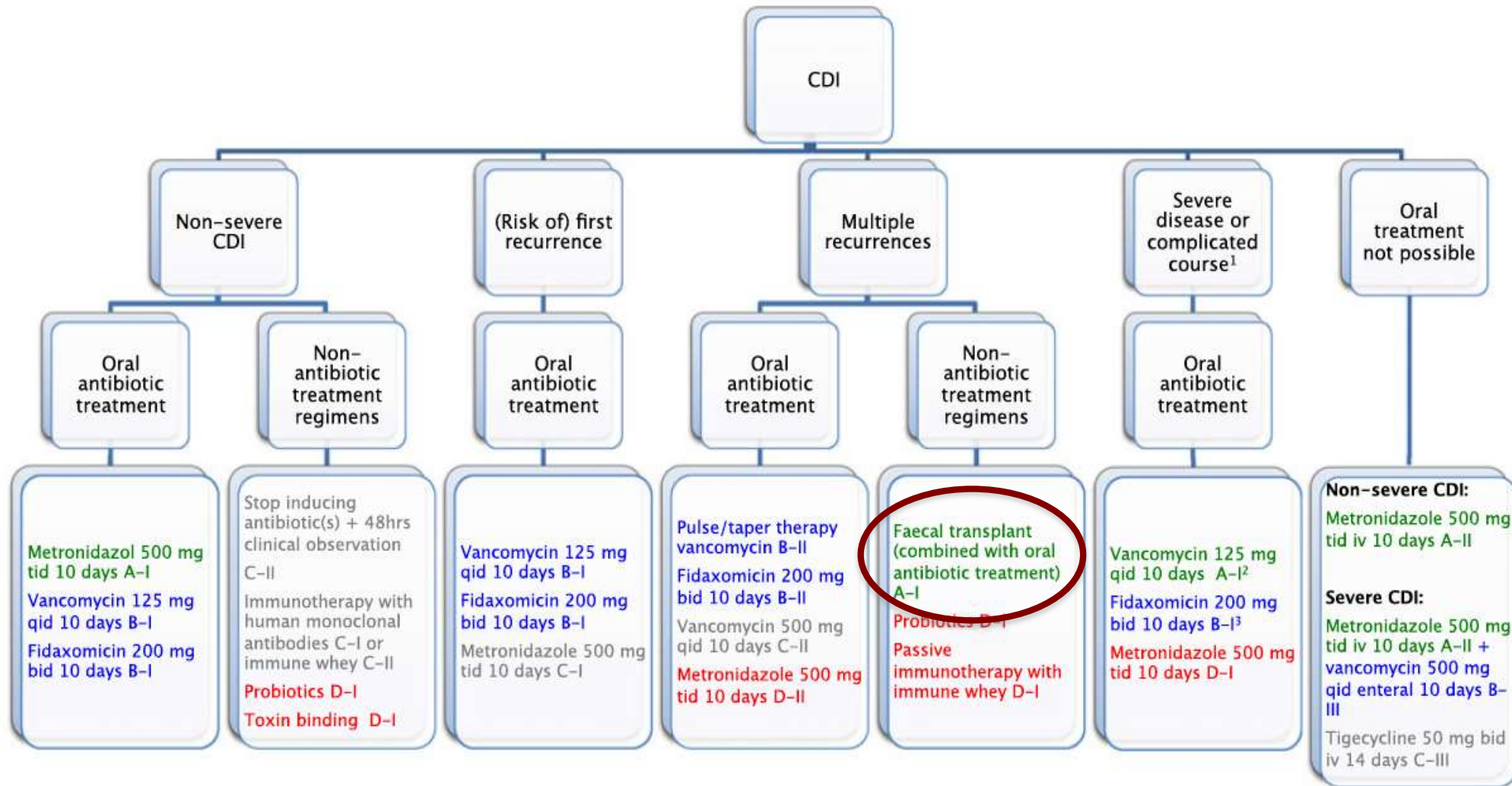
VOL. 368 NO. 5

Duodenal Infusion of Donor Feces for Recurrent *Clostridium difficile*

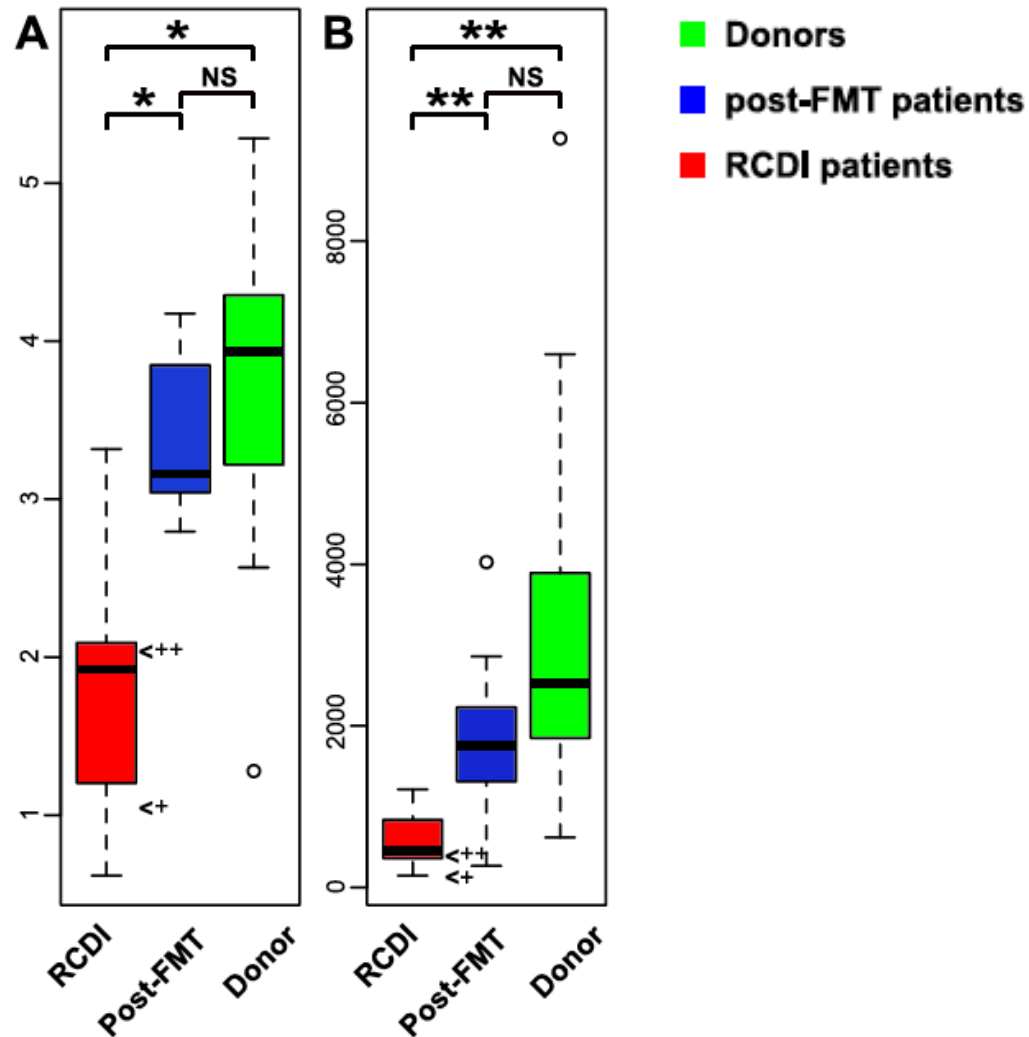
The study was stopped
after an interim analysis !



European Guidelines - 2014



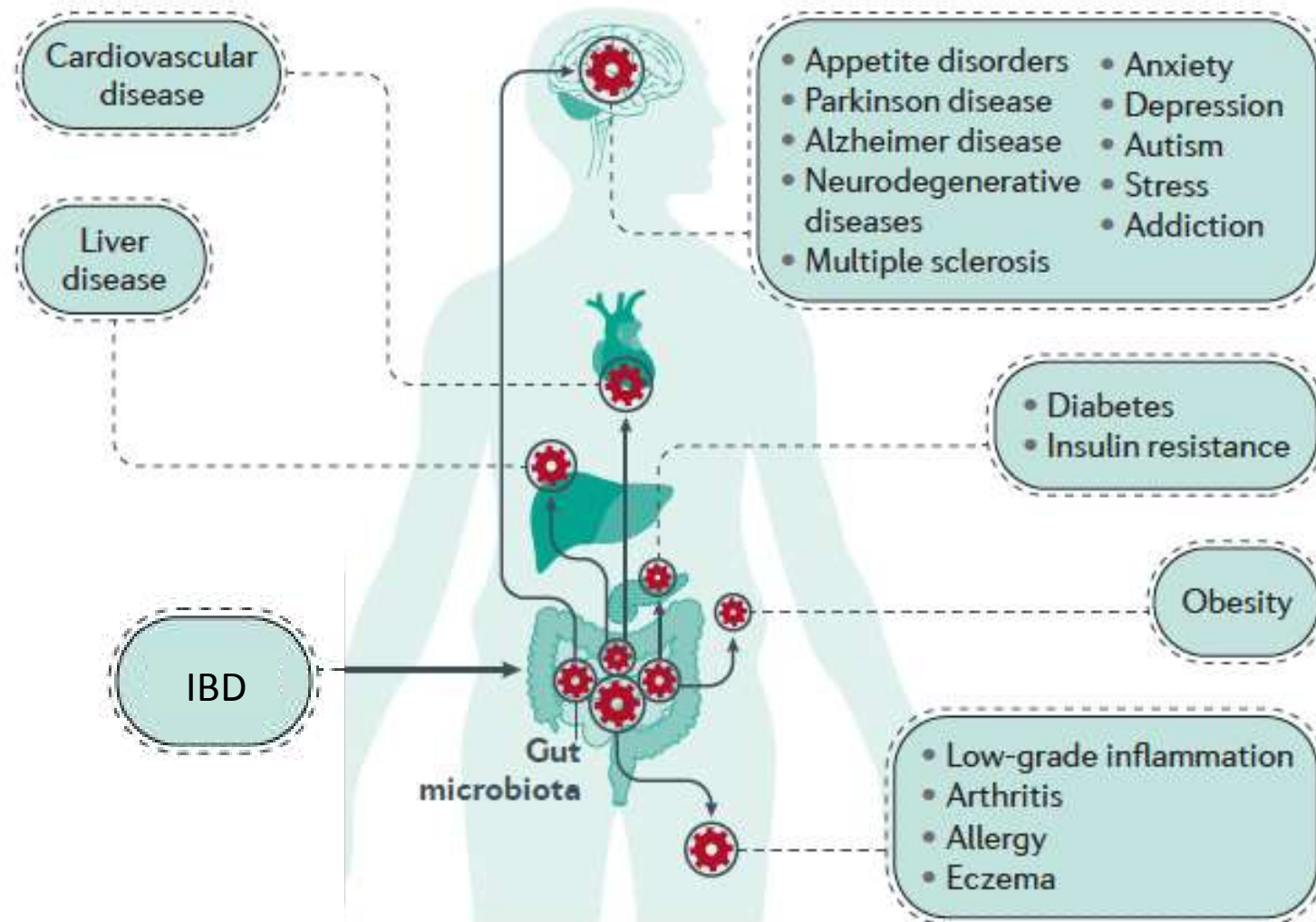
Le principe: restaurer la diversité du microbiote intestinal



Autres mécanismes hypothétiques

- Compétition pour les éléments nutritifs
- Suppression directe par des peptides antimicrobiens
- Inhibition de la germination des spores médiée par les acides biliaires
- Activation de la résistance à la colonisation médiée par le système immunitaire

Gut dysbiosis is widespread in many conditions!



Ulcerative colitis: 3 RCT

(1) 75 patients FMT (50 mL enema, unrelated healthy donor) or placebo (50 mL water enema) once weekly for 6 weeks

-> clinical and endoscopic remission at 7 weeks (24% vs. 5%)

-> Donor effect: 7/9 patients in remission after FMT received fecal material from a single donor.

(2) 48 patients FMT (via nasogastric tube, healthy donor) or placebo (autologous fecal microbiota) at 0 and 3 weeks

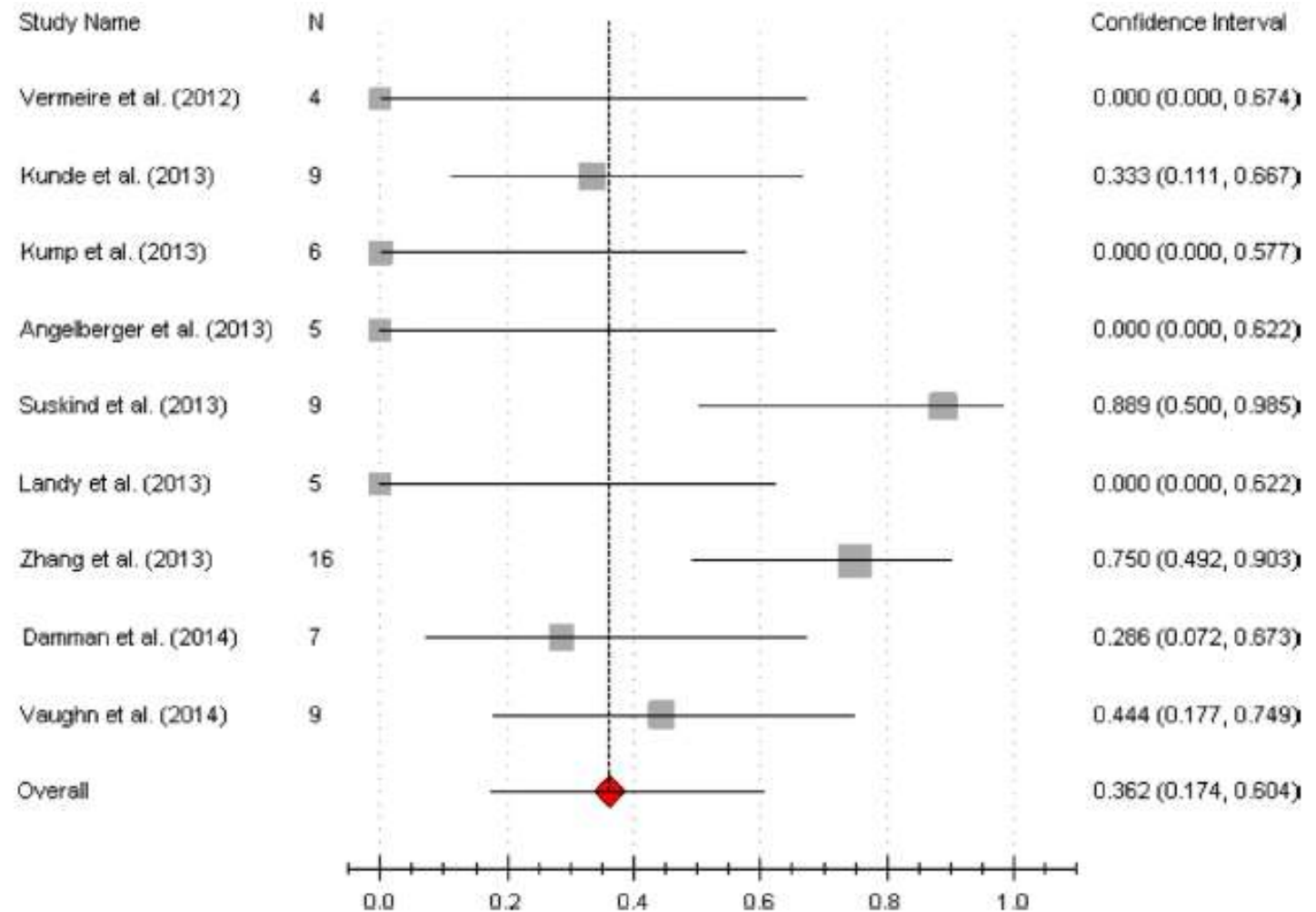
-> No statistically significant difference in remission at 12 weeks (30% vs. 20%)

(3) 85 patients FMT (150 mL enema, blended stool from 3 to 7 unrelated donors) or placebo (150 mL enema) 5 days per week for 8 weeks

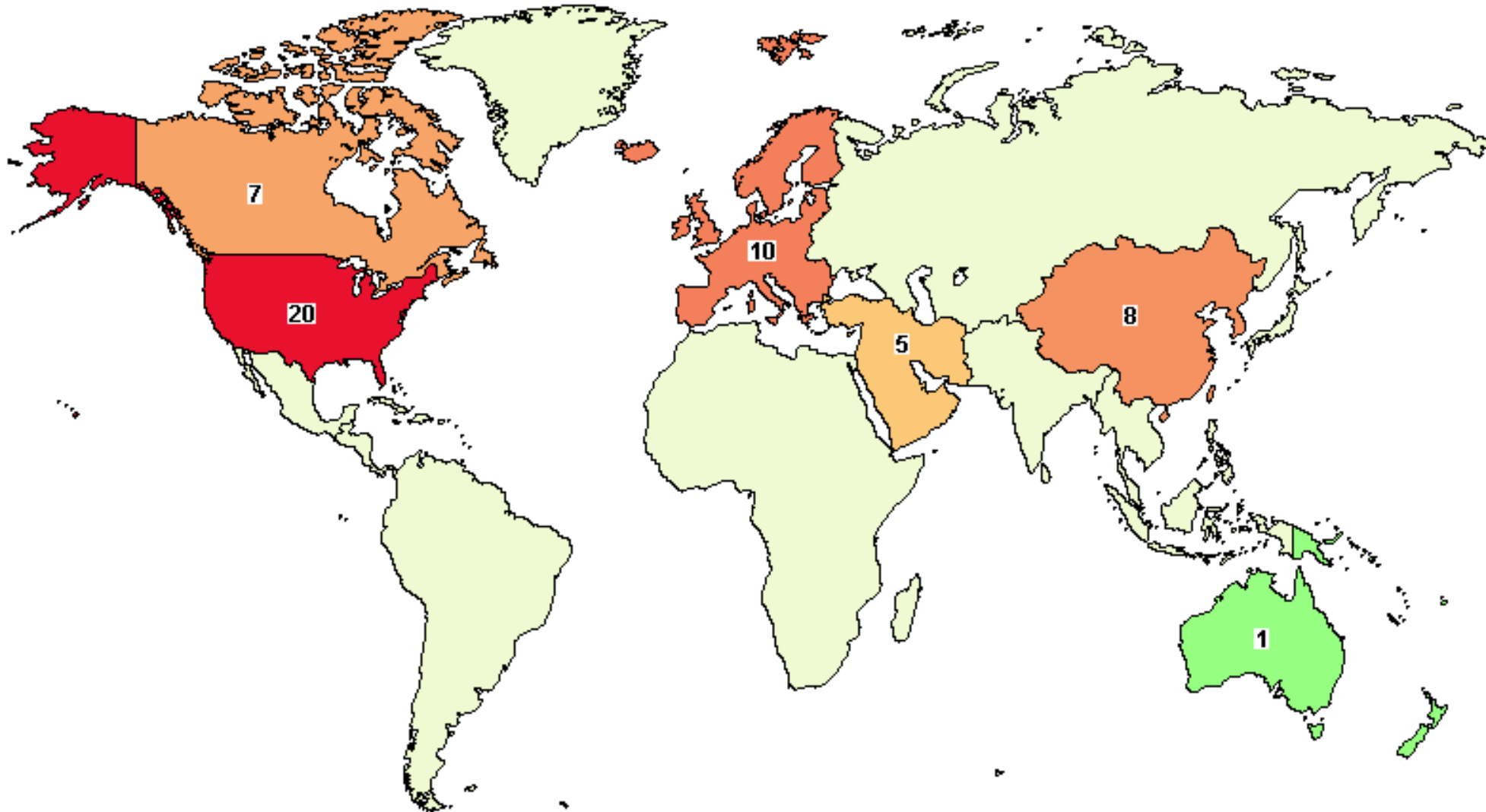
-> clinical (steroid-free) and endoscopic remission at 8 weeks (27% vs. 8%)

Crohn: Meta-Analysis of cohort studies

Overall pooled estimate of clinical remission of 36.2% (95% CI 17.4%-60.4%)



51 ongoing clinical trials (FMT for IBD)...



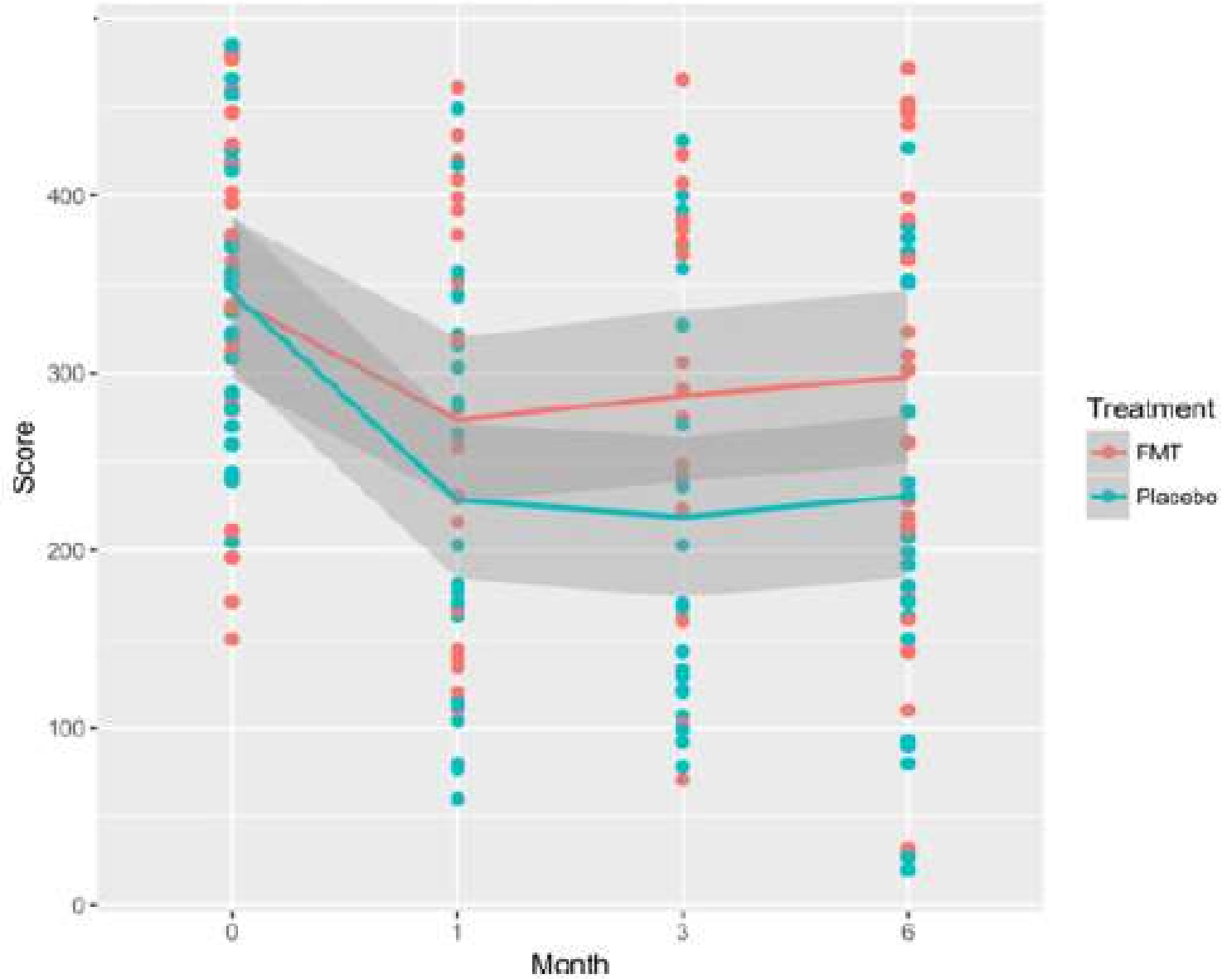
IBS

- 90 participants and randomly assigned them to active treatment (n=60) or placebo (i.e. patient own faeces: n=30)
- Response at 3 months after FMT:
 - 36 (**65%**) of 55 active treatment group vs 12 (**43%**) of 28 placebo group (p=0,049)
- Response at 12 months after FMT:
 - 31 (**56%**) of 55 active treatment group vs ten (**36%**) of 28 placebo group (p=0,075)

Faecal microbiota transplantation alters gut microbiota in patients with irritable bowel syndrome: results from a randomised, double-blind placebo-controlled study

Sofie Ingdam Halkjær,¹ Alice Højer Christensen,² Bobby Zhao Sheng Lo,¹ Patrick Denis Browne,³ Stig Günther,² Lars Hestbjerg Hansen,³ Andreas Munk Petersen¹

Change in IBS Symptom Severity Score



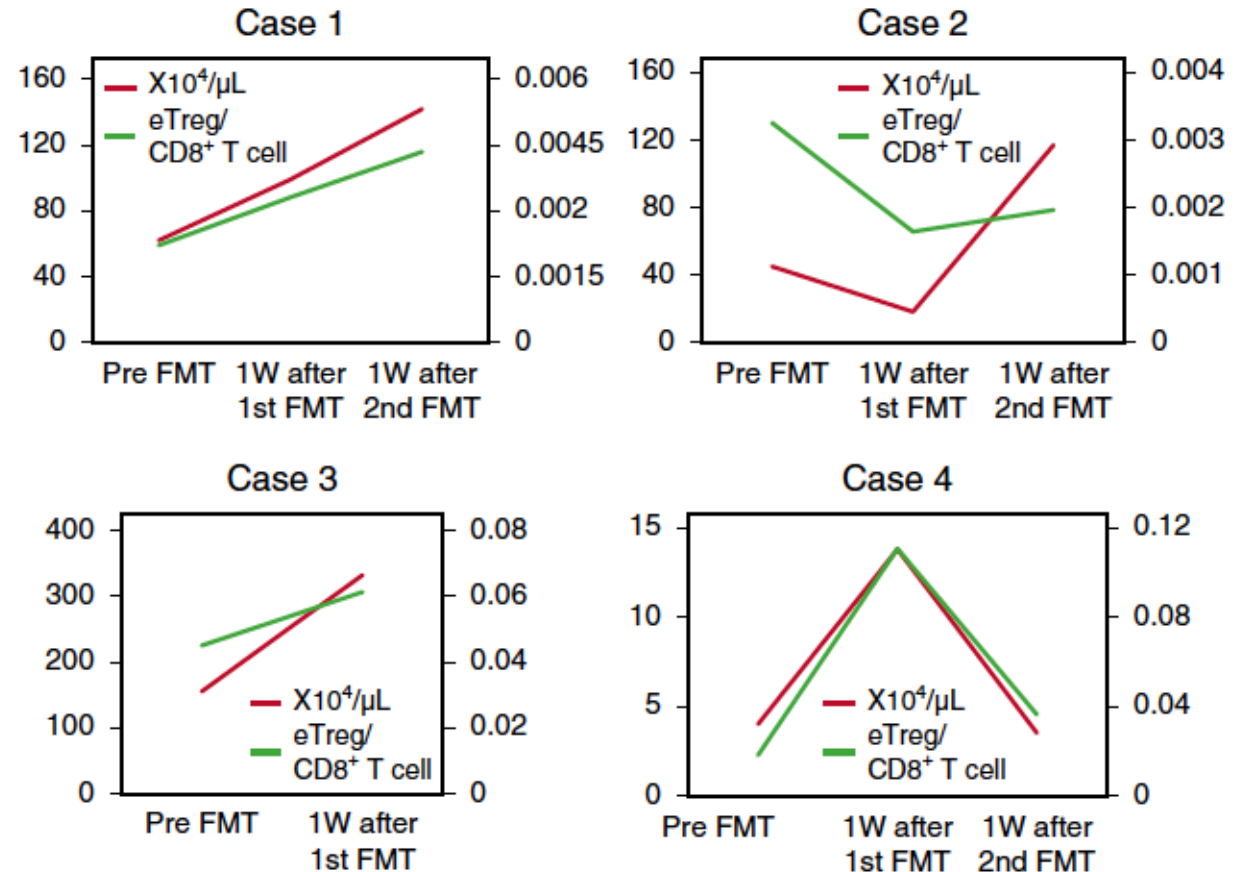
Fecal microbiota transplantation for patients with steroid-resistant acute graft-versus-host disease of the gut

Kazuhiko Kakihana,^{1,*} Yuki Fujioka,^{2,3,*} Wataru Suda,^{4,5,*} Yuho Najima,¹ Go Kuwata,⁶ Satoshi Sasajima,⁷ Iyo Mimura,⁸ Hidetoshi Morita,⁸ Daisuke Sugiyama,² Hiroyoshi Nishikawa,² Masahira Hattori,^{4,9} Yutaro Hino,¹ Shuntaro Ikegawa,¹ Keita Yamamoto,¹ Takashi Toya,¹⁰ Noriko Doki,¹ Koichi Koizumi,⁶ Kenya Honda,^{5,7,11} and Kazuteru Ohashi¹

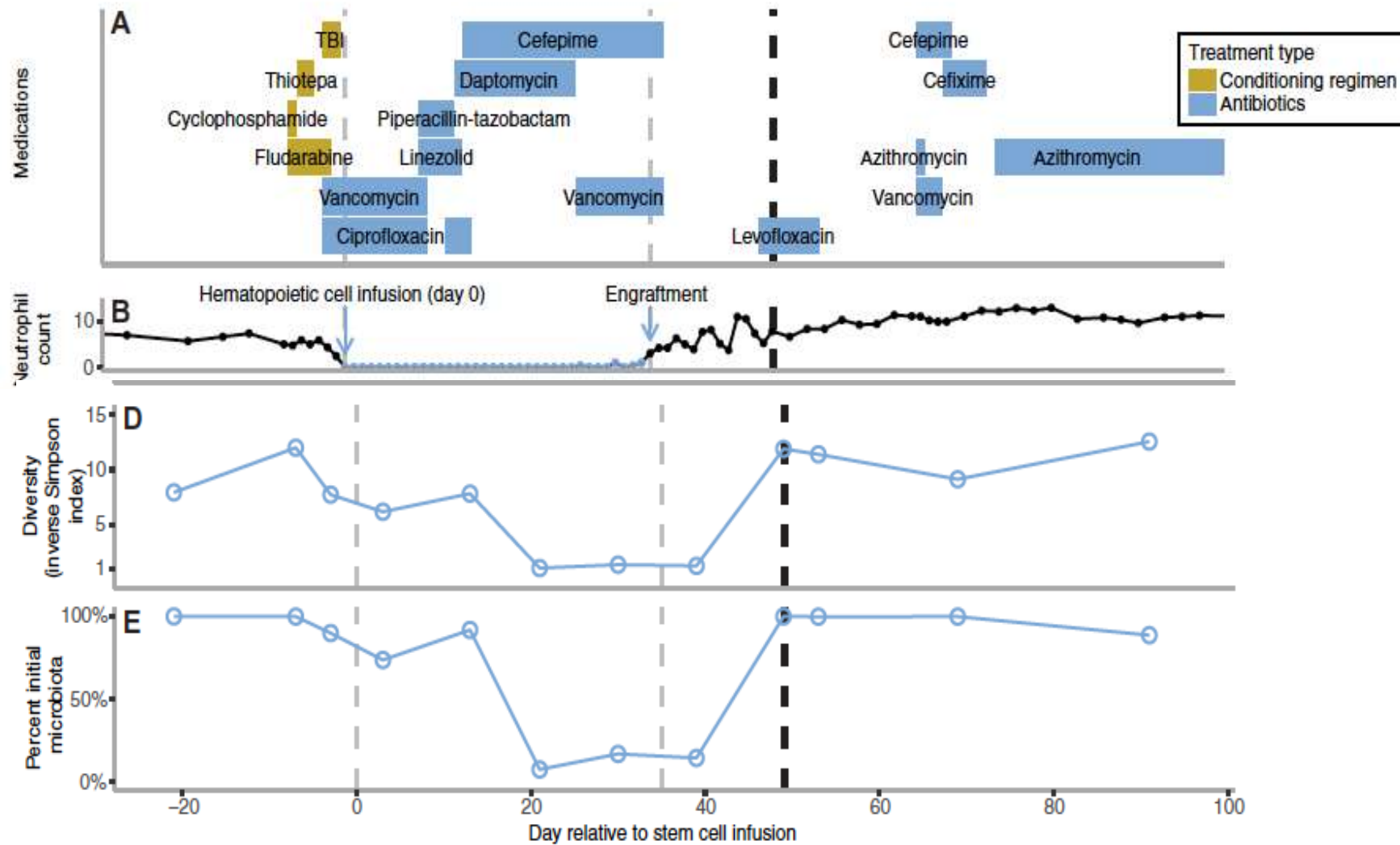
4 patients with steroid-resistant/dependent gut aGVHD received FMT

All patients responded to FMT, with 3 complete responses and 1 partial response

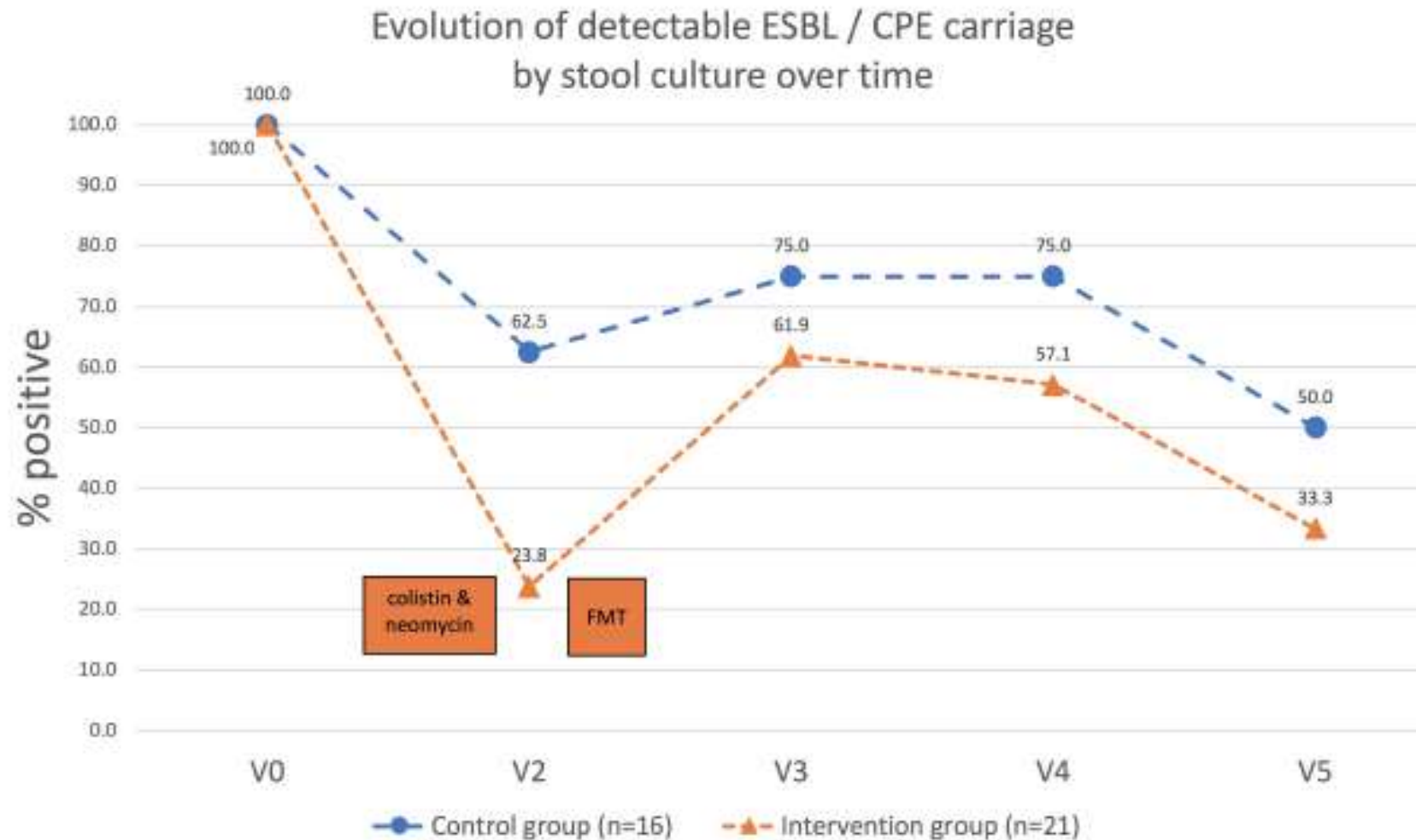
No severe adverse events attributed to FMT were observed.



Reconstitution of the gut microbiota of AB-treated patients by autologous FMT in HSCT



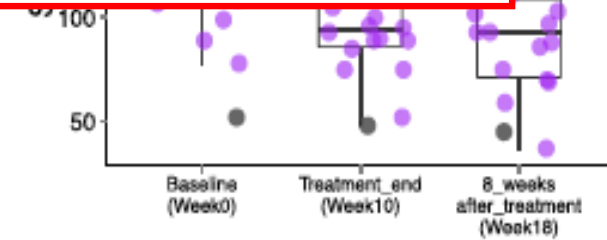
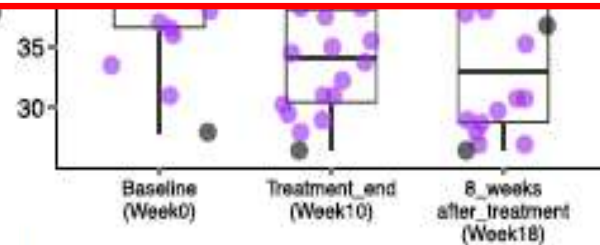
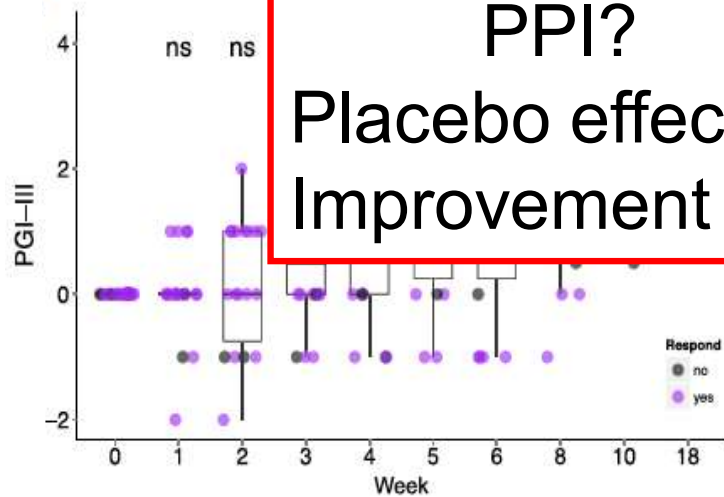
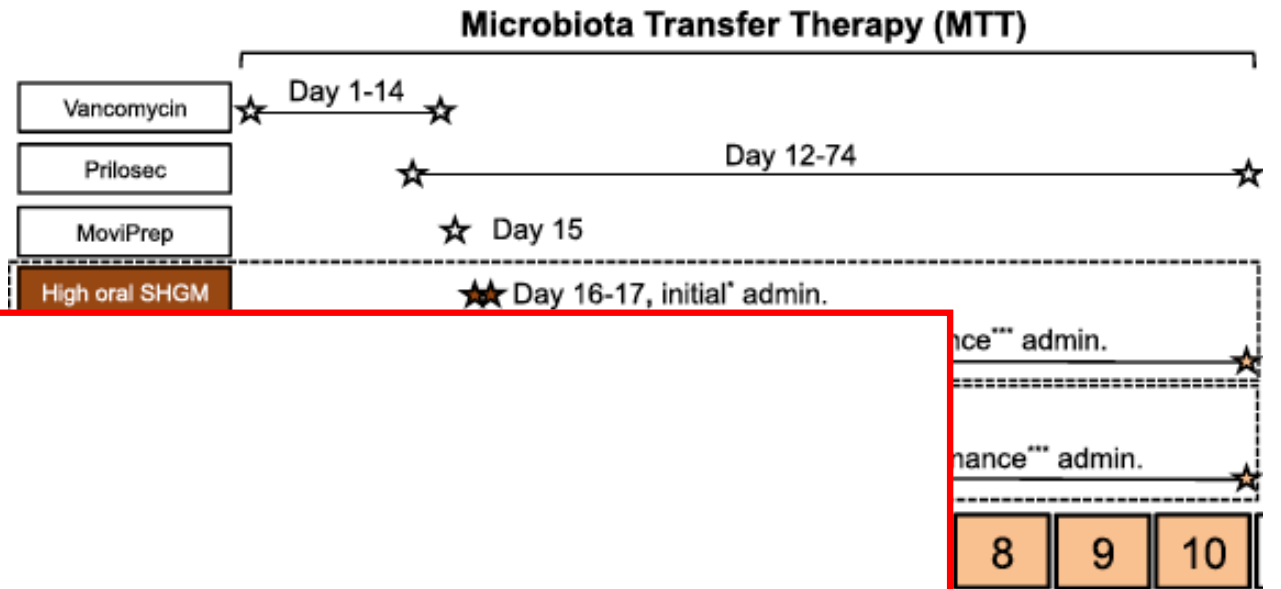
Eradication BMR (R-GNOSIS)



Autism: 1 open study

18 children (7-16 yrs)
 Autism + GI symptoms
 Treatment
 Follow-up

Effect of
 Vancomycin?
 Initial dose?
 Maintenance dose?
 PPI?
 Placebo effect?
 Improvement of GI symptoms?



8 9 10

Epilepsy



*World Journal of
Gastroenterology*

Fecal microbiota transplantation cured epilepsy in a case with Crohn's disease: The first report

Zhi He, Bo-Ta Cui, Ting Zhang, Pan Li, Chu-Yan Long, Guo-Zhong Ji, Fa-Ming Zhang

22-year-old girl, with a 17-year history of epilepsy

FMT x 3 (Trial: NCT01793831)

Donor = primary school girl

During the 20 months of follow-up, FMT has proved its efficacy in preventing relapse of seizures after withdrawing the antiepileptic drugs

CASE REPORT | COLON

Hair Growth in Two Alopecia Patients after Fecal Microbiota Transplant

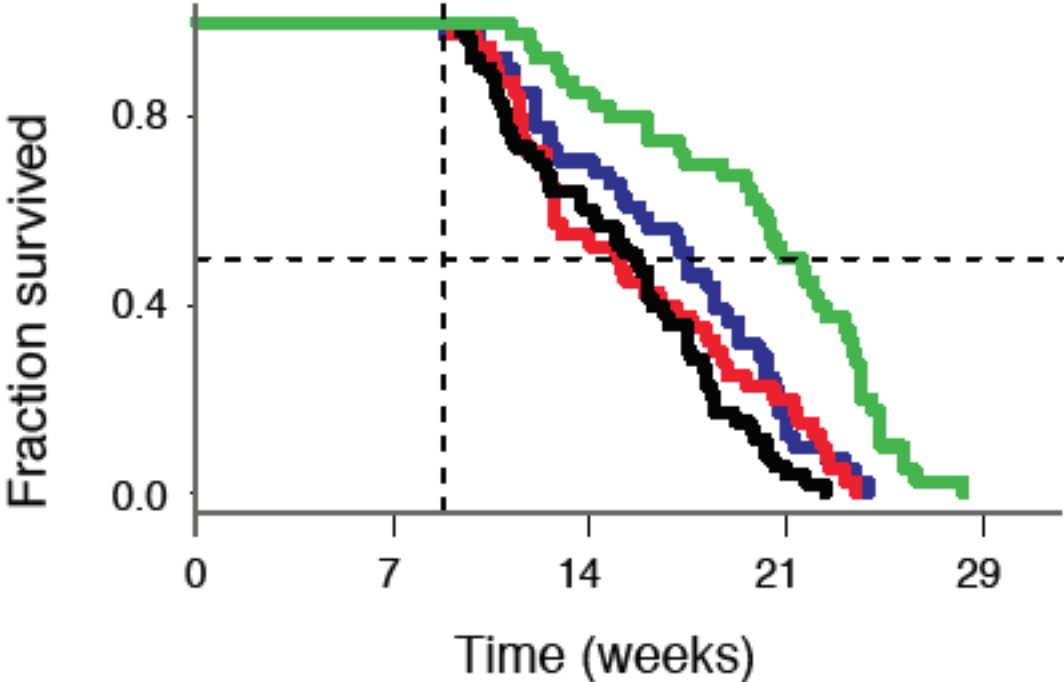
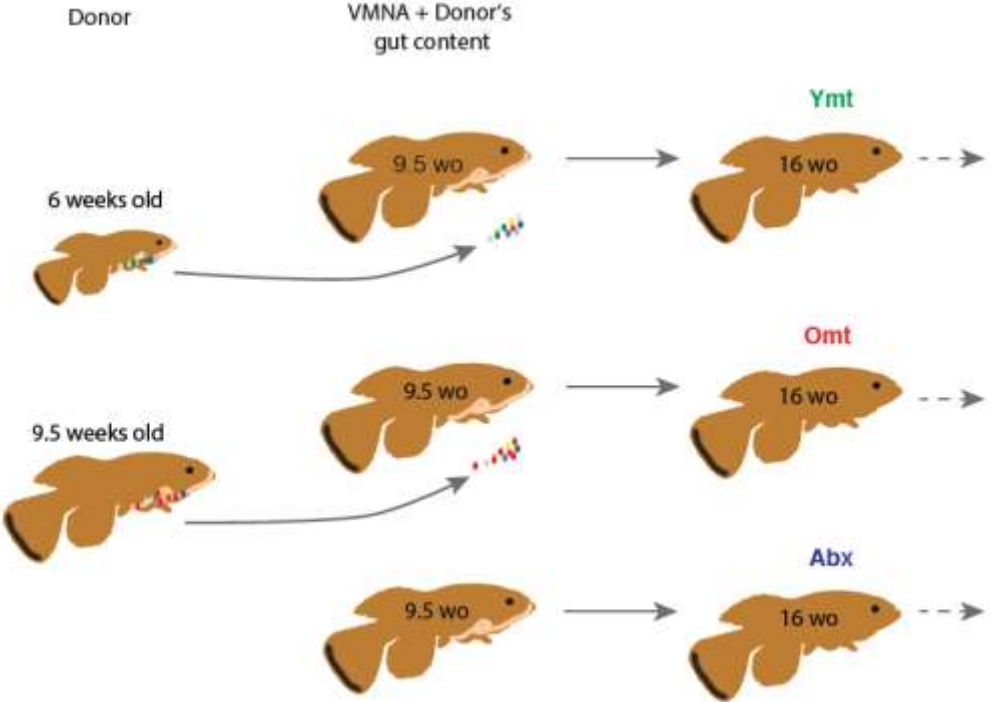
Dionne Rebello, MD¹, Elaina Wang, BS¹, Eugene Yen, MD³, Peter A. Lio, MD⁴, and Colleen R. Kelly, MD, FACG^{1,2}



Many ongoing clinical trials

- IBD: 51
- IBS: 11
- Metabolic diseases: 8
- Obesity: 7
- Liver diseases: 7
- Brain diseases: 5
- ...

The quest for the holy grail!!!!

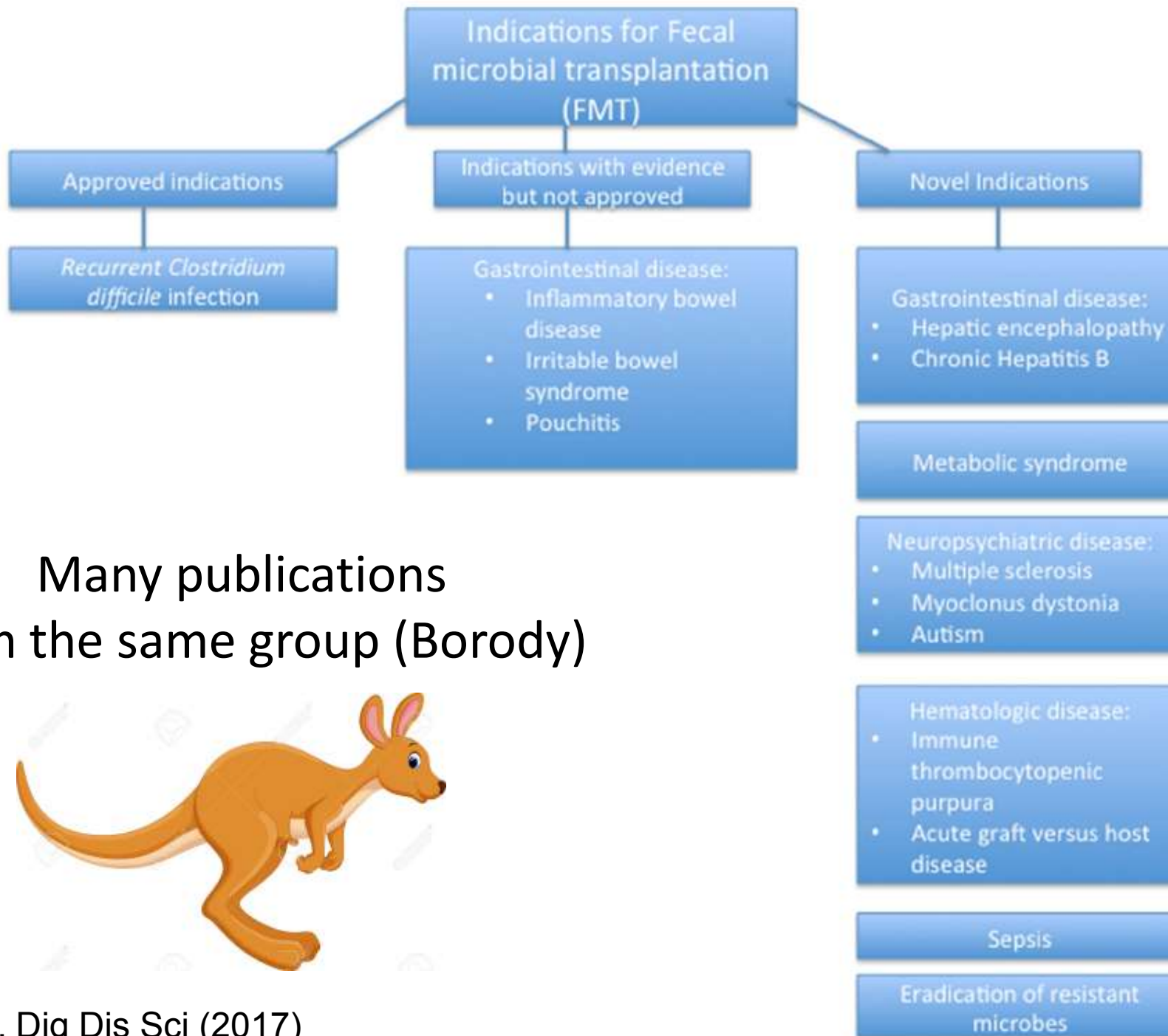


Median lifespan was 41% longer



"Prediction is very difficult, especially if it's about the future "

Nils Bohr (1885-1962)
Nobel laureate in Physics



Many publications
from the same group (Borody)



FMT

Are you a super pooper?

Posted on January 23, 2019 in Featured News, Health

- Multiple
- Donor s
 - Rich
 - Bact
 - Micro
 - SCFA
 - ...
- Donor I
- Recipe



Stool transplants from 'super donors' have high success rates in trials for conditions like IBD and type 2 diabetes. Image: Shutterstock.

Gastroenterol, 2017



Monocytes
ungi
Metabolites, Protists, Other
14(7): e1002503

TMF Koala

