



**LIVING WITH IBD**

— Seminar & workshop —

# ALTERNATIVE MEDICINES

*with*

**PROF.  
MICHAEL SCHULTZ**



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# Alternative Medicines in IBD

**Michael Schultz**



@GastroOtago

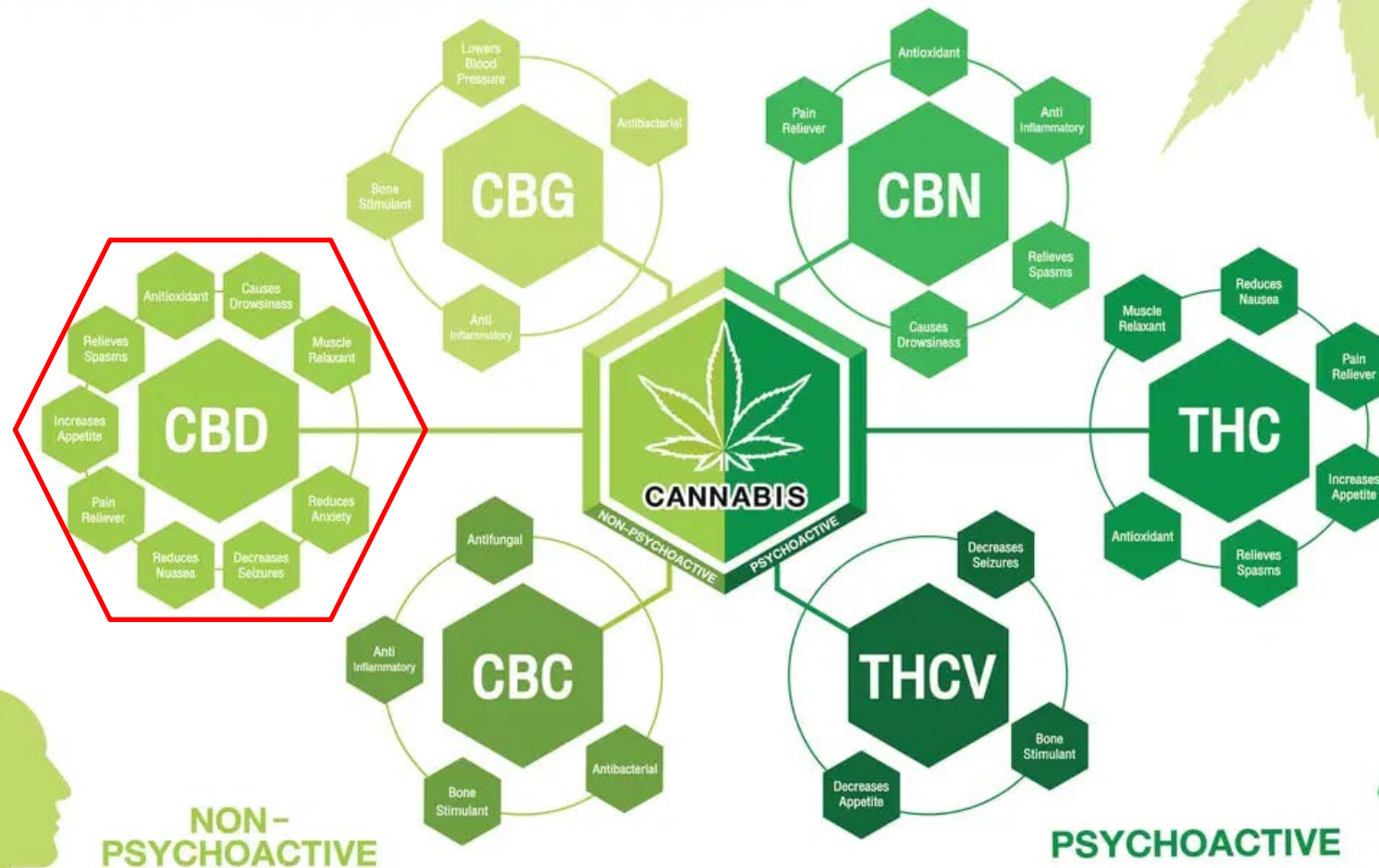


- Cannabis
- Naltrexone
- Probiotics
- FMT



## CANNABINOID GUIDE

CANNABINOIDS ARE THE GROUP OF CHEMICAL COMPOUNDS FOUND IN THE CANNABIS PLANT THAT HAVE PHYSICAL AND MENTAL AFFECTS WHEN THEY INTERACT WITH CANNABINOID RECEPTORS IN YOUR CELLS.

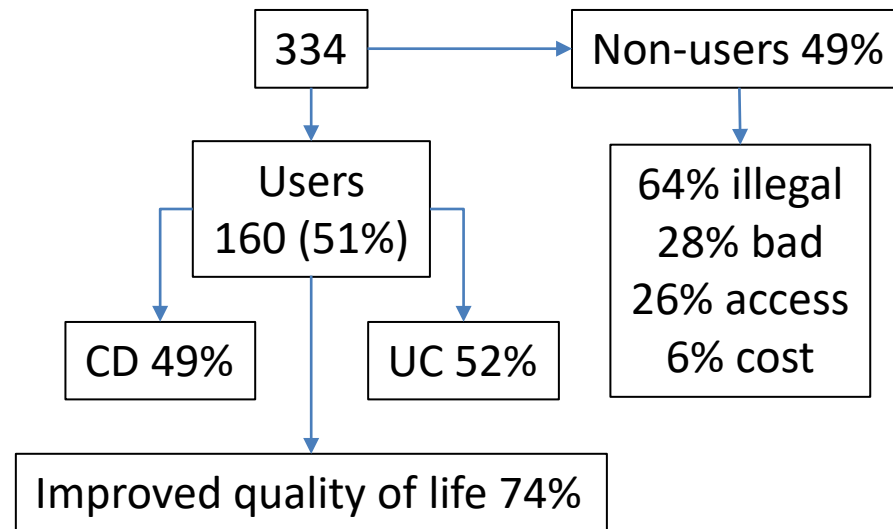


# Attitudes towards and use of cannabis in New Zealand patients with inflammatory bowel disease: an exploratory study.

Appleton K, Whittaker E, ..., Schultz M

The New Zealand Medical Journal Vol 134 No 1530: 19 February 2021  
Te ara tika o te hauora hapori

## Cannabis



Symptoms	Very effective, % (n)	Moderately effective, % (n)	Not effective at all, % (n)	I do not suffer from this symptom, % (n)	I don't know, % (n)
Abdominal pain/cramps	56.5 (39)	39.1 (27)	0.0 (0)	1.5 (1)	2.9 (2)
Frequent diarrhoea	10.3 (7)	26.5 (18)	30.9 (21)	10.3 (7)	22.1 (15)
Urgency	11.6 (8)	30.4 (21)	26.1 (18)	11.6 (8)	20.3 (14)
Fevers	11.9 (8)	19.4 (13)	10.5 (7)	32.8 (22)	25.4 (17)
Loss of appetite	46.3 (31)	34.3 (23)	3.0 (2)	13.4 (9)	3.0 (2)
Nausea/vomiting	41.2 (28)	38.2 (26)	1.5 (1)	11.8 (8)	7.4 (5)
Tiredness/fatigue	8.7 (6)	39.1 (27)	34.8 (24)	2.9 (2)	14.5 (10)
Other (eg, joint pain, skin conditions, eye inflammation)	39. (26)	37.8 (25)	3.0 (2)	10.6 (7)	9.1 (6)



# Alternative and Complementary Approaches for the Treatment of Inflammatory Bowel Disease: Evidence From Cochrane Reviews

Chande N, Costello SP, Feagan BG

*Inflamm Bowel Dis* 2020

*“The endogenous cannabinoid pathway in the GI tract has roles in immune function, epithelial growth, motility, and secretion and is upregulated in states of inflammation.”*

UC n = 60

Capsules with 4.7% THC vs placebo

No difference in remission or response

## Cannabis

### Important research

#### Crohn's disease study

by Naftali et al. in 2013

21 patients

81% side effects

115 mg of THC  
via a cannabis cigarette  
or placebo, twice a day

experienced  
clinical remission



#### Crohn's disease study

by Naftali et al. in 2017

22 patients

10 mg of CBD oil  
or placebo under  
the tongue, twice a day

experienced remission



\*The difference was not statistically significant.  
\*The lack of significant effect of CBD could be due to the small doses of CBD or to a lack of synergism with other cannabinoids.

#### Crohn's disease & ulcerative colitis questionnaire

by Storr et al. in 2014

313 patients



Cannabis improved



Cannabis use was associated with higher risk of surgery in patients with Crohn's disease.

## Opioid Receptors $\kappa$ , $\delta$ , $\mu$ :

- Central nervous system
- GI tract → motility and secretion

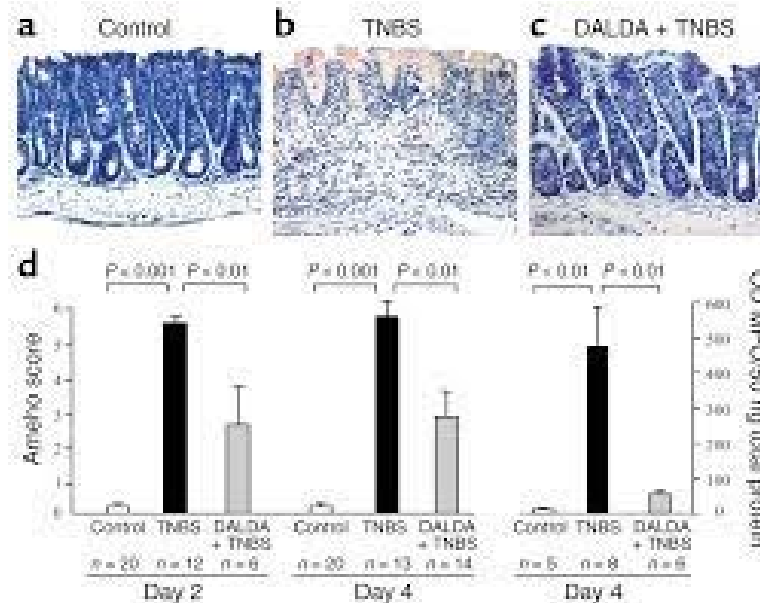
## Naltrexone

### Anti-inflammatory properties of the $\mu$ opioid receptor support its use in the treatment of colon inflammation

David Philippe, ... , Brigitte L. Kieffer, Pierre Desreumaux

*J Clin Invest.* 2003;111(9):1329-1338

IBD →  $\uparrow\mu$  by CD4/8<sup>+</sup> T-cells





Type of Study (Number of Subjects)	Treatment Duration	Notable Outcomes	Reference
Open label prospective (17 adult patients affected by Crohn's disease)	12 weeks + 4 weeks follow-up	<ul style="list-style-type: none"> <li>Majority responded with a 70-point decrease in Crohn's disease activity index (89%) and achieved remission (67%)</li> <li>Well tolerated, 7 patients reported sleep disturbances</li> </ul>	Smith et al. [38]
Pediatric case report on Crohn's disease (1)	4 weeks + 3 months follow-up	<ul style="list-style-type: none"> <li>Patient achieved remission after failing multiple standard regimens</li> </ul>	Shannon et al. [60]
Cochrane review of placebo- controlled trials (34 adult and 12 pediatric patients affected by Crohn's disease)	12 weeks (adults) and 8 weeks (children)	<ul style="list-style-type: none"> <li>Drug was safe and tolerable</li> <li>Small sample precluded strong conclusions, but LDN may provide clinical benefits</li> </ul>	Parker et al. [61]
Open label prospective (19 adult patients affected by Crohn's disease and 28 by ulcerative colitis)	12 weeks	<ul style="list-style-type: none"> <li>Clinical improvement in majority (74.5%) of patients who previously had intractable disease, while some (25.5%) achieved remission</li> <li>Drug was well tolerated and 4 patients reported vivid dreams which resolved upon morning drug administration instead of bedtime</li> </ul>	Lie et al. [44]
Quasi-experimental pharmacoepidemiological cohort of patients affected by inflammatory bowel disease (582)	4 years	<ul style="list-style-type: none"> <li>LDN use was associated with significant reduction in consumption of anti-inflammatory medications in cohort</li> </ul>	Raknes et al. [62]

## Alternative and Complementary Approaches for the Treatment of Inflammatory Bowel Disease: Evidence From Cochrane Reviews

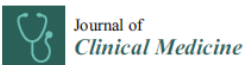
Chande N, Costello SP, Feagan BG

*Inflamm Bowel Dis* 2020

No concerning findings but more research needed.

Probiotic Used	Study	Sample Size	Studied Group	Result of the Intervention
<i>Escherichia coli</i> Nissle 1917	Kruis W. et al. Aliment Pharmacol. Ther. 1997 [30]	120	adults	efficacy in maintaining remission and preventing relapse comparable to mesalazine
	Rembacken BJ. et al. Lancet. 1999 [31]	116	adults	efficacy in maintaining remission after exacerbation of UC comparable to mesalazine
	Kruis W. et al. Gut. 2004 [32]	327	adults	efficacy and safety in maintaining remission comparable to mesalazine
	Henker J. et al. Zeitschrift Für Gastroenterologie, 2008 [33]	34	children	efficacy in maintaining remission comparable to mesalazine
	Matthes H. et al. BMC Complement Altern Med. 2010 [34]	90	adults	possibility of dose-dependent efficacy in inducing remission of the rectal probiotic compared to placebo
	Petersen AM et al. J Crohns Colitis. 2014 [35]	100	adults	no benefit in the use of probiotic as an additional therapy to conventional treatment
<i>Lactobacillus</i> GG	Zocco MA, Aliment Pharmacol Ther. 2006 [36]	187	adults	higher efficacy of probiotic as add-on therapy in prolonging the relapse-free time compared to mesalazin monotherapy
<i>Bifidobacterium breve</i> , <i>Bifidobacterium bifidum</i> , <i>Lactobacillus acidophilus</i> YIT 0168 (Bifidobacteria-Fermented Milk- BFM)	Ishikawa et al. J Am Coll Nutr 2003 [37]	21	adults	higher efficacy of probiotic mixture as add-on therapy in maintaining remission and preventing relapse compared to convantional therapy alone
	Kato K. et al. Aliment. Pharmacol. Ther. 2004 [38]	20	adults	higher efficacy of probiotic as add-on therapy in maintaining remission compared to convantional therapy alone
<i>Saccharomyces boulardii</i>	Guslandi M. et al. Eur J Gastroenterol Hepatol. 2003 [39]	24	adults	higher efficacy of probiotic as add-on therapy in inducing and maintaining remission compared to mesalazin monotherapy
<i>Lactobacillus reuteri</i> ATCC 55730	Oliva S. et al. Aliment Pharmacol Ther. 2012 [40]	40	children	higher efficacy of probiotic enema as add-on therapy additional to oral mesalazin in improving mucosal inflammation compared to conventional therapy
<i>Lactobacillus casei</i> , <i>Lactobacillus plantarum</i> , <i>Lactobacillus acidophilus</i> and <i>Lactobacillus delbrueckii</i> subsp. <i>Bulgaricus</i> , <i>Bifidobacterium longum</i> , <i>Bifidobacterium breve</i> and <i>Bifidobacterium infantis</i> , <i>Streptococcus salivarius</i> subsp. <i>Thermophils</i> (VSL#3)	Tursi A. et al. Am J Gastroenterol. 2010 [41]	144	adults	higher efficacy of probiotic mixture as add-on therapy to conventional treatment in patients with relapsing disease compared to placebo
	Sood A. et al. Clinical Gastroenterology and Hepatology 2009 [42]	147	adults	higher efficacy in inducing and maintaining remission compared to placebo
	Miele E. et al. Am J Gastroenterol. 2009 [43]	29	children	higher efficacy in maintaining remission compared to placebo

# Probiotics



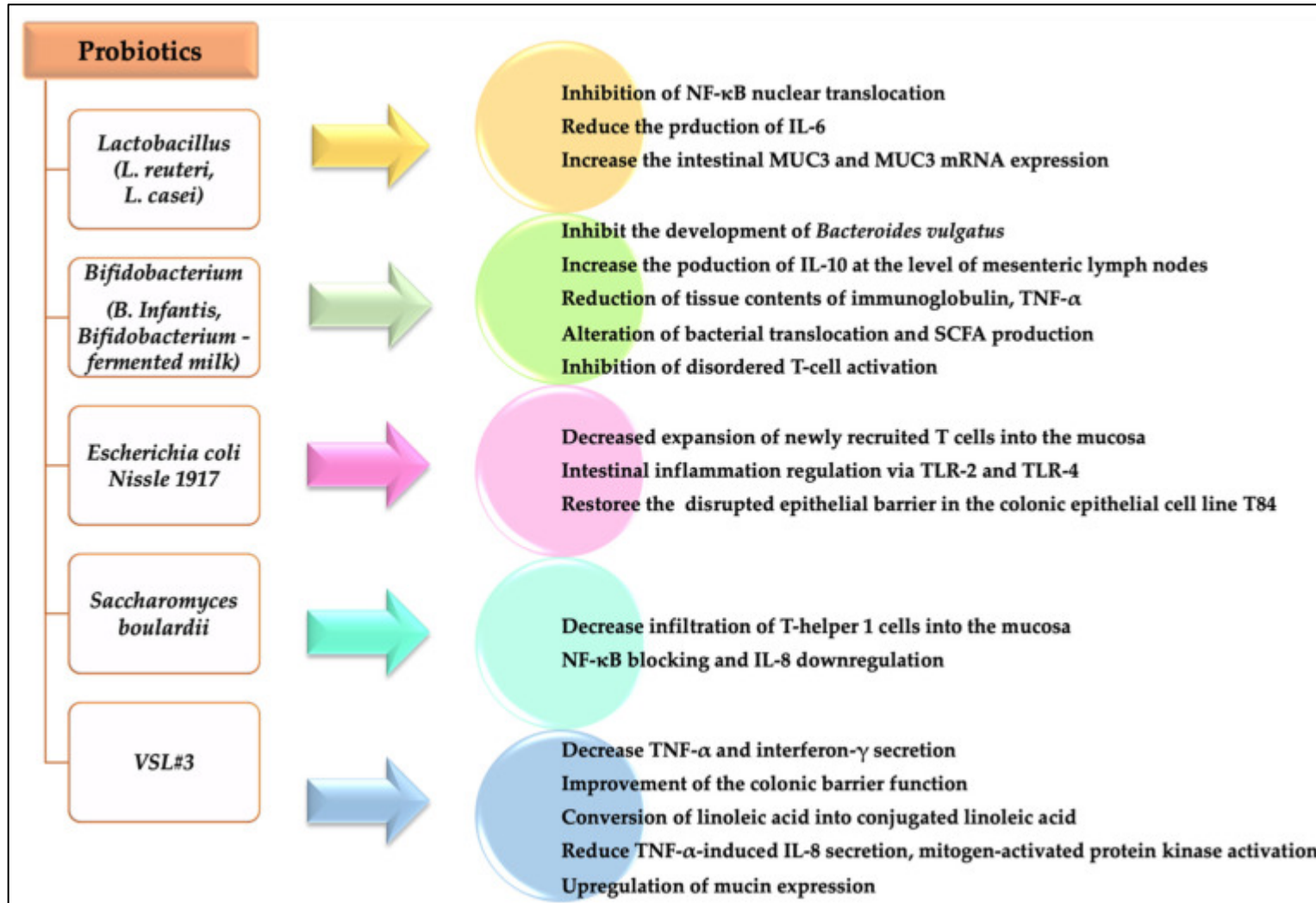
Review  
**Probiotics, Prebiotics and Synbiotics in Inflammatory Bowel Diseases**  
 Katarzyna Akutko \*<sup>†</sup> and Andrzej Stawarski <sup>‡</sup>  
*J. Clin. Med.* **2021**, *10*, 2466.

Effective as add-on in ulcerative colitis

# Probiotics

Probiotic Used	Study	Sample Size	Studied Group	Result of the Intervention
<i>Lactobacillus GG</i>	Schultz M. et al. BMC Gastroenterology 2004 [52]	11	adults	no benefit in the use of probiotic as an additional therapy to conventional treatment
	Gupta P. et al. JPGN 2000 [53]	4	children	higher efficacy of probiotic as an add-on therapy in improving gut barrier function and clinical status
	Prantera C. et al. Gut 2000 [54]	45	adults	no benefit in preventing endoscopic relapses or reducing the severity of inflammation
	Bousvaros A. et al. Inflamm Bowel Dis. 2005 [55]	75	children	no benefit in use probiotic as add-on therapy to conventional treatment in prolonging of relapse-free time
<i>Saccharomyces boulardii</i>	Plein K. et al. Gastroenterol. 1993 [56]	20	adults	higher efficacy of probiotic as an add-on therapy in reducing in the number of stools compared to placebo
	Bourreille A. et al. Clin. Gastroenterol. Hepatol. 2013 [57]	165	adults	no benefit in maintaining remission as add-on therapy after conventional treatment
<i>Lactobacillus casei</i> , <i>Lactobacillus plantarum</i> , <i>Lactobacillus acidophilus</i> and <i>Lactobacillus delbrueckii</i> subsp. <i>Bulgaricus</i> , <i>Bifidobacterium longum</i> , <i>Bifidobacterium breve</i> and <i>Bifidobacterium infantis</i> , <i>Streptococcus salivarius</i> subsp. <i>Thermophilus</i> (VSL#3)	Day AS. et al. Gastroenterology 2012 [58]	17	children	higher efficacy in reducing disease activity and improving weight and albumin levels compared to placebo
	Fedorak RN. et al. Clinical Gastroenterology and Hepatology. 2014 [59]	120	children over 16 years old, adults	no benefits in reducing endoscopic recurrence rates compared to placebo
<i>Escherichia coli</i> Nissle 1917	Malchow HA et al. J. Clin. Gastroenterol 1997 [51]	28	adults	higher efficacy of probiotic as add-on therapy in preventing relapse and reducing the need for steroid treatment compared to conventional therapy alone

Possible effect in Crohn's disease

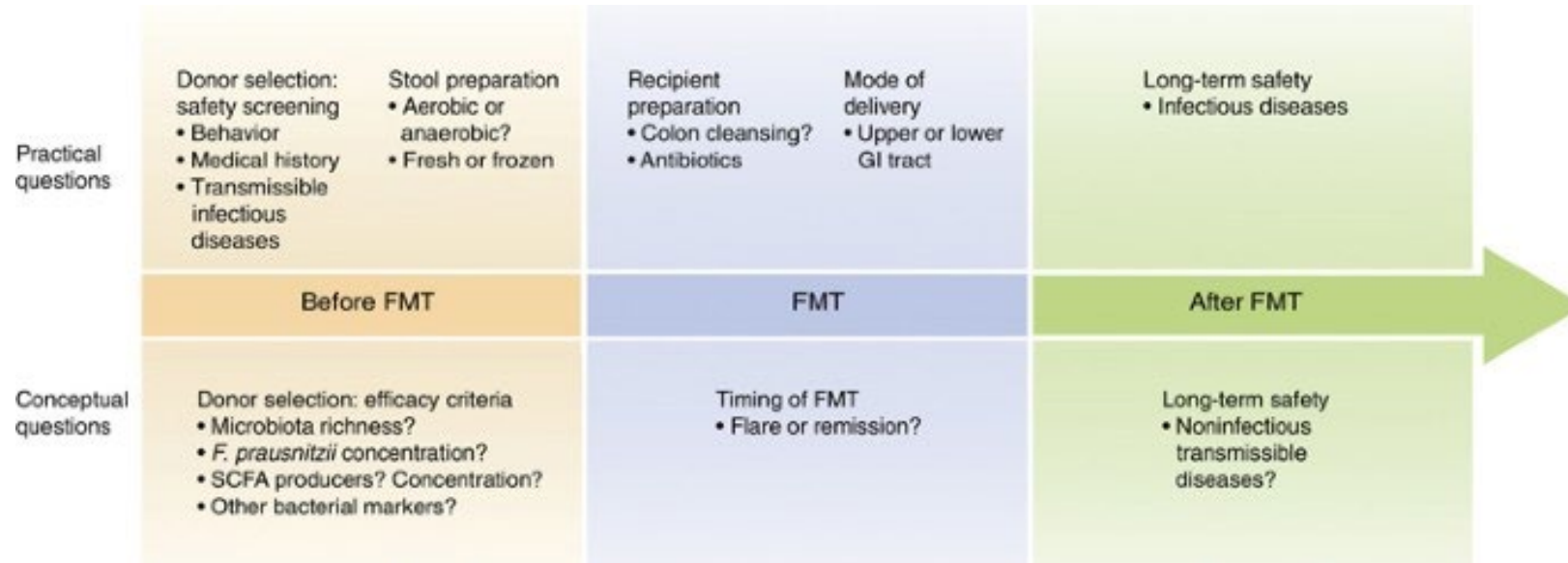


## Highlighting the Relevance of Gut Microbiota Manipulation in Inflammatory Bowel Disease.

Pavel FM, Vesa CM, Bungau S. Diagnostics (Basel). 2021;15:1090

Therefore, the additional benefits of these therapies should not be ignored as adjuvants to medical therapy.





More questions than answers but were getting there.

Clin remission at week 7-12: 28% vs 9% clinical and endoscopic remission  
Endoscopic remission at week 7-12: 30% vs 10%

### **Alternative Medicines:**

Cannabis – too early to say but little evidence

Naltrexone – promising

Probiotics – as add-on to conventional medication

FMT - possibly