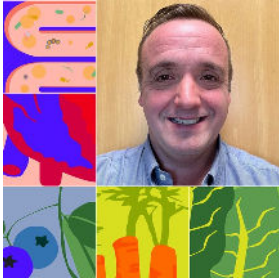


Microbiome, Gut and Systemic Health: New Frontiers in Personalised Nutrition




Dr. Jonathan Sutton

Poo Transplants: Pros and Cons of Faecal Microbial Transplantation (FMT)

2:45-3:30pm




An event by:

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Nutritional Medicine
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FMT – Pros and Cons

Dr Jonathan Sutton MbChB FRCP (UK)
Ysbyty Gwynedd
Bangor
Wales

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Overview

- Why FMT is important
- History of FMT
- CDI and FMT
- Cons ?
- How to do it
- Other potential indications:
 - IBS/functional bowel disorders
 - Inflammatory Bowel disease
 - Obesity
 - Hepatic encephalopathy

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Why?

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A good reliable set of
bowels is worth more
to a man than any
quantity of brains.

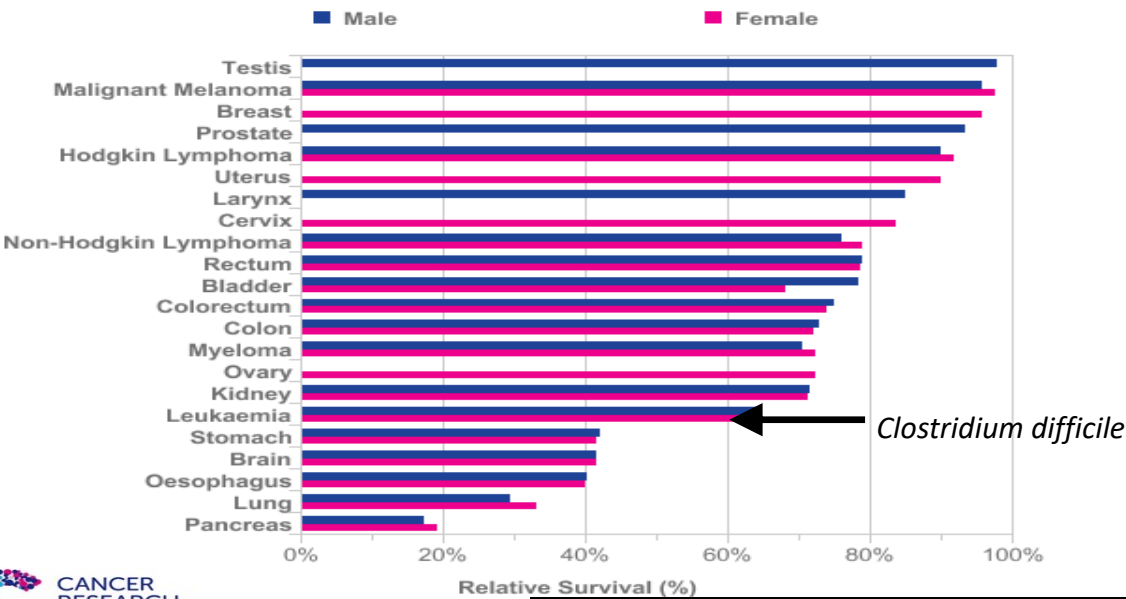
Josh Billings

www.STOREMYPIC.COM

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21 Common Cancers: Patients Diagnosed 2005 - 2009 and Followed up to 2010
One-Year Relative Survival, Ages 15–99, England



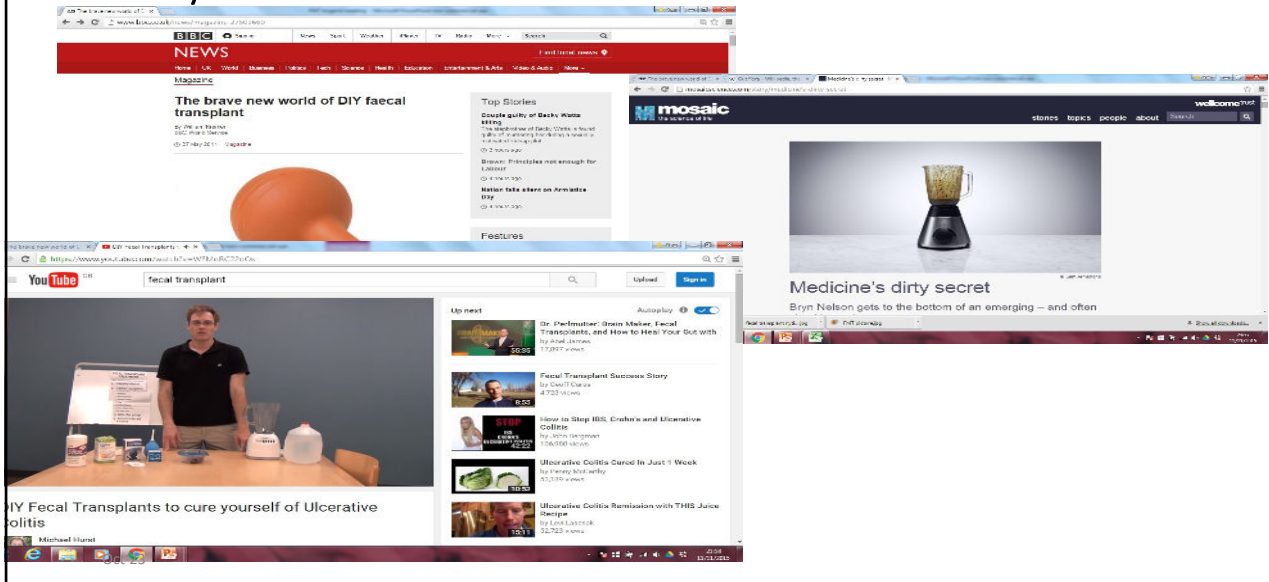
CANCER RESEARCH UK

Prepared by Cancer Research UK
Original data source: ONS Statistical Bulletin (2011) Cancer

Courtesy of Dr Robert Porter

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Why FMT?



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History of FMT

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Faecal Therapy

- First described in 4th Century- Ge Hong described using human faecal suspension for food poisoning and diarrhoea
- Li Shizhen described using 'yellow soup' to cure many abdominal symptoms C16th



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Fast forward.....

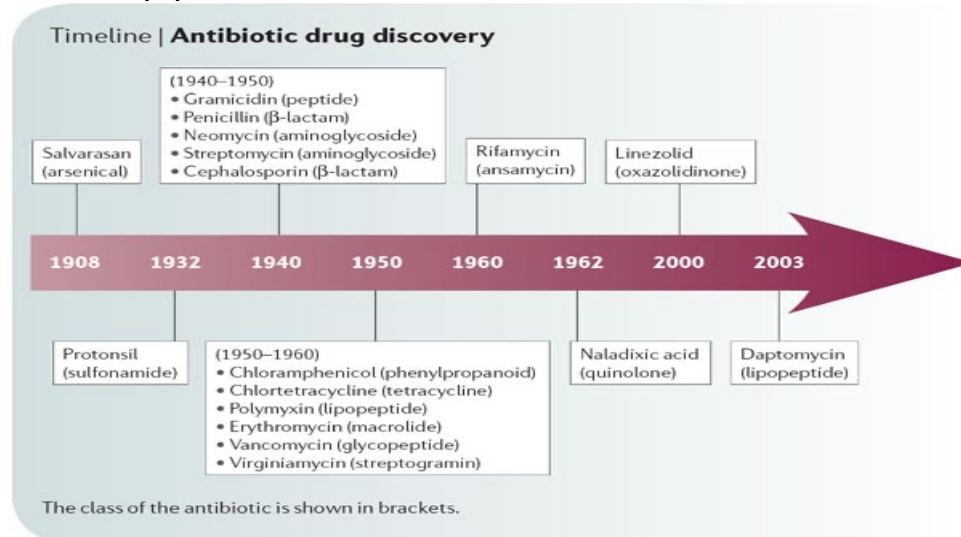
- Denver 1958
 - 'Fecal enema as an adjunct in the treatment of pseudomembranous enterocolitis'. *Eiseman et al Surgery 1958;44:854-9*



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What happened next



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1991 New York

- Dr Lawrence Brandt -Gastroenterologist
- Rediscovered FMT
- Thought it was a novel idea
- Produced a significant case series of data
- 90+% cure rate
- Picked up by enthusiasts

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CDI and FMT

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Recurrent CDI

- Most patients respond to initial antimicrobial therapy
- Approximately 25% have recurrence
- Second recurrence in 35-45%
- Subsequent recurrence rates higher than 50%

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Mr Roberts

- 85 year old
- Very active good quality of life
- Treated for cellulitis in July 2021
- Developed diarrhoea after discharge from hospital
- Diagnosed with CDI

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Mr Roberts

- Initially treated with vancomycin for 10 days
- Good improvement
- Recurred after 1 week
- Treated with fidaxomicin
- Recurred 1 week later
- 5 subsequent courses of treatment
- Recurrent relapses

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Mr Roberts

- Referred (tentatively) by GP after advice from microbiology
- On review
 - Perceived very poor quality of life due to frequent diarrhoea
 - Worried about leaving the house
 - Lost confidence
 - Worried that 'this might be it '

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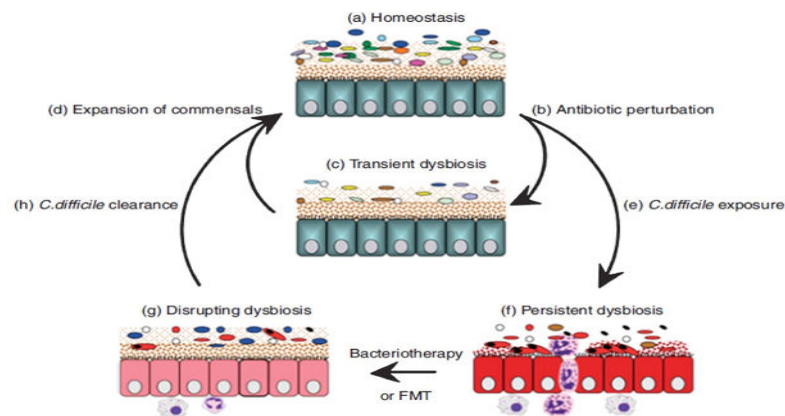
Mr Roberts

- Explained the rationale and risks of FMT
- Explained the practicalities of delivering FMT
- He agreed to go ahead
- One week later early February 2022 FMT given
- Symptom free since

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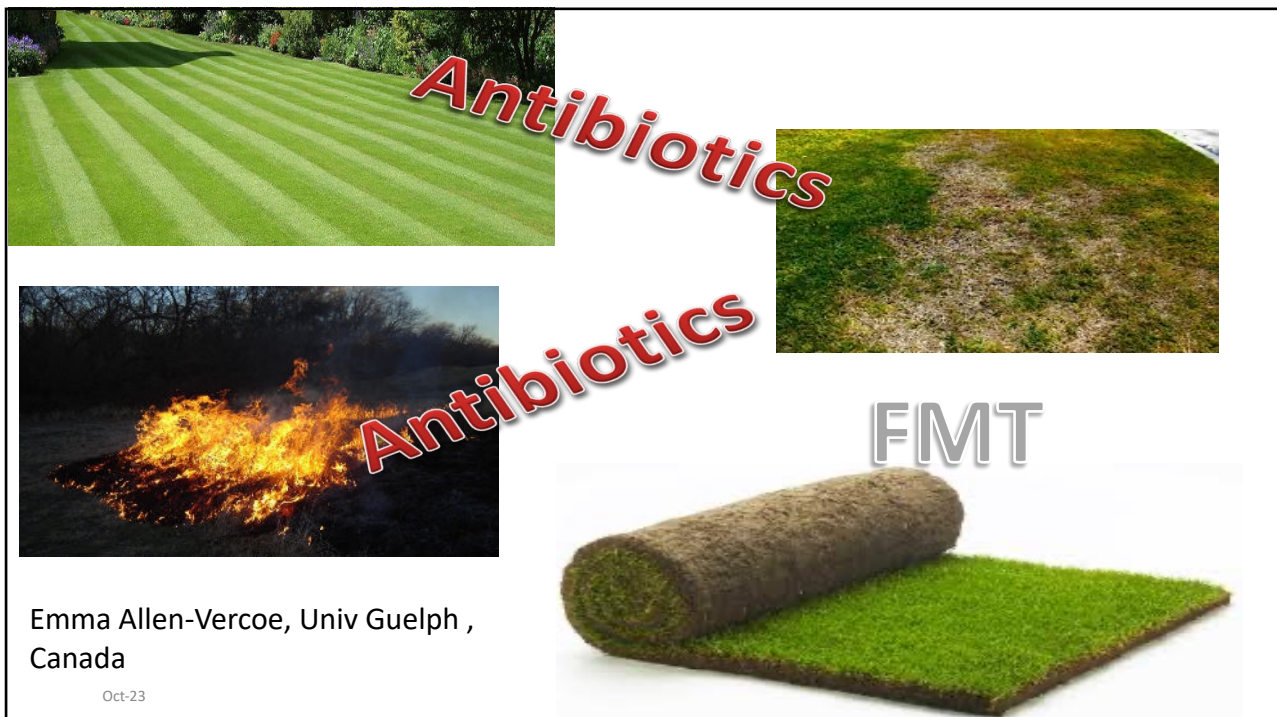
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Why does *C. diff* recur?



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Emma Allen-Vercoe, Univ Guelph ,
Canada

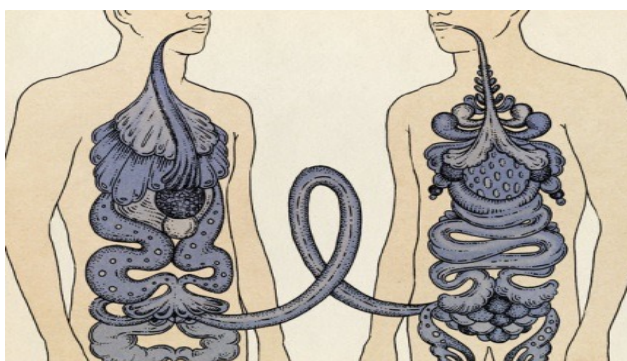
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Cons

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Why is fmt not commonly used?

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Patient Attitudes

- Study in healthy volunteers
- 192 people attending OPD clinics
- 2 hypothetical scenarios

Zipursky J et al. Clinical Infectious Diseases 2012;55(12):1652-8

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- Scenario 1

- Suffering with recurrent CDI, two treatment options
 1. Another antibiotic course with a 65% success rate
 2. Antibiotics plus 'floral reconstitution' with 90% success rate

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- Scenario 2

- Same clinical scenario but detailed information about what FR is including potential routes of administration

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Results

- Scenario 1
 - 85% chose antibiotics plus FR
- Scenario 2
 - 81% chose antibiotics plus FR
 - Increased to 94% if recommended by their doctor

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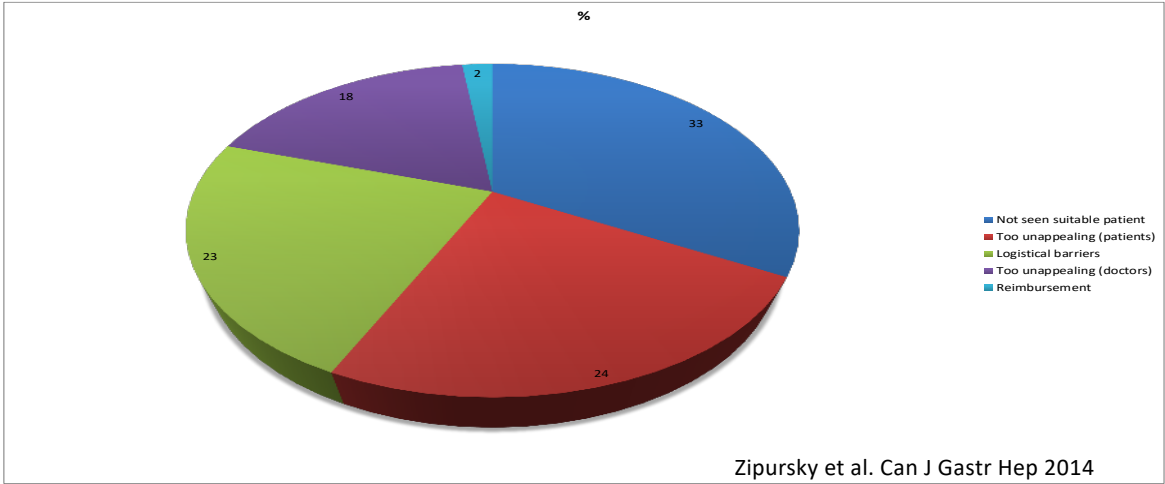
Physician attitudes toward FMT

- Survey of 135 physicians
- 100% had treated recurrent CDI
 - 20% had treated a patient with FMT
- 65% had neither offered or referred for FMT

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Of those



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Barriers to widespread adoption

Survey of 161 UK Infection and Gastroenterology specialists from 86 Trusts/Boards

Factor	Favours use %	Inhibits use %	Neither %	Don't know %
Evidence base	96.4	0	1.4	2.2
Benefit vs risk	90.8	0.7	5.7	2.8
Overall cost	41.8	9.9	29.8	18.4
Antimicrobial resistance	61	3.5	29.1	6.4
Patient safety	55.3	12.1	26.2	6.4

Porter, Clin Microbiol Infect, 2015, in press

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Barriers to widespread adoption

Factor	Favours use %	Inhibits use %	Neither %	Don't know %
Patient acceptance	23.4	41.1	26.2	9.2
Donor selection	9.3	47.9	32.1	10.7
Cost to local laboratory	10	32.9	45.7	11.4
Availability of prepared stool	33.6	47.1	11.4	7.9
Feasibility / practicality of procedure	24.8	57.4	13.5	4.3
Local expertise	32.1	45.7	17.1	5

Porter, Clin Microbiol Infect, 2015, in press

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Complications

- Complications of delivery method
 - Aspiration upper GI
 - Colonoscopy complications
- Transmission of infection (? Unknown)
- Unknown consequence of altering microbiome
 - ? Autoimmune disease

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How to do it

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Specialist equipment



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PARENTAL
ADVISORY
EXPLICIT CONTENT

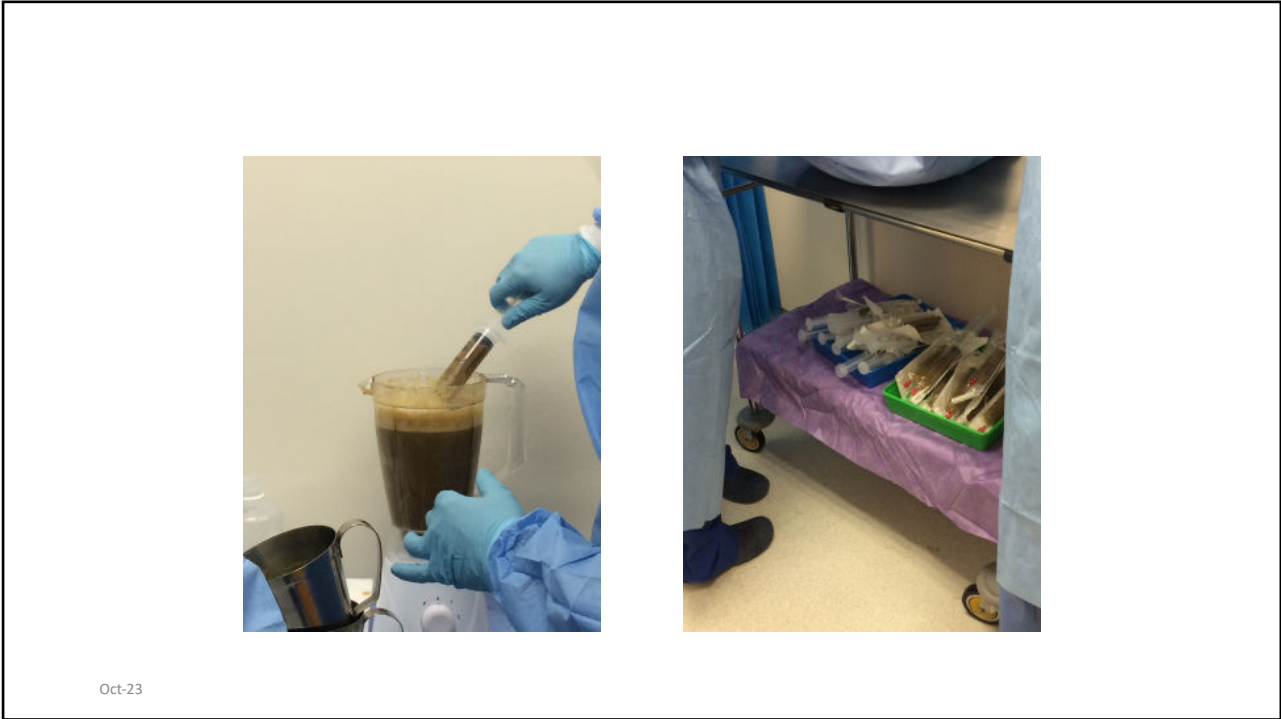
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Problems with suitable donors



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The solution

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Route of administration

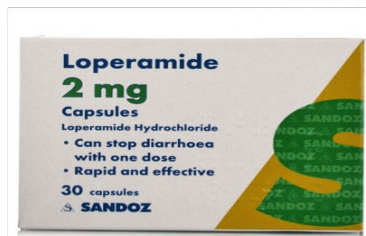
- Top
 - NGT
 - NJT
 - OGD
 - Capsules
- Bottom
 - Colonoscopy
 - Enema
- Lower GI
 - Primary cure rate 93.2%
 - Overall recurrence 6.0%
- Upper GI
 - Primary cure rate 81.8%
 - Overall recurrence 8.2%

Y.-T. Li et al. APT 2016 43(445-457)

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Preparing the patient



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My recipe

- Either NGT (or colonoscopy). Not via gastroscopy
- Stop antibiotics 24 to 48 hrs prior
- No bowel prep for upper GI route
- Patient greater than 45 degrees (close to 90 as possible)
- Administered behind the head
- Pt can sip juice during the procedure
- Leave NGT in for 30 minutes post administration

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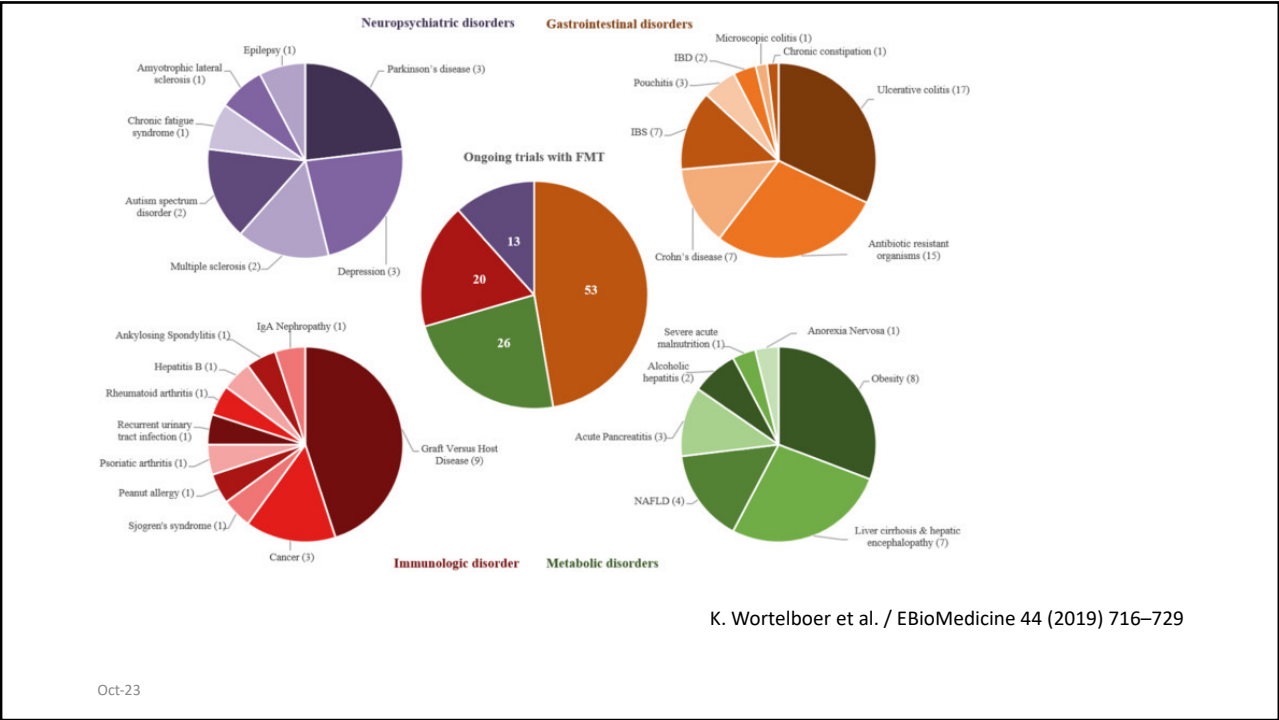
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FMT beyond rCDI



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Obesity



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Obesity

- Animal models show that in mice models FMT can cause weight loss
- 1 RCT in humans - no benefit over 6 month follow up.
- Ridaura VK, Faith JJ, Rey FE, et al.. Gut microbiota from twins discordant for obesity modulate metabolism in mice. *Science*. 2013;341(6150)
- Lahtinen P et al Effectiveness of Fecal Microbiota Transplantation for Weight Loss in Patients With Obesity Undergoing Bariatric Surgery. *JAMA Netw Open*. 2022 Dec; 5(12)

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Hepatic encephalopathy

- Reversible neurolocognitive dysfunction
- Chronic liver disease and portosystemic hypertension shunts toxins to the brain
- Ammonia main toxin

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Hepatic encephalopathy

- Hypothesis
 - FMT may change microbiome composition reducing urease activity
 - FMT may establish integrity of intestinal barrier decreasing ammonia uptake
- Early RCTs show potential benefit for HE but further larger trials required to establish role.
- References
 - Bajaj JS, Kassam Z, Fagan A, et al. Fecal microbiota transplant from a rational stool donor improves hepatic encephalopathy: a randomized clinical trial. *Hepatology* 2017;66:1354-5.
 - Bajaj JS, Salzman NH, Acharya C, et al. Fecal microbial transplant capsules are safe in hepatic encephalopathy: a phase 1, randomized, placebo-controlled trial. *Hepatology* 2019;70:1690-703.

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Irritable bowel disorders

- Chronic non-inflammatory GI disorders
- Pathophysiology not fully understood
- Studies have shown IBS to be associated with altered microbiota
- RCTs have produced contradictory results
 - 1 trial showing worsening of IBS symptoms 1 showing improvement
- Halkjaer SI et al *Gut*. 2018 Dec; **67**: 2107-2115
- *Lancet Gastroenterol Hepatol*. 2018 Jan; **3**: 17-24

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IBS

- In both studies microbiota diversity increased
- ? IBS subtype
- ? FMT administration strategy

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Inflammatory Bowel Disorder

- Ulcerative colitis and Crohn's disease
- Both have been associated with reduced diversity (reduced *Bacteroidetes* and *Firmicutes*)

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Ulcerative colitis

- 4 RCTS – systemic review by Cochrane
- Showed higher remission in the FMT (37%) c/w control arm (18%)
- Fecal transplantation for treatment of inflammatory bowel disease. *Cochrane Database Syst Rev.* 2018 Nov; **11**CD012774
- 'Superdonor' Donor B
 - ? Response is donor related (unlike rCDI)
 - Moayyedi et al 2015. Out of 9 responders 7 came received FMT from one donor
 - Moayyedi, P, Surette, M. G., Kim, P. T., Libertucci, J., Wolfe, M., Onischi, C., et al. (2015). Fecal microbiota transplantation induces remission in patients with active ulcerative colitis in a randomized controlled trial. *Gastroenterology* 149, 102–109

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IBD (UC)

- Other active 'ingredients' not just bacterial diversity?
 - SFA
 - BA
- Specific species e.g. *Eubacterium hallii* and *Roseburia inulinivorans*
- Pooled donors better than single donors?
- Single treatment or multiple sessions?
- More RCTs needed to answer these questions

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Summary

- FMT offers a therapeutic means of altering an individuals colonic microbiota
- Currently the only clear indication is rCDI
- There are other possible indications
- More trial data is needed to establish the role of FMT
- Not necessarily all about microbiome
- Faeces will not be the end product!

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Saturday 14th October

Featuring Dr. Gerard Mullin, Professor Glenn Gibson, Dr. Amrita Vijay, Justine Bold, Dr. Jonathan Sutton and Benjamin Brown

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