



# 21° Congresso Nazionale

Società Italiana di Tossicologia

**Pericolo, rischio  
e rapporto  
rischio-beneficio**

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**BOLOGNA**

20-22 Febbraio 2023

# Trapianto di microbiota intestinale: potenziali applicazioni per il trattamento di malattie sistemiche e non

**Gemelli**



Fondazione Policlinico Universitario Agostino Gemelli IRCCS  
Università Cattolica del Sacro Cuore

***Prof. Luca Masucci***

Responsabile UOS

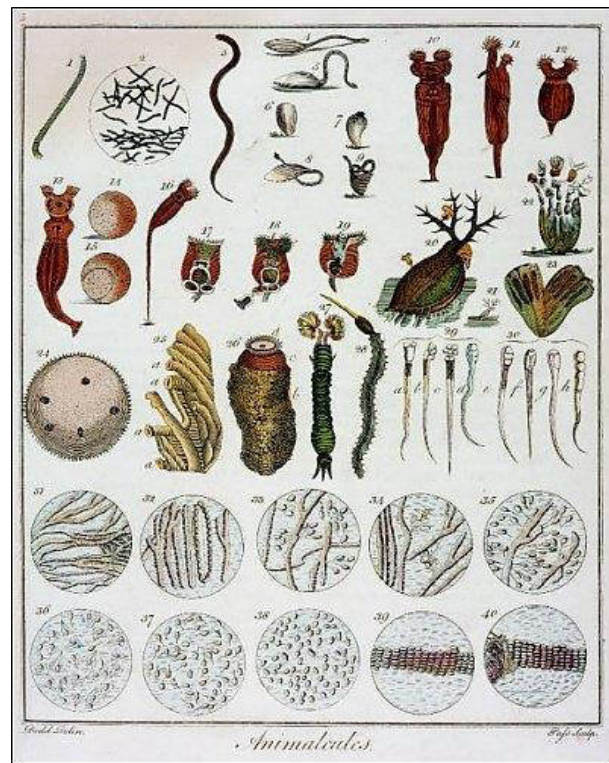
Diagnostica Molecolare e Manipolazione di Microbiota

Laboratorio di Microbiologia

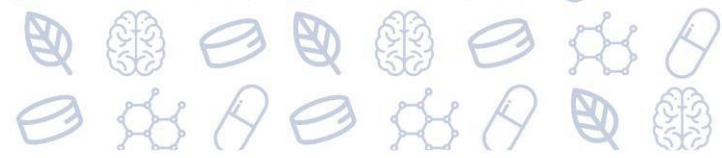
Direttore Prof. M. Sanguinetti



# Antony van Leeuwenhoek







BENGTSSON E

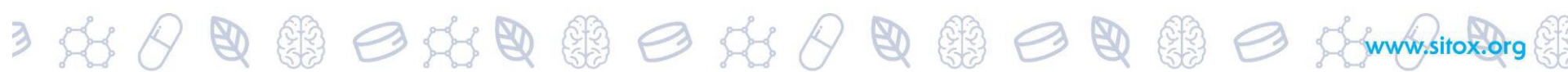
**FATIGUE AFTER PENICILLIN ADMINISTRATION**

Svenska läkartidningen 1951 Oct 5;48(40):2334-8.

FURBERG C, RINGQVIST T.

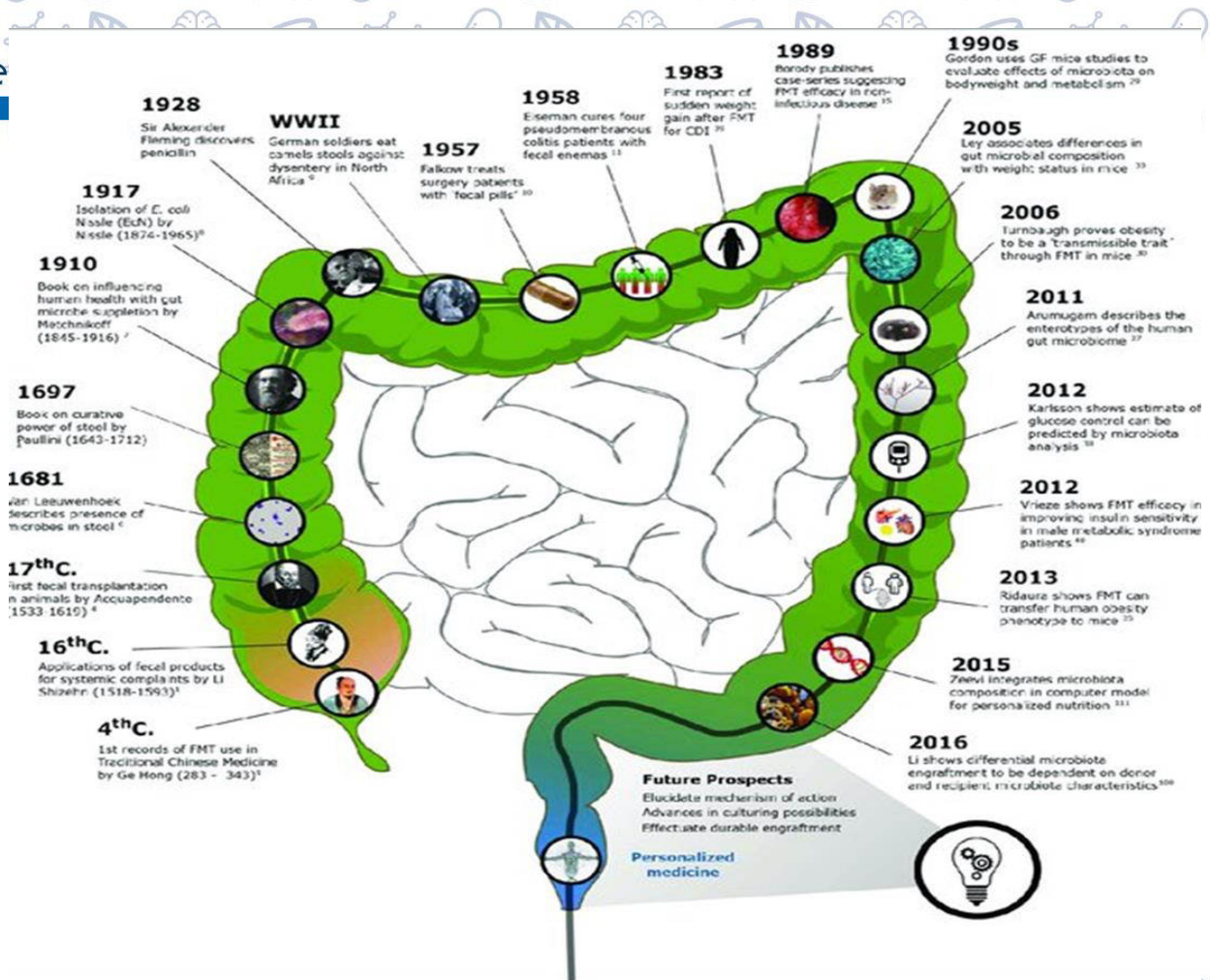
**EFFECT OF PENICILLIN ON THE PHYSICAL CAPACITY FOR  
WORK AND ON THE EXPERIENCE OF FATIGUE DURING  
WORK**

Sven Lakartidn. 1963 Sep 11;60:2650-5.





# Una «breve» storia



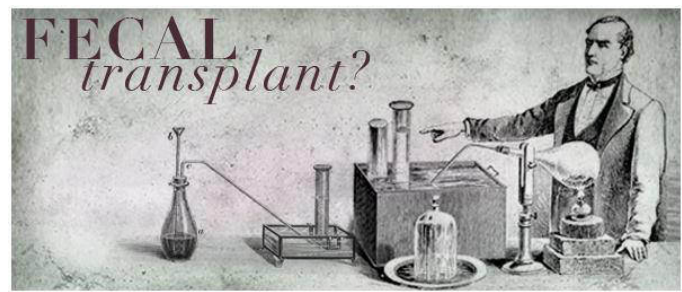
Manipolazione  
delle feci

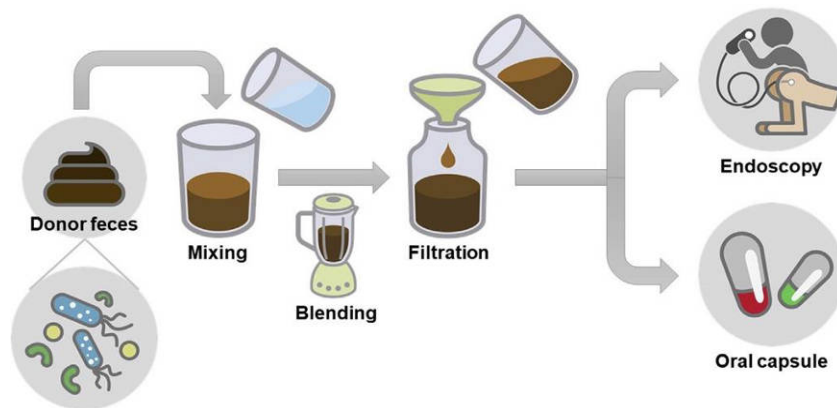


omogeneizzazione



purificazione







## Donor selection

### Guidelines

#### Box 1 Key issues to select potential donors at the preliminary interview

##### INFECTIOUS DISEASES

- ▶ History of, or known exposure to, HIV, HBV or HCV, syphilis, human T-lymphotropic virus I and II, malaria, trypanosomiasis, tuberculosis
- ▶ Known systemic infection not controlled at the time of donation
- ▶ Use of illegal drugs
- ▶ Risky sexual behaviour (anonymous sexual contacts; sexual contacts with prostitutes, drug addicts, individuals with HIV, viral hepatitis, syphilis; work as prostitute; history of sexually transmittable disease)
- ▶ Previous reception of tissue/organ transplant
- ▶ Previous (<12 months) reception of blood products
- ▶ Recent (<6 months) needle stick accident
- ▶ Recent (<6 months) body tattoo, piercing, earring, acupuncture
- ▶ Recent medical treatment in poorly hygienic conditions
- ▶ Risk of transmission of diseases caused by prions
- ▶ Recent parasitosis or infection from rotavirus, *Giardia lamblia* and other microbes with GI involvement
- ▶ Recent (<6 months) travel in tropical countries, countries at high risk of communicable diseases or traveller's diarrhoea
- ▶ Recent (<6 months) history of vaccination with a live attenuated virus, if there is a possible risk of transmission
- ▶ Healthcare workers (to exclude the risk of transmission of multidrug-resistant organisms)
- ▶ Individual working with animals (to exclude the risk of transmission of zoonotic infections)

##### GI, METABOLIC AND NEUROLOGICAL DISORDERS

- ▶ History of IBS, IBD, functional chronic constipation, coeliac disease, other chronic GI disorders
- ▶ History of chronic, systemic autoimmune disorders with GI involvement
- ▶ History of, or high risk for, GI cancer or polyposis
- ▶ Recent appearance of diarrhoea, hematochezia
- ▶ History of neurological/neurodegenerative disorders
- ▶ History of psychiatric conditions
- ▶ Overweight and obesity (body mass index >25)

##### DRUGS THAT CAN IMPAIR GUT MICROBIOTA COMPOSITION

- ▶ Recent (<3 months) exposure to antibiotics, immunosuppressants, chemotherapy
- ▶ Chronic therapy with proton pump inhibitors

*European consensus conference on faecal microbiota transplantation in clinical practice.*

European FMT Working Group.  
Gut. 2017 Apr;66(4):569-580. doi: 10.1136/gutjnl-2016-313017.  
Epub 2017 Jan 13.

# Laboratory tests

## Box 3 Blood and stool testing to check donors for any potentially transmittable disease

### GENERAL BLOOD TESTING

- ▶ Cytomegalovirus
- ▶ Epstein-Barr virus
- ▶ Hepatitis A
- ▶ HBV
- ▶ HCV
- ▶ Hepatitis E virus
- ▶ Syphilis
- ▶ HIV-1 and HIV-2
- ▶ *Entamoeba histolytica*
- ▶ Complete blood cell count with differential
- ▶ C-reactive protein and erythrocyte sedimentation rate
- ▶ Albumin
- ▶ Creatinine and electrolytes
- ▶ Aminotransferases, bilirubin, gamma-glutamyltransferase, alkaline phosphatase

### BLOOD TESTING IN SPECIFIC SITUATIONS

- ▶ Human T-lymphotropic virus types I and II antibodies
- ▶ *Strongyloides stercoralis*

### GENERAL STOOL TESTING

- ▶ Detection of *Clostridium difficile*
- ▶ Detection of enteric pathogens, including *Salmonella*, *Shigella*
- ▶ *Campylobacter*, *Escherichia coli* O157 H7, *Yersinia*, vancomycin-resistant enterococci, methicillin-resistant *Staphylococcus aureus*, Gram-negative multidrug-resistant bacteria
- ▶ Norovirus
- ▶ Antigens and/or acid fast staining for *Giardia lamblia* and *Cryptosporidium parvum*
- ▶ Protozoa (including *Blastocystis hominis*) and helminths
- ▶ Faecal occult blood testing

### STOOL TESTING IN SPECIFIC SITUATIONS

- ▶ Detection of *Vibrio cholera* and *Listeria monocytogenes*
- ▶ Antigens and/or acid fast staining for *Isospora* and *Microsporidia*
- ▶ Calprotectin
- ▶ *Helicobacter pylori* faecal antigen
- ▶ Rotavirus

European consensus conference on faecal microbiota transplantation in clinical practice.

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Gut. 2017 Apr;66(4):569-580. doi: 10.1136/gutjnl-2016-313017.  
Epub 2017 Jan 13.

### FRESH FAECAL MATERIAL

- ▶ Fresh stool should be used within 6 hours after defecation
- ▶ To protect anaerobic bacteria, the storage and preparation should be as brief as possible
- ▶ Until further processing, the stool sample can be stored at ambient temperature (20°C–30°C)
- ▶ Anaerobic storage and processing should be applied if possible
- ▶ A minimum amount of 30 g of faeces should be used
- ▶ Faecal material should be suspended in saline using a blender or manual effort and sieved in order to avoid the clogging of infusion syringes and tubes
- ▶ A dedicated space, disinfected using measures that are effective against sporulating bacteria, should be used
- ▶ Protective gloves and facial masks should be used during preparation

### FROZEN FAECAL MATERIAL

- ▶ At least 30 g of donor faeces and 150 mL of saline solution should be used
- ▶ Before freezing, glycerol should be added up to a final concentration of 10%
- ▶ The final suspension should be clearly labelled and traceable, and stored at –80°C
- ▶ On the day of faecal infusion, faecal suspension should be thawed in a warm (37°C) water bath and infused within 6 hours from thawing
- ▶ After thawing, saline solution can be added to obtain a desired suspension volume
- ▶ Repetitive thawing and freezing should be avoided

*European consensus conference on faecal microbiota transplantation in clinical practice.*

European FMT Working Group.  
Gut. 2017 Apr;66(4):569-580. doi: 10.1136/gutjnl-2016-313017.  
Epub 2017 Jan 13.





WHO Collaborating Centre  
For Vaccine and Serological  
Research, Child, Tissues and Organs

*Roma*, 07/08/2020

Prot. 1386/CNT2020

Ai Centri FMT Nazionali  
Loro sedi  
E, p.c. Direzione Generale della Prevenzione Sanitaria  
Ministero della Salute

**Oggetto:** emendamento al “Programma Nazionale sul trapianto di microbiota fecale umano”  
(FMT - Fecal Microbiota Transplantation)

Con riferimento all'emendamento in oggetto presentato dal CNT (24 febbraio 2020 Prot 452 CNT/2020), con il quale si richiedeva che il Programma Nazionale sul trapianto di FMU prevedesse anche l'impiego di materiale fecale congelato, il Consiglio Superiore di Sanità (CSS), nelle sedute del 9 giugno e del 14 luglio 2020, si è espresso con parere favorevole.

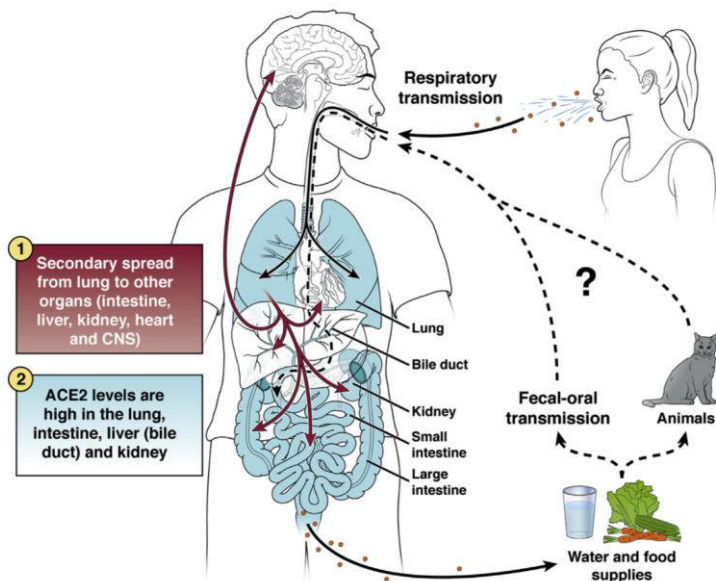
Pertanto, il “Programma Nazionale sul Trapianto di Microbiota Fecale umano (FMT) – aspetti regolatori, clinici e organizzativi” è stato integrato con il protocollo per la preparazione del materiale fecale congelato e con altre indicazioni procedurali correlate, incluse alcune raccomandazioni del CSS.

Si allega il nuovo documento in cui sono evidenziate le revisioni apportate alle pag: 3,5,8,10, All 2 (pag 12 e 13).

Il Direttore del Centro Nazionale Trapianti  
Dr. Massimo Cardillo



## INFEZIONE DA SARS-CoV-2

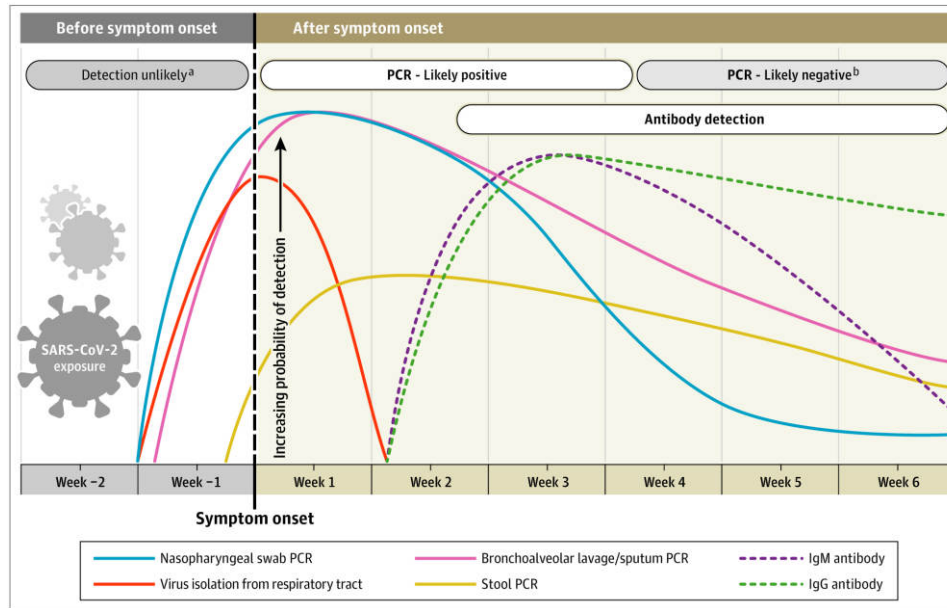


Ding et al. *Gastroenterology* (2020)

**SYMPTOMS 2019-nCoV**

- Headache
- Dry Cough
- Cold
- Fever
- Shortness of breathe


## LA VIA RESPIRATORIA È L'UNICA VIA DI TRASMISSIONE?





ORIGINAL ARTICLE

## Laboratory handling practice for faecal microbiota transplantation

G. Quaranta<sup>1</sup>, G. Fancello<sup>2</sup>, G. Ianiro<sup>3</sup>, R. Graffeo<sup>2</sup>, A. Gasbarrini<sup>3,4</sup>, G. Cammarota<sup>3,4</sup>, M. Sanguinetti<sup>1,2</sup> and L. Masucci<sup>1,2</sup> 

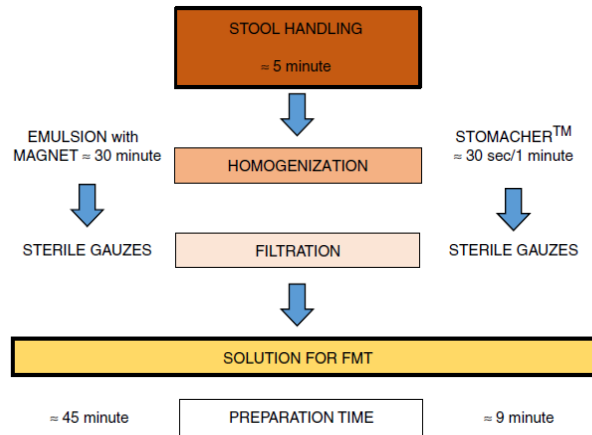



Figure 1 FMT Experimental overview for both methods. [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

ORIGINAL ARTICLE

## Laboratory handling practice for faecal microbiota transplantation

G. Quaranta<sup>1</sup>, G. Fancello<sup>2</sup>, G. Ianiro<sup>3</sup>, R. Graffeo<sup>2</sup>, A. Gasbarrini<sup>3,4</sup>, G. Cammarota<sup>3,4</sup>, M. Sanguinetti<sup>1,2</sup> and L. Masucci<sup>1,2</sup> 

**Table 1** Microbial load of anaerobes and aerobes (CFU per ml) in both methods for fresh preparation

| Stool sample | MPE                    |                        | SSE                     |                        |
|--------------|------------------------|------------------------|-------------------------|------------------------|
|              | ANA                    | AE                     | ANA                     | AE                     |
| #1           | 10 <sup>13</sup>       | 1.4 × 10 <sup>12</sup> | 1.13 × 10 <sup>13</sup> | 3.3 × 10 <sup>12</sup> |
| #2           | 4.6 × 10 <sup>3</sup>  | 10 <sup>11</sup>       | 10 <sup>4</sup>         | 10 <sup>11</sup>       |
| #3           | 10 <sup>4</sup>        | 6.4 × 10 <sup>9</sup>  | 9.2 × 10 <sup>3</sup>   | 3.5 × 10 <sup>9</sup>  |
| #4           | 2.3 × 10 <sup>8</sup>  | 7 × 10 <sup>9</sup>    | 2.5 × 10 <sup>8</sup>   | 3 × 10 <sup>10</sup>   |
| #5           | 3 × 10 <sup>9</sup>    | 4.5 × 10 <sup>9</sup>  | 3.2 × 10 <sup>9</sup>   | 3 × 10 <sup>9</sup>    |
| #6           | 4 × 10 <sup>7</sup>    | 3 × 10 <sup>8</sup>    | 3.8 × 10 <sup>7</sup>   | 2.7 × 10 <sup>8</sup>  |
| #7           | 5.2 × 10 <sup>10</sup> | 10 <sup>12</sup>       | 7 × 10 <sup>10</sup>    | 10 <sup>12</sup>       |
| #8           | 3.4 × 10 <sup>7</sup>  | 2.1 × 10 <sup>9</sup>  | 4 × 10 <sup>7</sup>     | 3.1 × 10 <sup>9</sup>  |
| #9           | 2 × 10 <sup>4</sup>    | 10 <sup>6</sup>        | 4 × 10 <sup>4</sup>     | 5 × 10 <sup>5</sup>    |
| #10          | 6.2 × 10 <sup>5</sup>  | 10 <sup>9</sup>        | 5.5 × 10 <sup>5</sup>   | 3.1 × 10 <sup>9</sup>  |

Abbreviations: MPE, emulsion magnet plate; SSE: emulsion SEWARD STOMACHER®.



ORIGINAL ARTICLE

### Laboratory handling practice for faecal microbiota transplantation

G. Quaranta<sup>1</sup>, G. Fancello<sup>2</sup>, G. Ianiro<sup>3</sup>, R. Graffeo<sup>2</sup>, A. Gasbarrini<sup>3,4</sup>, G. Cammarota<sup>3,4</sup>, M. Sanguinetti<sup>1,2</sup> and L. Masucci<sup>1,2</sup>

Table 2 Microbial load of aerobes and anaerobes (CFU per ml) in both methods after defrosting

| Methods | Sample | Growth conditions | T0                     | 15 days                | 30 days                | 90 days                |
|---------|--------|-------------------|------------------------|------------------------|------------------------|------------------------|
| MPE     | #1     | AE                | 10 <sup>13</sup>       | 10 <sup>13</sup>       | 10 <sup>13</sup>       | 10 <sup>13</sup>       |
|         |        | ANA               | 1.4 × 10 <sup>12</sup> | 1.5 × 10 <sup>12</sup> | 1.4 × 10 <sup>12</sup> | 10 <sup>12</sup>       |
|         | #2     | AE                | 4.6 × 10 <sup>3</sup>  | 4.6 × 10 <sup>3</sup>  | 5 × 10 <sup>3</sup>    | 4.6 × 10 <sup>3</sup>  |
|         |        | ANA               | 10 <sup>11</sup>       | 10 <sup>11</sup>       | 10 <sup>11</sup>       | 10 <sup>11</sup>       |
|         | #3     | AE                | 10 <sup>4</sup>        | 3.8 × 10 <sup>3</sup>  | 10 <sup>4</sup>        | 1.3 × 10 <sup>4</sup>  |
|         |        | ANA               | 6.4 × 10 <sup>9</sup>  | 5.8 × 10 <sup>9</sup>  | 6 × 10 <sup>9</sup>    | 6 × 10 <sup>9</sup>    |
| SSE     | #1     | AE                | 1.1 × 10 <sup>13</sup> | 10 <sup>13</sup>       | 10 <sup>13</sup>       | 1.3 × 10 <sup>13</sup> |
|         |        | ANA               | 3.3 × 10 <sup>12</sup> | 3 × 10 <sup>12</sup>   | 3.6 × 10 <sup>12</sup> | 2.8 × 10 <sup>12</sup> |
|         | #2     | AE                | 10 <sup>4</sup>        | 10 <sup>4</sup>        | 10 <sup>4</sup>        | 10 <sup>4</sup>        |
|         |        | ANA               | 10 <sup>11</sup>       | 9.4 × 10 <sup>10</sup> | 10 <sup>11</sup>       | 10 <sup>11</sup>       |
|         | #3     | AE                | 9.2 × 10 <sup>3</sup>  | 9 × 10 <sup>3</sup>    | 8.7 × 10 <sup>3</sup>  | 8.4 × 10 <sup>3</sup>  |
|         |        | ANA               | 3.5 × 10 <sup>9</sup>  | 4 × 10 <sup>9</sup>    | 3.8 × 10 <sup>9</sup>  | 3.2 × 10 <sup>9</sup>  |





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25 glu  
2013

MEDICINA E RICERCA

## Al Gemelli di Roma il primo trapianto nel Lazio di flora batterica intestinale

Il trapianto - effettuato da un'équipe coordinata da Antonio Gasbarrini, responsabile dell'Unità operativa complessa di medicina interna e gastroenterologia del Gemelli - è stato effettuato attraverso una colonscopia eseguita da Giovanni Cammarota della Uoc di gastroenterologia e il microbiota del donatore (un parente) è stato preparato e purificato da Luca Masucci nell'ambito di una collaborazione con l'Istituto di microbiologia dell'Università Cattolica diretto da Maurizio Sanguinetti.

**10 anni FMT e infezione da *Clostridioides difficile*  
~450 procedure su ~400 pazienti.**



Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: [www.elsevier.com/locate/dld](http://www.elsevier.com/locate/dld)



## Faecal transplantation for *Clostridium difficile* infection. Three cases treated in Italy

Giovanni Cammarota\*  
Gianluca Ianiro  
Antonio Gasbarrini

*Department of Clinical Sciences, Division of Internal  
Medicine and Gastroenterology, A. Gemelli University  
Hospital, Rome, Italy*

Luca Masucci  
Maurizio Sanguinetti  
*Institute of Microbiology, A. Gemelli University  
Hospital, Rome, Italy*

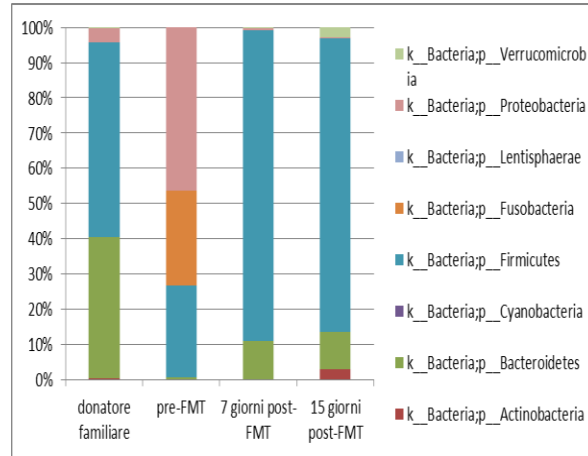


# Trapianto fecale (FMT)

## **RAZIONALE**

- ricostituire una flora intestinale normale in grado di competere con *C.difficile* e/o modulare una disbiosi mediante l'instillazione di una sospensione liquida contenente flora enterica ottenuta da un donatore sano

## Pyrosequencing analysis donatore e ricevente - Phylum



### Donatore:

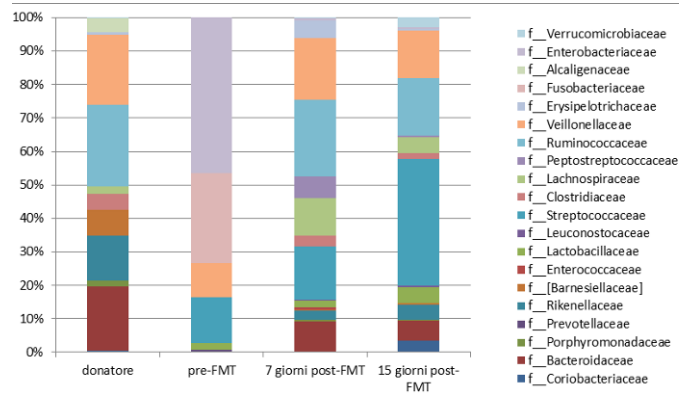
Firmicutes 55 %  
Bacteroidetes 40%  
Proteobacteria 4%

### Ricevente:

Proteobacteria 46%  
Fusobacteria 27%  
Firmicutes 26%  
Bacteroidetes 11%



## Pyrosequencing analysis donatore e ricevente - Famiglia



### Donatore:

*Ruminococcaceae* (23%)  
*Veillonellaceae* (20%)  
*Bacteroidaceae* (19%)  
*Rikenellaceae* (12%)  
*Clostridiaceae* (5%)

### Ricevente:

*Enterobacteriaceae* (46%)  
*Fusobacteriaceae* (27%)  
*Streptococcaceae* (13%)  
*Veillonellaceae* (10%)

### RICEVENTE a 7 GIORNI

*Ruminococcaceae* (19%), *Veillonellaceae* (16%),  
*Streptococcaceae* (13%), *Bacteroidaceae* (8%),  
*Lachnospiraceae* (9%), *Peptostreptococcaceae*  
(5%), *Clostridiaceae* (3%), *Lactobacillaceae* (2%) e  
*Rikenellaceae* (2%).

# FMT?



# Clostridium difficile PCR ribotype 027: assessing the risks of further worldwide spread

Lancet Infect Dis 2010;  
10: 395-04

Review

Archie CA Clements, Ricardo J Soares Magalhães, Andrew J Tatem, David L Paterson, Thomas V Riley

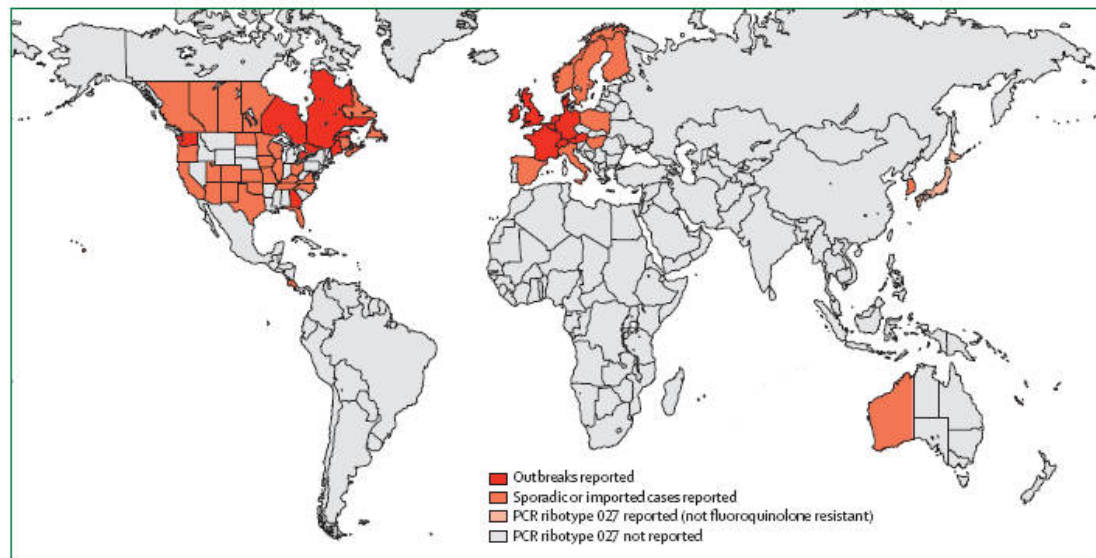
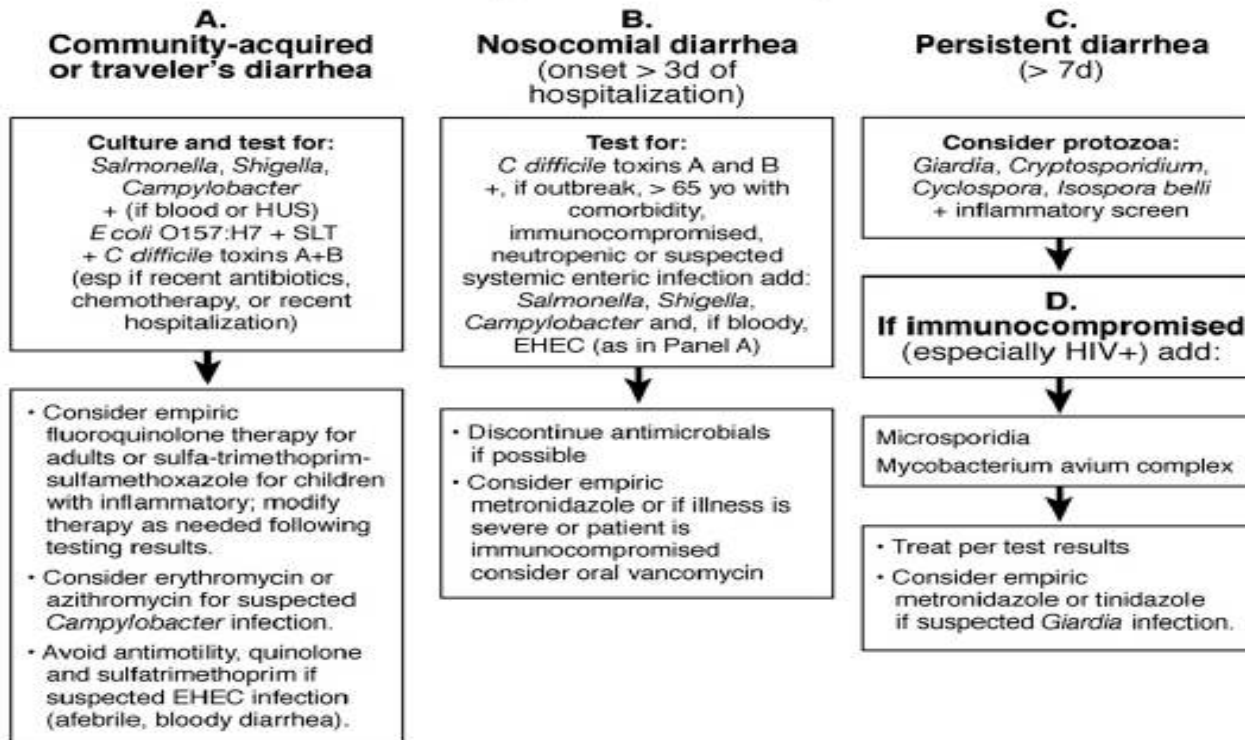


Figure 1: Countries\* where *Clostridium difficile* PCR ribotype 027 has been reported

Sources of information include reports from the USA<sup>3,34</sup> and Canada,<sup>35</sup> reporting hospital outbreaks since 2001; the UK,<sup>28,36</sup> the Netherlands,<sup>37-39</sup> Belgium,<sup>40</sup> and Ireland,<sup>41</sup> reporting hospital outbreaks since 2005; France,<sup>34,42</sup> Switzerland,<sup>43</sup> and Luxembourg,<sup>44</sup> reporting hospital outbreaks since 2006; Germany,<sup>45-47</sup> reporting hospital outbreaks since 2007; and Austria<sup>38,48</sup> and Denmark,<sup>44,45,49</sup> reporting hospital outbreaks since 2008. Sporadic or imported cases of infection caused by *C difficile* PCR ribotype 027 have also been reported from Costa Rica,<sup>50</sup> Finland,<sup>34,51</sup> Hungary,<sup>45,52</sup> Italy,<sup>53</sup> Norway,<sup>54</sup> Poland,<sup>44,45</sup> Spain,<sup>45</sup> Sweden,<sup>38</sup> Western Australia,<sup>57</sup> South Korea,<sup>58</sup> and Hong Kong.<sup>59</sup> The earliest known isolate from the Netherlands was collected in 2002,<sup>37</sup> but—like earlier strains of PCR ribotype 027 in North America, isolates from Japan,<sup>60,61</sup> and the majority of recent isolates from Sweden<sup>1,62</sup>—it was susceptible to fluoroquinolones and is thought a historic strain not associated with the recent international epidemic. \*And states or provinces of the USA, Canada, and Australia.



## Diagnosis and Treatment of Acute or Persistent Diarrhea





# *C. difficile*

principali fattori di rischio (Baxter, ICHE 2008)

- Esposizione agli antibiotici
- Soppressione dell'acidità gastrica
- Età

## New trends in *Clostridium difficile* virulence and pathogenesis

C. Denève<sup>a</sup>, C. Janoir<sup>a</sup>, I. Poilane<sup>b</sup>, C. Fantinato<sup>b</sup>, A. Collignon<sup>a,b,\*</sup>

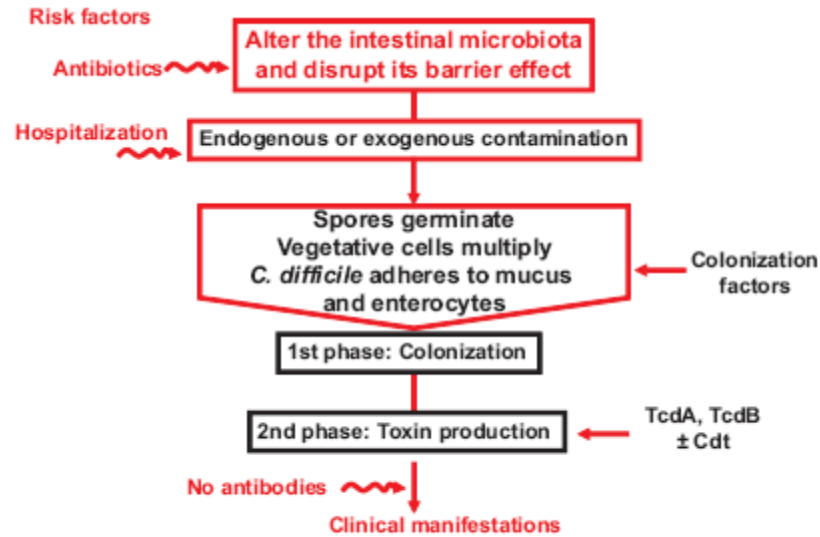


Fig. 1. Pathogenesis of *Clostridium difficile*.

AP&T Alimentary Pharmacology and Therapeutics

## Randomised clinical trial: faecal microbiota transplantation by colonoscopy vs. vancomycin for the treatment of recurrent *Clostridium difficile* infection

G. Cammarota\*, L. Masucci†, G. Ianaro\*, S. Bibbò\*, G. Dinoi\*, G. Costamagna‡, M. Sanguinetti† & A. Gasbarrini\*

\*Institute of Internal Medicine,  
Catholic University, Faculty of  
Medicine and Surgery, Rome, Italy.

†Institute of Microbiology, Catholic  
University, Faculty of Medicine and  
Surgery, Rome, Italy.

‡Institute of Surgery, Catholic  
University, Faculty of Medicine and  
Surgery, Rome, Italy.

Luglio 2013 giugno 2014

39 pazienti (F = 23, M = 16, età media 73aa)

FMT (20 soggetti, F = 12, M = 8, età media: 71aa)

In terapia con Vancomicina (19 soggetti, F = 11, M = 8, età media 75aa).

AP&T Alimentary Pharmacology and Therapeutics

Randomised clinical trial: faecal microbiota transplantation by colonoscopy vs. vancomycin for the treatment of recurrent *Clostridium difficile* infection

G. Cammarota\*, L. Masucci<sup>1</sup>, G. Ianiro\*, S. Bibbò\*, G. Dinio\*, G. Costamagna<sup>2</sup>, M. Sanguinetti<sup>3</sup> & A. Gasbarrini\*

FMT ha mostrato una significativa efficacia più che vancomicina

**A un anno dall'inizio, dopo aver interpellato una commissione indipendente di 2 internisti e 1 gastroenterologo lo studio è stato fermato.**

**TRATTAMENTO TERAPEUTICO È PROSEGUITO**



Randomised clinical trial: faecal microbiota transplantation by colonoscopy vs. vancomycin for the treatment of recurrent *Clostridium difficile* infection

G. Cammarota<sup>1</sup>, L. Masucci<sup>1</sup>, G. Ianiro<sup>1</sup>, S. Bibbò<sup>1</sup>, G. Dinoi<sup>1</sup>, G. Costamagna<sup>1</sup>, M. Sanguinetti<sup>1</sup> & A. Gasbarrini<sup>1</sup>

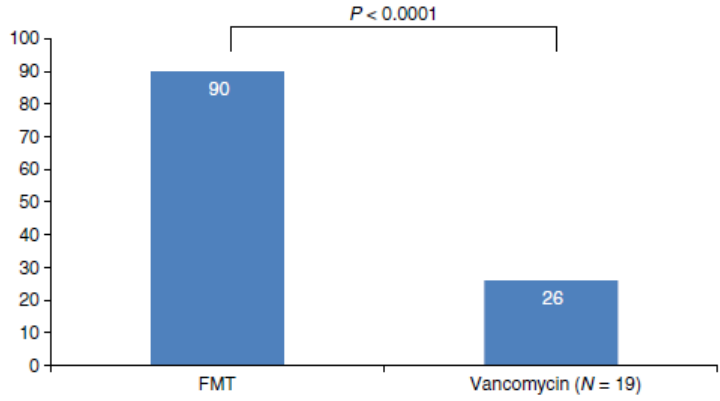


Figure 2 | Percentage of patients cured.

# FMT?

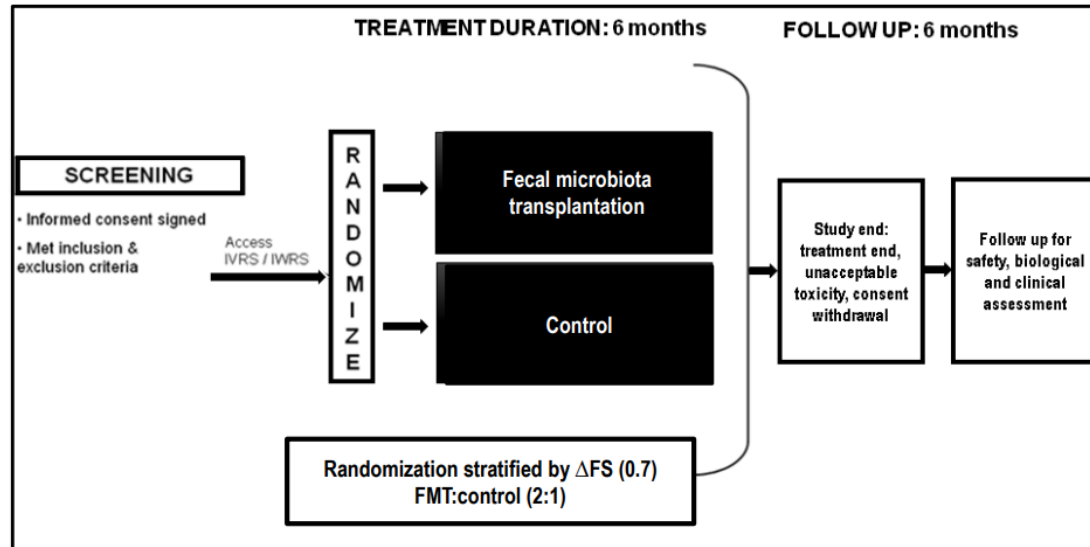




## FETR-ALS Study Protocol: A Randomized Clinical Trial of Fecal Microbiota Transplantation in Amyotrophic Lateral Sclerosis

Jessica Mandrioli<sup>1</sup>, Amedeo Amedei<sup>2\*</sup>, Giovanni Cammarota<sup>3,4</sup>, Elena Nicolai<sup>2</sup>, Elisabetta Zucchi<sup>1,5</sup>, Roberto D'Amico<sup>6</sup>, Federica Ricci<sup>2</sup>, Gianluca Quaranta<sup>7,8</sup>, Teresa Spanu<sup>7,9</sup> and Luca Masucci<sup>7,8</sup> on behalf of The FETR-ALS Working Group

- ❖ Valutare la modulazione del microbiota luminale e mucosale dei pazienti in seguito all'FMT
- ❖ Valutare la modulazione del sistema immunitario dopo l'infusione, in particolare delle popolazioni linfocitarie

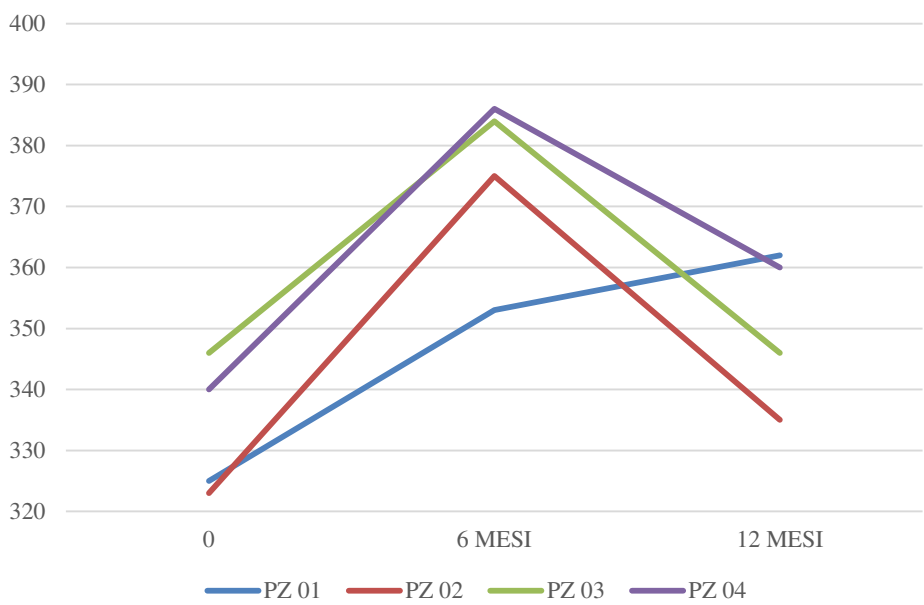


# Risultati

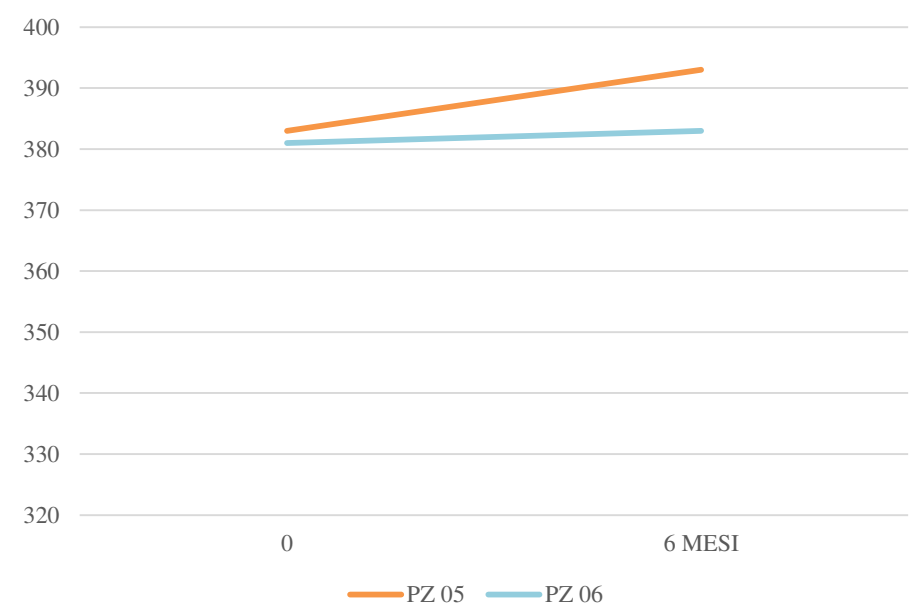
## Analisi di sequenziamento su campioni di feci

$\alpha$ -diversità

Pazienti FMT



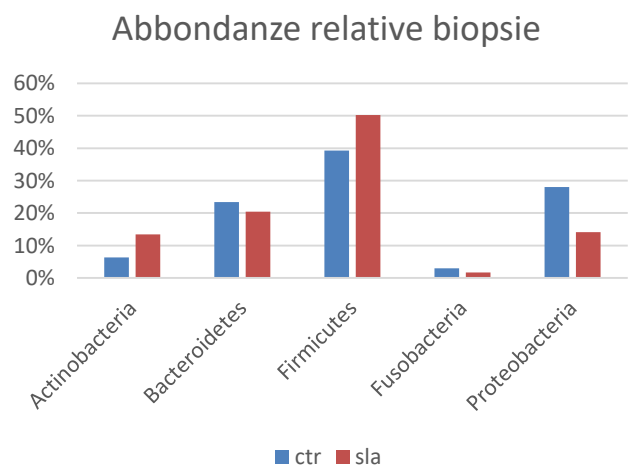
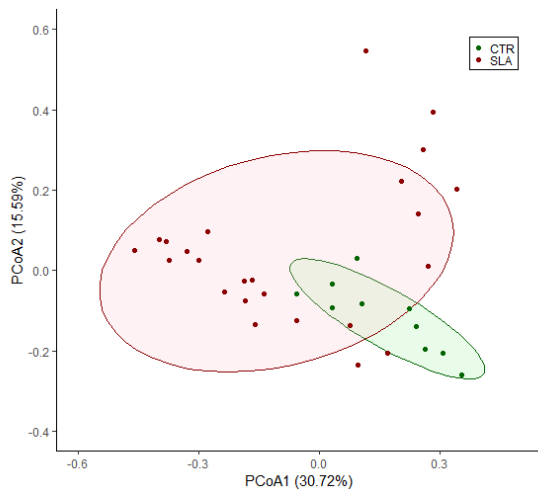
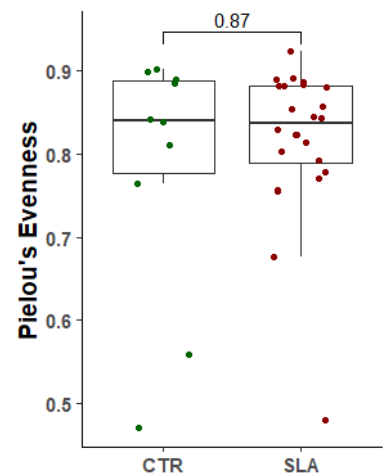
Pazienti CTR





## Analisi di sequenziamento su campioni biotici

### $\alpha$ -diversità e $\beta$ -diversità

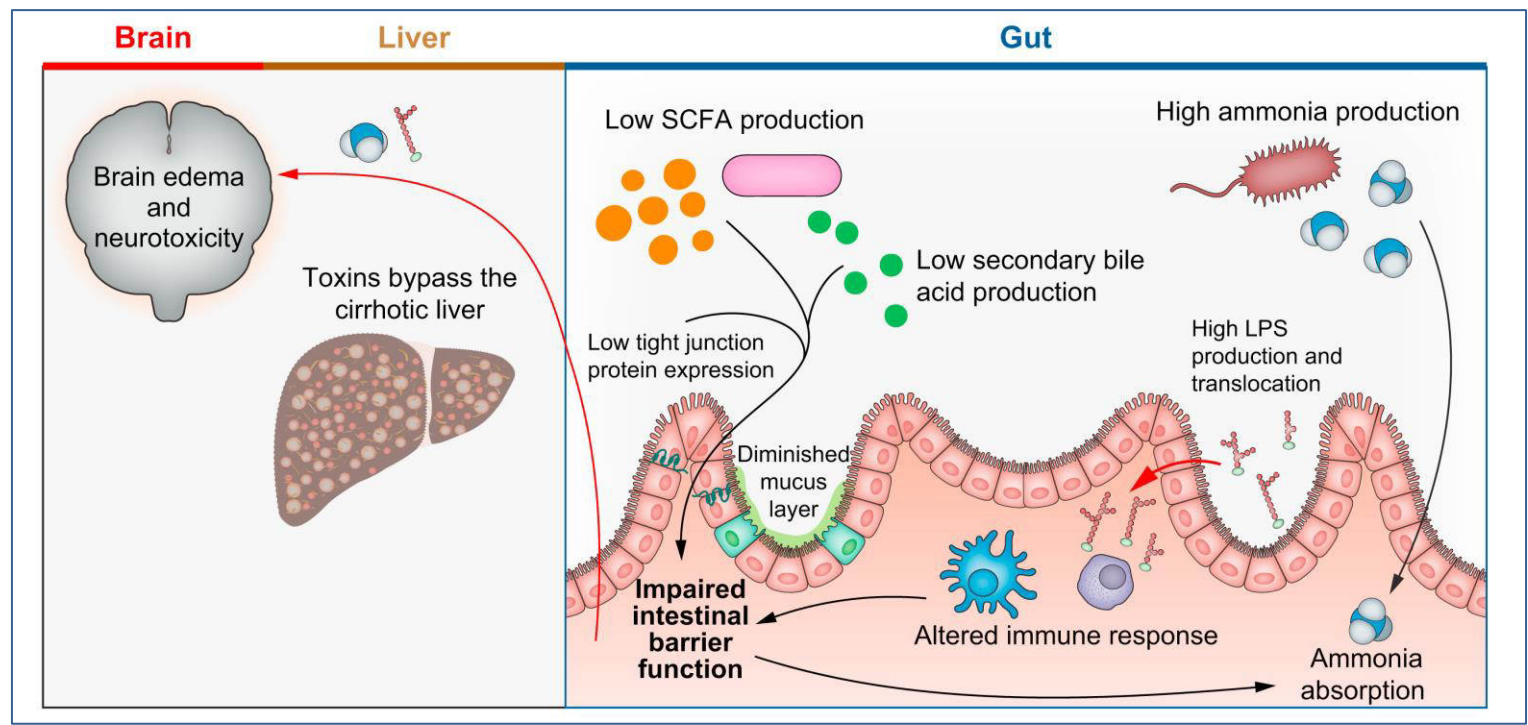


# FMT?



# **Il trapianto di microbiota fecale (FMT) mediante capsule orali: un approccio terapeutico in pazienti con cirrosi ed encefalopatia epatica refrattari ai trattamenti convenzionali**

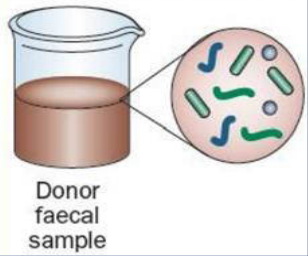
## Gut-brain axis



**Bloom et al., *Journal of Hepatology*, 2021**

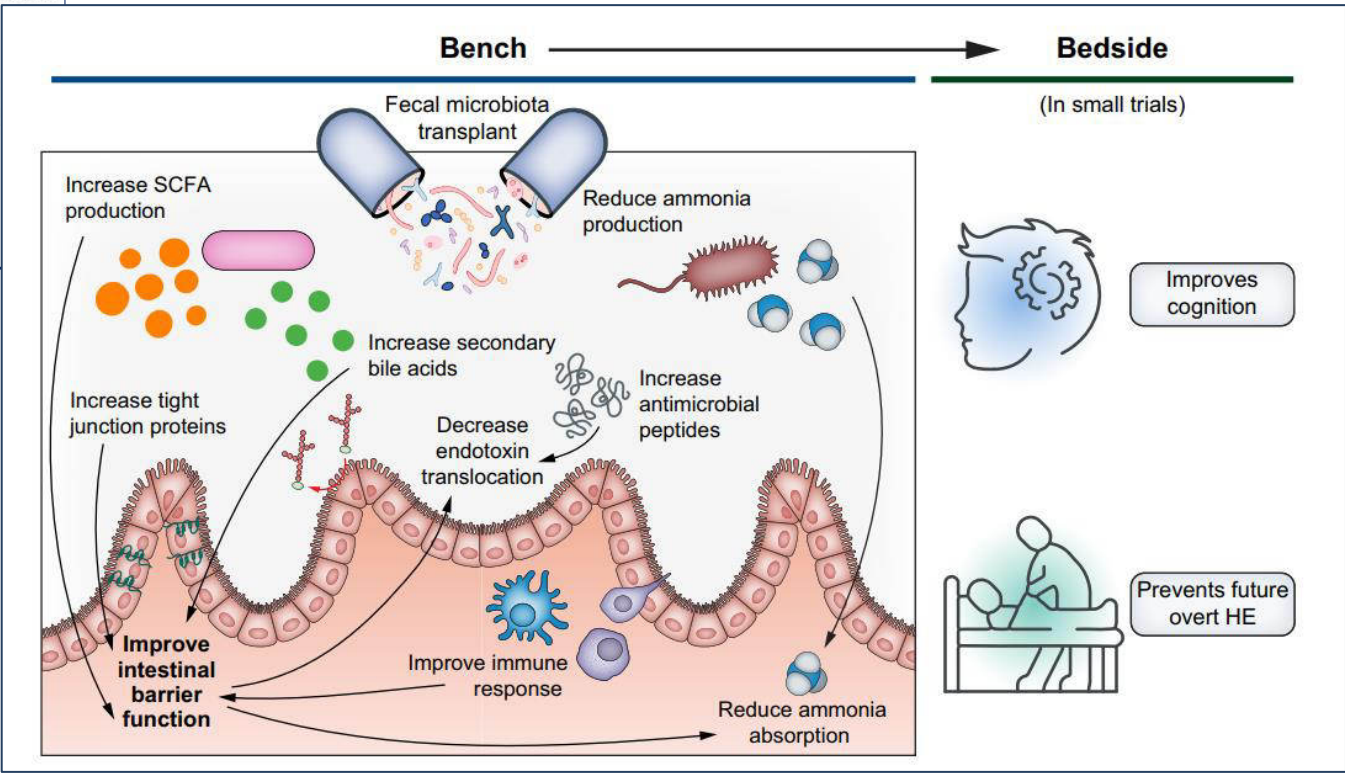
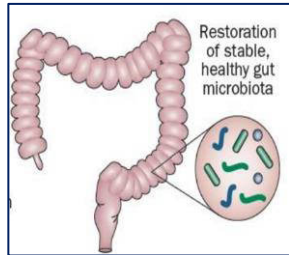


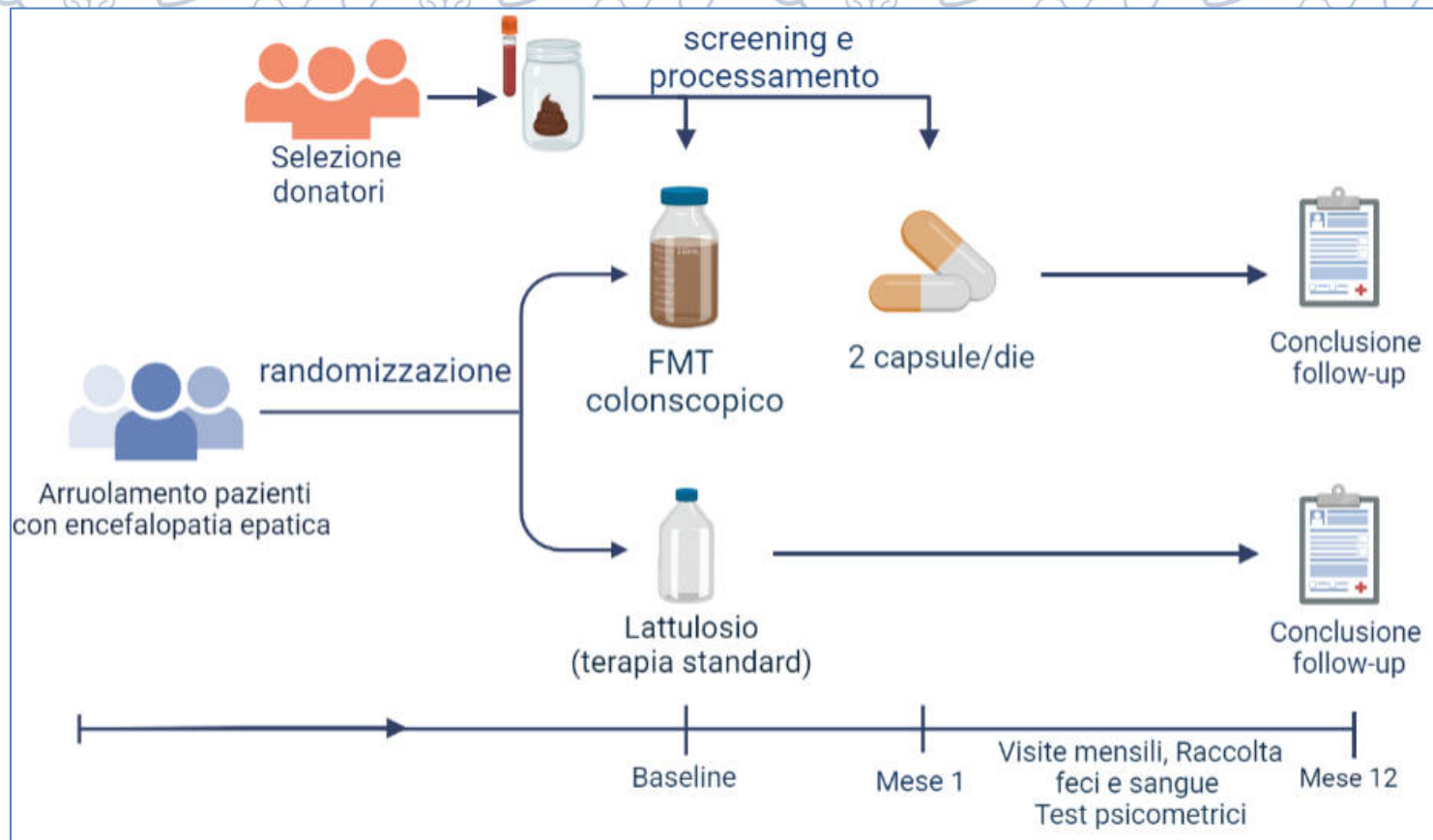
**Faecal microbiota transplantation**



**Administration by:**

- Enema
- Transcolonic infusion
- Nasoduodenal or nasogastric infusion
- Oral capsules





# Materiali e metodi

Parametri microbiologici

- Estrazione Acidi nucleici
- Analisi metagenomica 16S targeted su campioni fecali

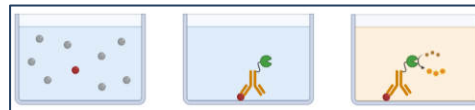
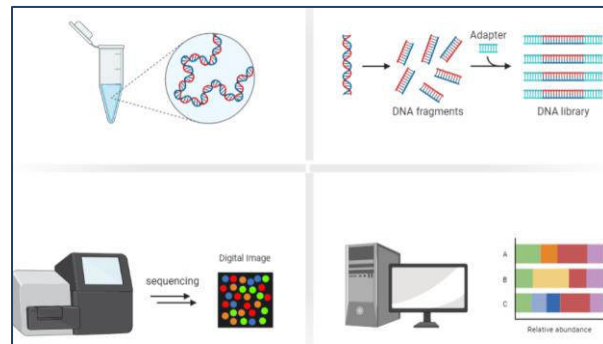
Parametri biochimici

Dosaggio della calprotectina fecale (CLIA)

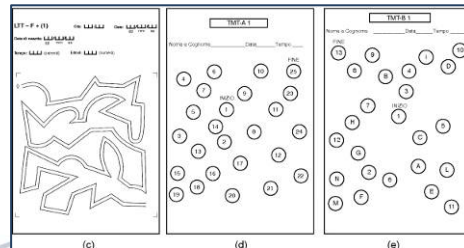
Dosaggio dell'ammoniaca sierica (saggio enzimatico)

Parametri clinici

Psychometric Hepatic Encephalopathy Score (PHES)

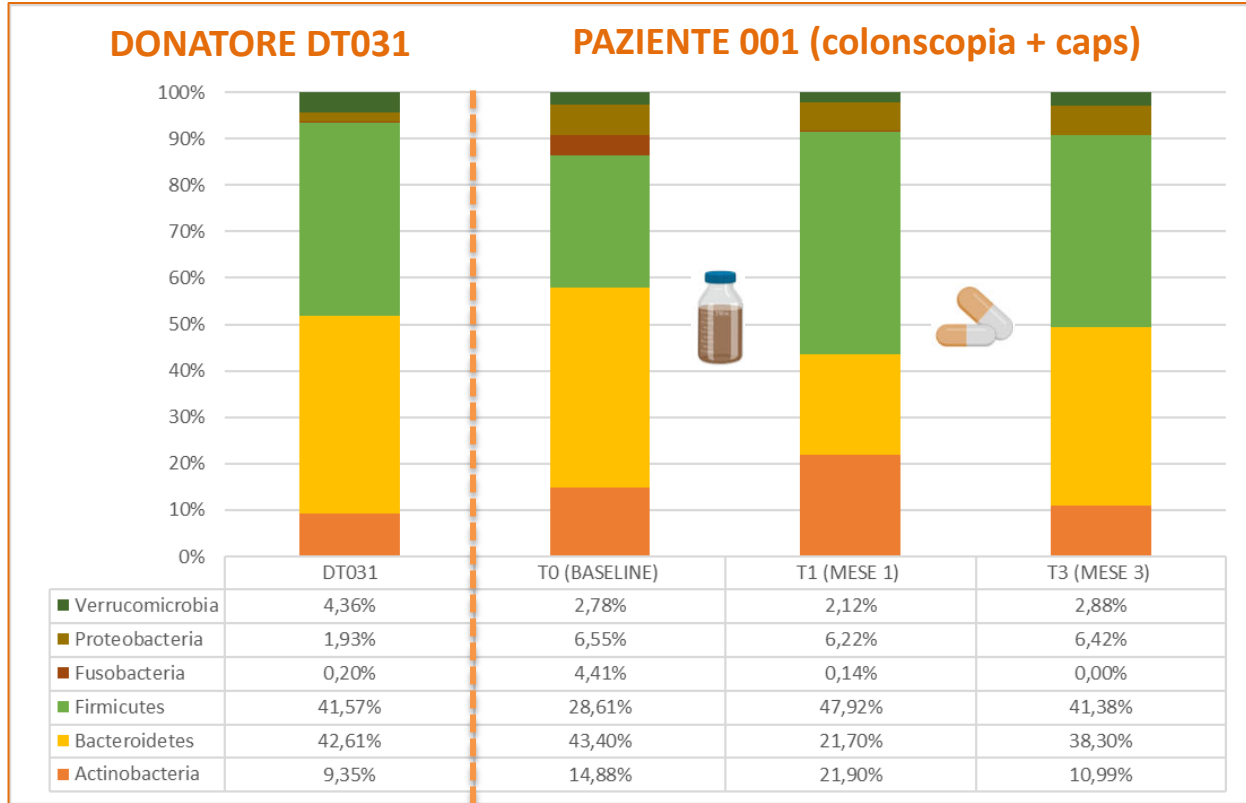


GLDH



# RISULTATI

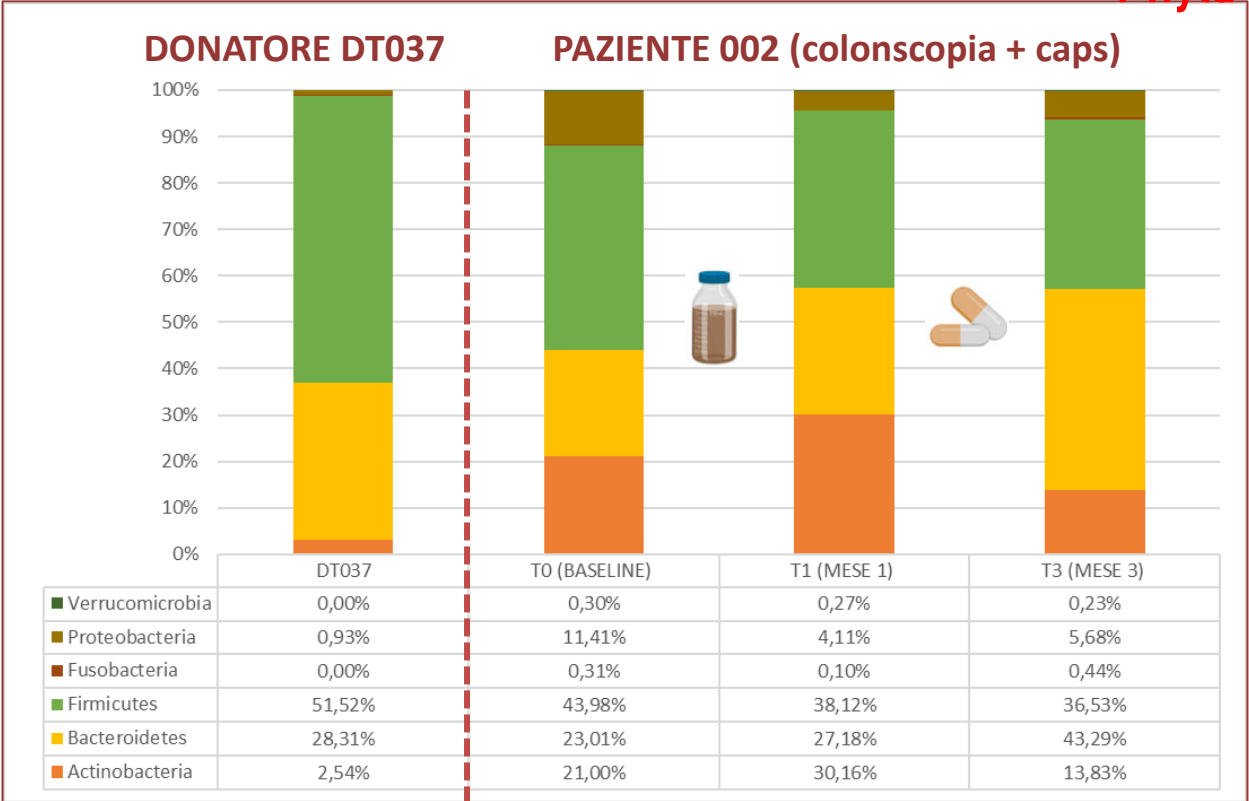
## Next Generation Sequencing (NGS) Phyla



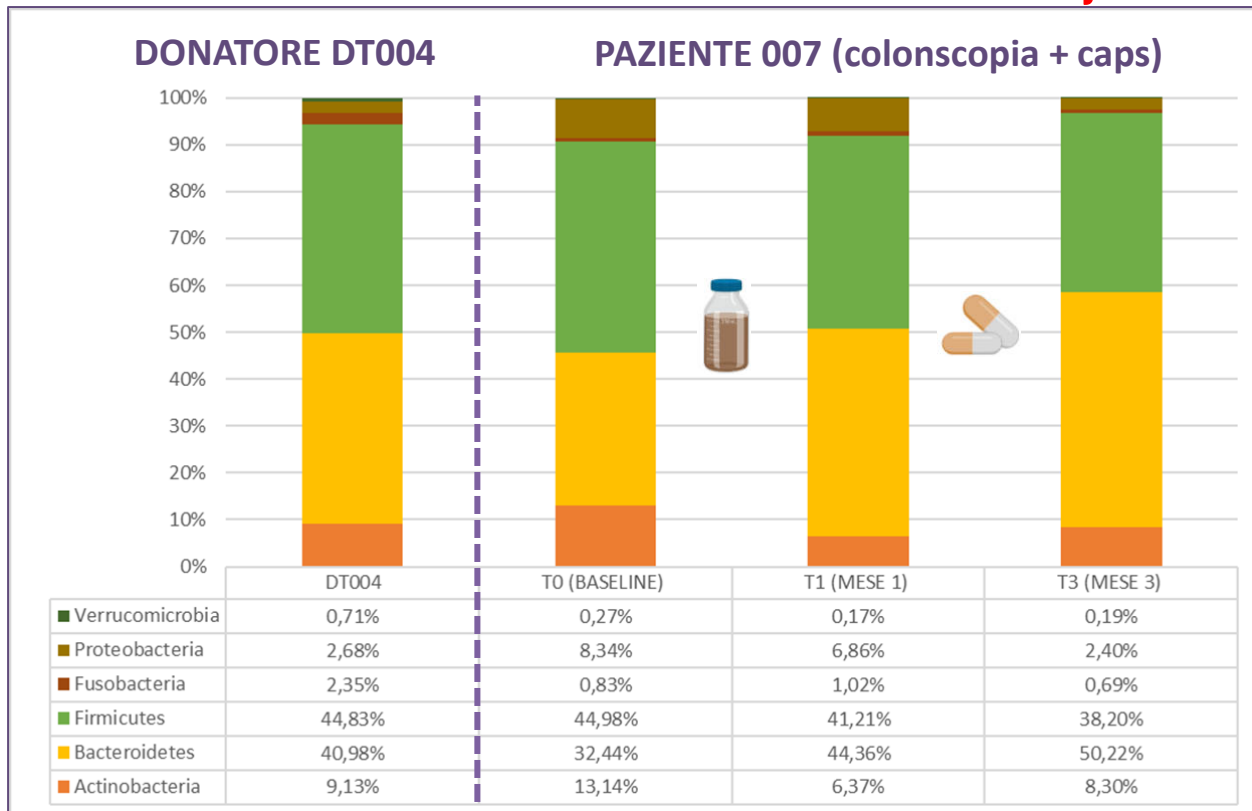


# RISULTATI

## Next Generation Sequencing (NGS) Phyla



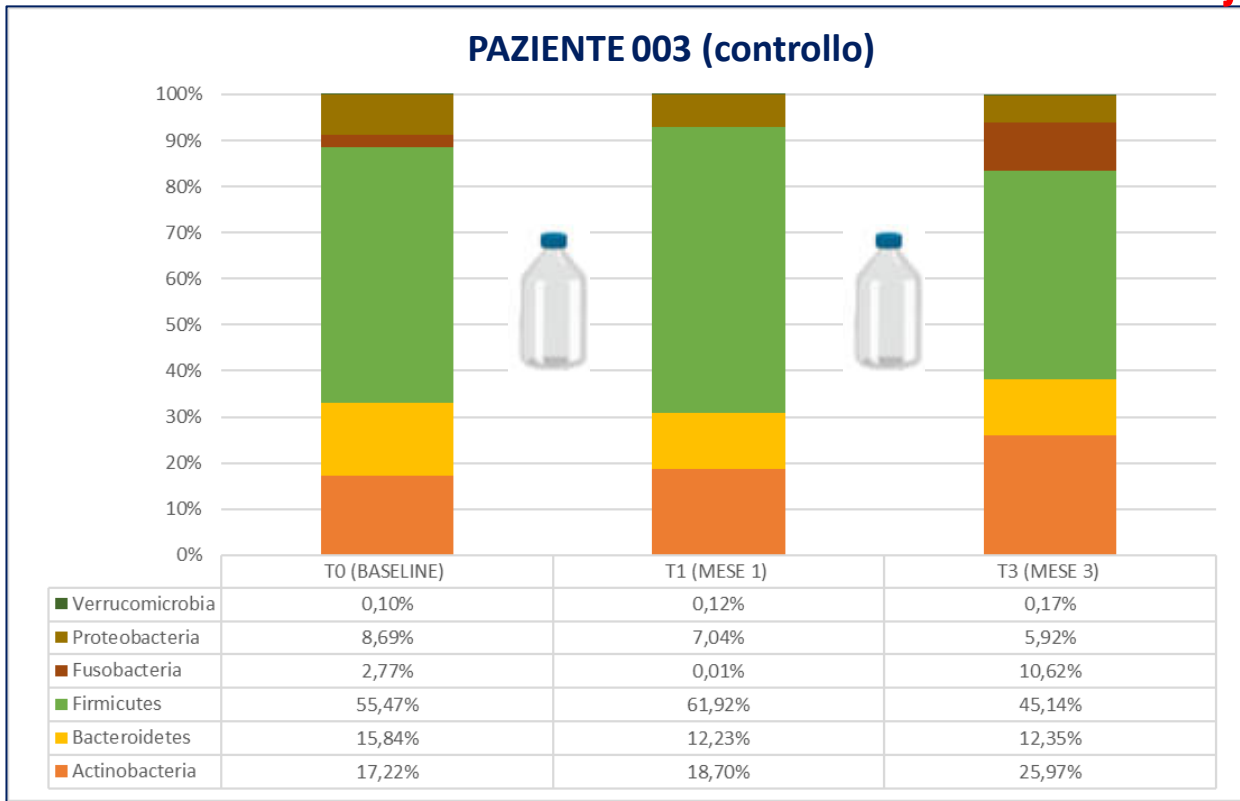
# RISULTATI Next Generation Sequencing (NGS) Phyla

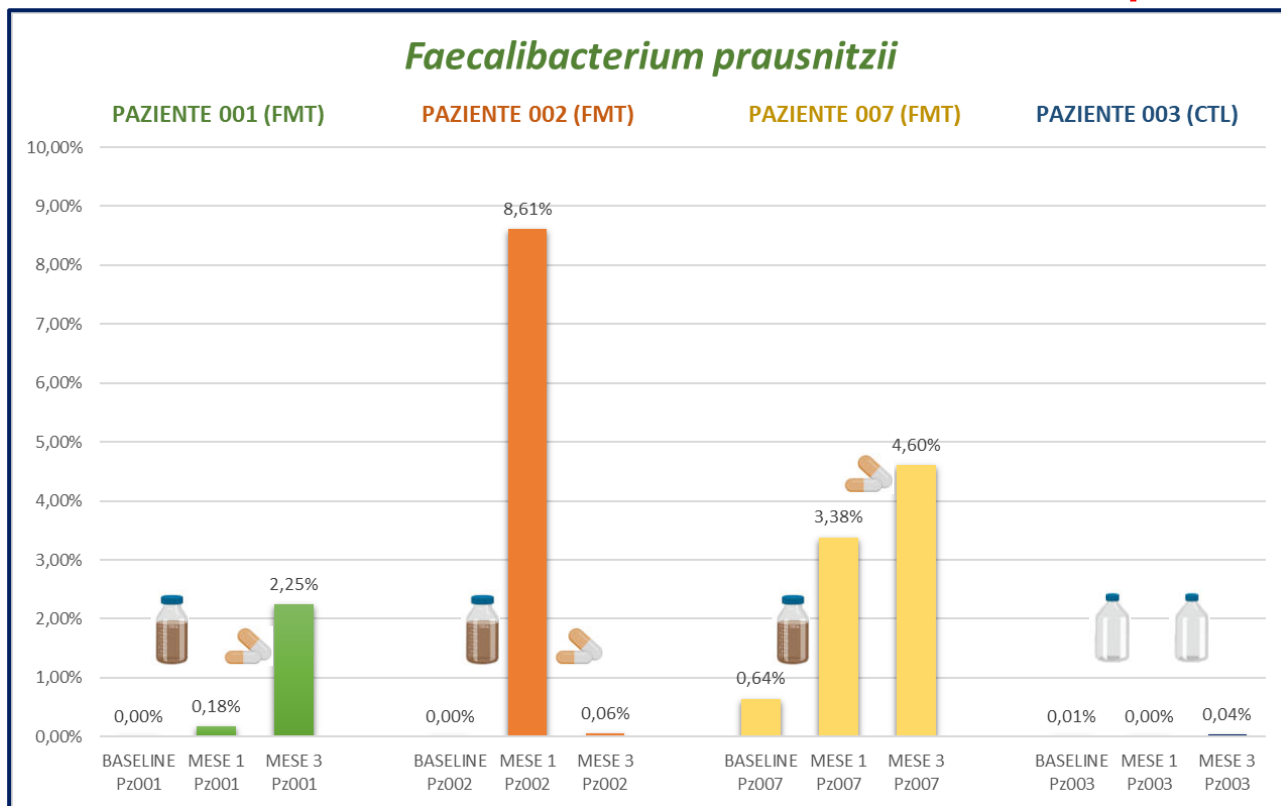


# RISULTATI

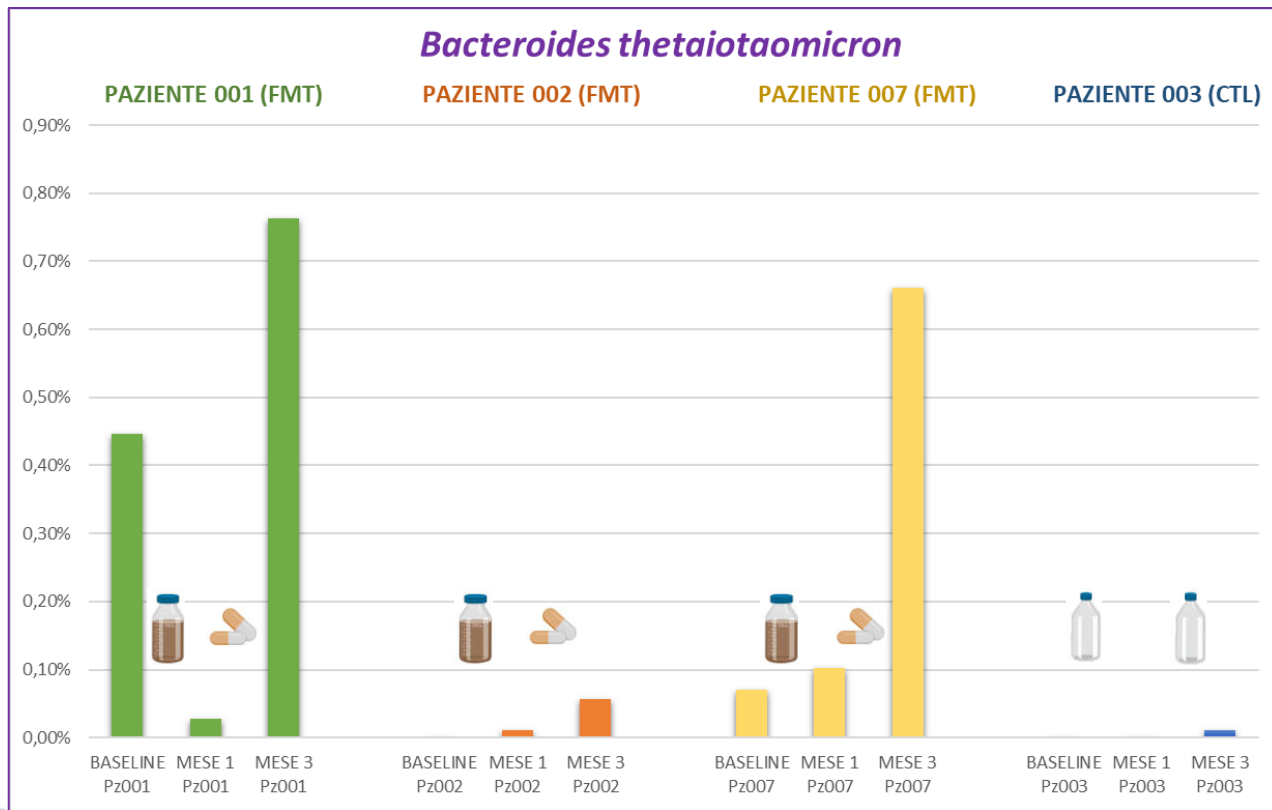
## Next Generation Sequencing (NGS)

### Phyla









# FMT?



Hindawi


BioMed Research International

Volume 2022, Article ID 5787373, 9 pages

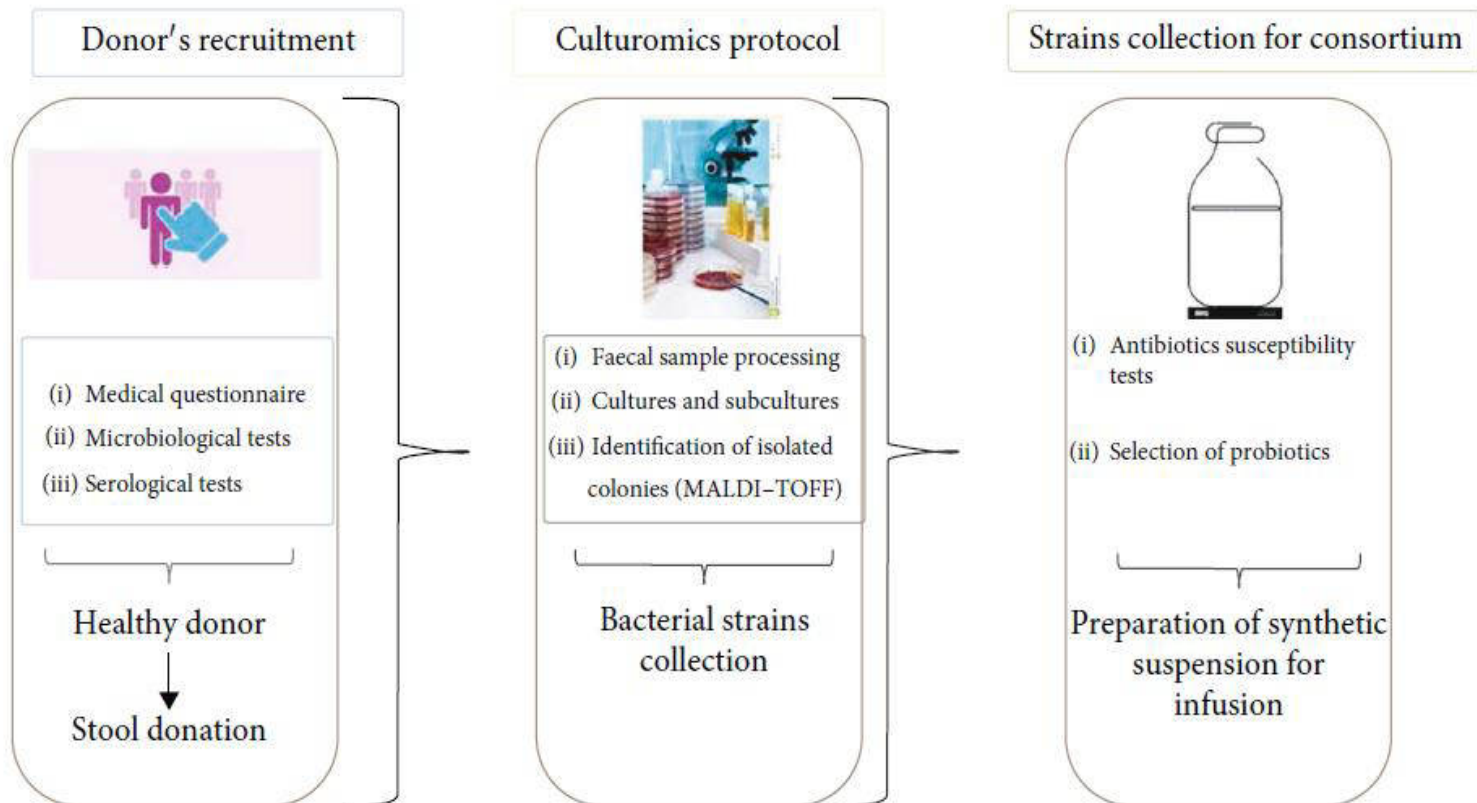
<https://doi.org/10.1155/2022/5787373>

*Research Article*

# “Bacterial Consortium”: A Potential Evolution of Fecal Microbiota Transplantation for the Treatment of *Clostridioides difficile* Infection

Gianluca Quaranta <sup>1</sup>, Gianluca Ianiro <sup>2</sup>, Flavio De Maio <sup>1</sup>, Alessandra Guarnaccia <sup>1</sup>,  
Giovanni Fancello <sup>1</sup>, Chiara Agrillo,<sup>1</sup> Federica Iannarelli,<sup>1</sup> Stefano Bibbo <sup>2</sup>,  
Amedeo Amedei <sup>3</sup>, Maurizio Sanguinetti <sup>1,4</sup>, Giovanni Cammarota <sup>2</sup>,  
and Luca Masucci <sup>1,4</sup>

# “Bacterial Consortium”: A Potential Evolution of Fecal Microbiota Transplantation for the Treatment of *Clostridioides difficile* Infection





# “Bacterial Consortium”: A Potential Evolution of Fecal Microbiota Transplantation for the Treatment of *Clostridioides difficile* Infection

BioMed Research International

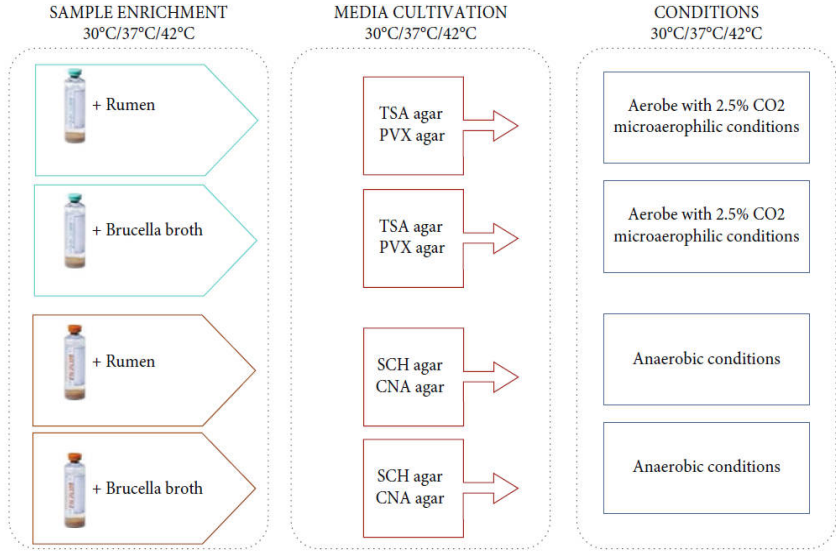


FIGURE 2: Culturomics protocol conditions used for bacterial isolation and BC synthesis.

| Bacterial strain                  | Concentration (CFU/mL) | MIC values         |
|-----------------------------------|------------------------|--------------------|
| <i>Acidaminococcus intestini</i>  | $5 \times 10^8$        | Not applicable     |
| <i>Bacteroides fragilis</i>       | $5 \times 10^8$        | MER 1 S            |
|                                   |                        | CLI 64 R           |
|                                   |                        | MRD 1 S<br>TZP 4 S |
| <i>Bacteroides ovatus</i>         | $5 \times 10^8$        | MER 0.25 S         |
|                                   |                        | CLI 4 S            |
|                                   |                        | MRD 8 R<br>TZP 4 S |
| <i>Bacteroides uniformis</i>      | $5 \times 10^8$        | MER 0.25 S         |
|                                   |                        | CLI 2 S            |
|                                   |                        | MRD 4 S<br>TZP 4 S |
| <i>Bifidobacterium longum</i>     | $5 \times 10^8$        | Not applicable     |
| <i>Clostridium scindens</i>       | $5 \times 10^8$        | Not applicable     |
| <i>Lactobacillus casei</i>        | $5 \times 10^8$        | Not applicable     |
| <i>Lactobacillus gasseri</i>      | $5 \times 10^8$        | Not applicable     |
| <i>Lactobacillus rhamnosus</i>    | $5 \times 10^8$        | Not applicable     |
| <i>Lactobacillus parabuchneri</i> | $5 \times 10^8$        | Not applicable     |
| <i>Parabacteroides distasonis</i> | $5 \times 10^8$        | Not applicable     |
| <i>Propionibacterium avidum</i>   | $5 \times 10^8$        | Not applicable     |
| <i>Ruminococcus gnavus</i>        | $5 \times 10^8$        | Not applicable     |

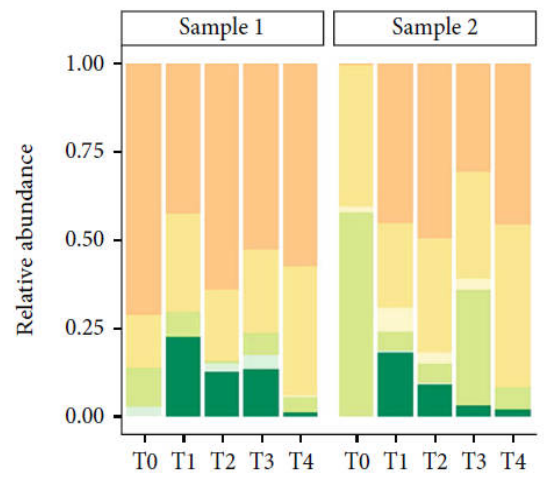
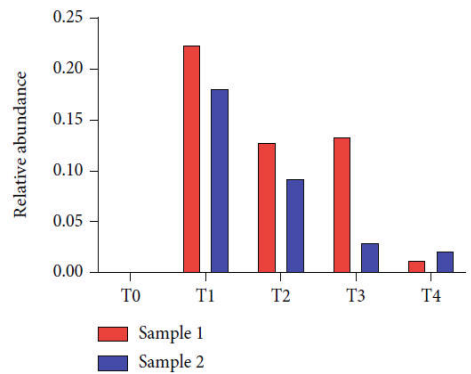
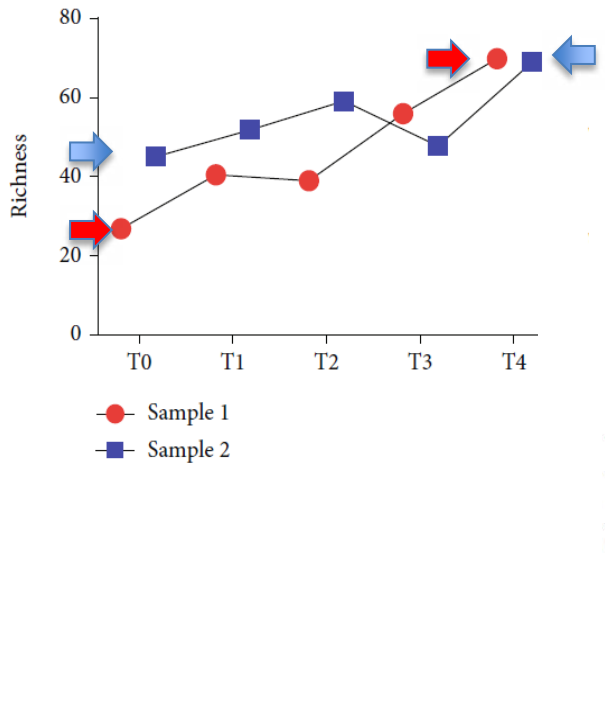


FIGURE 5: Relative abundance of *Akkermansia muciniphila* in PZ1 (sample 1) and PZ 2 (sample 2).









ARTICLE



<https://doi.org/10.1038/s41467-020-18127-y>

OPEN

# Faecal microbiota transplantation for the treatment of diarrhoea induced by tyrosine-kinase inhibitors in patients with metastatic renal cell carcinoma

Gianluca Ianiro <sup>1,7</sup>, Ernesto Rossi <sup>2,7</sup>, Andrew M. Thomas <sup>3</sup>, Giovanni Schinzari<sup>2</sup>, Luca Masucci <sup>4</sup>, Gianluca Quaranta<sup>4</sup>, Carlo Romano Settanni<sup>1</sup>, Loris Riccardo Lopetuso<sup>1</sup>, Federica Armanini<sup>3</sup>, Aitor Blanco-Miguez<sup>3</sup>, Francesco Asnicar<sup>3</sup>, Clarissa Consolandi<sup>5</sup>, Roberto Iacovelli <sup>2</sup>, Maurizio Sanguinetti <sup>4</sup>, Giampaolo Tortora<sup>2</sup>, Antonio Gasbarrini<sup>1</sup>, Nicola Segata <sup>3,6,7</sup> & Giovanni Cammarota <sup>1,7</sup>✉

cell carcinoma (ClinicalTrials.gov number: NCT04040/12). The primary outcome is the resolution of diarrhoea four weeks after the end of treatments. Twenty patients are randomised to receive FMT from healthy donors or placebo FMT (vehicle only). Donor FMT is more effective than placebo FMT in treating TKI-induced diarrhoea, and a successful engraftment is observed in subjects receiving donor faeces. No serious adverse events are

- FMT rappresenta una valida opzione terapeutica in CDI e in disbiosi
- Studi su patologie sistemiche che abbiano un substrato scientifico sono indubbiamente da promuovere e verificare
- Ridurre la via colonscopica, attualmente più utilizzata, con capsule gastroresistenti contenenti o consorzi batterici o soluzione fecale congelata o soluzione fecale liofilizzata.

- Progressi futuri sono rivolti all'utilizzo di **CONSORZI BATTERICI** ossia insieme di batteri fecali selezionati e controllati con saggi di sensibilità agli antibiotici ottenuti da donatori sani, da assumere in capsule o per via colonscopica
- Sospensioni polibatteriche formulate in base alle esigenze dei pazienti
- Sospensioni polibatteriche garantiranno una ottimizzazione nella gestione e nella sicurezza.



# Vincenzo Tiberio



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