Inflammatory Bowel Disease and the Microbiome: Clinical Progress and Questions Left Unanswered

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What is the Microbiome?

• Defined as the ecological community of commensal, symbiotic and pathogenic microorganisms that literally share our body space

• The human microbiome consists of about 100 trillion microbial cells

• Outnumber human cells 10:1
The human gut is like a rainforest

- High diversity of species
- Healthy ecosystem
- Balance
- Resistance to disease

- Low diversity of species
- Sick ecosystem
- Imbalance
- Susceptibility to disease
Dysbiosis Disrupts Health

Datasheet:
- Diverse and abundant microbiota
- Firmicutes, Bacteroidetes and Actinobacteria dominant
- Healthy levels of SCFA production
- Intact mucosal barrier
- No overt inflammation

**Therapeutic disruption of dysbiosis**
- Antibiotics
- Probiotics
- Dietary intervention/Prebiotics
- Faecal transplantation

**Dysbiosis-related diseases**
- Chronic gastrointestinal infections
- Antibiotic-associated diarrhoea
- Pseudomembranous colitis
- Inflammatory bowel disease
- Necrotizing enterocolitis

Datasheet:
- Microbiota diversity reduced
- Elevated *Enterobacteriaceae*/opportunistic pathogens
- Skewed SCFA profile
- Disruption of mucosal barrier
- Host inflammatory response initiated

Dysbiosis in IBD
<table>
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<tr>
<th>Microbial composition</th>
<th>Microbial function</th>
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<td>Decrease in α diversity</td>
<td>Decrease in SCFAs, butyrate</td>
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<td>Decrease in <em>Bacteroides</em> and Firmicutes</td>
<td>Decrease in butanoate and propanoate metabolism</td>
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<td>Increase in Gammaproteobacteria</td>
<td>Decrease in amino acid biosynthesis</td>
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<td>Presence of <em>E coli</em>, specifically adherent-invasive <em>E coli</em></td>
<td>Increase in auxotrophy</td>
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<td>Presence of <em>Fusobacterium</em></td>
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<td>Decrease in Clostridia, Ruminococcaceae, <em>Bifidobacterium</em>, <em>Lactobacillus</em></td>
<td>Increase in sulfate transport</td>
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<td>Decrease in <em>F prausnitzii</em></td>
<td>Increased oxidative stress</td>
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<td>Increase in type II secretion system, secretion of toxins</td>
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Therapeutic Manipulations of the Microbiome in IBD

• Crohn’s disease: role seems clear
  ➢ Diversion of fecal stream is effective
  ➢ Antibiotics are beneficial in subsets of CD patients
  ➢ Role for TPN/bowel rest

• Ulcerative colitis: role less clear
  ➢ Diversion not effective
  ➢ No clear role for antibiotics or TPN/bowel rest
  ➢ VSL #3 & E. coli Nissle 1917 effective
The Emergence of FMT
Fecal Microbiota Transplantation

- Instillation of minimally manipulated microbial communities from stool of a healthy donor into a patient’s GI tract.

- FMT is distinguished from a defined consortia of microorganisms, highlighting the degree of complexity and functionality of the microbiome.

- Can be considered both a “drug” and a “biologic or tissue”
Regulations: US

• May use to treat C. difficile not responding to standard therapy
• No IND required

• Informed consent
  – State it is investigational
  – Discuss real and theoretical risks

• Draft guidance March 2016
  – Would enforce IND requirement for stool banks
Recurrent CDI

- Recurrence of symptoms after successful initial therapy for *C. difficile*
  - endogenous persistence of *C. difficile* spores
  - acquisition of a new strain from an exogenous source.

- Strains Analysis:
  - two different serogroups in 21.5%
  - same serogroup in 78.5%

Barbut et al.
Recurrent CDI

• Recurrence is present when CDI re-occurs within 8 weeks
  – provided the symptoms from the previous episode resolved
  – May occurs within days
Recurrent CDI

- 15-20% of patients (regardless of initial therapy)
- 2\(^{nd}\) recurrence: 30-45%; 3\(^{rd}\) recurrence: 45-60%
- Relapses can continue for years
Recurrent CDI in IBD

- Prevalance 2.5 to 8 times higher
- 10% lifetime risk of CDI
- Higher rates of recurrence, chronic carriage and mortality
- CDI can illicit flares, worsen disease severity and overall course
Recurrent CDI: Why does it occur?

- Impaired host response
- Altered intestinal microbiome
Impaired Host Response

Impaired Host Response
Altered Intestinal Microbiome

- Decreased phylogenetic richness
- *Bacteroidetes* and *Firmicutes* are reduced in patients with recurrent CDI, not in patients with just one episode

• Not just microbial membership but function
• Antibiotics disturb not only the structure of the microbiome but also the function
  – Fermentation of SCFA
  – Lipid metabolism
  – Protein digestion
  – Bile salt metabolism
• CDI is communicated by ingestion of spores.
• Spores:
  ① are resistant to heat and antibiotics and are able to survive outside of the colon.
  ② germinate in the GI tract and become vegetative cells which can produce toxin.
  ③ Germination is critical to initiate CDI.
  ④ Bile acids are vital to the germination process.
The Relationship between CDI and Bile Acids

- In vitro primary bile acids can stimulate germination of *C. difficile* spores:
- The secondary bile acid deoxycholate can inhibit growth of the vegetative form.
  - Antibiotic therapy may ablate critical members of the microbiota that generate inhibitory (protective) secondary bile acids.
    - Stool extracts from antibiotic treated mice have higher concentrations of primary bile acids and form untreated mice have relatively higher secondary bile acids.
- The relationship between the host microbiome and bile salt metabolism is poorly defined in humans with CDI.
Bile Salt Analysis in Stool

For Primary Bile Acids:
- Control vs. First Time: p=1.0
- Control vs. Recurrent: p=0.0024
- First Time vs. Recurrent: p<0.0001

For Secondary Bile Acids:
- Control vs. First Time: p=0.00065
- Control vs. Recurrent: p=0.52
- First Time vs. Recurrent: p<0.0001
Accuracy of Bile Salts as Predictors

[ROC Curve for Random Forest]

- True positive rate
- False positive rate

[Boxplot]
- Ratio of Deoxycholate:Glycocholate
- Control
- iCDI Patient Status
- iCDI
Treatment: Recurrent CDI

- **First recurrence**: In IBD vancomycin should be used.
- **Second recurrence**: pulsed vancomycin regimen
  - 125 mg orally four times daily for 14 days
  - 125 mg orally twice daily for 7 days
  - 125 mg orally once daily for 7 days
  - 125 mg orally every other day for 7 days
  - 125 mg orally every 3 days for 14 days

*Alternative: fidaxomicin*

- **Third recurrence**: Fecal Microbiota Transplantation
Fidaxomicin

- Trade Name: Dificid
- Non-systemic (minimally absorbed)
- Bactericidal
- Dose 200mg BID x 10 days
Non-antibiotic Therapies

• IVIG
  – no RCT data, no role in severe fulminant disease
  – 400 mg/kg once every 3 weeks for a total of 2 or 3 doses

• Probiotics
  – *Saccharomyces boulardii* or lactobacillus species may be added during the final 2 weeks of the vancomycin taper and for at least 4 weeks thereafter (preferably 8 weeks).

• The efficacy of probiotics in preventing recurrent *C. difficile* infection is unclear
Considerations

Prior to Initiating Therapy for rCDI:

• Consider other etiologies of diarrhea: post infectious IBS, IBD flare
• Retesting not recommended after therapy unless moderate to severe diarrhea
• In patients with persistent diarrhea despite appropriate treatment with vancomycin or flagyl – other causes must be considered

C. difficile is rarely if ever resistant to flagyl or vancomycin
Fecal Transplantation: the Basics
Steps of FMT: The Four D’s

1. **Decision**: is FMT indicated?

2. **Donor Selection**:
   - Patient directed vs. universal
   - Fresh or frozen

3. **Delivery Modality**:
   - Enema
   - Colonoscopy / sigmoidoscopy
   - NG/NJ tube
   - Capsules

4. **Discharge and Follow-up**
Step 1: Decision ➔ Patient Selection

Appropriate candidates are:

– patients who have **confirmed** relapsing CDI (a history of 3 or more episodes, or 2 episodes that required hospitalization)

– patients with refractory disease that is unresponsive to traditional antibiotics.
# Step 2: Donor Selection

## Patient Directed
- **Source:** Family or Friend
- **Pros:**
  - Patient comfort
- **Cons:**
  - Multiple tests
  - Expensive
  - Delays care
  - Physician’s time

## Universal Donor
- **Pros:**
  - Routinely tested
  - Healthy individual
  - Proven donor track
  - Minimize cost
- **Cons**
  - Billing
  - Food allergies
Donors

• Donors must be ≥ 18 years old
• Donors may be relatives or friends to the recipient
• Donors should be otherwise healthy and have daily formed BMs.
• They should not have a history of Inflammatory Bowel Disease or chronic constipation.
• No antibiotics within the last 3 months
# Intestinal Microbiome Restoration

**Donor Screening Checklist**

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<th>Inclusion Criteria: Answers must ALL be Yes</th>
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<th>No</th>
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<tr>
<td>Healthy adult</td>
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<td>Has daily formed bowel movements</td>
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<table>
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<th>Exclusion Criteria: Answers must ALL be No</th>
<th>Yes</th>
<th>No</th>
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<tr>
<td>Currently taking an antibiotic</td>
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<td>Taken antibiotics in the last 3 months</td>
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<td>Currently taking any other medication for an infection</td>
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<td>Traveled to areas of the world where risk of traveler’s diarrhea is high</td>
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<td>History of chronic constipation, or chronic laxative use</td>
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<tr>
<td>Personal history of Inflammatory Bowel Disease (Crohn’s disease or Ulcerative Colitis)</td>
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<tr>
<td>History of chronic diarrhea or microscopic colitis</td>
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<td>Personal history of GI malignancy or polyposis</td>
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<td>History of gastric bypass</td>
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<td>Taking daily probiotics or daily PPI</td>
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<td>Taking major immunosuppressive agents: steroids, biologics etc.</td>
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<tr>
<td>Currently on systemic chemotherapy</td>
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</table>

**The following conditions should be avoided in donors if possible:**

- Metabolic syndrome/ Obesity
- Autoimmune conditions: MS, psoriasis, vasculitis, RA
- Atopic disease: asthma and eczema and eosinophilic disorders of the GI tract
Frozen vs. Fresh Stool

• Randomized, double blind, non-inferiority trial
• 232 adults with recurrent or refractory CDI
• Up to 2 FMT by enema
• Clinical Resolution @ 13 weeks
  – mITT: 75% (frozen) & 70% (fresh)
  – Per Protocol: 83.5% (frozen) & 85.1% (fresh)

Screening

• Blood:
  • Hepatitis A (IgG and IgM)
  • Hepatitis B (HBsAg/Ab and HBcAb)
  • Hepatitis C Ab
  • HIV-1/2 (Ab and viral load)
  • Syphilis (TP-IgG) during

• Stool:
  • C. difficile (by culture)
  • Routine stool culture
  • Giardia antigen
  • Cryptosporidium antigen
  • O&P

Food Allergies
Frozen stool from a bank: OpenBiome Model

1 Clinician orders fecal preparations from a stool bank

2 Stool bank provides rigorously screened, processed, frozen material

3 The clinician thaws material and performs FMT

Donor Assessment
- 109-point clinical assessment for transmissible infectious diseases and potentially microbiome-mediated conditions
  - E.g. IBD, IBS, depression, anxiety, age, obesity, metabolic syndrome, autoimmune diseases and others

Stool & Serological Testing
- Stool testing
  - C. diff toxin PCR, Ova & Parasites, Isospora, Cyclospora, Giardia EIA; Cryptosporidium EIA; H. pylori Ag, Common enteric pathogens (e.g. Salmonella, Shigella, E. coli, Campylobacter, Vibrio, Norovirus PCR, Adenovirus EIA, Rotovirus EIA, VRE culture, Microsporidium
  - Serological testing
    - HIV 1 & 2, HAV, HBV, HCV, HTLV 1 & 2, Treponema pallidum. CBC, LFTs

Processing, Monitoring & Re-testing
- 60-day quarantine procedure
- Continuous requalification
- Processing controls
- Filtering & homogenization
- Safety aliquots
- Storage & shipping controls
- Traceability
- 16s rRNA (microbiome) sequencing & characterization

<5% pass rate
Step 3: Mode of Delivery

- Nasogastric or nasoduodenal tube
  - Uncomfortable
  - Requires radiology

- Retention enemas
  - Variable patient ability to tolerate

- Lower endoscopy
  - Enables examination of mucosa

- Encapsulation
  - Decreased procedure related risk & cost

Aas et al. 2003; Rubin et al 2012; Van Nood 2013; Silverman et al. 2010; Kassam et al 2012; Lee et al 2014;
Cumulative evidence

- 87%-89% experienced clinical resolution
- No adverse events associated with FMT reported

Cammarota G. J Clin Gastroenterol 2014
Kassam Z, Am J Gastroenterol 2013
Preparation

• Recipient:
  – Standard bowel prep required
  – Continue Abx until day before

• Donor:
  – MOM the night before is ok
  – Stool volume: 50-200gm
  – Collected within 6 hrs of procedure
  – Stool should not be refrigerated
  – *Avoid food allergens
Stool Preparation

- Stool is blended with 500cc NS for 1 min until liquid
- Solution is passed through a strainer into an emesis basin
- Drawn up into 60cc syringes
- Solution can be instilled through the scope
- Full colonoscopy to the TI is performed
- Instillation in the TI and right colon
Step 4: Discharge and Follow Up Post FMT

- Retain slurry for 2-6 hours
- Imodium post-procedure
- Avoid future antibiotics
I had recurrent *C. difficile*. I was treated with a fecal transplant on ____ 20___.

**Questions to ask about new medications:**

1. Is this an antibiotic?
2. Will it put me at undue risk of a *C. difficile* recurrence?
3. Can I avoid oral antibiotic therapy? Are there other treatment options? Will it compromise my care to delay antibiotics and see if my condition improves?
“What if I Need an Antibiotics Again?”

N=152

10.5 % Overall Post FMT CDI recurrence rate

16

10 (63%) received antibiotics

6 (37%) did not receive antibiotics

Fischer/Allegretti DDW 2016
“If I take an antibiotic, should I take a prophylactic antibiotic or probiotic with it to prevent c.diff, and if so which ones?”

Recurrence Rates:

- with neither: 23% (4/17)
- with probiotic only: 21% (3/14)
- with anti-CDI antibiotic only: 0% (0/12)
- with concomitant anti-CDI antibiotic + probiotic: 20% (3/15)
  - with concomitant anti-CDI antibiotics and/or probiotic 15% (6/41)
What if They Need Antibiotics Again?

- **Reassure:** recurrence rates are low post FMT
- Suggest the most narrow spectrum antibiotics
- Prophylactic Flagyl or Vancomycin **not recommended**
  - No proven benefit, possible harm
How Effective is FMT?
How Effective is FMT for recurrent CDI?

• Multiple systematic reviews and meta analyses: shows 90% efficacy
  – Guol APT 2012
  – Sofi Scand J Gastro 2013;
  – Kassam Am J Gastroenterol 2013
  – Drekonja JAMA 2015

• Now, 4 randomized controlled trials
  – VanNood
  – Youngster
  – Cammarota
  – Kelly C.
Duodenal Infusion of Donor Feces for Recurrent Clostridium difficile

Summary: 89.7%, 95% CI 84%-93%)

Kassam et al. AM J Gastroenterol, 2013
How Effective is FMT for recurrent CDI in IBD?

- 67 patients with IBD who underwent FMT

CDI Outcomes:
- 79% efficacy at clearing CDI

IBD Outcomes:
- 46.3% improved
- 35.8% unchanced
- 17.9% worsened
Safety profile in IBD

• Mild Adverse Events: Vomiting, diarrhea, flatulence, bloating

• Infection Transmission:
  – CMV after self-administered-FMT
  – Life-threatening Listeria infection in UC patient

• Disease Flare:
  – Fevers, elevated inflammatory markers and abdominal tenderness post-FMT
  – IBD patients on immunosuppressive therapy who underwent FMT for CDI
    • 5/36 IBD (14%) experienced IBD flare post FMT

Vermeire S. Gastroenterology 2012
Surawicz C. personnel communications
<table>
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<tr>
<th>Study name</th>
<th>Event rate</th>
<th>Lower limit</th>
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Capsules: The Future of FMT Research in IBD
## Capsules

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<th>Pros</th>
<th>Cons</th>
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| • avoid a procedure, anesthesia  
• lower cost  
• No bowel prep | • motility  
• large pills  
• many pills  
• **Dose unknown** |
**FMT capsules: Current Landscape**

A recent proof-of-concept case series suggested a version of oral FMT capsules may be effective.

**Method:**
- Stool suspension generated in saline
- Sequentially sieved & centrifuged
- Resuspend pellet in saline/glycerol
- Size 00 capsules and frozen (-80°C)
- Mean stool per capsule: 1.6g

**Dosing:**
- 15 capsules on 2 consecutive days
- Total of 48 grams of stool
- If non-response, re-treated with 15 capsules on 2 consecutive days

**Results:**
- Single course: 70% clinical cure
- Extended course: 90% clinical cure
- No serious adverse events

**Issues:**
1. Unstable formulation – aqueous attack on gelatin vehicle
   Propensity for degradation
2. Time consuming & non-scalable
3. Arbitrary dose

- The minimum effective dose of capsule based FMT is unknown.
- Current dosing standards:
  - 25 grams of stool in 250mls of saline for lower GI administration
  - 12.5 grams of stool in 30mls of saline for upper GI administration.

Youngster et al JAMA 2014
Novel FMT Capsule: Microbial Emulsion Matrix

Highly stable at room temperature

Scalable process
- >25,000 capsules produced

Dosing
- Mean stool per capsule: 0.75g

Viability

Stability

Mendolia, Kassam et al, ACG 2015
Methods: Study Overview

Open-label, cluster dose-finding study performed at two academic, quaternary care hospitals

Inclusion criteria
- Outpatient recurrent CDI (3 or more episodes) referred for FMT
- Failed to maintain CDI cure after standard therapy

Key exclusion criteria
- Dysphagia / ‘test’ capsule failure
- History of aspiration
- Severe-complicated CDI
- IBD

Endpoints
1. Safety (grade 2+) between high & low dose
2. Clinical resolution of diarrhea with no CDI recurrence at 8-weeks

Allegretti DDW 2016
Results: Single FMT capsule course

No adverse events attributed to FMT were observed in either group

<table>
<thead>
<tr>
<th></th>
<th>High Dose N=7</th>
<th>Low Dose N=10</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical remission at 72 hours</td>
<td>7 (100%)</td>
<td>8 (80%)</td>
<td>0.56</td>
</tr>
<tr>
<td>Clinical cure at 8 week</td>
<td>5 (71%)</td>
<td>7 (70%)</td>
<td>0.33</td>
</tr>
</tbody>
</table>
Results

• Overall 5 patients were non-responders
  ▪ 3 low dose group
  ▪ 2 high dose group
• After re-treatment with high dose capsule FMT, 4/5 (80%) had resolution of symptoms
• 1 patient underwent successful FMT by colonoscopy
• **Aggregate FMT capsule response rate:** 16/17 (94%)
• Treatment algorithm: initial course of low dose capsules followed by high dose retreatment for non-responders
Severe CDI

- 14-18% 30 day all-cause mortality
- Surgery for refractory/complicated infection:
  - Total abdominal colectomy with end ileostomy procedure of choice
  - 30 day perioperative mortality 30-80%
  - “not good surgical candidates”

Jaber M. Am J Gastro; 2008
Schmic D. J Infect Pub Health 2014
Fischer Protocol

- Sequential FMT
- 29 patients: 10 severe & 19 severe complicated 5 toxic megacolon
  - 59% female; mean age 65
- 27/29 (93%) cured
  - Single FMT 62%
  - 2 FMT 31%
  - 3 FMT 7%
- 30 day all cause mortality 7%

Fischer M. Aliment Pharm Thera 2015.
FMT for the Treatment of IBD
• Cannot be performed in the US for clinical care currently
• IND from the FDA is required
• Ongoing Clinical Trials
Case Reports for FMT in IBD

• 1989: Bennet et al. self treated with fecal enemas for UC
  – Clinical and histologic remission

• 2012 Systematic Review: 41 patients with IBD and CDI
  – Reduction of symptoms (76%)
  – Disease remission (62%)

Bennet JD. Lancet 1989
Meta-analysis

36.2% achieved clinical remission (95% CI 17.4%-60.4%)
-60.5% of CD patients (95% CI 28.4%-85.6%)
-64% of younger patients (95% CI 10.6%-96.4%)
-22% of UC patients (95% CI 10.4%-40.8%)

Colman RJ, JCC 2014
## Randomized Controlled Trials

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Study design</strong></td>
<td>Double blind randomized (1:1), controlled</td>
<td>Double blind randomized (1:1), controlled</td>
</tr>
<tr>
<td><strong>Study population</strong></td>
<td>Adult patients with mild to moderate UC</td>
<td>Adult patients with mild to moderate UC</td>
</tr>
<tr>
<td><strong>Subjects randomized</strong></td>
<td>75</td>
<td>50</td>
</tr>
<tr>
<td><strong>Number completing therapy</strong></td>
<td>70</td>
<td>37</td>
</tr>
<tr>
<td><strong>Anti-TNF permitted</strong></td>
<td>Yes- stable doses</td>
<td>No</td>
</tr>
<tr>
<td><strong>Placebo</strong></td>
<td>Water</td>
<td>Autologous FMT</td>
</tr>
<tr>
<td><strong>Route</strong></td>
<td>Retention Enema</td>
<td>Naso-duodenal tube</td>
</tr>
<tr>
<td><strong>Schedule</strong></td>
<td>Weekly for 6 weeks</td>
<td>2 doses (week 0 and 6)</td>
</tr>
<tr>
<td><strong>Donor stool</strong></td>
<td>6 volunteers; fresh or frozen</td>
<td>15 volunteers; fresh</td>
</tr>
<tr>
<td><strong>Primary endpoint</strong></td>
<td>Remission: Mayo score ≤ 2 and endoscopic score of 0 at week 7.</td>
<td>Clinical remission: Simple clinical colitis activity score ≤ 2 combined with ≥ 1 point decrease in Mayo endoscopic score at week 12.</td>
</tr>
<tr>
<td><strong>Subjects who achieved Primary endpoint</strong></td>
<td>9/38 (24%) FMTvs 2/37 (5%) controls p=0.03</td>
<td>7/23 (30%) FMT vs 5/25 (20%) controls (p=0.51)</td>
</tr>
</tbody>
</table>
Focus Trial

- Double-blinded multi center RCT
- Included: active UC resistant to standard treatments
- Randomized to receive:
  - a single FMT via colonoscopic on day 1 followed by enema 5 days/week for 8 weeks
  - Placebo FMT via colonoscopy followed by placebo enemas
- Active treatment: 3 to 7 unrelated donors.
- Primary endpoint: steroid-free clinical remission + endoscopic response/remission
Results

- 81 patients enrolled.
- Steroid-free clinical remission + endoscopic response:
  - 11 of 41 (27%) patients receiving FMT vs 3 of 40 (8%) patients receiving placebo ($p = 0.02$)
Microbiome changes associated with sustained eradication of *Clostridium difficile* after single faecal microbiota transplantation in children with and without inflammatory bowel disease

S. K. Hourigan*†, L. A. Chen*†, Z. Grigoryan†, G. Laroche*, M. Weidner*, C. L. Sears* & M. Oliva-Hemker*
**CDI**
- Single Infusion
- Symptom reversal is rapid
- Will work in majority of patients
- Success: no symptoms, negative stool

**IBD**
- Multiple Infusions
- Symptom reversal is slower and may be transient
- Will work in a subset of patients
- Success: no symptoms, normal histology
• Ongoing Studies at BWH:
  – Post Op Crohn’s
  – PSC
  – Obesity
Patient Perspectives
Patient willingness to undergo FMT

Participant’s self-reported disease severity and willingness to undergo FMT

Adapted from C.Kelly DDW 2015
Kahn S. Inflamm Bowel Dis 2013
What about the patients?
Fecal transplants beat antibiotics for curing diarrhea caused by C. difficile

The treatment may sound appalling, but it works.

Self-Prescribed Fecal Transplant Saves Canadian Man's Life

Fecal Transplants: They Work, the Regulations Don’t

Fecal transplants successful in treating intestinal ailments

Fecal transplants show promise in infection fights
The FMT Coach
A Guide to Fecal Microbiota Transplantation

Matt Robinson

POOP POWER
STORY & GUIDE BOOK
How a man used Fecal Transplants at home to permanently cured himself of Insensitive Tcell
The gut microbiome contains a highly complex and dense community of microbes that include bacteria, fungi and viruses, many of which have not been fully characterized.

It is a dynamic and living consortium that can change over time in ways that scientists cannot currently fully predict.
Safety and Ethical Concerns

**Acute Concerns:**
- bacterial, viral, parasitic infections
- acute allergic reactions

**Long-term concerns**
- is it possible that we are predisposing the recipient to the diseases the donor will develop in his/her lifetime?
- Animal models suggests the microbiome may play a role in the pathogenesis of several human diseases.
  - Metabolic syndrome
  - Heart disease
  - Behavior
Conclusions

- FMT is an effective therapy for recurrent CDI infections in patients with and without IBD
- It is a therapy that shows promise for the treatment of IBD
- Patients and clinicians are eager for alternative therapies
- Safety Profile is good and risk of flares is low
- Long term consequences remain unclear
Thank You