Our Vision
To provide every patient with the care we want for those we love the most

Norfolk and Norwich University Hospitals NHS

Faecal microbiota transplantation

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NNUH

Aims

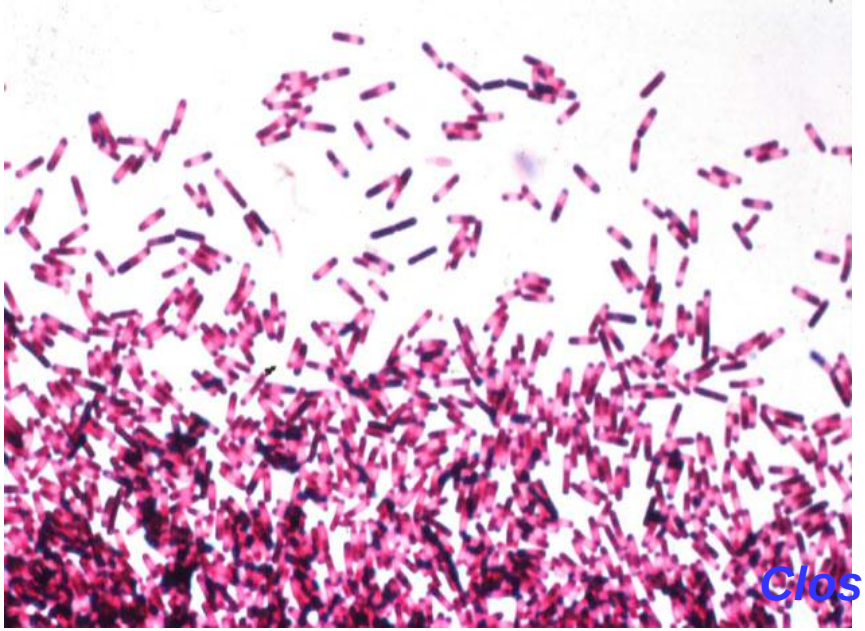
- Why faecal microbiota transplantation (FMT) at NNUH?
- How we set up our service
- Our experience so far
- Next stage

History of FMT

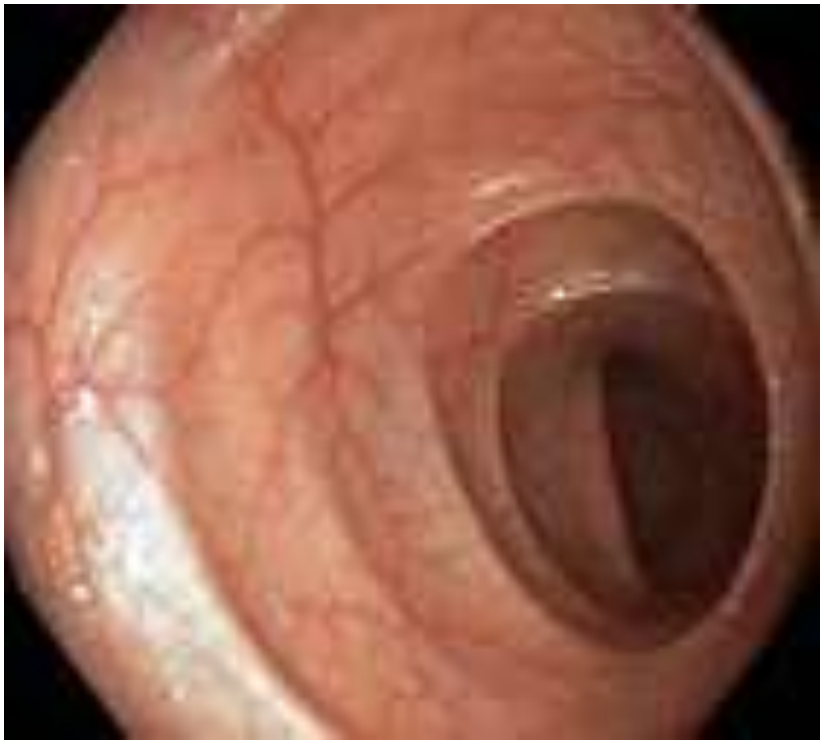
- Bacteriotherapy, faecal transfusion, faecal transplant, stool transplant, faecal enema, and human probiotic infusion (HPI).
- 4th century China (yellow soup, golden syrup)- food poisoning, severe diarrhea
- 1958 first publication Ben Eiseman et al, Colorado, Surgery 1958;44:854-859 (PMC)
- Centre for Digestive Diseases in Sydney, Australia, offering FMT for more than 20 years
- Some baby animals eat their mothers' faeces (coprophagia)

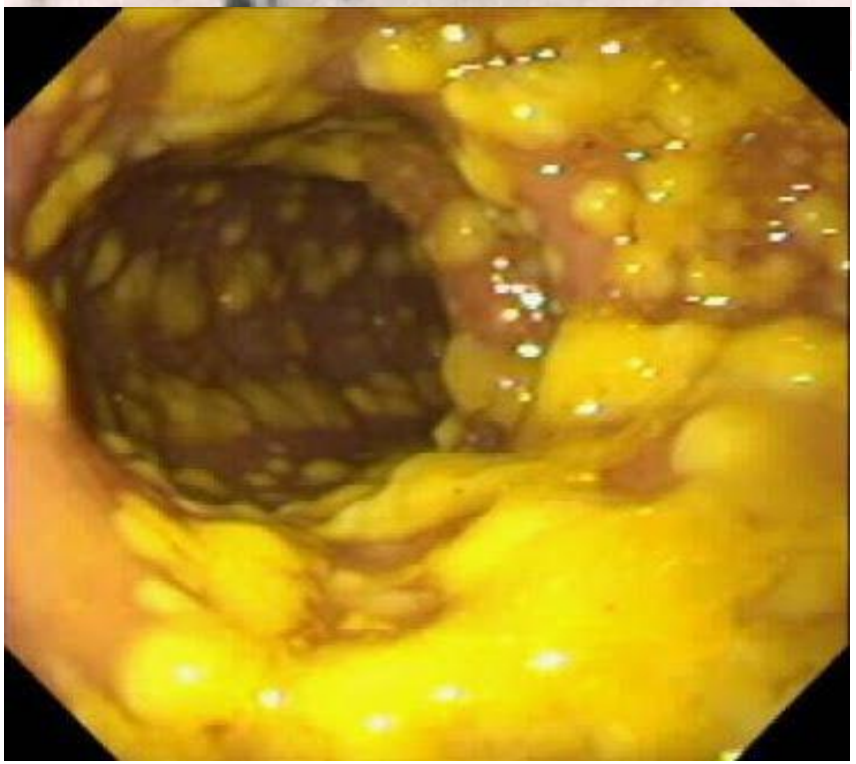
The problem

- UK-20,488 cases (2010), 12000 (2014), 3000 relapses
- USA-100,000 cases,14,000 deaths
- 1:3 to1: 4 have at least one relapse
- Of these 60% further relapses
- Destruction of gut diversity by antibiotics



Clostridium difficile





C. difficile chain of infection

Infectious agent
C. difficile

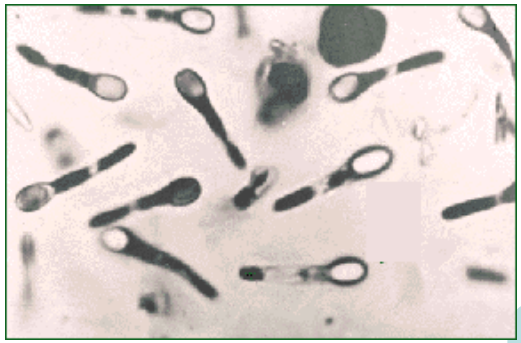
Reservoir
Large bowel

Portal of exit
Faeces

Means of transmission
Faecal-oral

Portal of entry
ingestion

Susceptible host
immunocompromised, >65, broad spectrum Antibiotic use, healthcare contact



NICE National Institute for Health and Care Excellence

Faecal microbiota transplant for recurrent Clostridium difficile infection

Issued: March 2014
NICE interventional procedure guidance 485
guidance.nice.org.uk/ipg485

NICE **Recommendations**

- 1.1 Current evidence on the **efficacy** and **safety** of faecal microbiota transplant for recurrent *Clostridium difficile* infection is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit.

- 1.2 This procedure should **only** be considered for patients with recurrent *C. difficile* infections that have failed to respond to antibiotics and other treatments.

- 1.3 Clinicians should ensure that a confidential record is kept of the donor and recipient of each faecal microbiota transplant.

- 1.4 NICE encourages further research into faecal microbiota transplant for *C. difficile* infection, specifically to investigate optimal dosage, mode of
- administration and choice of donor.

- "Implementation of this guidance is the responsibility of local commissioners and/or providers".

Why FMT?

- Real problem
- Real and lasting solution (improve patient care)
- Break the vicious cycle, Possibility of cure
- Discourage DIY and unregulated practice
- Current CDI treatments not effective-Vanc, Mtz, HNIG, pulsed, tapering, Fidaxomicin, ? Tigecycline
- Existing interest and expertise in *C. difficile*

Evidence-Faecal microbiota transplant (FMT)

Van Nood, N. Eng j, Jan 2013

- Via nasogastric tube, nasoduodenal tube, NJ, rectal enema or via the biopsy channel of a colonoscope
- 42 patients-faecal transplant/ Vancomycin, with a bowel lavage /Vancomycin only. Primary cure rates 81% /23%/ 31% respectively at 10-week follow-up.
- Relapse rates 6%, 54% and 62%
- FMT overall cure rate of 94%

Aim of FMT

- Replace with healthy flora
- Right composition
- Microbial diversity

Stages of FMT

- Pre-screened donor register
- Identify eligible pt
- Notify donor and FMT lab
- Administer donor questionnaire
- Book endoscopy, prep patient
- Prepare donor material
- Infuse FMT
- Store aliquots (donor and recipient)
- Follow up

Donor exclusion criteria for fecal microbiota transplant

Absolute
Risk of infectious agent
Known HIV, hepatitis B or C infections
Known exposure to HIV or viral hepatitis (within the previous 12 months)
High-risk sexual behaviors
Use of illicit drugs
Tattoo or body piercing within six months
Incarceration or history of incarceration
Known current communicable disease (eg, upper respiratory tract infection)
Risk factors for variant Creutzfeldt-Jakob disease
Travel (within the last six months) to areas of the world where diarrheal illnesses are endemic or risk of traveler's diarrhea is high
Gastrointestinal comorbidities
History of inflammatory bowel disease
History of IBS, idiopathic chronic constipation, or chronic diarrhea
History of gastrointestinal malignancy or known polyposis
Factors that can or do affect the composition of the intestinal microbiota
Antibiotics within the preceding three months
Major immunosuppressive medications (eg, calcineurin inhibitors, exogenous glucocorticoids, biological agents, etc)
Systemic antineoplastic agents
Additional recipient-specific considerations
Recent ingestion of a potential allergen (eg, nuts) where recipient has a known allergy to this (these) agent(s)
Relative exclusion criteria that might be appropriate to consider
History of major gastrointestinal surgery (eg, gastric bypass)
Metabolic syndrome
Systemic autoimmunity (eg, multiple sclerosis, connective tissue disease)
Atopic diseases including asthma and eczema, eosinophilic disorders of the gastrointestinal tract
Chronic pain syndromes (eg, chronic fatigue syndrome, fibromyalgia)

HIV: human immunodeficiency virus; IBS: irritable bowel syndrome.
Data from: Bakken JS, Borody T, Brandt LJ, et al. Treating Clostridium difficile infection with fecal microbiota transplantation. Clin Gastroenterol Hepatol 2011; 9:1044.

NNUH donor screening

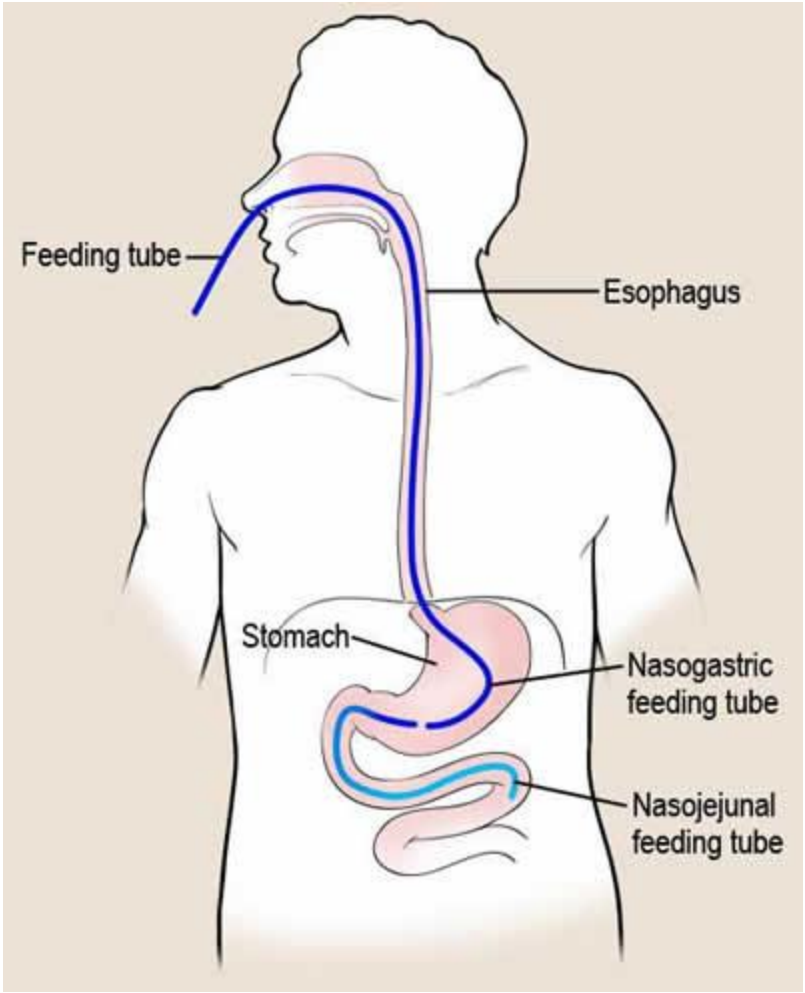
- Serum sample for:
- HIV 1+2 antibodies
- HTLV I/II antibodies (Ref lab.)
- Hepatitis A IgM
- Hepatitis BsAg, cAb,
- Hepatitis C antibody
- Hepatitis E antibody (Ref lab)
- Syphilis ELISA for total antibody
- CMV/EBV IgG
- Strongyloides and Entamoeba histolytica serology (Ref lab.)

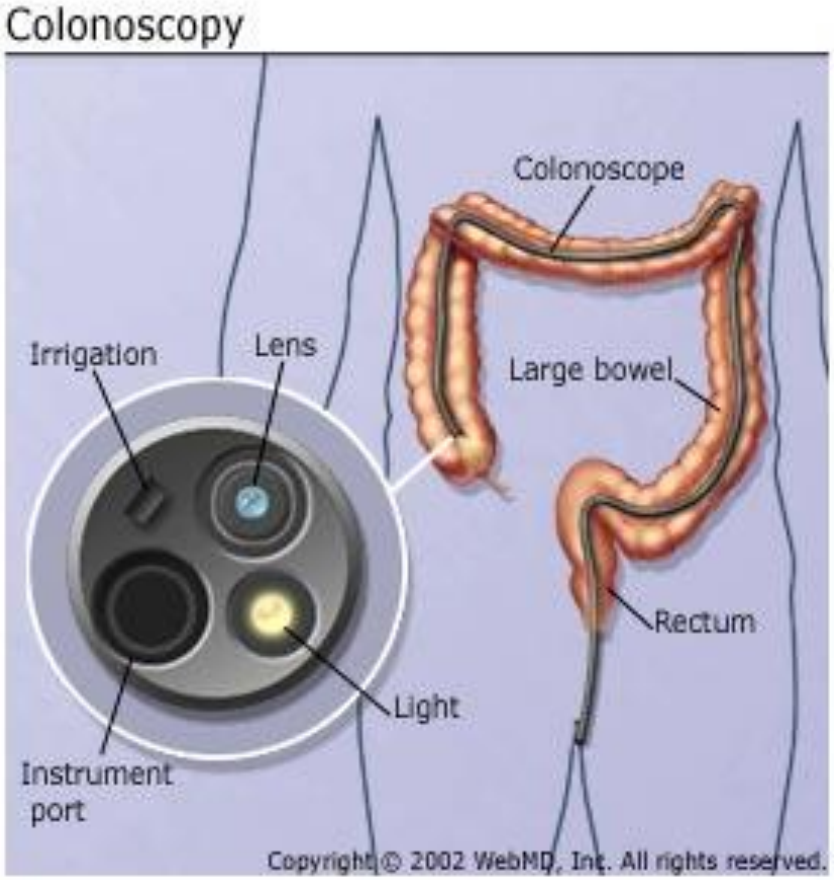
- **NNUH uses Unrelated donors, motivated, well informed**

- Stool specimen testing for:
- Microscopy for Ova, cysts and parasites by concentration
- Culture for Salmonella, Shigella, Campylobacter, E. coli 0157
- *C. diff* GDH and Tox A/B
- Norovirus PCR
- Screen for extended spectrum beta lactamase producing organisms (ESBLs)
- Screen for Vancomycin resistant enterococci (VRE)
- Screen for Meticillin resistant *Staphylococcus aureus* (MRSA)
- Screen for Carbapenemase producing Enterobacteriaceae (CPE)

Patient prep

- Consent
- Oral Vanc 500mg qds commence 4 days prior to FMT
- Bowel prep day before if possible
- NJ tube insertion
- Slurry infusion
- Can eat 30mins after infusion
- Can go home after one bowel motion


Feeding tube
Esophagus
Stomach
Nasogastric feeding tube
Nasojejunal feeding tube


Colonoscopy
Colonoscope
Irrigation
Lens
Large bowel
Rectum
Light
Instrument port
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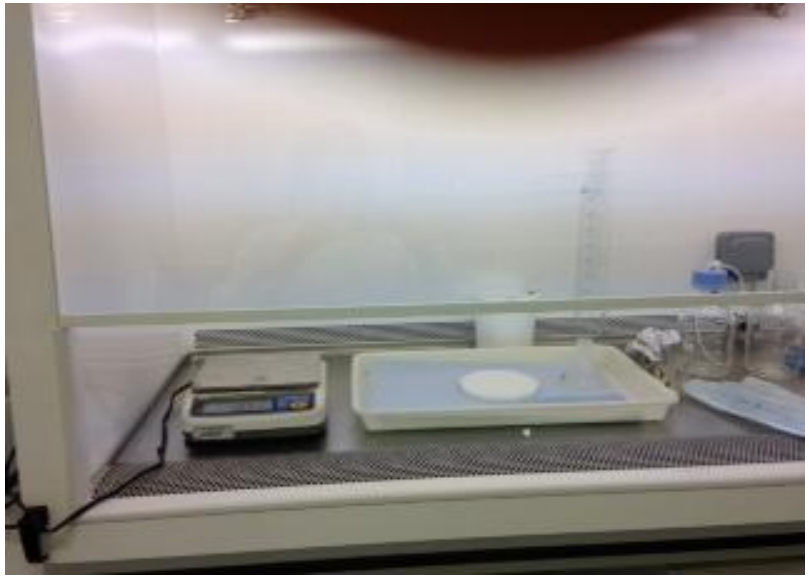
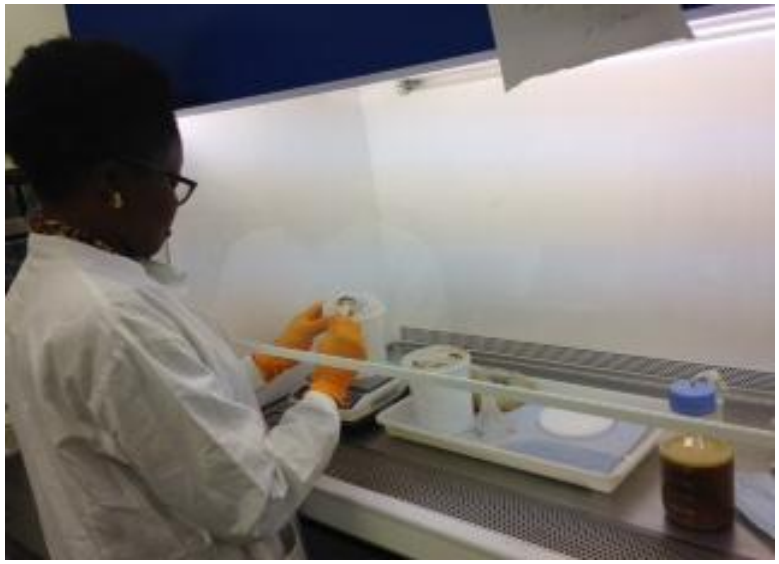
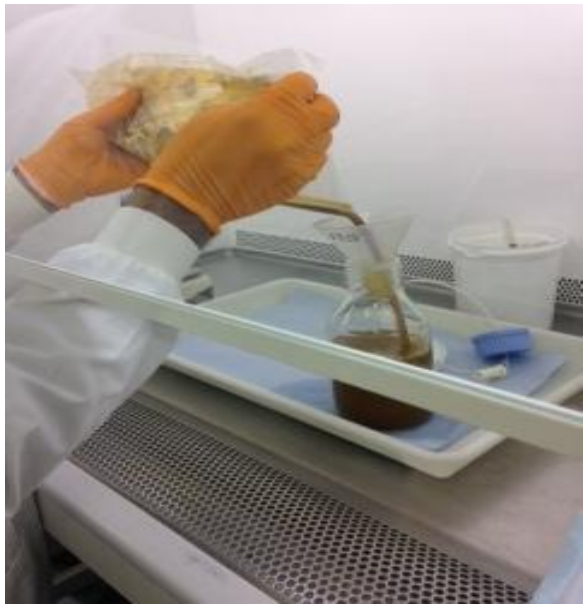


FMT preparation in a dedicated laboratory





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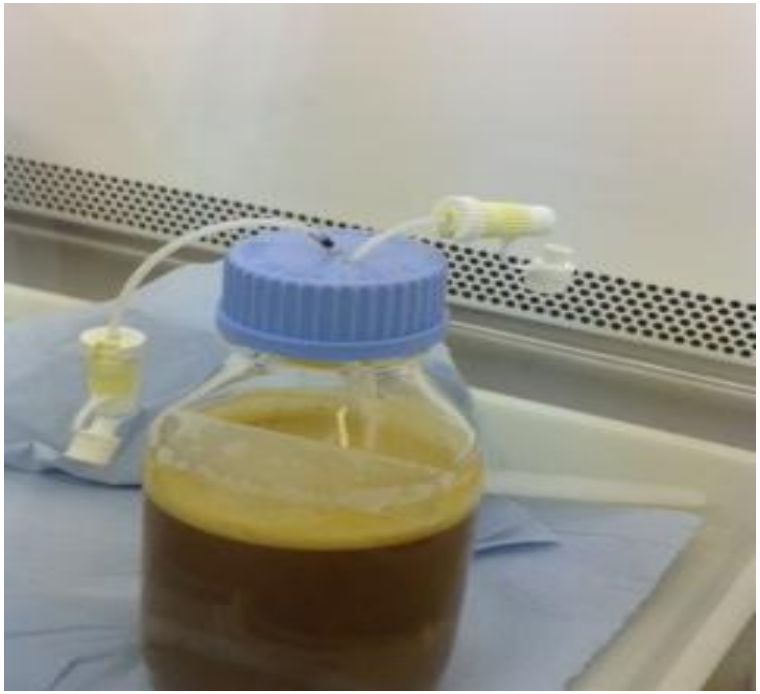

NNUH experience so far

- 1st case Aug 2015
- 12 cases so far
- 11(91%) response (8 wks to 8months)
- 1 patient's FMT compromised due to co-admin of needed atbs
- Business case in progress

Side effects from literature-- Minor & infrequent

- Belching, abdominal cramps, tummy pain (Risk is 1 in 5 patients)
- Diarrhoea on the day of the transplant (all patients due to volume of suspension given)
- Infections of the stomach, bowel and the tissue lining the inside of the abdomen (tummy) from commensal organisms (peritonitis or enteritis) within 2 days of having the procedure (Risk 1 in 50 patients).
- **Risks from access route provision**
- Possibility of infection, obesity??
- No serious adverse effect so far in our 12 patients

Patients/ carers ….

Pre- treatment:

- I just want to go back to my wife, she is alone and losing her sight.
- Pt is palliative and difficult to manage due to symptoms
- I want to go to my step father's funeral
- Care home does not want the pt
- I hate being in isolation. I need my exercises and my rehab
- I was embarrassed at a wedding
- Can't get carers in
- Symptoms keep coming back

Post-treatment:

- I did not want to flush the toilet, haven't done anything this good for a long time!
- I hadn't slept through the night for months until last night
- I'll personally come and speak to any patient who is reluctant to take this treatment

Future developments

- Optimum dose, route
- Match donor with recipient
- Super donor
- Any difference based on ribotype e.g. 027?
- Microbial cocktail
- Long term follow up
- Age restriction?
- Use as first line?

Future developments

- Fresh/ frozen
- Stored autologous
- Capsules
- Related/ unrelated donors
- Research, research, research!
- MDRO
- Organ transplant
- Metabolic medicine
- Etc
- Relapses/ re-infection
- Access to out patients and other hospitals

Expanding rapidly

- Now over 500 centers in USA,
- 7 centre in the UK (BMJ 2015)
- open Biome stool bank, USA
- Netherlands stool bank

Conclusion

- 90% efficacy (95% if two FMTs)
- Natural product
- No supply problems
- No direct cost
- No over dose
- No under dose
- No drug reaction
- No drug interaction
- No contraindications
- No age limits
- Logistics and technical considerations
- Reduce antibiotic resistance
- Improve patient care
- Reduce spread in hosp
- Cost effective

ACKNOWLEDGMENT

FMT collaborators

- Institute of food research (IFR)
- Dedicated donors
- Microbiology lab, EPA
- Gastroenterology colleagues/ endoscopy unit
- NNUH Infection control team