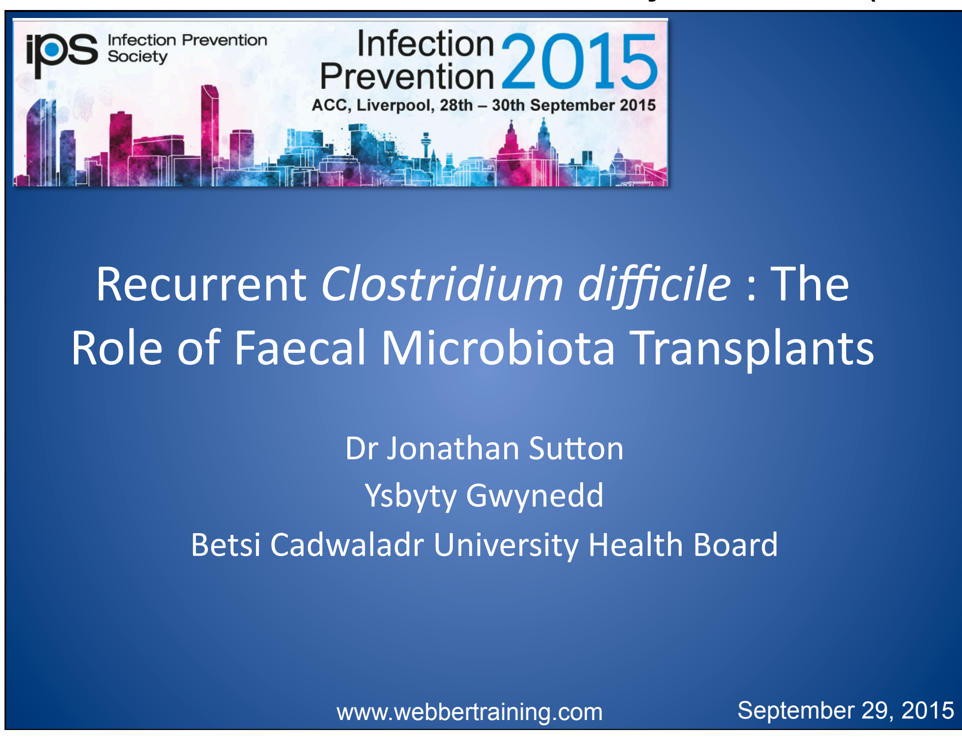
ips Infection Prevention Society
Infection Prevention 2015
ACC, Liverpool, 28th – 30th September 2015
Recurrent Clostridium difficile : The Role of Faecal Microbiota Transplants
Dr Jonathan Sutton
Ysbyty Gwynedd
Betsi Cadwaladr University Health Board
www.webbertraining.com
September 29, 2015

'Toying with human motions'
*Borody et al. Journal of clinical gastroenterology 38(6) 2004
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The Power of Poop
The POWER of POOP
promoting safe, accessible fecal microbiota transplant
for all who need it
ABOUT
SUCCESS STORIES
E-PATIENTS
RESOURCES
FACEBOOK GROUP
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Bob's Story
In August, Bob a much loved 57 year old husband, father and state administrator was having regular outpatient treatment in the local hospital in Kentucky, USA, for a non-gut-related condition. One day he had his regular treatment, developed diarrhea that... Read More ›
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Meet Your Microbiome
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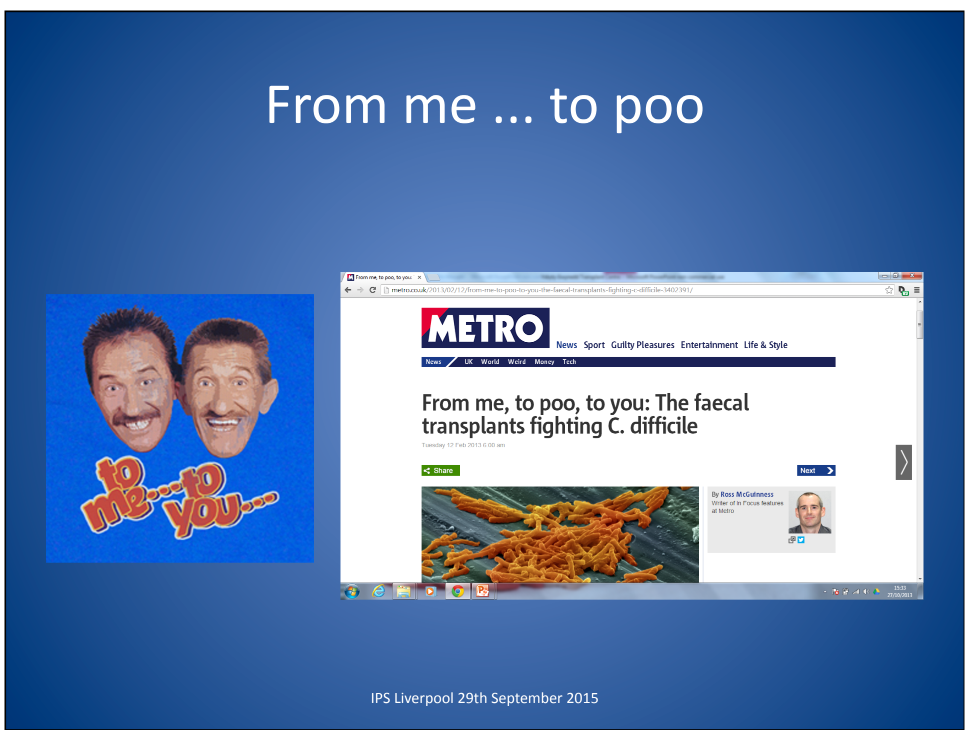
From me … to poo
to me...to you...
METRO
From me, to poo, to you: The faecal transplants fighting C. difficile
IPS Liverpool 29th September 2015

Overview

- Case history
- Recurrent CDI
- Why FMT?
- History of FMT
- Our journey
- The future?

Case history

- Mr MW 76 year old man
- Admitted to local hospital July 2014
  - Severe CAP- managed in ITU
  - Cardiac arrest on ITU
  - Coronary angioplasty
  - Developed ARF
  - Haemodialysis
- Developed C diff
  - Metronadazole 14 days
  - Vancomycin 14 days
  - Vancomycin + metronidazole 28 days
  - Fidaxomicin 10 days

Referral

Sent: Tuesday, December 23, 2014 10:41 AM
To: Jonathan Sutton (BCUHB - Medical)
Subject: Stool transplant
Hi,

I am trying to get hold of the gastroenterologist who does stool transplants. Is that you?

We have a patient I would like to discuss.

Thanks

MW

- Wife – post splenectomy on long term antibiotics
- Daughter – recent tonsillitis
- 2 grandsons aged 8 and 12
- Opted to treat with frozen material
- 8 months later no recurrence

Clostridium difficile

- Difficult or obstinate
- Gram positive, spore forming organism
- Can be a minor part of normal colonic microbiota
- Causes disease when competing bacteria are wiped out following antibiotic use

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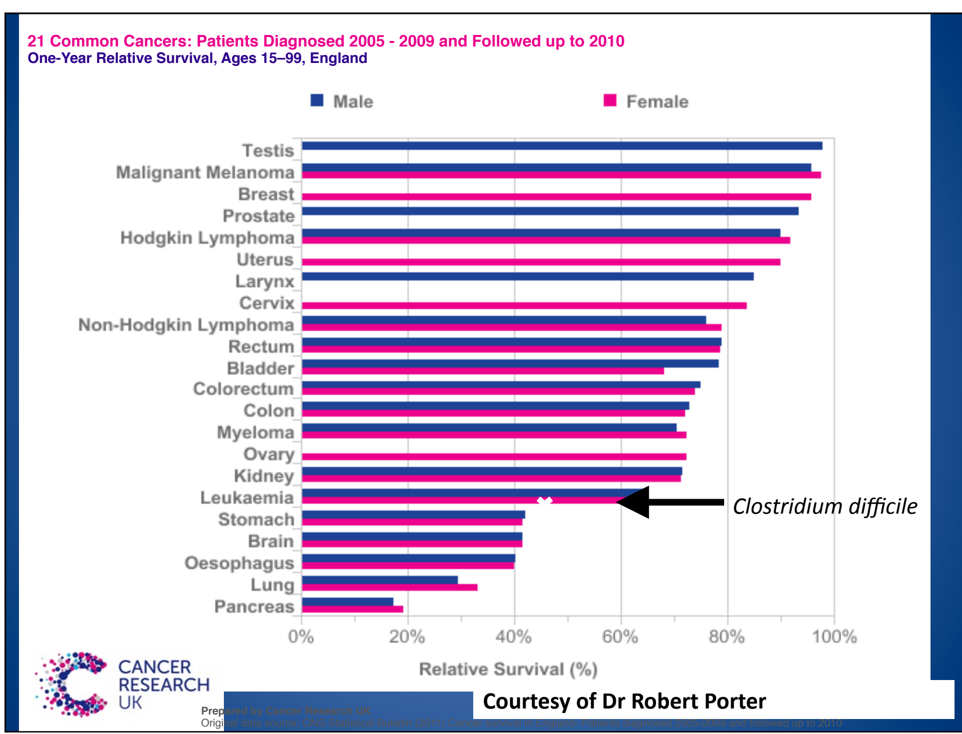

Recurrent CDI

- Complete abatement of symptoms whilst on appropriate treatment followed by reappearance of diarrhoea after treatment stopped
- Molecular methods suggest up to 50% are reinfections rather than relapses.

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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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Management of recurrence

- Tapered or pulsed dose vancomycin
  - Persistent spores
  - Recurrence rates 31% compared with 45%

- Fidaxomicin narrow spectrum antibiotic – less damaging to background microbiota.
  - Similar efficacy to vancomycin but less recurrence

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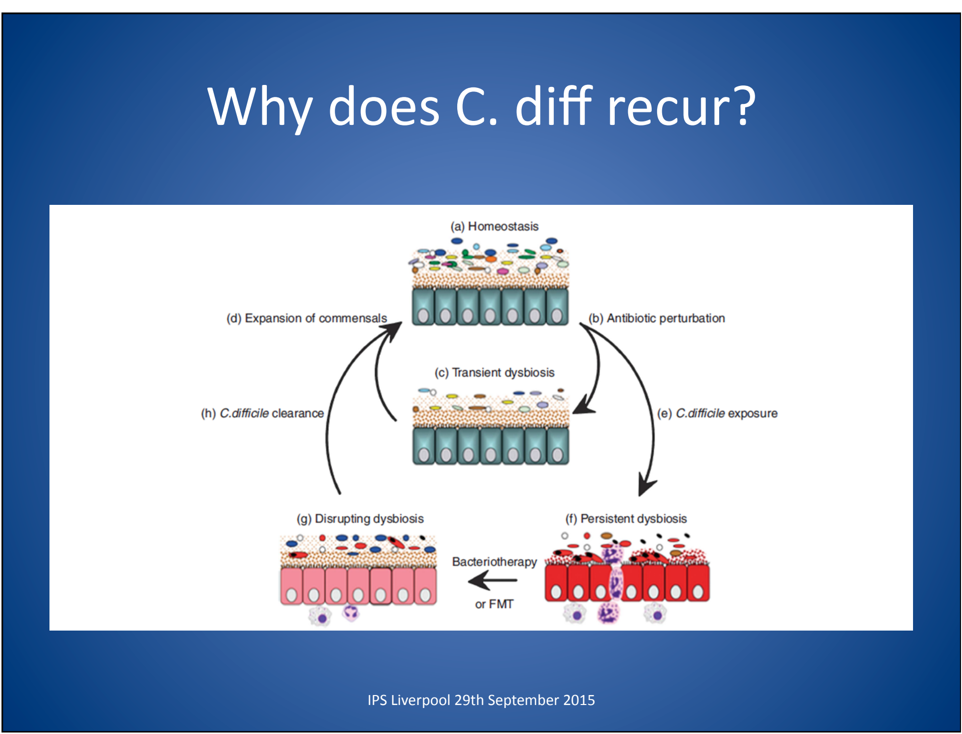
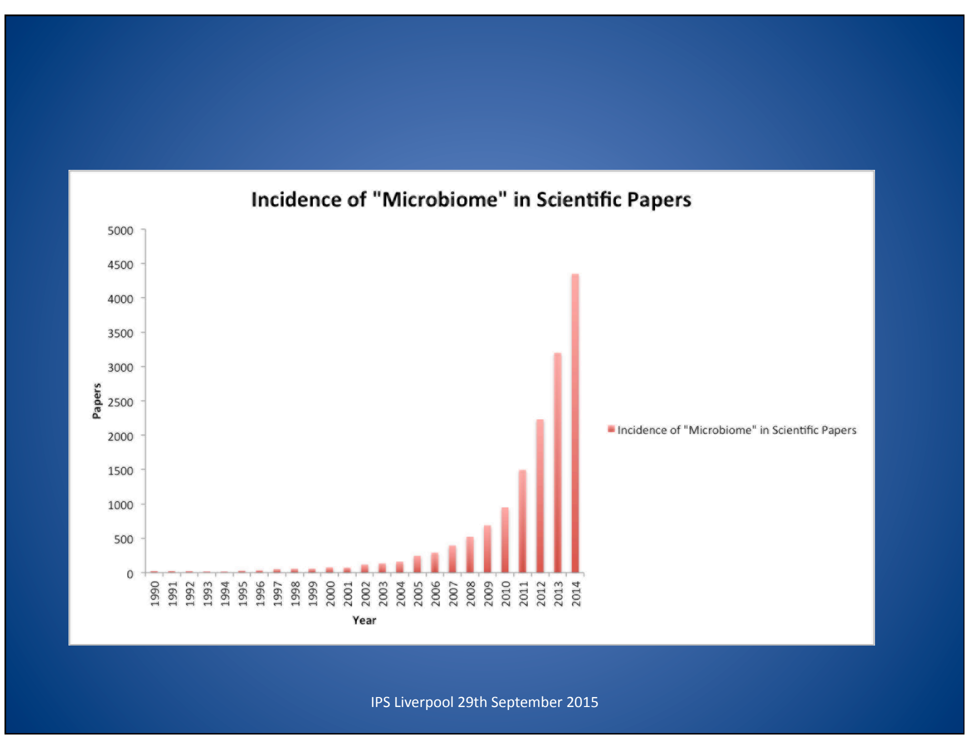


Antibiotics
Antibiotics
FMT
Emma Allen-Vercoe, Univ Guelph , Canada


Incidence of "Microbiome" in Scientific Papers
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
Papers
1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014
Year
Incidence of "Microbiome" in Scientific Papers
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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*
- Data limited to case reports and case series

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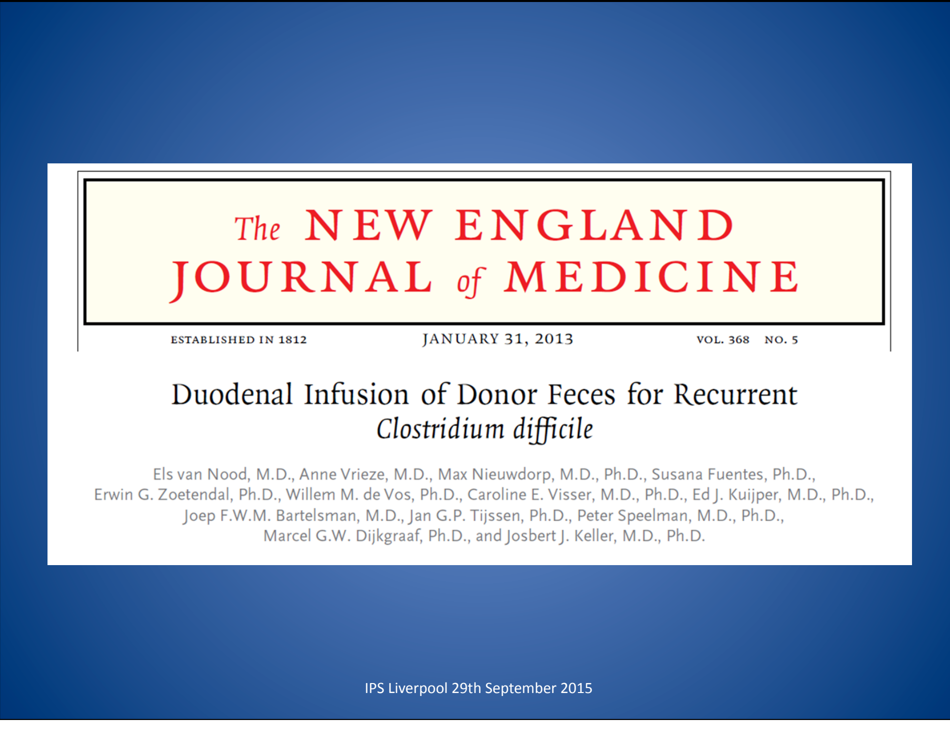

- Open labelled, RCT
- 3 treatment arms
  - Vancomycin , bowel lavage, FMT
  - Standard vancomycin regimen
  - Standard vancomycin +bowel lavage

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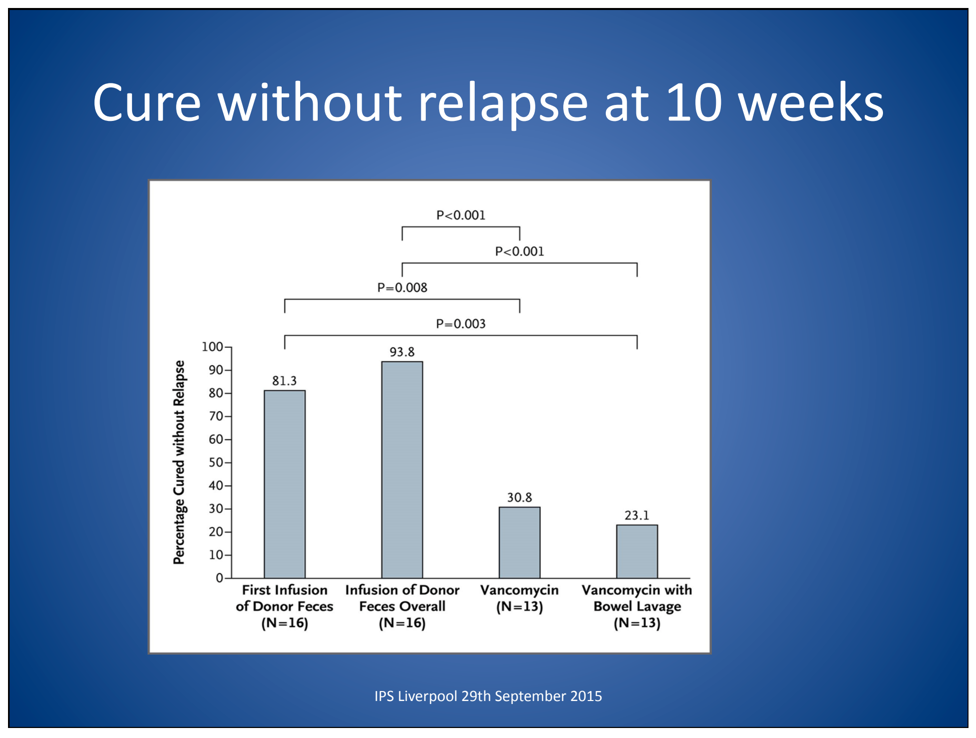
Cure without relapse at 10 weeks
P<0.001
P<0.001
P=0.008
P=0.003
Percentage Cured without Relapse
100
90
80
70
60
50
40
30
20
10
0
81.3
93.8
30.8
23.1
First Infusion of Donor Feces (N=16)
Infusion of Donor Feces Overall (N=16)
Vancomycin (N=13)
Vancomycin with Bowel Lavage (N=13)
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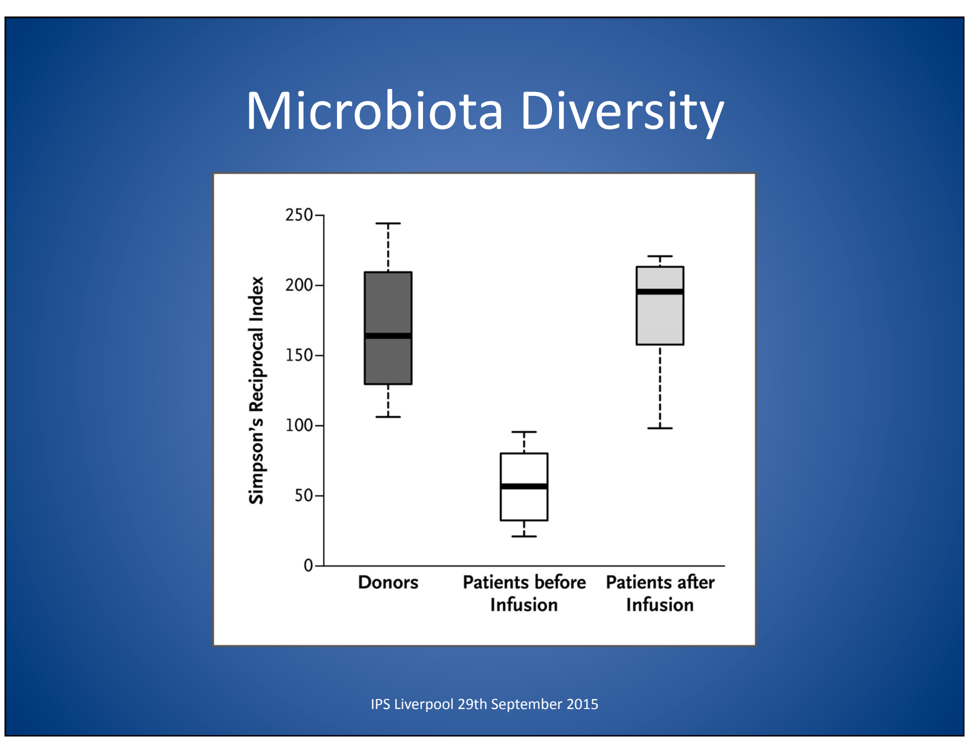
Microbiota Diversity
Simpson's Reciprocal Index
250
200
150
100
50
0
Donors
Patients before Infusion
Patients after Infusion
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- Trial stopped early as almost all the patients in the 2 control arms had recurrence
- Success rate for FMT 80% consistent with case series data

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Acceptable to patients?

- Clinicians often state no patient would ever agree to this procedure
- No patient (in YG)who has been considered for procedure has refused it.

Zipursky J. et al. Can J Gastroenterol Hepatol 2014 28(6):319-24

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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

Results

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

Safety of FMT

- Most current data is retrospective
- Minor
  - Abdominal symptoms immediately post FMT are common
- Serious
  - Related to mode of administration
  - Transmission of infection
- Potential
  - Transmission of infective agent
  - Induction of chronic disease by altering the microbiome

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Our Journey

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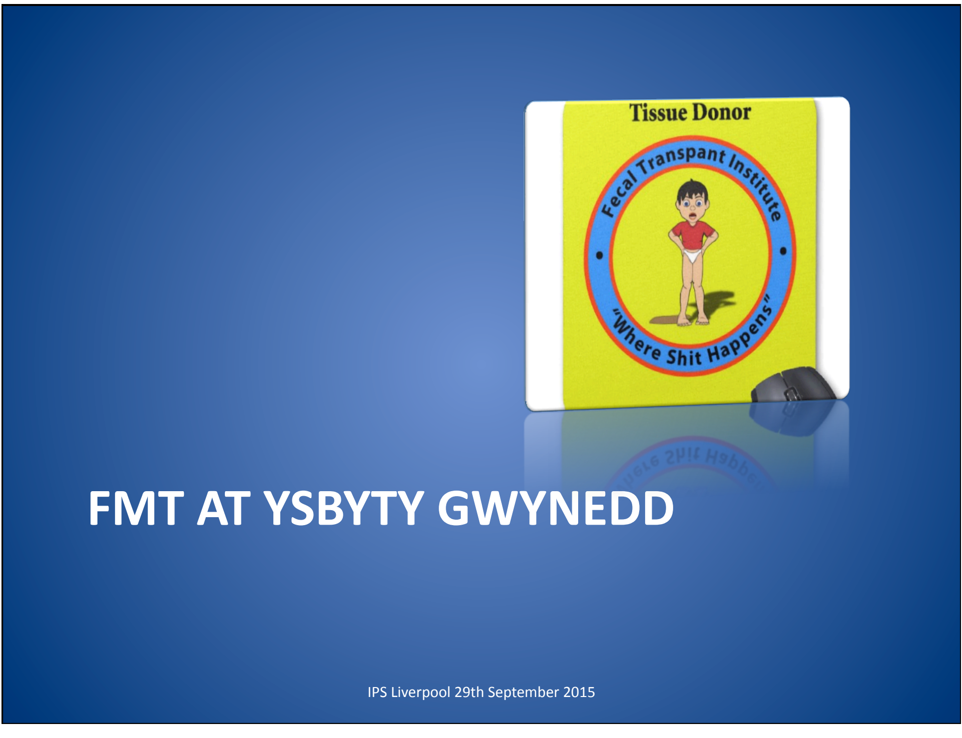

Multidisciplinary

- Interested in the concept
- Lack of effective treatment for recurrent disease
- Discussed with local microbiologists
- Discussed with gastroenterology colleagues
- RCT was trigger to look at developing a service

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Who, where and how?

- Must have had 2 relapses – tapered vancomycin
- Opted to use colonoscopy as preferred method
- Preferred to use relatives as donor
  - Screening confirmed

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Donor selection

- Pt relative
- BMI < 30
- No bowel symptoms (IBS/IBD)
- No autoimmune disease
- No antibiotic use for 3 months prior to transplant

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Screening of Donors

Table S1. Screening of blood and feces from candidate donors.

Blood tests:	Cytomegalovirus (IgG and IgM)
	Epstein-Barr Virus (VCA IgM, VCA IgG, VCA, antiEBNA)
	Hepatitis A (total antibodies, *and if positive also Hepatitis A IgM*)
	Hepatitis B (HbsAg, antiHbsAg)
	Hepatitis C (anti HCV)
	HIV-1 and HIV-2 (Combined HIV Antigen/Antibody test)
	Human T-lymphotropic virus types I and II (HTLV) (antibodies)
	Treponema pallidum (TPHA)
	Entamoeba histolytica (agglutination and dipstick test)
	Strongyloides stercoralis (ELISA)
Fecal tests:	Bacteriological evaluation by local standards
	Parasitological evaluation by local standards (triple feces test)
	Test for *Clostridium difficile (toxin ELISA and culture)*

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Specialist equipment
TESCO
JUG BLENDER

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Transplant

- Procedure performed in endoscopy unit
- Donor provides sample on arrival
- Material processed
  - 2 staff masked and gowned
  - Mixed with N/saline in household blender
  - Homogenised
  - Drawn in 50ml syringes and capped

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Patient

- Vancomycin continued until 48 hours prior to transplant
- Full bowel prep given
- Colonoscopy performed to terminal ileum
  - 10 x 50mls donor material given through the scope.
- Loperamide given immediately
- Bed rest for 6 hours
- Loperamide repeated at 6 hours

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PARENTAL
ADVISORY
EXPLICIT CONTENT
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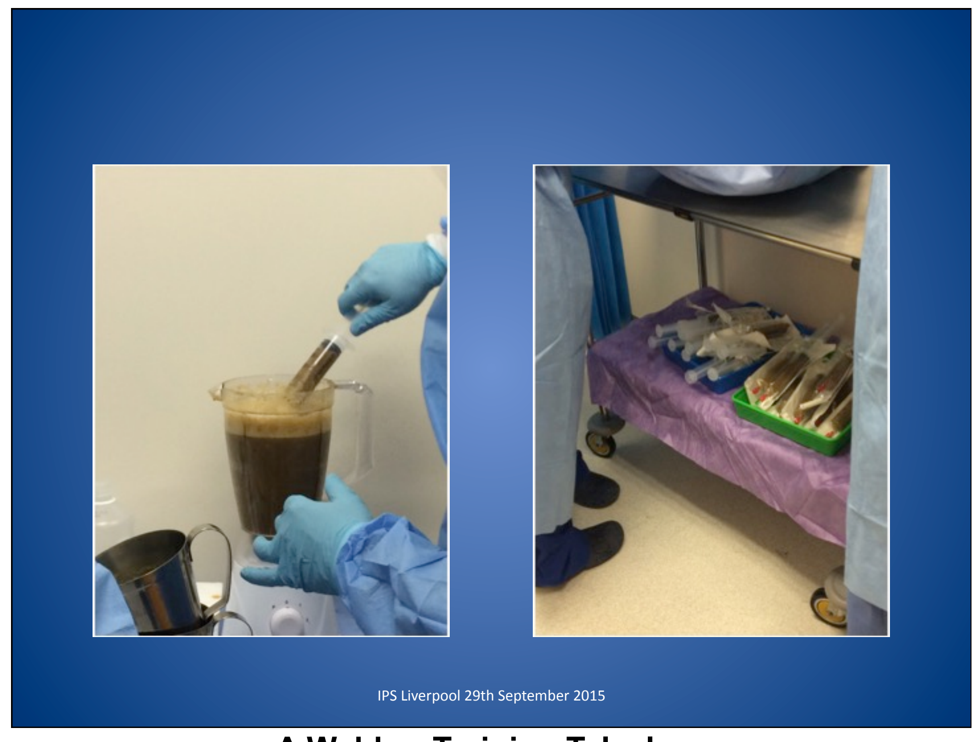
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Problems with suitable donors
www.bbc.co.uk/news/health-31168511
NEWS HEALTH
7 February 2015 Last updated at 01:19
Woman's stool transplant leads to 'tremendous weight gain'
By James Gallagher
Health editor, BBC News website
Top Stories
Putin: War with Ukraine 'unlikely'
Greece 'delays reform plan deadline'
MPs Rifkind and Straw suspended
Pregnant MP hits back at job doubts
Syria trio 'not radicalised' at school
Features
Cakeage and corkage
And the other extra charges that restaurants levy
Best pictures
Images of the ceremony and backstage on Oscars night
Forgotten interview
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Problems

- Can be difficult to find donors who fulfil criteria
- Takes time to perform screening
- Messy to prepare stool!

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Openbiome

- Non profit making company in Boston USA
- Mission statement to make FMT:
  - Easier
  - Cheaper
  - Safer
  - Widely available

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Easier?

- Material provided screened, mixed, filtered and frozen
- 6 months shelf life in a -20°C freezer
- No more donor finding or screening
- Allows patients to be treated quickly

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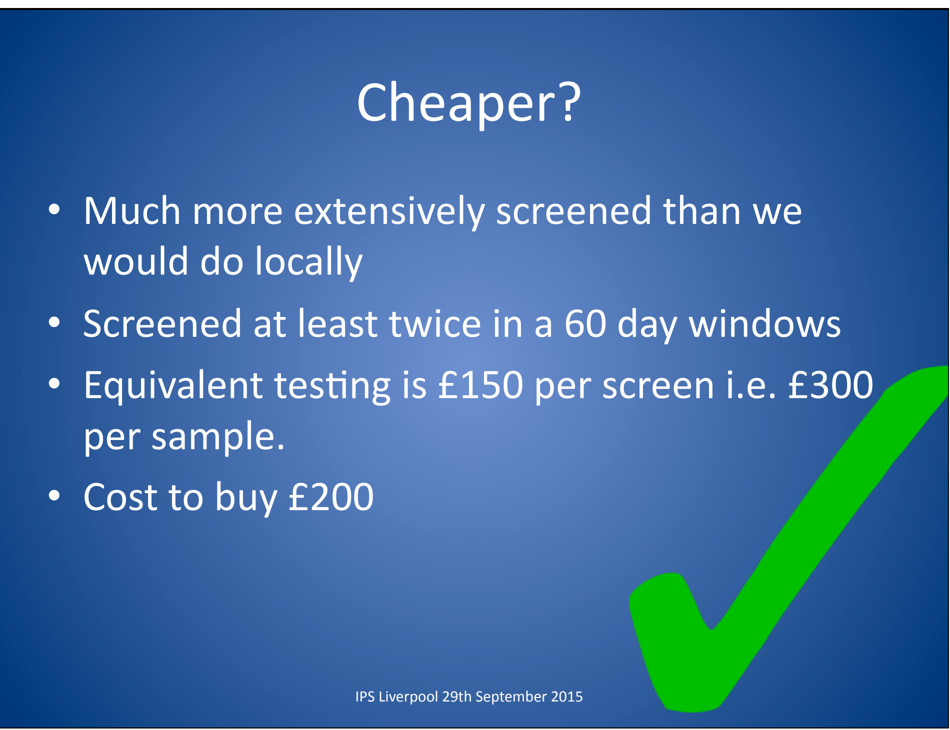
Cheaper?
• Much more extensively screened than we would do locally
• Screened at least twice in a 60 day windows
• Equivalent testing is £150 per screen i.e. £300 per sample.
• Cost to buy £200
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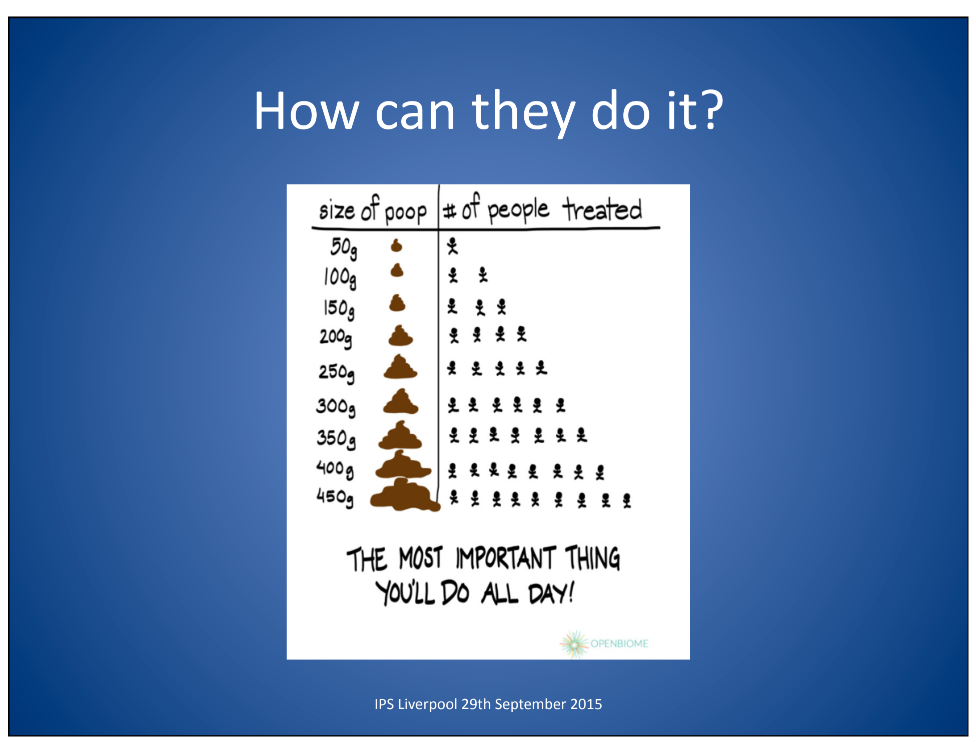
How can they do it?
size of poop
# of people treated
50g
100g
150g
200g
250g
300g
350g
400g
450g
THE MOST IMPORTANT THING YOU'LL DO ALL DAY!
OPENBIOME
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Payment by results

- $40 per sample
- If they donate 5 days in a week $50 bonus
- Earn prizes
  - Biggest single donation of the month
  - Most donations in a month

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Safer?

- More extensively screened
- Better quality control
- Traceability
  - Tracker codes
  - Deep frozen reference samples
- Established adverse event reporting system
- Reduced hazard of processing locally

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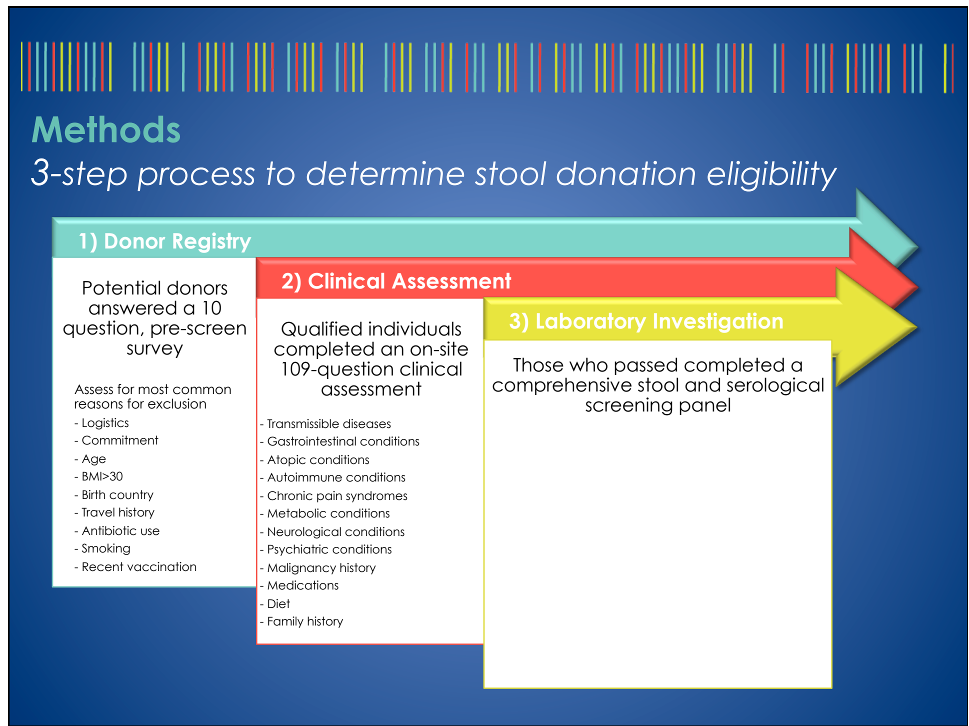
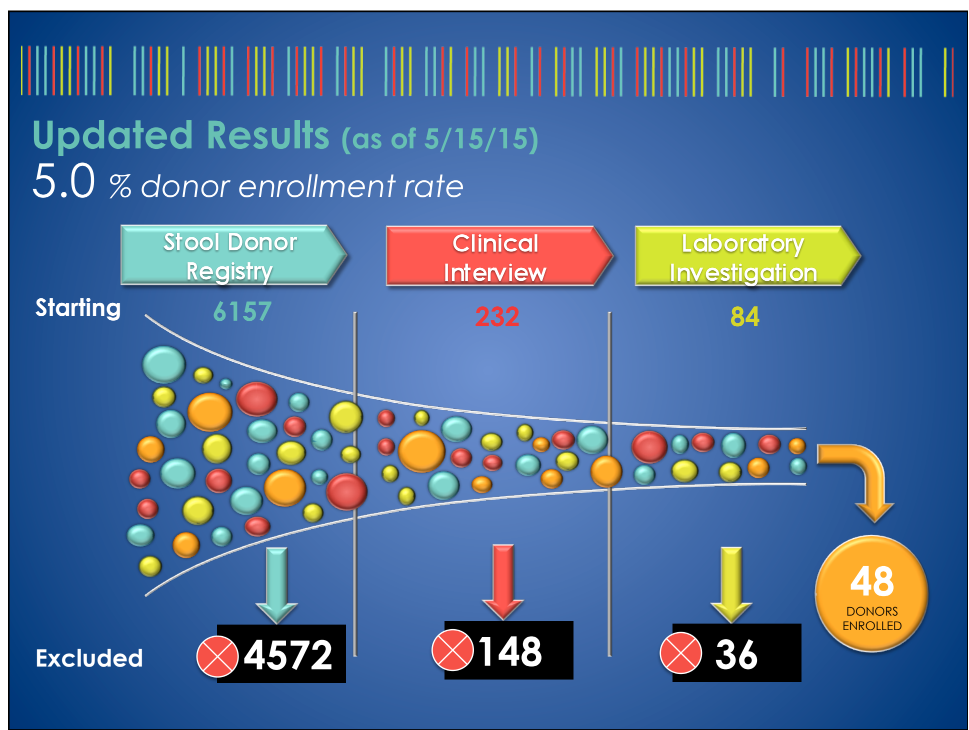

Methods
3-step process to determine stool donation eligibility
1) Donor Registry
Potential donors answered a 10 question, pre-screen survey
Assess for most common reasons for exclusion
- Logistics
- Commitment
- Age
- BMI>30
- Birth country
- Travel history
- Antibiotic use
- Smoking
- Recent vaccination
2) Clinical Assessment
Qualified individuals completed an on-site 109-question clinical assessment
- Transmissible diseases
- Gastrointestinal conditions
- Atopic conditions
- Autoimmune conditions
- Chronic pain syndromes
- Metabolic conditions
- Neurological conditions
- Psychiatric conditions
- Malignancy history
- Medications
- Diet
- Family history
3) Laboratory Investigation
Those who passed completed a comprehensive stool and serological screening panel


Updated Results (as of 5/15/15)
5.0 % donor enrollment rate
Stool Donor Registry
Clinical Interview
Laboratory Investigation
Starting
6157
232
84
Excluded
4572
148
36
48
DONORS ENROLLED

OPENBIOME IN YG
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Specialist equipment
JUG BLENDER
LABCOLD
SPARKFREE
LABFREEZER
DR SUTTON'S POO
PANTRY
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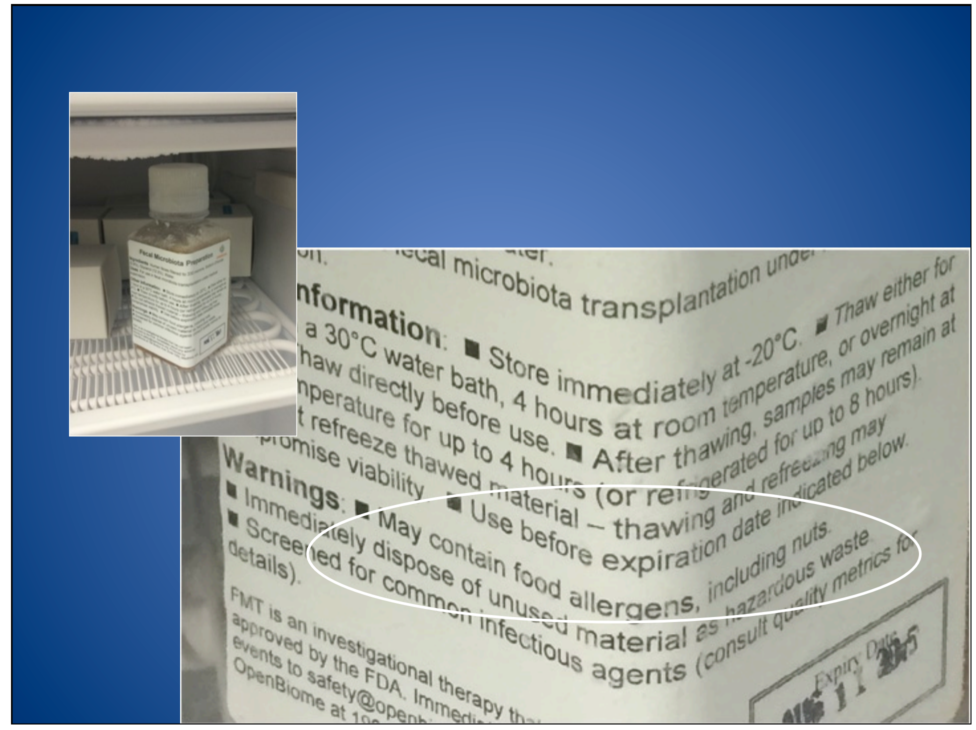

So far..

- 15 patients treated
  - 8 with Openbiome
  - 7 'blender'
- No non-responders
- 2 relapses following antibiotic treatment
  - 1 treated with repeat FMT
  - 1 with Fidaxomicin

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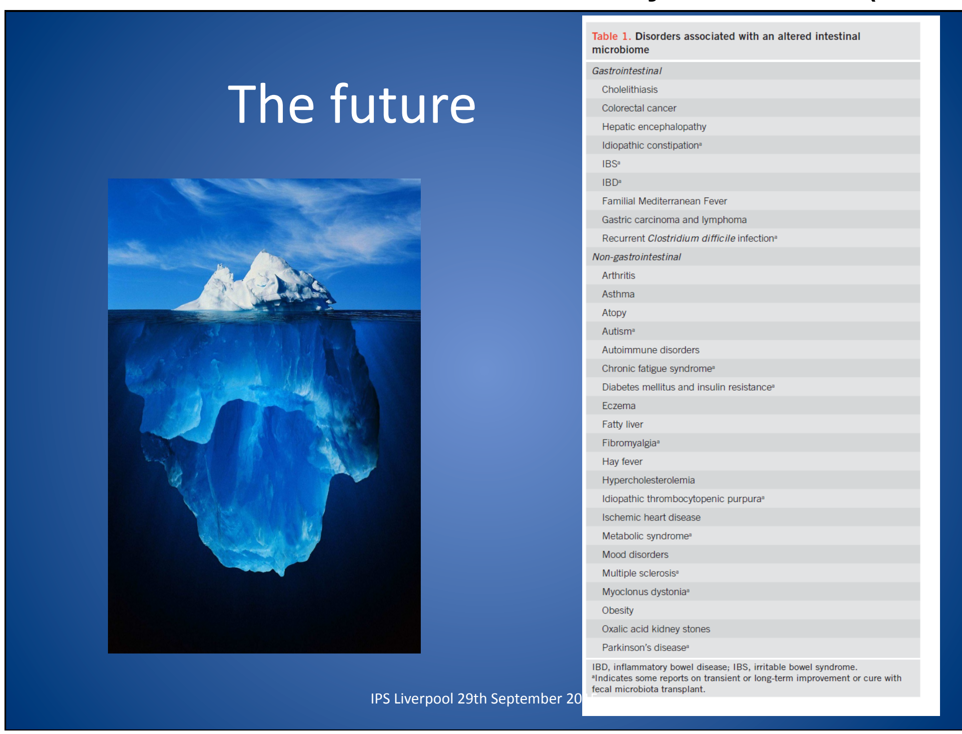
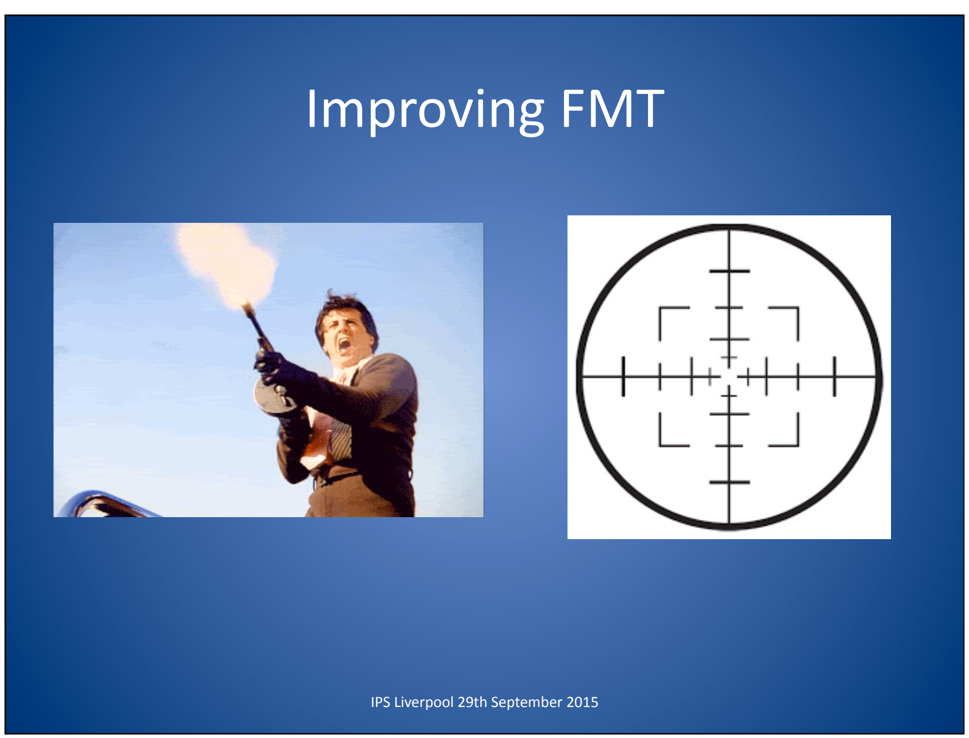
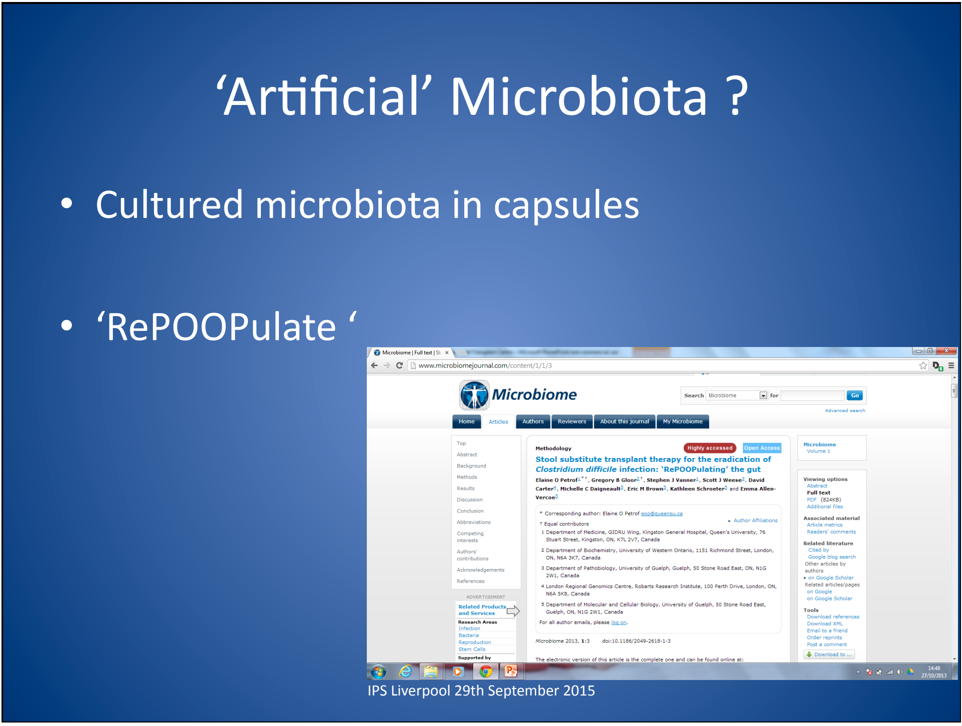


Table 1. Disorders associated with an altered intestinal microbiome

Gastrointestinal
Cholelithiasis
Colorectal cancer
Hepatic encephalopathy
Idiopathic constipation[a]
IBS[a]
IBD[a]
Familial Mediterranean Fever
Gastric carcinoma and lymphoma
Recurrent *Clostridium difficile* infection[a]
Non-gastrointestinal
Arthritis
Asthma
Atopy
Autism[a]
Autoimmune disorders
Chronic fatigue syndrome[a]
Diabetes mellitus and insulin resistance[a]
Eczema
Fatty liver
Fibromyalgia[a]
Hay fever
Hypercholesterolemia
Idiopathic thrombocytopenic purpura[a]
Ischemic heart disease
Metabolic syndrome[a]
Mood disorders
Multiple sclerosis[a]
Myoclonus dystonia[a]
Obesity
Oxalic acid kidney stones
Parkinson's disease[a]

IBD, inflammatory bowel disease; IBS, irritable bowel syndrome.
[a]Indicates some reports on transient or long-term improvement or cure with fecal microbiota transplant.





Summary

- FMT is a very effective treatment for recurrent CDI
- More long-term safety data is needed especially if indications expand
- Stool banks may improve availability and safety
- Optimisation of therapy
  - More focused therapy
  - Cultured material
  - Best route

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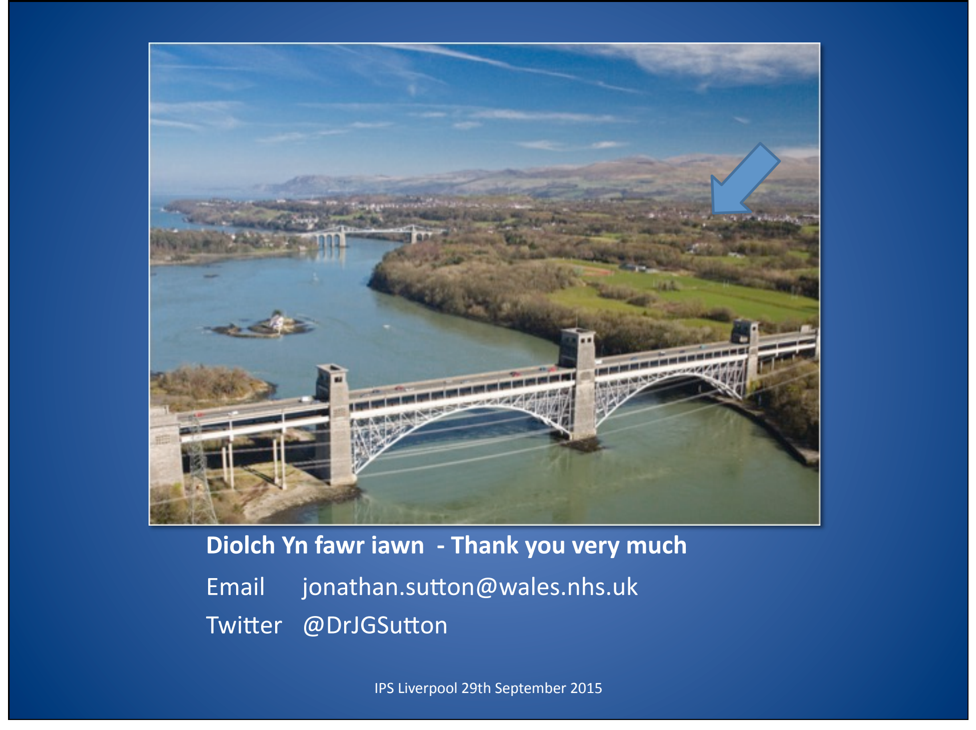
Diolch Yn fawr iawn - Thank you very much
Email jonathan.sutton@wales.nhs.uk
Twitter @DrJGSutton
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