UNIVERSITY OF COPENHAGEN

Amager og Hvidovre Hospital

Microhealth

Aleris Hamlet

Inflammatory bowel disease (IBD) and the gut microbiota – An overview

-Correlation between gut dysbiosis and inflammatory bowel disease

-Current knowledge from trials changing the gut microbiota through Fecal Microbiota Transplantation (FMT)

-Where do we go from here?

Contact:
Frederik Cold, MD, PhD-student
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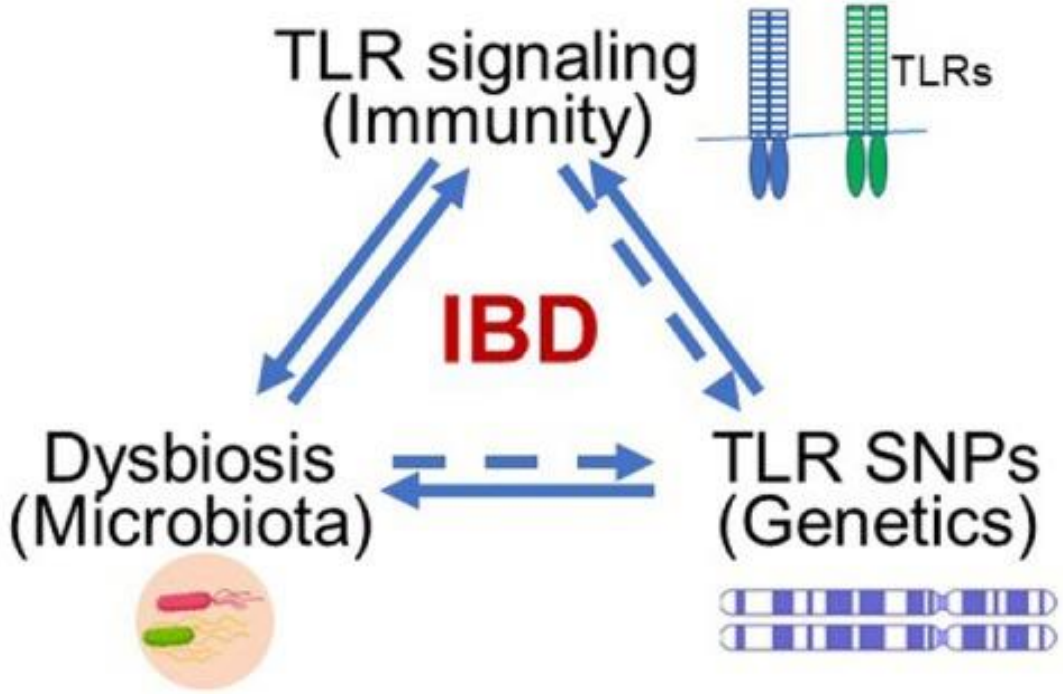
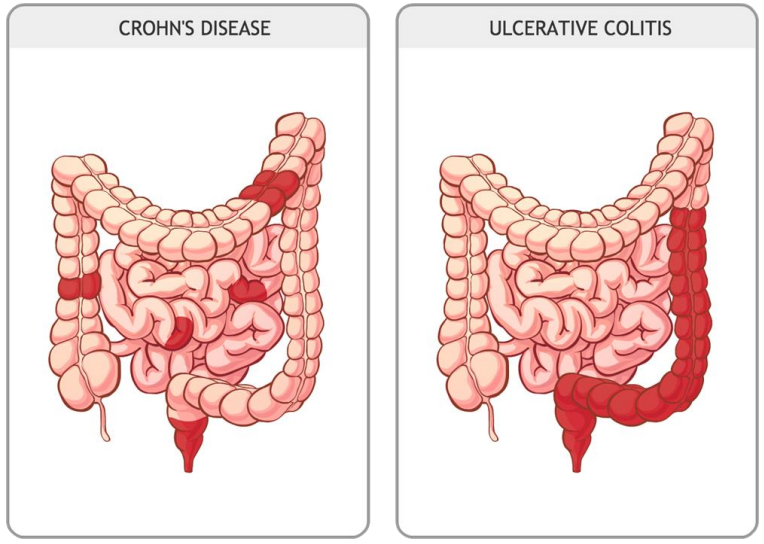
Inflammatory Bowel Disease (IBD)

-Ulcerative Colitis
-Mb Crohn

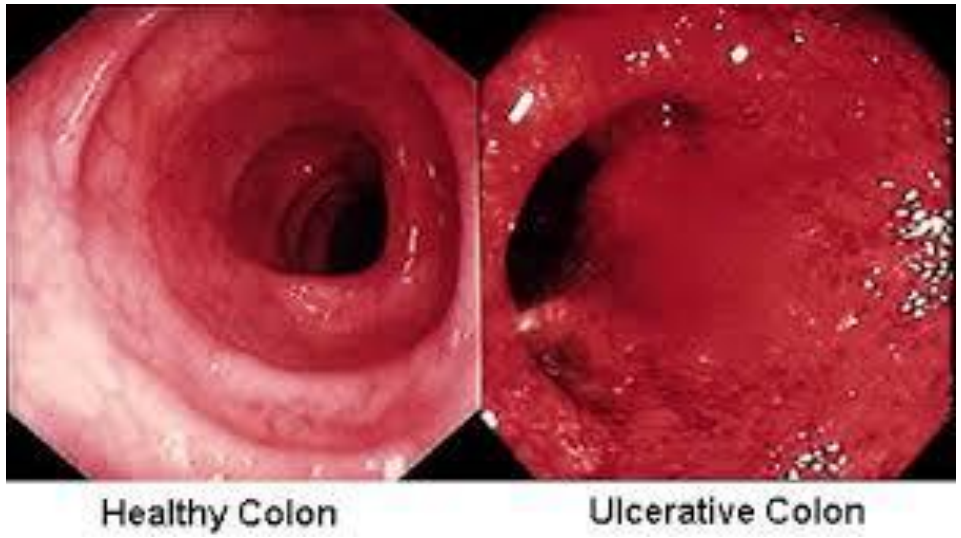
-Etiology: Environmental, genetic, and microbial factors

-Incidence is increasing





NG et al, 2018, Lancet



Lu et al, 2018, Front Immunol

Gut microbiota and IBD

-Decreased microbial diversity
-Changed composition of bacteria
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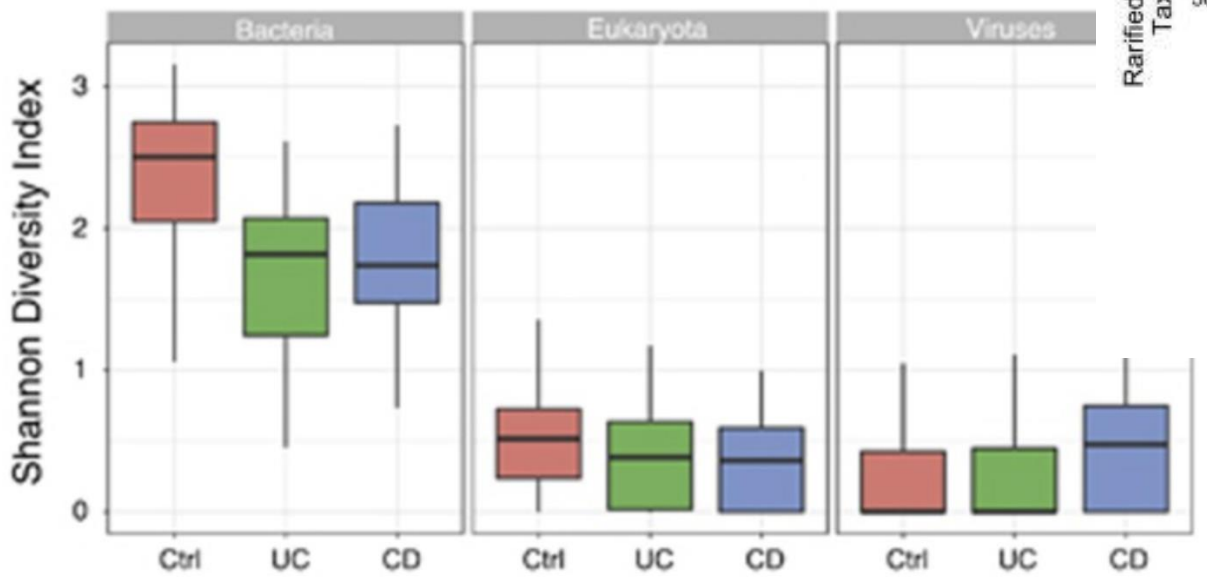
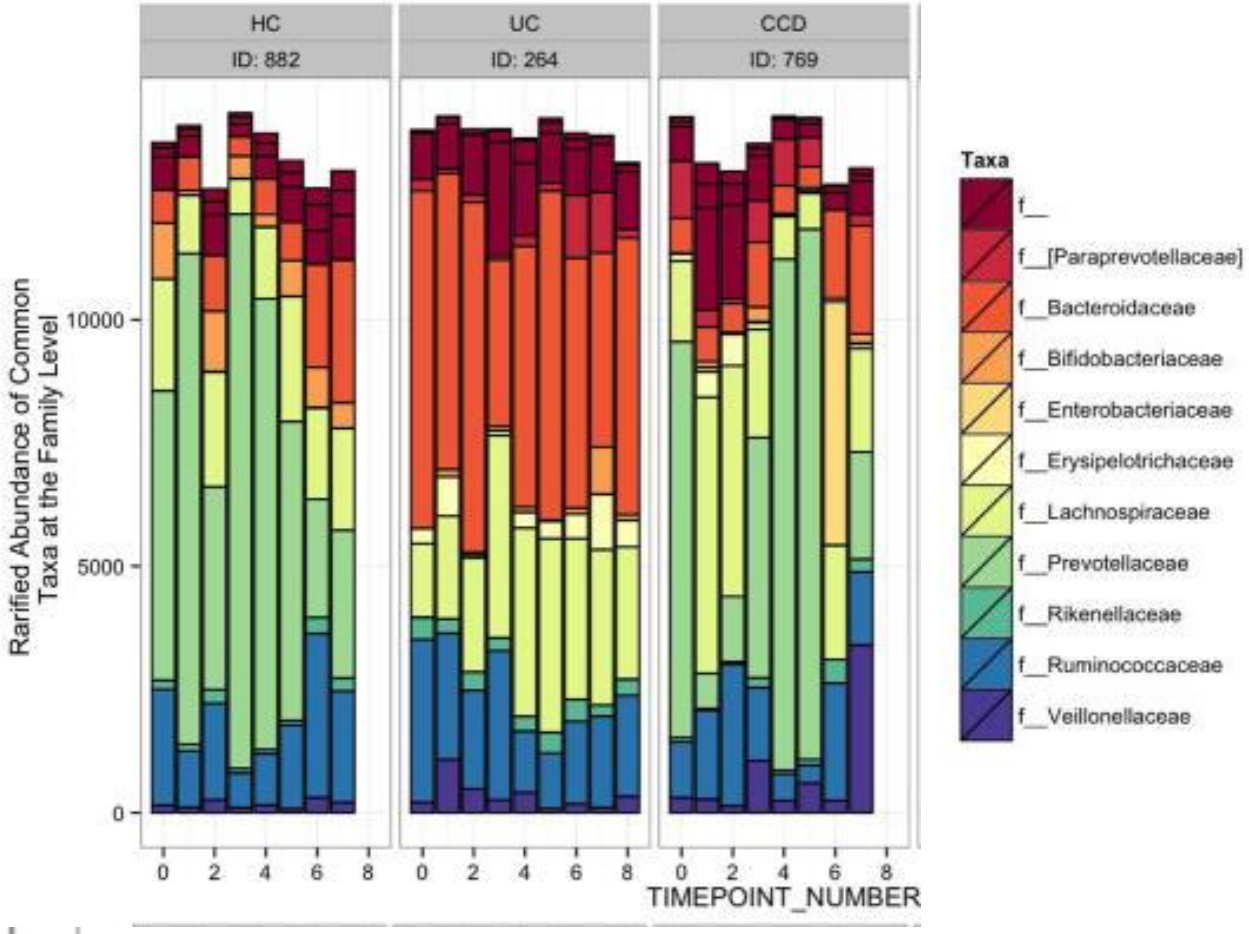


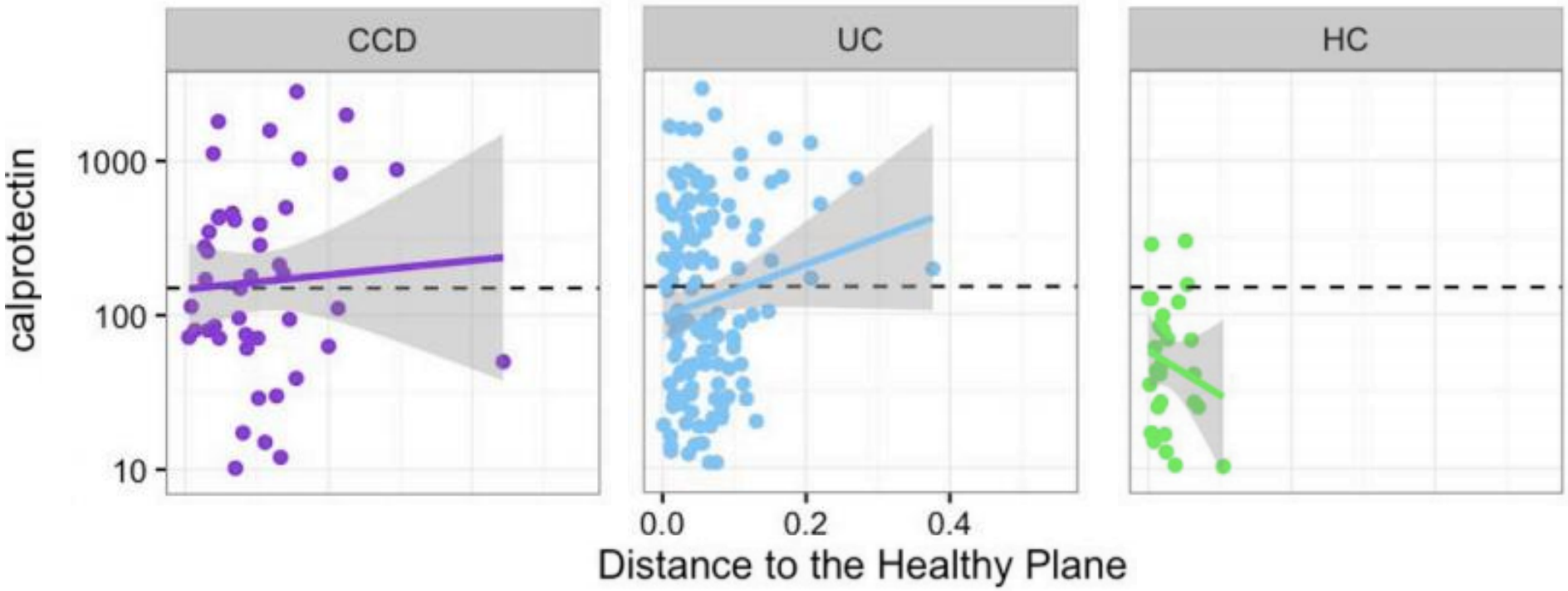


Moustafa et al, 2017, Clin Trans Gastroenterol

Halfvarson et al, 2017, Nat Microbiol

Gut microbiota and IBD

-Changes according to disease activity and treatment



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The effects of FMT in IBD

-Increased diversity
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-Multidonor FMT better than single donor FMT
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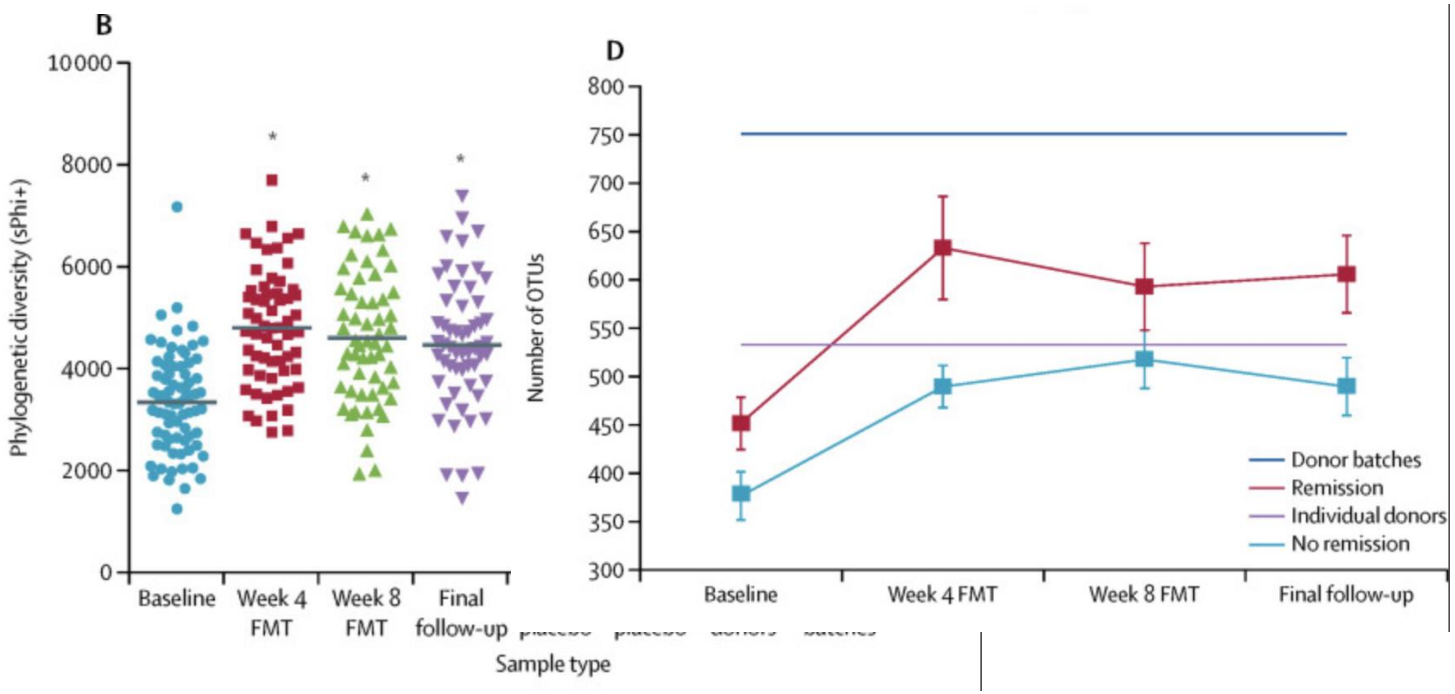


Paramsothy S, et al. Lancet 2017; 389:1218 1228

Effects of FMT on Ulcerative Colitis

-Remission of symptoms (25%)
-Improves symptoms (50%)

Study or Subgroup	Donor transplant Events	Total	Placebo Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Year
Rossen 2015	7	23	5	25	28.2%	1.75 (0.47, 6.57)	2015
Moayyedi 2015	9	38	2	37	19.0%	5.43 (1.09, 27.15)	2015
Paramsothy 2017	11	41	3	40	26.5%	4.52 (1.16, 17.70)	2017
Costello 2017	12	38	3	35	26.4%	4.92 (1.25, 19.31)	2017
Total (95% CI)		140		137	100.0%	3.67 (1.82, 7.39)	
Total events	39		13				

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.70$, df = 3 (P=.64); $I^2 = 0\%$
Test for overall effect: $Z = 3.63$ (P=.0003)

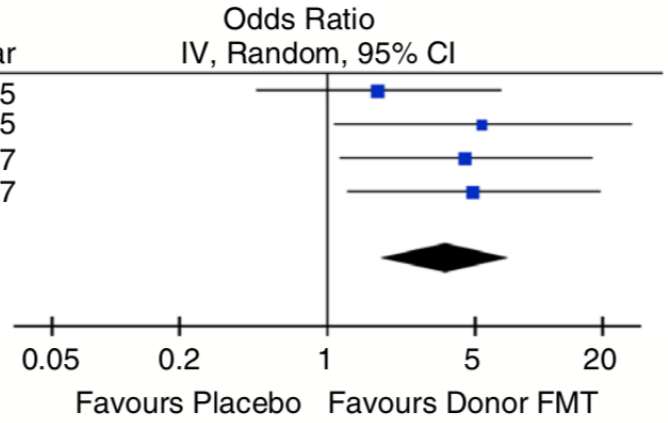


FIGURE 2 Forest plot for remission in randomised controlled trials of faecal microbiota transplant (FMT) for ulcerative colitis. Remission was variably defined as per Table 3

Study or Subgroup	Donor FMT Events	Total	Placebo Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Rossen 2015	11	23	13	25	22.7%	0.85 (0.27, 2.63)
Moayyedi 2015	15	38	9	37	25.9%	2.03 (0.75, 5.48)
Paramsothy 2017	22	41	9	40	26.7%	3.99 (1.52, 10.45)
Costello 2017	21	38	7	35	24.7%	4.94 (1.74, 14.07)
Total (95% CI)		140		137	100.0%	2.48 (1.18, 5.21)
Total events	69		38			

Heterogeneity: $\tau^2 = 0.30$; $\chi^2 = 6.21$, df = 3 (P=.10); $I^2 = 52\%$
Test for overall effect: $Z = 2.40$ (P=.02)

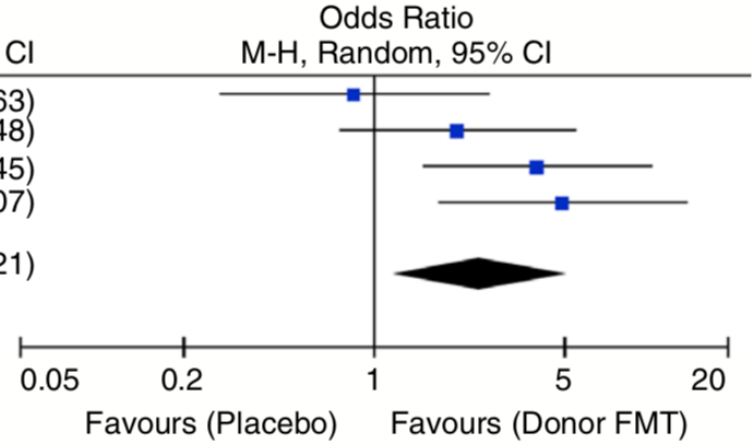
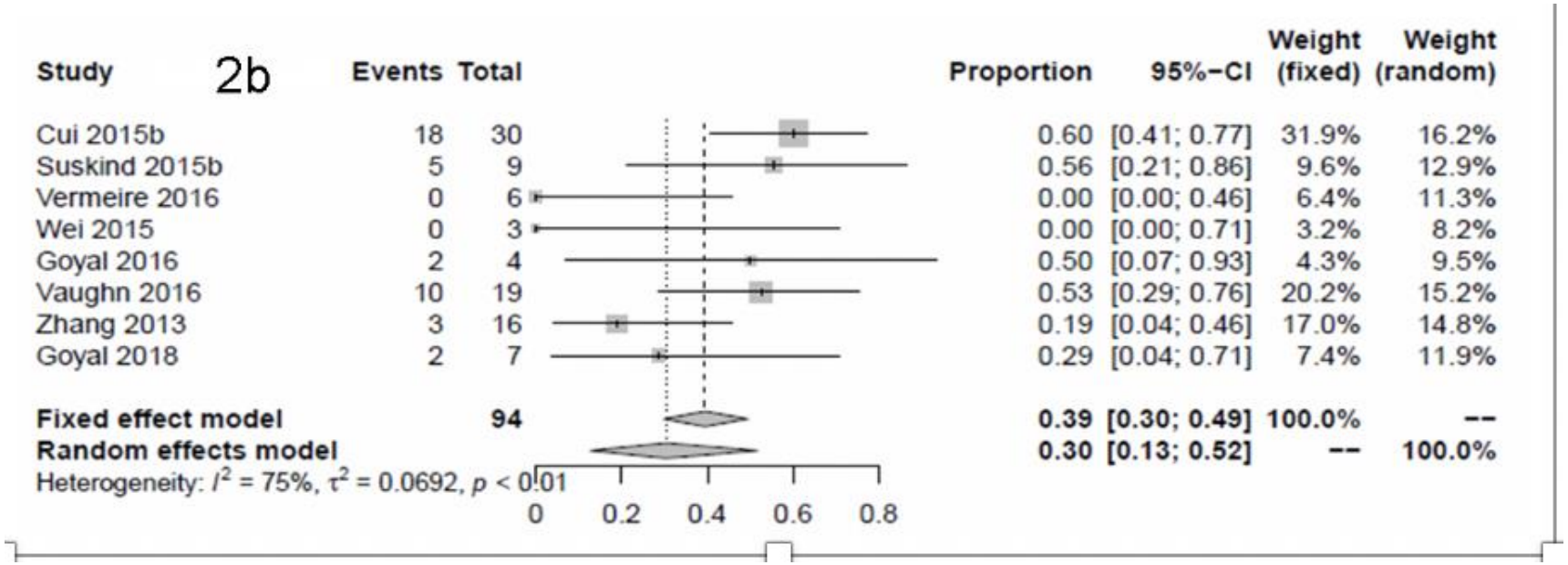


FIGURE 3 Forest plot for clinical response in randomised controlled trials of faecal microbiota transplant (FMT) for ulcerative colitis. Clinical response variably defined as per Table 3

Costello et al, 2017, Aliment Pharmacol Ther.

Effects of FMT on Mb Crohn

-No randomized trials
-Case-studies indicates good response



Fang et al, 2018, Biomed Res Int.

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Microhealth

Aleris Hamlet

Experiences with FMT Capsules from Aleris-Hamlet Hospitals

Open-label Pilot study:

-Seven patients with active Ulcerative Colitis

-A daily dose of 25 multidonor capsules for 50 days

-180 days follow-up

Amager og Hvidovre Hospital

Participants

-Seven patients with active disease

- Simple Clinical Colitis Activity Index (SCCAI) between 4 and 10

- Fecal calprotectin >250 mg/kg

Baseline table	
Variable	
Participants, n	7
Age, median, years [range]	38 [27-51]
Gender, n	Male (5), Female (2)
Disease duration, median, years [range]	9 [5-20]
Current concomitant medication:	
Systemic 5-asa, n [%]	3 [43%]
Systemic and local 5-asa, n [%]	2 [29%]
Local 5-asa, n [%]	1 [14%]
None, n [%]	1 [14%]
Earlier treatment:	
Corticosteroids, n [%]	3 [43%]
Corticosteroids, thiopurines and biological treatment, n [%]	3 [43%]
Corticosteroids and thiopurines, n [%]	1 [14%]
Disease extension at last colonoscopy:	
Pancolitis, n [%]	3 [43%]
Left-sided colitis, n [%]	2 [29%]
Proctosigmoiditis, n [%]	1 [14%]
Rectal, n [%]	1 [14%]

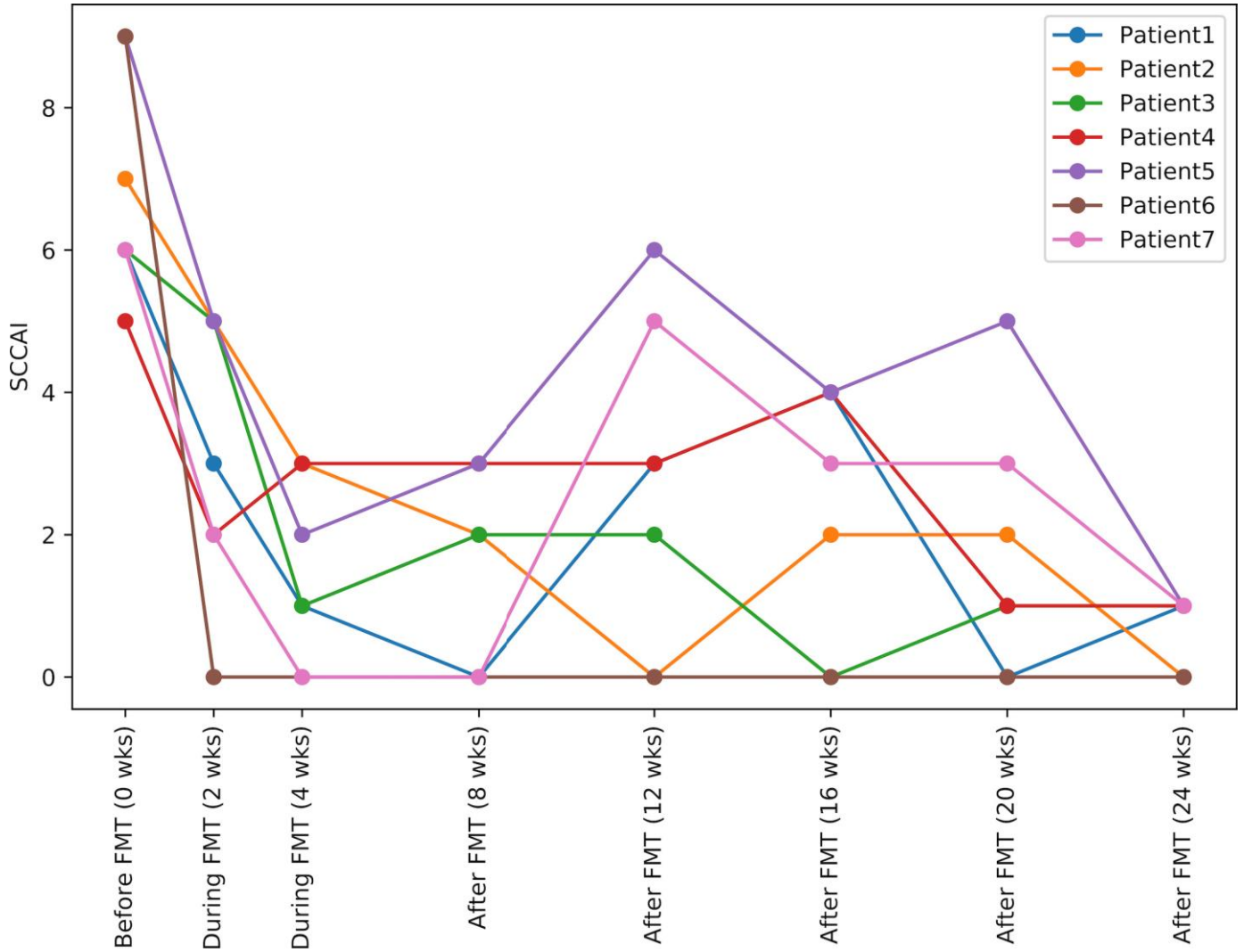
Cold et al, 2019, Scand J Gasteroenterol

Effects of FMT capsules on symptoms

-All participants experienced beneficial effects after four and eight weeks

-Three of the seven participants experienced flare-up/relapse after the treatment period

Symptom	Score
Bowel frequency (day)	
1-3	0
4-6	1
7-9	2
>9	3
Bowel frequency (night)	
1-3	1
4-6	2
Urgency of defecation	
Hurry	1
Immediately	2
Incontinence	3
Blood in stool	
Trace	1
Occasionally frank	2
Usually frank	3
General Well Being	
Very well	0
Slightly below par	1
Poor	2
Very poor	3
Terrible	4
Extracolonic features	1 point per manifestation



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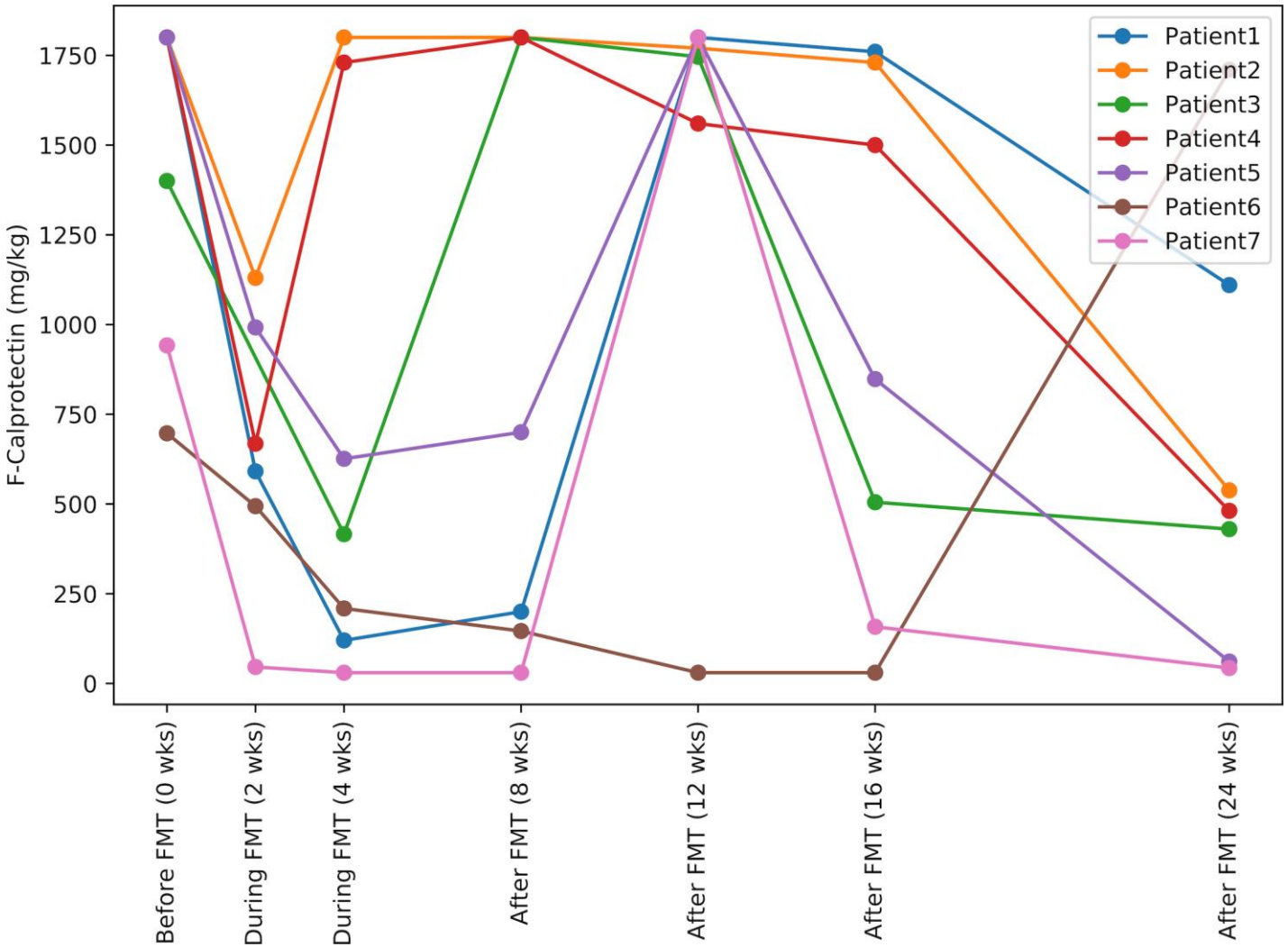
-Increased to baseline levels after twelve weeks



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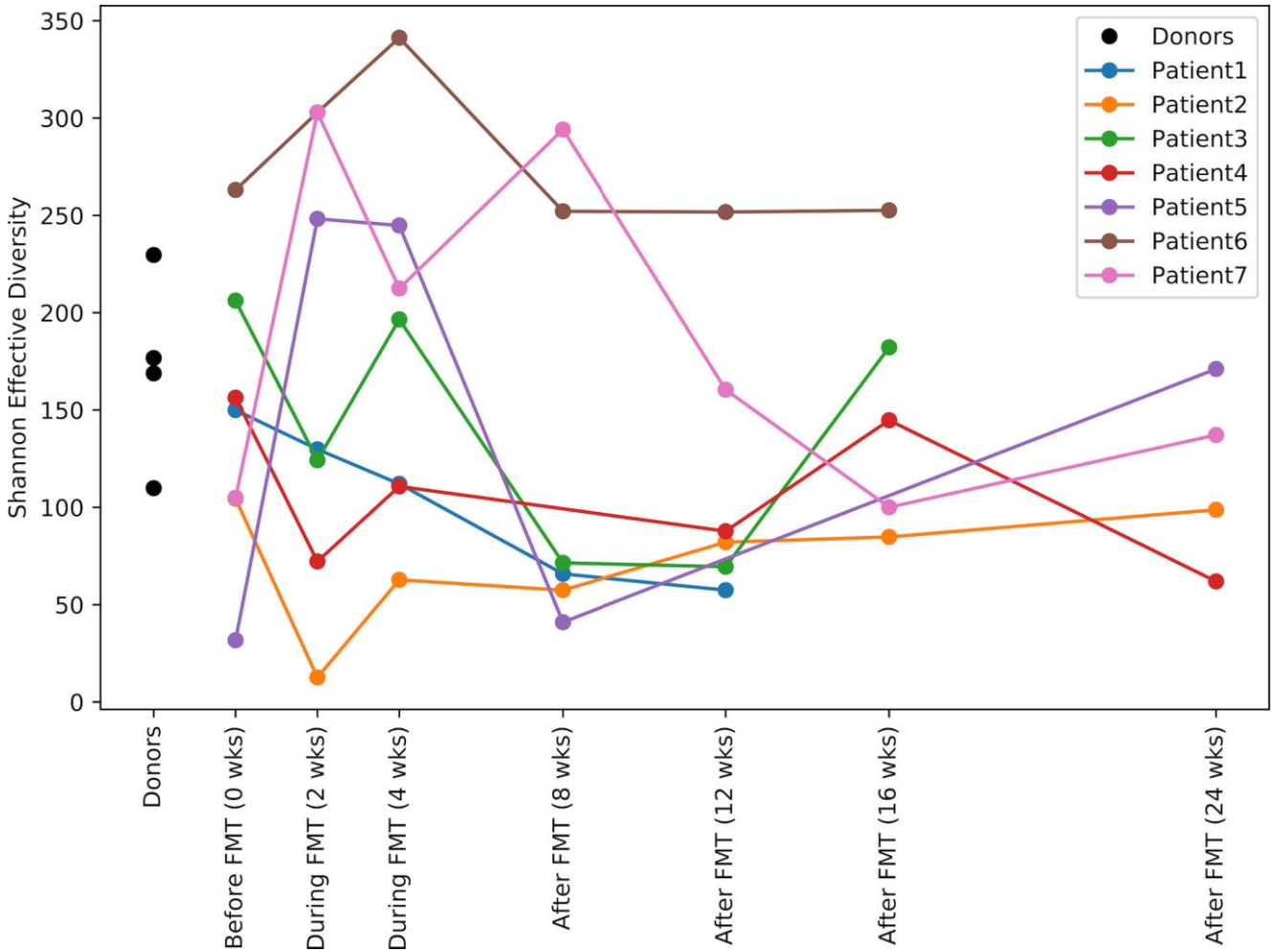
Effects of FMT capsules on fecal bacterial diversity

-Alpha-diversity surprisingly did not increase in the treatment period



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Inflammatory bowel diseases and the gut microbiota

-Correlation between gut dysbiosis and inflammatory bowel disease

-FMT seems to improves symptoms in Ulcerative Colitis, but the effects in Mb Crohn is poorly investigated

-Where do we go from here?

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Microhealth trial

-80 patients with UC randomized (1/1) to either 28 days of treatment with FMT Capsules or Placebo. ***First randomized clinical trial with FMT capsules***

-Six months follow up. ***Long term follow up***

Amager og Hvidovre Hospital

Microhealth trial

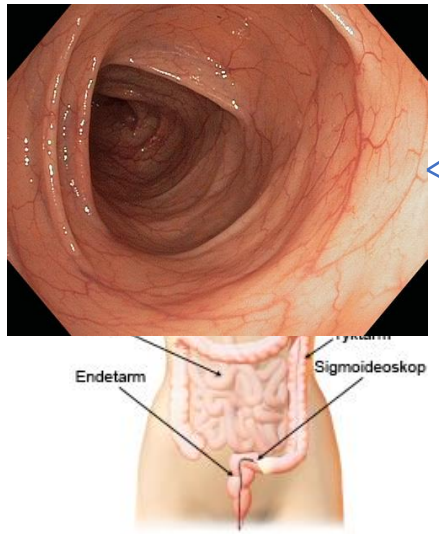
Screening visit (visit 1) 1-4 weeks prior to enrollment

80 participants with active Ulcerative Colitis

	40 participants FMT group	40 participants Placebo group
Baseline (visit 2)	Sigmoidoscopy, symptomscore, blood and fecal samples	Sigmoidoscopy, symptomscore, blood and fecal samples
Week one (Visit 3)	Collection of new capsules	Collection of new capsules
Week two (Visit 4)	Symptomscore and fecal samples	Symptomscore and fecal samples
Week three (Visit 5)	Collection of new capsules	Collection of new capsules
Week four (visit 6) End of active treatment	Sigmoidoscopy, symptomscore, blood and fecal samples	Sigmoidoscopy, symptomscore, blood and fecal samples
Week eight (visit 7)	Symptomscore and fecal samples	Symptomscore and fecal samples
Week 26 (visit 8) End of follow-up	Symptomscore and fecal samples	Symptomscore and fecal samples

Active treatment period Four weeks

Follow-up period 22 weeks



Long-term follow up

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What we would like to know

-Does FMT improve symptoms in patients with UC? (possibly)

-Can the treatment be delivered through capsules? (maybe)

-How long and how often should the treatment be given? (we don't know!)

-What is a good donor? (we have an idea)

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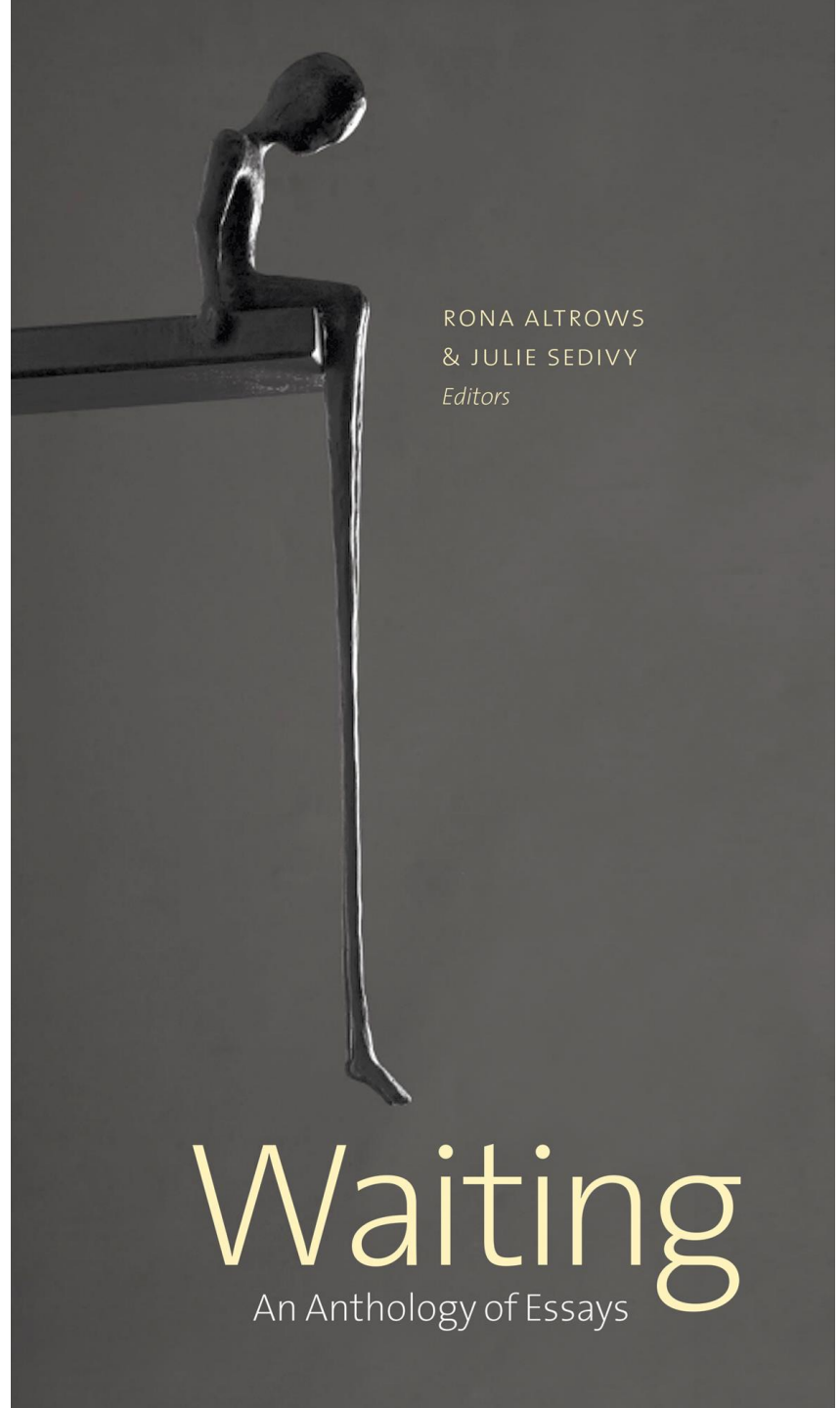
REGION Amager og Hvidovre Hospital


RONA ALTROWS
& JULIE SEDIVY
Editors
Waiting
An Anthology of Essays

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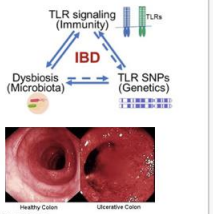

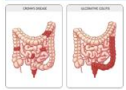

NG et al, 2018, Lancet

Li et al, 2016, Front Immunol

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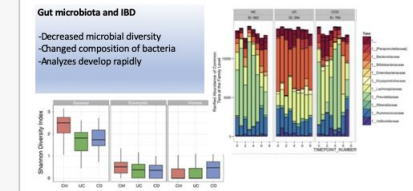

Mosca et al, 2017, Clin Trans Gastroenterol

Halfvarson et al, 2017, Nat Microbiol

3

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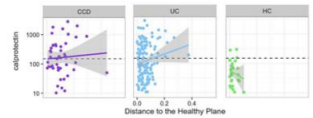

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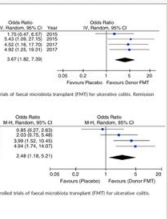

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5

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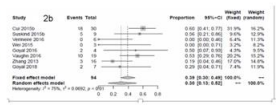

Song et al, 2018, Biomed Res Int.

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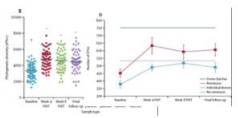

Paramsothy S, et al. Lancet 2017; 389:1218-1228

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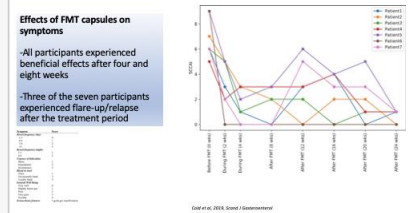

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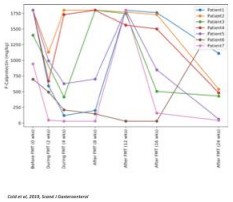

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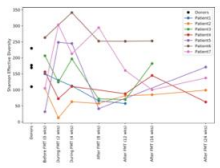

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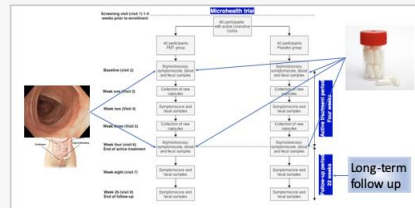

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