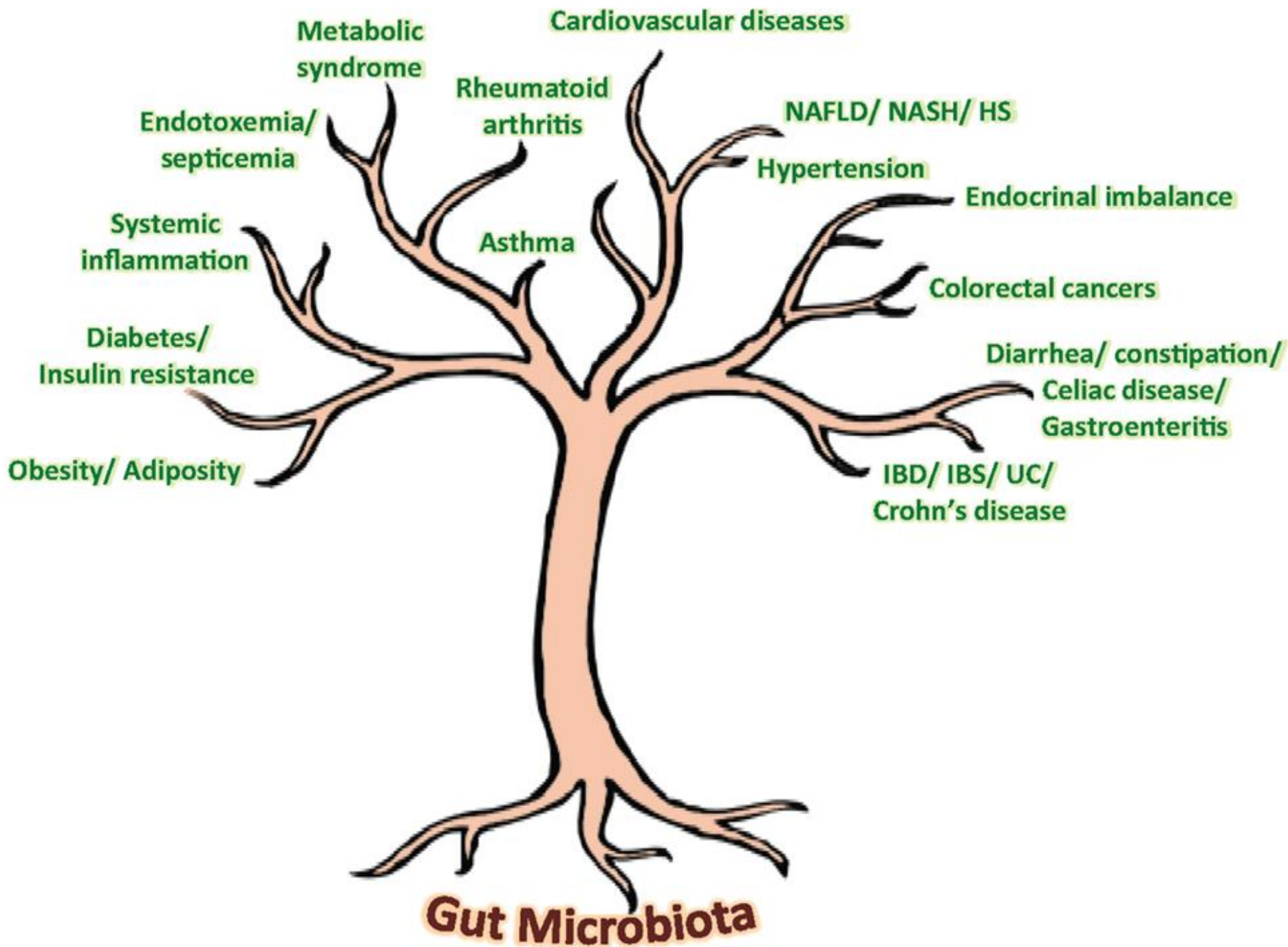


# FEKAL MİKROBİYOTA TRANSPLANTASYONU

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# Tanım

- Fekal mikrobiyota transplantasyonu (FMT)
  - Sağlıklı bir insanın dışkısından elde edilen mikrobiyal solusyonun değişik yollarla hasta kişiye nakledilmesidir.
  - Bu işlemin amacı bozulmuş barsak mikrobiyotasını sağlıklı bakteri topluluğu ile baskılamak, işlevini değiştirmektir.



# Tarihçe

- FMT yeni bir tedavi değil, ancak yeni popülerite kazanan bir tedavidir.
- Özellikle son yıllarda bakteri genetiği ve işlevi daha iyi araştırıldığı için FMT uygulaması artmıştır.
- Çin’de 4. yüzyılda besin zehirlenmesi ve şiddetli ishalde insan dışkısının ağızdan uygulandığı Ge Hong tarafından bildirilmiştir.

» Am J Gastroenterol 2012

- 16. yy da Li Shizhen dışkının diyare, ateş, ağrı, kusma ve kabızlıkta tedavide kullanıldığını bildirmiştir.
- 17. yy da veterinerlikte transfaunation olarak tanımlanmıştır.

» J Clin Gastroenterol 2004; 38:475–483

- İnsanlarda ilk kez psödomembranöz kolit için Eiseman tarafından 1958 de kullanılmıştır.

» Surgery 1958; 44:854–859.

# Teknik





# Fecal transplants can save lives



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Hastaların bakış açısının sorgulandığı bir anket çalışmasında, Hastaların işleme sıcak baktığı doktorların işlemden kaçındığı bulunmuştur.

# İdeal Donör Nasıl olmalı?



# Kan testleri

|       | Bakken et al., 2011   | Van Nood et al., 2014   | ANSM 2014*   |
|-------|---|---|--|
| Blood | <p>HIV type 1 and 2<br/>HAV IgM<br/>HBsAg, anti-HBc (both IgG and IgM), and anti-HBs.<br/>HCV Ab<br/>RPR and FTA-ABS</p> <p>Confirmatory tests will be performed when a positive or reactive screening test result is received for such purposes as donor counseling or investigating discordant test results.<br/>Serologic testing of the recipient for these agents is optional.</p> | <p>HIV types 1 and 2<br/>Human T-lymphotropic virus type I and II<br/>HAV (total antibodies, if positive and not vaccinated also hepatitis A IgM)<br/>HBV (HbsAg, anti-HbsAg, anti-HBcore)<br/>HCV C (anti-HCV)<br/>CMV (IgG and IgM)<br/>EBV (VCA IgM, VCA IgG, VCA, anti-EBNA)<br/><i>Treponema pallidum</i> (TPHA)<br/><i>Entamoeba histolytica</i> (agglutination and dipstick test)<br/><i>Strongyloides stercoralis</i> (ELISA)</p> | <p>HIV types 1 and 2 (serology and viral load)<br/>Human T-lymphotropic virus<br/>Hepatitis A, B (serology and viral load), C (serology and viral load)and E<br/>CytomégaloVirus Virus<br/>Epstein-Barr Virus (to confirm the absence of any sero-discordance with the recipient)<br/><i>Treponema pallidum</i><br/><i>Strongyloides stercoralis</i><br/><i>Trichinella sp.</i><br/><i>Toxoplasma gondii</i> (to confirm the absence of any sero-discordance with the recipient)</p> |



# Dışkı testleri

|       |  |   |  |
|-------|--|---|--|
| Stool | <i>C. difficile</i> toxin B by PCR; if unavailable, then toxins A and B by EIA.<br>Routine bacterial culture for enteric pathogens<br>Fecal <i>Giardia</i> antigen<br>Fecal <i>Cryptosporidium</i> antigen                       | Test for <i>C. difficile</i> (toxin ELISA and culture or PCR)<br>Bacteriological evaluation by local standards<br>Parasitological evaluation by local | Bacterial culture for:<br><i>C. difficile</i><br><i>Listeria monocytogenes</i><br><i>Vibrio cholerae</i> / <i>Vibrio parahemolyticus</i><br><i>Salmonella</i><br><i>Shigella</i><br><i>Multirésistant bacteria</i>   |
|       | Acid-fast stain for <i>Cyclospora</i> , <i>Isospora</i> and, if antigen testing unavailable, <i>Cryptosporidium</i><br>Ova and parasites<br><i>Helicobacter pylori</i> fecal antigen (for upper GI routes of FMT administration) | standards (triple feces test or PCR)  | <i>Strongyloïdes stercoralis</i><br><i>Cryptosporidium</i> sp.<br><i>Cyclospora</i> sp.<br><i>Entamoeba histolytica</i><br><i>Giardia intestinalis</i><br><i>Isospora</i> sp.<br><i>Microsporidies</i><br>Adénovirus<br>Astrovirus<br>Rotavirus<br>Calcivirus (norovirus, sapovirus)<br>Picornavirus<br>(entérovirus, Aichi virus) |

# Donör dışlama kriterleri-1

|  |  |
|--|--|
| <p>Risk of infectious agent</p> <ul style="list-style-type: none"><li>• Known HIV, Hepatitis B or C infections</li><li>• Known exposure to HIV or viral hepatitis (within the previous 12 months.)</li><li>• High-risk sexual behaviors (examples: sexual contact with anyone with HIV/AIDS or hepatitis, men who have sex with men, sex for drugs or money)</li><li>• Use of illicit drugs</li><li>• Tattoo or body piercing within 6 months</li><li>• Incarceration or history of incarceration</li><li>• Known current communicable disease (e.g., upper respiratory tract infection)</li><li>• Risk factors for variant Creutzfeldt-Jakob disease</li><li>• Travel (within the last 6 months) to areas of the world where diarrheal illnesses are endemic or risk of traveler's diarrhea is high</li><li>• <i>Past of typhoid fever (French regulatory agency)</i></li><li>• <i>Hospitalization abroad for more than 24 hours in the last 12 months (including members of the entourage) (French regulatory agency)</i></li><li>• <i>Residence of several years in the tropics(French regulatory agency)</i></li></ul> |  |
| <p>Gastrointestinal co-morbidities</p> <ul style="list-style-type: none"><li>• History of inflammatory bowel disease (IBD)</li><li>• History of irritable bowel syndrome, idiopathic chronic constipation, or chronic</li></ul>  | <p>Gastrointestinal co-morbidities</p> <ul style="list-style-type: none"><li>• History of major gastrointestinal surgery (e.g., gastric bypass, short bowel)</li><li>• <i>Family history of IBD, autoimmune disease and colonic cancer (French</i></li></ul> |

# Donör dışlama kriterleri-2

|   |  |
|---|--|
| <p>diarrhea</p> <ul style="list-style-type: none"><li>• History of gastrointestinal malignancy or known polyposis</li><li>• <i>Acute diarrhea during the last 3 months (French regulatory agency)</i></li></ul>   | <p><i>regulatory agency)</i></p>   |
| <p>Factors that can or do affect the composition of the intestinal microbiota</p> <ul style="list-style-type: none"><li>• Antibiotics within the preceding 3 months</li><li>• Major immunosuppressive medications, e.g., calcineurin inhibitors, exogenous glucocorticoids, biologic agents, etc.</li><li>• Systemic anti-neoplastic agents</li></ul> | <p>Factors that can or do affect the composition of the intestinal microbiota</p> <ul style="list-style-type: none"><li>• <i>Age &gt; 65 years (French regulatory agency)</i></li><li>• <i>BMI &gt; 30kg/m2 (French regulatory agency)</i></li></ul>   |
| <p>Additional recipient-specific considerations</p> <ul style="list-style-type: none"><li>• Recent ingestion of a potential allergen (e.g., nuts) where recipient has a known allergy to this (these) agent(s).</li></ul>   | <p>Additional recipient-specific considerations</p> <ul style="list-style-type: none"><li>• Metabolic syndrome</li><li>• Systemic autoimmunity, e.g., multiple sclerosis, connective tissue disease</li><li>• Atopic diseases including asthma and eczema, eosinophilic disorders of the gastrointestinal tract</li><li>• Chronic pain syndromes, (e.g., chronic fatigue syndrome, fibromyalgia)</li></ul> |

# FMT uygulama yolları

|                                 | Recipient preparation   | Preparation and administration of FMT   | Disadvantages and or risk   | Situations requiring precautions                             |
|---------------------------------|---|---|---|--|
| colonoscopy                     | Large volume bowel prep<br>± Loperamide before and/or after procedure | Large volume (>300ml) in one procedure requiring generally a sedation   | Anesthesia<br>Risk of colonic perforation<br>Cost                                       | Severe colitis<br>Colonic distension<br>Severe comorbidities |
| Retention enema                 | Variable volume of bowel prep   | Small volume ( 50ml) requiring 4 or 5 consecutive days of rectal administration                                   | Frequent stool losses   | Patients with diminished rectal sphincter tone               |
| Nasogastric or nasojejunal tube | PPI night before and the morning<br>No necessary bowel prep           | Generally small volume ( 25 to 50ml) through a nasoenteric tube requiring a radiological control before procedure | Inconfort of tube placement<br>Risk of aspiration, vomiting<br>Diarrhea after procedure | Gastroparesia<br>Motility disorder                           |

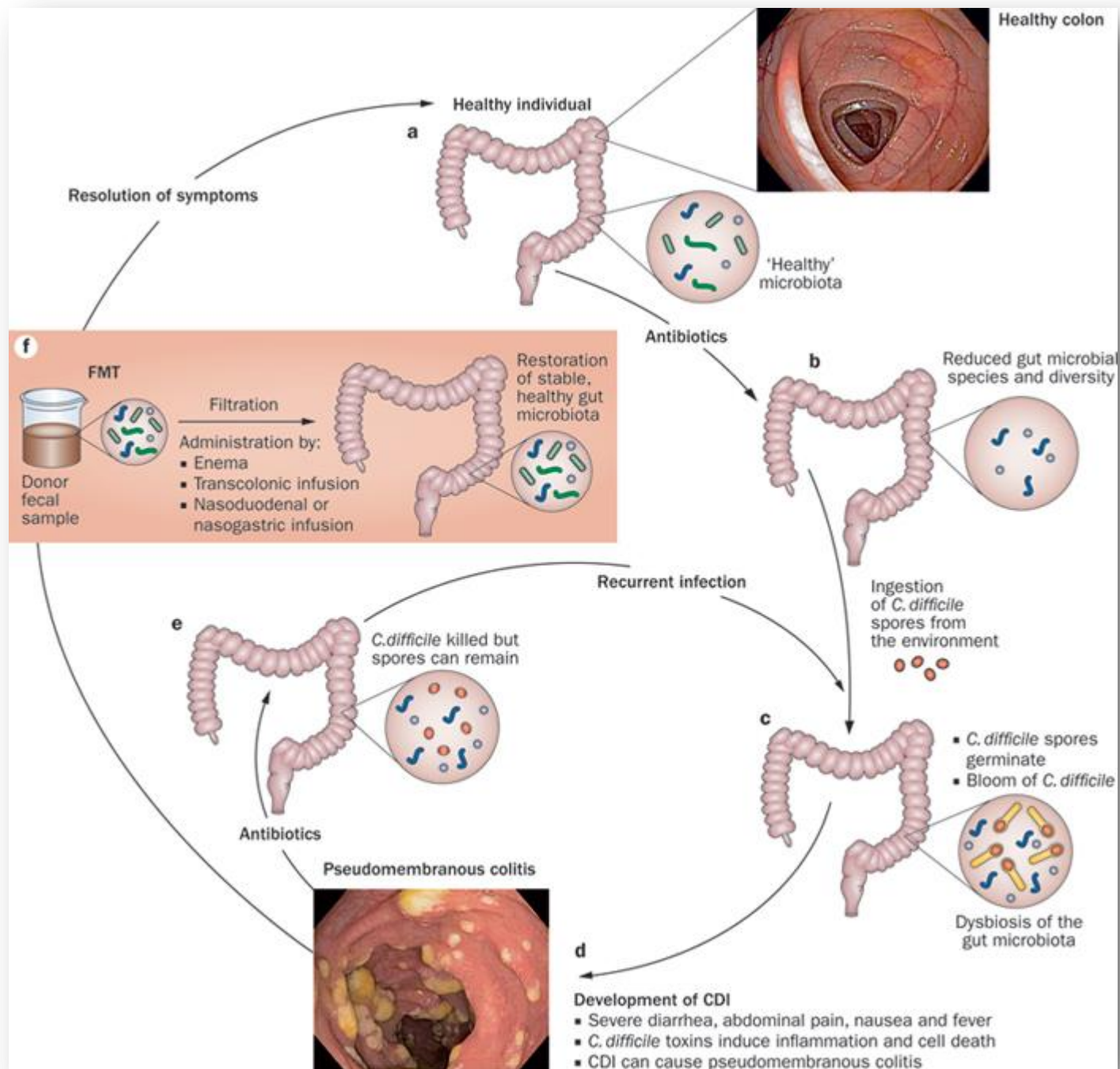
# Endikasyonlar

- Kesinleşmiş endikasyon
  - Kronik Clostridium difficile enfeksiyonu
- Araştırma aşamasında
  - Ülseratif kolit
  - Crohn hastalığı
  - İBS
  - Kabızlık
  - Diyabetes mellitus
  - Metabolik sendrom
  - Obezite



# C.Difficile

- Antibiyotik kullanımı sonrası gelişen psödomembranöz enterokolit etkeni
- Literatürde CD için FMT ile ilgili birçok yayın olgu serisi şeklinde.
- Tek yayın randomize kontrollü
- Başarı (kür) oranı %98 ! Oldukça yüksek
- Semptomlar birkaç gün içinde normale geliyor.



|                                |                          |         |            |   |                  |                |  |            |   |
|--------------------------------|--------------------------|---------|------------|---|------------------|----------------|--|------------|---|
| Eiseman <sup>13</sup> (1958)   | Journal article (US)     | 4 (3/1) | 56 (45–68) | /(retention enemas)   | 1–3              | Healthy adults | Severe diarrhoea ceased within 48 h  | 4/4 (100%) | None  |
| Cutolo LC <sup>76</sup> (1959) | Journal article (US)     | 1 (1/0) | 65         | Two ounces of faeces and 10 ounces of yogurt in a quart of normal saline) (Cantor tube) | 3/day for 7 days | Healthy humans | The first formed stool was passed 36 h later, after 48 h the diarrhoea ceased. A response was obtained and both clinical and laboratory evidence revealed the elimination of the staphylococcus from the intestine | 1/1 (100%) | Died of upper GI haemorrhage (not related to the FMT therapy) |
| Fenton <sup>77</sup> (1974)    | Journal article (Canada) | 1 (0/1) | 57         | -/500 mL saline (enema)   | 1                | /              | Marked improvement occurred and continued to complete resolution of the clinical and sigmoidoscopic abnormalities within 4 days.   | 1/1 (100%) | None  |

|                             |                           |         |            |   |                                 |                      |   |            |      |
|-----------------------------|---------------------------|---------|------------|---|---------------------------------|----------------------|---|------------|------|
| Schwan <sup>24</sup> (1984) | Journal article (Sweden)  | 1 (0/1) | 67         | 450 mL mixture contain faeces and saline (retention enemas) | 2 (over three consecutive days) | Husband              | Prompt and complete normalisation of the bowel function with disappearance of IBS symptoms. Stools of normal consistency, colour and smell have thereafter been passed daily or every other day. Weight gain 6 kg | 1/1 (100%) | None |
| Tvede <sup>78</sup> (1989)  | Journal article (Denmark) | 2 (1/1) | 60 (59–60) | 50 g faeces suspended in 500 mL saline (Enema)              | 1–2                             | Husband and daughter | Patient 1: complete clinical recovery with eradication of <i>C. difficile</i> and its toxin after 1 infusion; Patient 2 had 2 infusions but did not respond (but did respond to a cultured bacterial mixture)     | 1/2 (50%)  | None |
| Borody <sup>44</sup> (1989) | Letter (Australia)        | 1 (0/1) | 35         | Retention enemas (/)  | /                               | /                    | The patient appear to be 'cured' by resolution of symptoms dramatically.  | 1/1 (100%) | None |

|                                     |                       |         |            |   |   |   |   |            |      |
|-------------------------------------|-----------------------|---------|------------|---|---|---|---|------------|------|
| Patterson-1 <sup>79</sup><br>(1994) | Letter<br>(Australia) | 1 (Q/1) | 39         | Single daily retention enemas for 3 days (400 mL consisting of 200 mL stool mixed with 200 mL saline (Rectal tube)  | 3 | Husband                                     | No recurrence of diarrhoea in 2 years   | 1/1 (100%) | None |
| Patterson-2 <sup>79</sup><br>(1994) | Letter (Australia)    | 6 (-/-) | 56 (30–80) | Single daily retention enemas for 3 days (400 mL consisting of 200 mL stool mixed with 200 mL saline) (Rectal tube) | 3 | Relative                                    | All patients experienced rapid resolution of disabling persistent <i>C. difficile</i> infection without relapse   | 6/6 (100%) | None |
| Persky <sup>80</sup> (2000)         | Journal article (US)  | 1 (Q/1) | 60         | (500 mL containing stool mixed in saline) (colonoscopy)   | 1 | Husband                                     | Immediate and complete resolution of diarrhoea with normal bowel movements that was maintained long term. Repeat <i>C. difficile</i> toxin assay negative | 1/1 (100%) | None |
| Faust <sup>81</sup> (2002)          | Abstract (Canada)     | 6 (1/5) | 53 (37–74) | /(/)  | 1 | Family members (spouse 4, brother 1, son 1) | All patients responded promptly and continued to be asymptomatic; 4/6 patients <i>C. difficile</i> toxin negative   | 6/6 (100%) | None |



|  |                      |            |       |  |   |  |   |                     |      |
|--|----------------------|------------|-------|--|---|--|---|---------------------|------|
| Broody (CD SYNDROMES) <sup>61</sup> (2003) | Abstract (Australia) | 24 (11/13) | 19–59 | 200–300 g stool diluted in 200–300 mL saline (The suspension was infused into the colon) (colonoscopy and/or rectal enema and/or nasojejunal tube (Combination of colonoscopy and rectal enema was the most common (46%) delivery method)) | Daily for 1 (3/24, 13%), 5 (11/24, 46%) or 10 days (10/24, 42%) | Relatives or unrelated healthy individuals | Eradication of <i>C. difficile</i> was confirmed by negative Cd toxin and culture results in 20/24 patients (83%, $P < 0.0001$ ) post-treatment. 2/24 unsuccessful, 2/24 nonresponse, (including 1/24 recurrent)  | 20/24 (83%)         | †    |
| Wettstein <sup>38</sup> (2007)             | Abstract (Australia) | 16 (5/11)  | 11–87 | 200–300 g/200–300 mL Saline with added psyllium [Colonoscopy (day 1) Enema (between 5, 10, or 24 days)]  | 5–24  | Relatives or unrelated healthy individuals | Eradication of <i>C. difficile</i> was confirmed by negative Cd toxin A or B and culture results in 15/16 patients (93.5%) 4–6 weeks post-treatment   | Resolution in 15/16 | None |
| You <sup>62</sup> (2008)                   | Letter (US)          | 1 (1/0)    | 69    | 45 g/300 mL normal saline (Retention enema)  | 1   | Daughter                                   | The patient's blood pressure stabilised, the leucocyte count normalised, and oliguria resolved and both vasopressors and continuous venovenous hemofiltration was discontinued. The patient's bowel function returned, and abdominal distention decreased | 1/1 (100%)          | None |

|                                     |                          |           |              |   |                       |                            |  |               |      |
|-------------------------------------|--------------------------|-----------|--------------|---|-----------------------|----------------------------|--|---------------|------|
| Keller <sup>83</sup> (2009)         | Abstract (Netherlands)   | 11 (-/-)  | /            | >100 g/300–400 mL saline (infusion of suspension of donor faeces) (in jejunum (nasoduodenal tube) or in caecum and colon ascendens (via colonoscopy)) | 1                     | /                          | Successfully treated 11 patients with multiple recurrences of CDI  | 11/11 (100%)  | None |
| Maccanochie <sup>84</sup> (2009)    | Journal article (UK)     | 15 (1/14) | 81.5 (68–95) | 30 g faeces in 150 mL saline (30 mL of faecal fluid was administered) (Nasogastric tube)  | 1 (14/15) or 2 (1/15) | Healthy related volunteers | Patients were symptom free. 2 no responses; 2 relapsed (1 responded to the 2nd FMT)  | 12/15 (80%)   | None |
| Rubin <sup>85</sup> (2009)          | Letter (US)              | 16 (-/-)  | 70–99        | ~30 g or 2cm <sup>3</sup> /50–70 mL saline (30–60 mL suspense) (Nasogastric tube)   | 1                     | Family member              | 14/16 ambulatory patients are able to return to normal diet and activities immediately after the procedure   | 14/16 (87.5%) | None |
| Arkkila, P. E. <sup>86</sup> (2010) | Abstract (/)             | 37 (-/-)  | 69 (24–90)   | 20–30 mL mixed with 100–200 mL of water (colonoscopy)   | 1–2                   | Related to the recipient   | 34/37 (92%) patients were cured patients had relapse after 5–12 months after receiving new antibiotic treatment and they got successful faeces reinfusion thereafter. One noncured patient died after 1 month due to the toxic megacolon | 34/37 (92%)   | None |
| Silverman <sup>26</sup> (2010)      | Journal article (Canada) | 7 (4/3)   | 65 (30–88)   | 50 mL faeces in 200 mL saline (250 mL of faecal fluid was administered) (Retention enema)   | 1                     | Family member              | All of the patients were successfully cured  | 7/7 (100%)    | None |

|                              |                          |            |              |   |                               |   |  |              |  |
|------------------------------|--------------------------|------------|--------------|---|-------------------------------|---|--|--------------|--|
| Khoruts <sup>60</sup> (2010) | Journal article (US)     | 1 (0/1)    | 61           | 25 g/300 mL saline (250 mL of faecal fluid was administered) (colonoscopy)  | 1                             | Husband   | At 1 month after bacteriotherapy, stool studies were culture negative for <i>C. difficile</i>  | 1/1 (100%)   | ‡  |
| Rohlke <sup>87</sup> (2010)  | Journal article (US)     | 19 (2/17)  | 49 (29–82)   | ~350 mL saline (200–300 mL of faecal fluid was administered) (colonoscopy)  | 1 (majority) or 2 (1 patient) | Intimate domestic partners, family members and close friends. | All of the patients in this study maintained prolonged periods free of symptoms and are considered 'cured' after treatment with Faeces Flora Reconstitution  | 19/19 (100%) | /  |
| Yoon <sup>88</sup> (2010)    | Journal article (US)     | 12 (3/9)   | 66 (30–86)   | Unknown volume faeces in 1000 mL saline (250–400 mL of faecal fluid was administered) (colonoscopy)   | 1                             | Family member or partner                                      | Absence of diarrhoea, cramps, and fever. All patients experienced a durable clinical response to faeces transplantation  | 12/12 (100%) | None   |
| Garborg <sup>89</sup> (2010) | Journal article (Norway) | 40 (19/21) | 75 (53–94)   | 50–100/250 saline (200 mL of faecal fluid was administered) [Gastroscopy (38) or colonoscopy (2)]   | 1 (34/40) or 2 (6/40)         | Close relatives or other household members                    | A total of 33/40 patients (4 patients responded to the 2nd FMT) were successfully treated  | 33/40 (83%)  | None (5 unrelated deaths 3 weeks to 2 months post-FMT) |
| Kelly <sup>90</sup> (2010)   | Abstract (US)            | 12 (1/11)  | 55.6 (19–80) | 6–8 tablespoons of donor stool was added to 1 L of sterile water (740 mL (range 500–960 mL) of faeces suspension was delivered) (colonoscopy) | 1                             | Partner or family member                                      | Ten have remained symptom free. Two had diarrhoea after the procedure, but both were <i>C. difficile</i> negative. One responded to treatment with a fibre supplement and the other resumed vancomycin. None have had a documented recurrence of CDI to date | 12/12 (100%) | None   |

|                                |                               |                                      |   |  |                    |                                |  |               |   |
|--------------------------------|-------------------------------|--------------------------------------|---|--|--------------------|--------------------------------|--|---------------|---|
| Rubin <sup>41</sup> (2013)     | Journal article (US)          | 75 FMT courses (49/26) (74 patients) | 63 (6–94) two paediatric patients (age 6 and 8) | ~30 g (~3 cm <sup>3</sup> )/50–70 mL saline (25 mL) (nasogastric tube, or gastroscopy or through a PEG tube) | 1 or 2 (1 patient) | Healthy close household member | Fifty-nine FMT courses resulted in clinical resolution of diarrhoea for a primary cure rate of 79%. diarrhoea relapsed following 16 FMT courses; in 9 of these cases diarrhoea subsequently resolved after a single course of vancomycin. (paediatric patients: one experienced a clinical resolution following the FMT, while the other had a clinical relapse) | 59/75 (79.7%) | None  |
| Trubiano <sup>101</sup> (2013) | Journal article (Australia)   | 1 (0/1)                              | 75  | 30 g/70 mL saline (30 mL suspension of donor faeces) (delivered into the jejunum through gastroscopy)        | 1                  | Husband                        | The <i>C. difficile</i> -related symptoms were resolved. An abdominal computed tomography in the days before death showed no evidence of colitis, whereas stool cultures for <i>C. difficile</i> remained negative for culture and toxin on days 14, 20 and 30 after transplant  | 1/1 (100%)    | †   |
| Van Nood <sup>37</sup> (2013)  | Journal article (Netherlands) | 16 (8/8)                             | 73 ± 13   | Faeces were diluted with 500 mL of sterile saline (0.9%) (nasoduodenal tube)                                 | 1 (13/16) 2 (3/16) | Volunteers                     | The infusion of donor faeces was significantly more effective for the treatment of recurrent <i>C. difficile</i> infection than the use of vancomycin. 13 (81%) had resolution of <i>C. difficile</i> -associated diarrhoea after the first infusion. The 3 remaining patients received a second infusion with faeces from a different donor, with resolution in | 15/16 (94%)   | Mild diarrhoea and abdominal cramping on the infusion day |

# Complete Microbiota Engraftment Is Not Essential for Recovery from Recurrent *Clostridium difficile* Infection following Fecal Microbiota Transplantation

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*Clostridium difficile* için yapılan FMT nin başarılı olması için vercinin tüm mikrobiyotasının engrafmanı şart değil. Özellikle safra asit metabolize eden bakterilerin tutunması tedavide önemli

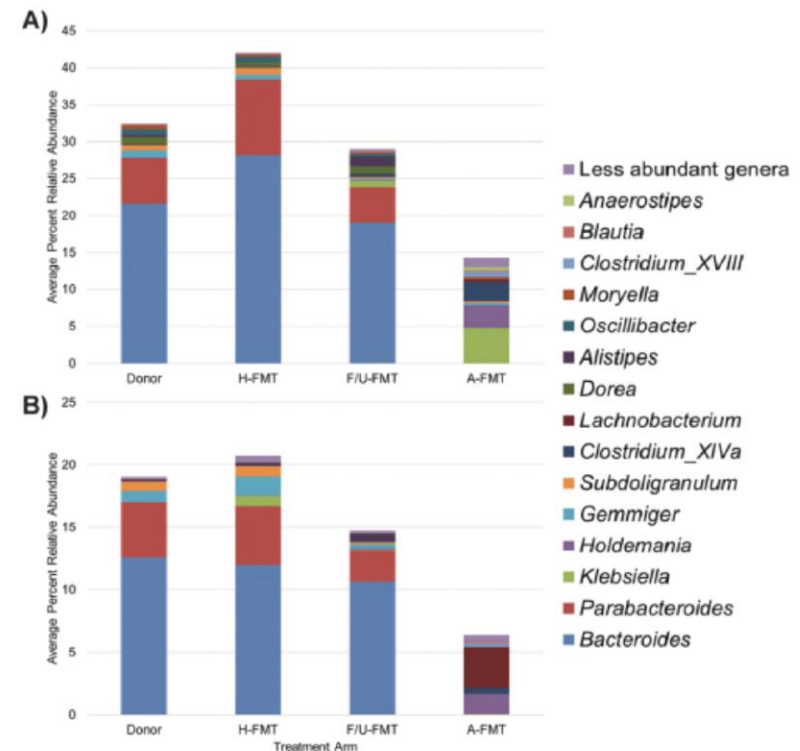


FIG 5 Genus-level classification of OTUs that differed significantly between treatment arms. Differences were evaluated by Kruskal-Wallis test at  $\alpha = 0.05$ . (A) Two weeks post-FMT and (B) 8 weeks post-FMT. H-FMT, heterologous FMT; F/U-FMT, follow-up heterologous FMT; A-FMT, autologous FMT.



İBH ve FMT

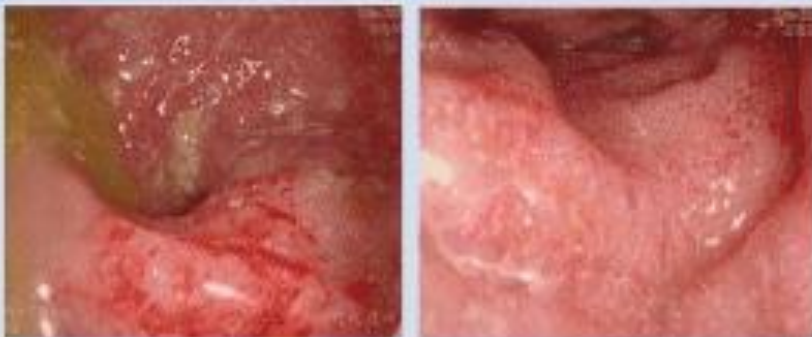




|           |     |  |                                   |         |                |   |                            |   |   |               |      |
|-----------|-----|--|-----------------------------------|---------|----------------|---|----------------------------|---|---|---------------|------|
| UC        |     | Bennet, J.<br>D <sup>102</sup><br>(1989) | Letter (US)                       | 1 (1/0) | /              | Large-volume<br>(Enema)   | 1                          | /   | Patient symptom-free (no bloody diarrhoea, cramping, tenesmus, skin lesions or arthritis) for the first time in 11 years without any medication   | 1/1 (100%)    | None |
| UC        |     | Borody <sup>44</sup><br>(1989)           | Letter<br>(Australia)             | 1 (1/0) | 45             | Retention<br>enemas (/)   | /                          | /   | The patient appear to be 'cured' by resolution of symptoms dramatically.  | 1/1 (100%)    | None |
| UC        |     | Broody <sup>103</sup><br>(2001)          | Journal<br>article<br>(Australia) | 3 (1/2) | 28, 38, 42     | Donor stool<br>suspended in<br>200 mL saline<br>with one<br>tablespoon of<br>psyllium<br>husks<br>(retention<br>enemas) | Single daily<br>for 5 days | Healthy<br>adults   | Disappearance of<br>symptoms within<br>1 month,<br>maintained long<br>term without<br>medications.  | 3/3<br>(100%) | None |
| UC        |     | Broody <sup>104</sup><br>(2003)          | Journal<br>article<br>(Australia) | 6 (3/3) | 36 (25–<br>53) | 200–300 g<br>stool diluted<br>in 200–<br>300 mL saline<br>(Retention<br>enema)  | 5                          | 1 Female<br>partner/1<br>Unrelated<br>Male/1 Brother<br>in<br>law/3 brother | All patients<br>showed complete<br>resolution of<br>symptoms by<br>4 months and<br>were able to<br>cease all UC<br>medications. No<br>clinical,<br>colonoscopic or<br>histological<br>evidence of UC at<br>long-term follow-up.     | 6/6<br>(100%) | None |
| UC<br>ITP | and | Borody <sup>105</sup><br>(ITP)<br>(2011) | Abstract<br>(Australia)           | 1 (0/1) | 39             | /(/)  | /                          | /   | In the months<br>following FMT the<br>patient<br>experienced an<br>abrupt rise in her<br>platelet count. A<br>marked reduction<br>in UC symptoms,<br>passing 2-3 semi-<br>formed stools<br>daily, without<br>bleeding or<br>urgency | 1/1 (100%)    | None |

|    |                                    |                         |            |            |   |                 |  |  |                 |  |
|----|------------------------------------|-------------------------|------------|------------|---|-----------------|--|--|-----------------|--|
| UC | Borody, T <sup>106</sup><br>(2012) | Abstract<br>(Australia) | 62 (40/22) | 45.4       | /(-)  | 1               | /  | Overall, 91.9% of patients responded to FMT. Of these, 67.7% of patients (42/62) achieved complete clinical remission, and 24.2% of patients (15/62) achieved partial response. The remaining 8% (5/62) were treatment failures. Improvement in CRP and ESR correlated with clinical response observed in FMT patients                   | 57/62<br>(91.9) | None   |
| UC | Brandt <sup>15</sup><br>(2012)     | Abstract<br>(US)        | 6 (2/4)    | 44 (26–73) | /(colonoscopy, self-administered faecal enemas) | 1               | First-degree relatives, spouses or otherwise related | All 6 of our patients reported improvement after FMT. Maximal benefit was seen in the subgroup of patients with concomitant CDI (n = 2) and newly diagnosed UC in the setting of antibiotic use (n = 1). FMT was not as effective in the 3 remaining patients, whose UC onset or worsening was not associated with CDI or antibiotic use | 6/6<br>(100%)   | None   |
| UC | Kunde <sup>43</sup><br>(2012)      | Abstract<br>(US)        | 3 (-/-)    | >7 and <21 | 8 oz faecal enemas (enema)                      | For over period | 5 days / 1 week                                      | Two of three subjects achieved clinical response by reduction in paediatric ulcerative colitis activity index (PUCAI) of 15 points or more. One of them had complete resolution of disease activity  | 3/3<br>(100%)   | Self-limiting symptoms from mild to moderate |



|    |                                    |                             |         |    |  |                      |                |   |             |  |
|----|------------------------------------|-----------------------------|---------|----|--|----------------------|----------------|---|-------------|--|
| UC | Angelberger S <sup>28</sup> (2012) | Abstract (Austria)          | 5 (3/2) | /  | 23.8 g (16.7–25 g) (nasojejunal tube); 20 g (6 g–21.7 g) (enema) stool was administered (nasojejunal tube and enema) | 3 (daily for 3 days) | Healthy adults | The general well-being improved from poor to very well at week 12 in 3 patients. The FMT might be safe but activates a temporary systemic immune response   | 3/5 (60%)   | *  |
| UC | Kump <sup>64</sup> (2013)          | Abstract (Austria)          | 6 (-/-) | /  | / (colonoscopy)  | 1                    | /              | Within the first 14 days all patients experienced a reduction in stool frequency. However, none of the 6 patients achieved a complete remission and only 2 of the 6 patients had a durable improvement in their clinical UC scores. Subsequently two patients underwent total colectomy and one additional patient was treated with ciclosporin | 2/6 (33.3%) | 1 patient had a self-limiting episode of fever after FMT |
| CD | Borody <sup>44</sup> (1989)        | Letter (Australia)          | 1 (1/0) | 31 | Retention enemas (/)   | /                    | /              | The patient appear to be 'cured' by resolution of symptoms dramatically.  | 1/1 (100%)  | None   |
| CD | Grehn <sup>45</sup> (2010)         | Journal article (Australia) | 1 (1/0) | 57 | NR/250 mL saline (200–400 mL of faecal fluid was administered) (Colonoscopy, nasojejunal tube, enema)                | 5–15 (9.1 ± 3.25)    | Unrelated male | /   | /           | /  |

|                              |                                     |                      |         |              |  |       |               |  |            |  |
|------------------------------|-------------------------------------|----------------------|---------|--------------|--|-------|---------------|--|------------|--|
| CD                           | Vermeire S <sup>65</sup> (2012)     | Abstract (/)         | 4 (1/3) | 37.5 (29–50) | -/- (200 g) (nasojunal tube, colonoscopy)          | 3     | Healthy donor | No change or ceased due to not working, none of the patients experienced clinical, biologic or endoscopic benefit  | 0/4 (0%)   | Transient fever developed in 3 out of 4 patients |
| Chronic refractory pouchitis | Landy <sup>107</sup> (2013)         | Abstract (UK)        | 8 (-/-) | /            | 30 g/50 mL saline (-) (nasogastric administration) | 1     | /             | FMT via nasogastric administration was not effective in achieving clinical remission for chronic refractory pouchitis with no change in PDAI or Cleveland global quality of life score (CGQoL) identified at 4 weeks after FMT | 0/8 (0%)   | None   |
| UC/CD                        | Borody T (IBD) <sup>59</sup> (2011) | Abstract (Australia) | 3 (1/2) | 33 (19–57)   | /(Enema)   | 33–69 | /             | Severe mixed IBD were successful reversal.   | 3/3 (100%) | None   |

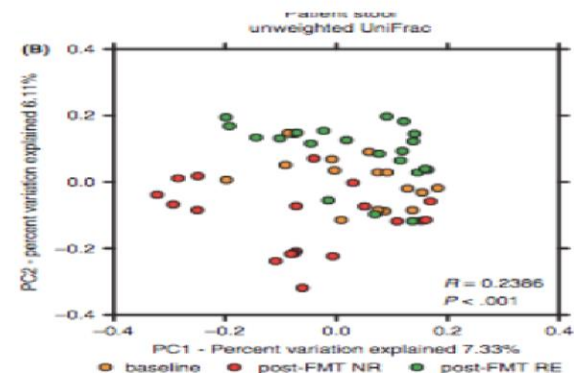
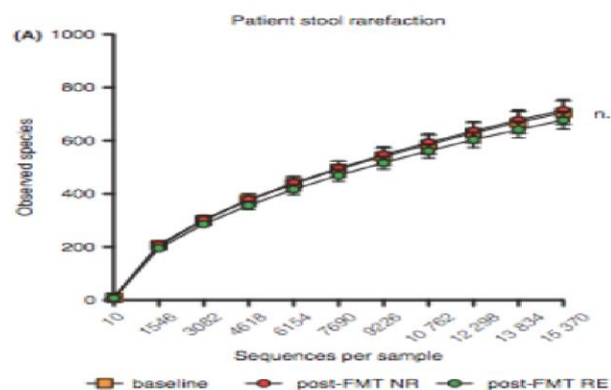
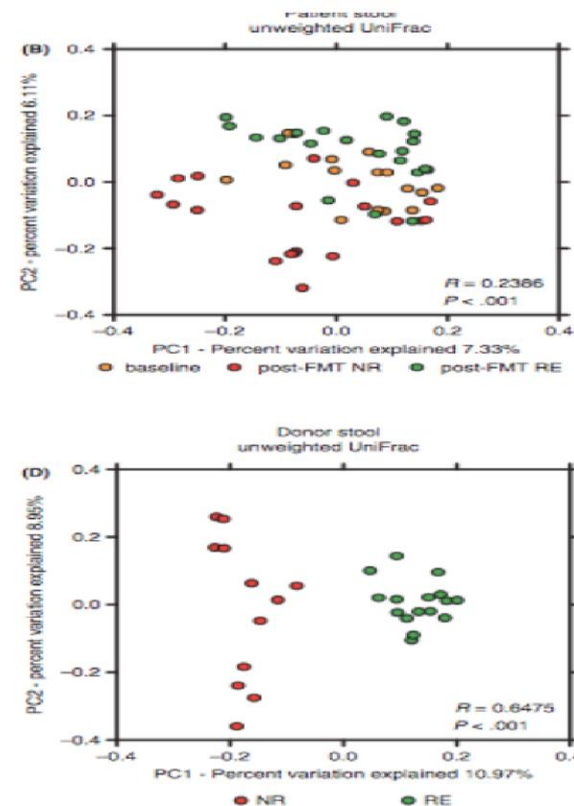
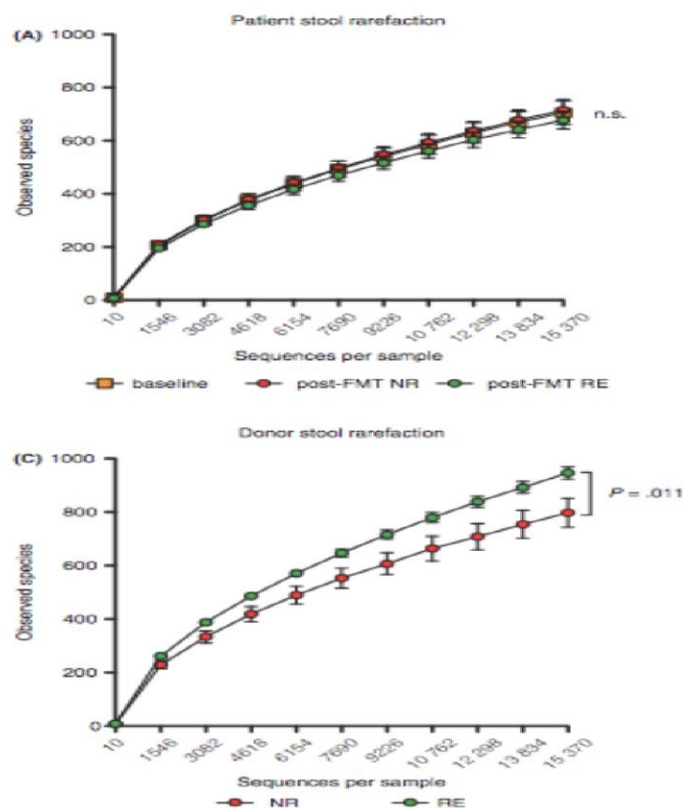


| Before  | After  |
|---|--|
|  |  <p><b>Rectum</b></p>         |
| <p><u><b>Above:</b></u> Rectum (L), Rectum (R)</p>                                |  |
|  |  <p><b>Sigmoid colon</b></p>  |
| <p><u><b>Above:</b></u> Sigmoid colon (L), terminal ileum (R)</p>                 |  <p><b>Sigmoid colon</b></p> |

# The taxonomic composition of the donor intestinal microbiota is a major factor influencing the efficacy of faecal microbiota transplantation in therapy refractory ulcerative colitis

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 B. Halwachs<sup>2,3,5</sup> | M. Wagner<sup>1</sup> | V. Stadlbauer<sup>1</sup> | A. Eherer<sup>1</sup> | K. M. Hoffmann<sup>6</sup> |  
 A. Deutschmann<sup>6</sup> | G. Reicht<sup>7</sup> | L. Reiter<sup>7</sup> | P. Slawitsch<sup>7</sup> | G. Gorkiewicz<sup>2,3,5</sup>  |  
 C. Högenauer<sup>1,2,5</sup> 







FMT ye yanıt veren hastaların donör örneklerinin çeşitliliği daha fazla.  
 Figure C



C.Difficle süperenfeksiyonu olan  
İBH'da FMT

|  |                         |           |            |  |   |        |   |  |                  |      |
|--|-------------------------|-----------|------------|--|---|--------|---|--|------------------|------|
| You <sup>108</sup><br>(2011)             | Abstract<br>(US)        | 1 (0/1)   | 33         | CD   | 75 g/200 mL<br>saline<br>(200 mL of<br>faecal fluid<br>was<br>administered)<br>(Nasogastric<br>tube)  | 1      | Husband   | Repeat<br><i>Clostridium<br/>difficile</i> PCR test<br>was negative.<br>The patient's<br>abdominal pain<br>markedly<br>improved, and<br>her<br>haematochezia<br>resolved   | 1/1<br>(100%)    | None |
| Duplessis <sup>109</sup><br>(2012)       | Journal<br>article (US) | 1 (0/1)   | 33         | CD   | 75 g/200 mL<br>saline<br>(200 mL of<br>faecal fluid<br>was<br>administered)<br>(Nasogastric<br>tube)  | 1      | Husband   | Bowel<br>movements<br>became less<br>frequent,<br>without<br>haematochezia,<br>and her<br>abdominal pain<br>improved and<br>fever abated.<br>Two days after<br>stool transfer, a<br>repeat <i>C. difficile</i><br>PCR was<br>negative. She<br>successfully<br>resumed<br>Crohn's colitis<br>therapy. | 1/1<br>(100%)    | None |
| Neelakanta<br>A <sup>110</sup><br>(2012) | Abstract<br>(US)        | 1 (0/1)   | 27         | CD   | /(Colonoscopy)  | 1      | Friend  | Able to<br>commence<br>Adalimumab.<br>Diarrhoea<br>improved but<br>did not<br>completely<br>resolve despite<br>negative stool<br>toxin studies for<br><i>Clostridium<br/>difficile</i> 2 weeks<br>post-procedure.  | 2/2<br>(100%)    | None |
| Hamilton <sup>30</sup><br>(2012)         | Journal<br>article (US) | 14 (3/11) | 44.6 ± 5.8 | 4/14UC, 6/<br>14 CD, 4/14<br>lymphocytic<br>colitis) | 50 g/250 mL<br>saline (220–<br>240 mL of<br>faecal fluid<br>was<br>administered)<br>[Colonoscopy<br>(1 patient<br>used upper<br>push<br>enteroscopy)] | 1 or 2 | Mothers,<br>daughters,<br>sons, wives,<br>husbands<br>and friends | Three other<br>patients were<br>treated with a<br>second infusion,<br>and all cleared<br>the infection<br>bringing the<br>overall success<br>rate to 85.7%.  | 12/14<br>(85.7%) | *    |

|                                       |                         |         |    |    |  |   |               |   |               |          |
|---------------------------------------|-------------------------|---------|----|----|--|---|---------------|---|---------------|----------|
| Singh <sup>42</sup><br>(2012)         | Abstract<br>(US)        | 1 (0/1) | 6  | UC | Fresh donor stool was mixed with saline then superfiltrated to 30 cc suspension (nasogastric tube) | 1 | Mother        | Stool calprotectin decreased from 504 at baseline to 76 by week 12. <i>C. diff</i> antigen and toxin were cleared by 3 weeks. Microbiome analysis of the donor stool and the patient's stool before and at 3 periods after bacteriotherapy are pending and will be finalised shortly. | 1/1<br>(100%) | None     |
| Watson <sup>62</sup><br>(2012)        | Abstract<br>(/)         | 1 (1/0) | 78 | UC | /(Colonoscopy)   | 1 | Wife          | No diarrhoea or abdominal pain.   | 1/1<br>(100%) | UC flare |
| Neelakanta A <sup>110</sup><br>(2012) | Abstract<br>(US)        | 1 (1/0) | 39 | UC | /(Colonoscopy)   | 1 | Family member | He has not had any relapse of CDI but still has evidence of active IBD in rectosigmoid on colonoscopy done a year after FMT.  | 1/1<br>(100%) | None     |
| Zainah, H <sup>111</sup><br>(2012)    | Journal article<br>(US) | 1 (1/0) | 51 | UC | 300 mL/- warm water (300 mL) (Colonoscopy)   | 1 | Wife          | The patient remained symptom free for 8 months and was able to stop oral vancomycin without CDI recurrence.   | 1/1<br>(100%) | None     |

| Before   | After   |
|--|---|
|  <p data-bbox="579 305 861 345"><b>Terminal ileum</b></p>               |  <p data-bbox="1406 305 1688 345"><b>Terminal ileum</b></p>                                 |
|  <p data-bbox="579 642 873 728"><b>Terminal ileum:<br/>erosions</b></p> |  <p data-bbox="1406 642 1688 682"><b>Terminal ileum</b></p>                                 |
|  <p data-bbox="579 1025 861 1065"><b>Terminal ileum</b></p>            |  <p data-bbox="1406 1025 1777 1110"><b>Terminal ileum: no<br/>visible inflammation</b></p> |

# Kronik Konstipasyon

## FMT



|                      |                                    |                             |         |             |   |                               |                |  |            |      |
|----------------------|------------------------------------|-----------------------------|---------|-------------|---|-------------------------------|----------------|--|------------|------|
| Chronic constipation | Borody <sup>44</sup> (1989)        | Letter (Australia)          | 1 (0/1) | 31          | /(Retention enemas)   | /                             | /              | The patient appear to be 'cured' by resolution of symptoms dramatically.   | 1/1 (100%) | None |
|                      | Andrews PJ <sup>46</sup> (1992)    | Journal article (Australia) | 1 (0/1) | 43          | /(Enema)  | Twice in two consecutive days | Husband        | Resolution of abdominal bloating and an unexplained disappearance of reflux symptoms with a pronounced reduction in the frequency of tension headaches | 1/1 (100%) | None |
|                      | Broody <sup>47</sup> (2001)        | Journal article (Australia) | 3 (1/2) | 16,17,68    | Donor stool suspended in 200 mL saline with one tablespoon of psyllium husks (retention enemas)       | Single daily for 5 days       | Healthy adults | Long-term restoration of normal bowel function to 1–2/day without laxatives.   | 3/3 (100%) | None |
|                      | Grehan <sup>45</sup> (2010)        | Journal article (Australia) | 4 (1/3) | 36.8(22–50) | NR/250 mL saline (200–400 mL of faecal fluid was administered) (Colonoscope, nasojejunal tube, enema) | 5–15 (9.1 ± 3.25)             | Unrelated male | /  | /          | /    |
|                      | Borody T <sup>48</sup> (MS) (2011) | Abstract (Australia)        | 3 (2/1) | 46 (29–80)  | /(/)  | 5–10                          | /              | Constipation was complete resolution. MS also progressively improved   | 3/3 (100%) | None |

Diğer hastalıklar  
FMT

# İBS ve karın ağrısı

|                    |                                |                             |         |            |   |                   |                |  |            |      |
|--------------------|--------------------------------|-----------------------------|---------|------------|---|-------------------|----------------|--|------------|------|
| IBS abdominal pain | or Grehan <sup>45</sup> (2010) | Journal article (Australia) | 5 (4/1) | 46 (38–56) | NR/250 mL saline (200–400 mL of faecal fluid was administered) (Colonoscope, nasojejunal tube, enema) | 5–15 (9.1 ± 3.25) | Unrelated male | /  | /          | /    |
|                    | Borody <sup>44</sup> (1989)    | Letter (Australia)          | 1 (0/1) | 21         | /(Retention enemas)   | /                 | /              | The patient appear to be 'cured' by resolution of symptoms dramatically. | 1/1 (100%) | None |

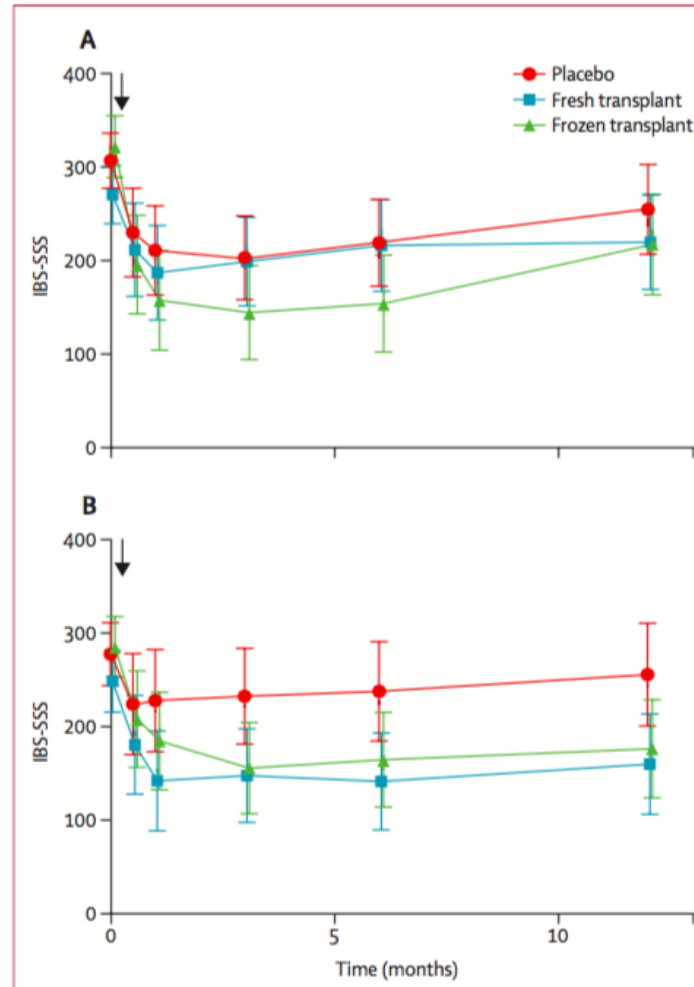
# Faecal microbiota transplantation versus placebo for moderate-to-severe irritable bowel syndrome: a double-blind, randomised, placebo-controlled, parallel-group, single-centre trial

Peter Holger Johnsen, Frank Hilpüsch, Jorunn Pauline Cavanagh, Ingrid Sande Leikanger, Caroline Kolstad, Per Christian Valle, Rasmus Goll

|   | Placebo (n=28)    | Active (n=55)     |
|---|-------------------|-------------------|
| Age (years)                                 | 45 (34 to 57)     | 44 (33 to 54)     |
| Sex   |                   |                   |
| Women                                       | 19 (68%)          | 36 (65%)          |
| Men   | 9 (32%)           | 19 (35%)          |
| IBS subtype                                 |                   |                   |
| IBS with diarrhoea and constipation (mixed) | 15 (54%)          | 24 (44%)          |
| IBS with diarrhoea only                     | 13 (46%)          | 31 (56%)          |
| Time with IBS (years)                       | 10 (6 to 16)      | 10 (5 to 19)      |
| IBS-SSS at inclusion                        | 278 (223 to 254)  | 260 (226 to 313)  |
| Functional disorder comorbidity*            | 9 (32%)           | 14 (25%)          |
| Total FODMAP before FMT (g/day)†            | 0.0 (-4.0 to 4.7) | 0.0 (-6.9 to 4.9) |

Data are median (IQR) or n (%). FODMAP=fermentable oligosaccharides, disaccharides, monosaccharides, and polyols. FMT=faecal microbiota transplantation. \*Self-reported by questionnaires at inclusion; includes fibromyalgia, chronic fatigue syndrome, jaw pain, and pelvic pain. †Calculated from the 5-day dietary record. IBS=irritable bowel symptom. SSS=severity scoring system.

**Table 1: Baseline characteristics**



FMT grubunda 36/55 (%65) vs plasebo 12/28 (%43) IBS semptomlarında azalma görüldü (p<0.05) (3.ay)

12. ayda ise FMT %56 vs plasebo %36 (NS)

# Antibiyotik ilişkili ishal

|     |                                      |                                |            |       |  |                       |               |  |                  |      |
|-----|--------------------------------------|--------------------------------|------------|-------|--|-----------------------|---------------|--|------------------|------|
| AAD | Gustafsson<br>A <sup>34</sup> (1999) | Journal<br>article<br>(Norway) | 32 (14/18) | 27-89 | 20 mL containing<br>5-10 g<br>homogenised<br>faeces in<br>ordinary<br>pasteurised<br>cow's milk<br>(Enema) | 1 or 2 (1<br>patient) | Healthy adult | 30 patients<br>were regarded<br>as clinically<br>normalised<br>within 1 week<br>and, in some<br>patients, even<br>after 1-2 days.<br>Two patients<br>received<br>additional<br>treatment<br>because of<br>persistent<br>symptoms;<br>one was given<br>a second<br>enema (day 3)<br>and<br>metronidazole<br>(day 8), and<br>the other<br>patient<br>vancomycin<br>(day 4), and<br>the diarrhoea<br>ceased after 3-4 days. | 30/32<br>(93.8%) | None |
|-----|--------------------------------------|--------------------------------|------------|-------|--|-----------------------|---------------|--|------------------|------|

# Metabolik sendrom

|                    |                            |                               |          |        |   |   |                              |  |              |      |
|--------------------|----------------------------|-------------------------------|----------|--------|---|---|------------------------------|--|--------------|------|
| Metabolic syndrome | Vrije <sup>54</sup> (2012) | Journal article (Netherlands) | 18 (-/-) | 50 ± 3 | The faeces was covered with sterile saline (500 mL 0.9% NaCl) (gastroduodenal tube) | 1 | Lean healthy Caucasian males | Insulin sensitivity of recipients increased (median rate of glucose disappearance changed from 26.2–45.3 mol/kg/min; $P < 0.05$ ) along with levels of butyrate-producing intestinal microbiota. | 18/18 (100%) | None |
|--------------------|----------------------------|-------------------------------|----------|--------|---|---|------------------------------|--|--------------|------|

# Özet-CDI ve FMT

| Indication  | Refractory/relapsing CDI (%)                  | Adults<br>N = 639/833 (76.7%)                       | Children<br>N = 5/11 (45.5%)                                      | Total<br>N = 644/844 (76.3%) |
|---|---|---|---|------------------------------|
| <b>(a) Characteristics and outcomes of FMT in adults and children with refractory/relapsing CDI.</b> <sup>11, 13, 14, 24, 26, 30, 31, 37-41, 44, 60, 61, 63, 71, 76-101</sup> |   |   |   |                              |
| Donor relationship  | Close relative or household member (%)        | 382/639 (59.8)                                      | 5/5 (100)   | 387/644 (60.1)               |
|   | Healthy voluntary donors (%)                  | 183/639 (28.6)                                      | 0   | 183/644 (28.4)               |
|   | Spouse or partner (%)                         | 60/639 (9.4)  | 0   | 60/644 (9.3)                 |
|   | Unknown (%)                                   | 14/639 (2.2)  | 0   | 14/644 (2.2)                 |
| Route of faecal instillation  | Colonoscopy (%)                               | 320/639 (50.1)                                      | 2/5 (40)  | 322/644 (50)                 |
|   | Nasogastric tube, gastroscope or PEG tube (%) | 161/639 (25.2)                                      | 3/5 (60)  | 164/644 (25.5)               |
|   | Enema or retention enemas (%)                 | 52/639 (8.1)  | 0   | 52/644 (8.1)                 |
|   | Nasojejunal or nasoduodenal tube (%)          | 17/639 (2.7)  | 0   | 17/644 (2.6)                 |
|   | Combined two or more of these above (%)       | 72/639 (11.3)                                       | 0   | 72/644 (11.2)                |
|   | Unstated (%)                                  | 17/639 (2.7)  | 0   | 17/644 (2.6)                 |
| Frequency   |   | 1-24  | 1-2   | /                            |
| Outcomes  | Success rate after FMT (%)                    | 580/639 (90.8)                                      | 4/5 (80)  | 584/644 (90.7)               |
|   | No response/recurrence after FMT (%)          | 62/639 (9.7)  | 1/5 (20)  | 63/644 (9.8)                 |
|   | Adverse events                                | Reported in four articles <sup>30, 37, 60, 61</sup> | Only one study reported some self-limiting symptoms <sup>43</sup> | /                            |



# Özet- CDI+İBH ve FMT

| Indication  | CDI in IBD (%)                                | Adults<br>N = 20/833 (2.4)             | Children<br>N = 1/11 (9.1) | Total<br>N = 21/844 (2.5) |
|---|---|--|----------------------------|---------------------------|
| <b>(c) Characteristics and outcomes of FMT in adults and children with CDI in IBD.</b> <sup>30, 42, 62, 108–111</sup> |   |  |                            |                           |
| Donor relationship  | Close relative or household member (%)        | 15/20 (75)                             | 1/1 (100)                  | 16/21 (76.2)              |
|   | Healthy voluntary donors (%)                  | 1/20 (5)                               | 0                          | 1/21 (4.8)                |
|   | Spouse or partner (%)                         | 4/20 (20)                              | 0                          | 4/21 (19.0)               |
| Route of faecal instillation  | Colonoscopy (%)                               | 18/20 (90)                             | 0                          | 18/21 (85.7)              |
|   | Nasogastric tube, gastroscope or PEG tube (%) | 2/20 (10)                              | 1/1 (100)                  | 3/21 (14.3)               |
| Frequency   |   | 1–2                                    | 1/1                        | /                         |
| Outcomes  | Success rate after FMT (%)                    | 18/20 (90.0)                           | 1/1 (100)                  | 19/21 (90.5)              |
|   | No response/recurrence after FMT (%)          | 2/20 (10)                              | 0                          | 2/21 (9.5)                |
|   | Adverse events                                | Reported in one articles <sup>62</sup> | /                          | /                         |

FMT, faecal microbiota transplantation; CDI, *Clostridium difficile* infection; IBD, inflammatory bowel disease; AAD, antibiotic-associated diarrhoea; PEG, percutaneous endoscopic gastroscopy.

The success means resolving *C. difficile* in the patients, as measured by negative stool sample enterotoxin for CDI; achieving clinical remission, disappearance of symptoms or reduction in disease activity index for IBD; resolving *C. difficile* and improved response to IBD medications for CDI in IBD; and resolution of symptoms for others.

# Özet-İBH ve FMT

| Indication  | IBD (%)                                       | Adults<br>N = 108/833 (13.0)<br>(including 94 UC, 14<br>CD and 3 UC/CD)          | Children<br>N = 3/11 (27.3)<br>(including 3 UC) | Total<br>N = 111/844 (13.2)                                 |
|---|---|--|---|---|
| <b>(b) Characteristics and outcomes of FMT in adults and children with IBD.</b> <sup>15, 28, 43-45, 59, 64, 65, 102-107</sup> |   |  |   |   |
| Donor relationship  | Close relative or household member (%)        | 10/108 (9.3)   | 0   | 10/111 (9.0)  |
|   | Healthy voluntary donors (%)                  | 14/108 (13.0)  | 0   | 14/111 (12.6)   |
|   | Spouse or partner (%)                         | 1/108 (1.0)  | 0   | 1/111 (0.9)   |
|   | Unknown (%)                                   | 83/108 (76.9)  | 3/3 (100)                                       | 86/111 (77.5)   |
| Route of faecal instillation  | Colonoscopy (%)                               | 6/108 (5.6)  | 0   | 6/111 (5.4)   |
|   | Nasogastric tube, gastroscope or PEG tube (%) | 8/108 (7.4)  | 0   | 8/111 (7.2)   |
|   | Enema or retention enemas (%)                 | 15/108 (13.9)  | 3/3 (100)                                       | 18/111 (16.2)   |
|   | Combined two or more of these above (%)       | 16/108 (14.8)  | 0   | 16/111 (14.4)   |
|   | Unstated (%)                                  | 63/108 (58.3)  | 0   | 63/111 (56.8)   |
| Frequency   |   | 1-69   | 5   | /   |
| Outcomes  | Success rate after FMT (%)                    | 84/108 (77.8)<br>(1 patients unstated)<br>(including 80 UC,<br>1 CD and 3 UC/CD) | 3/3 (100)<br>(including<br>3 UC)                | 87/111 (78.4%)<br>(including 83<br>UC, 1 CD and<br>3 UC/CD) |
|   | No response/recurrence after FMT (%)          | 22/108 (20.4)  | 0   | 22/111 (19.8)   |
|   | Adverse events                                | Reported in two articles <sup>64, 65</sup>                                       | /   | /   |

## ORIGINAL RESEARCH

## Effect of Vegan Fecal Microbiota Transplantation on Carnitine- and Choline-Derived Trimethylamine-N-Oxide Production and Vascular Inflammation in Patients With Metabolic Syndrome

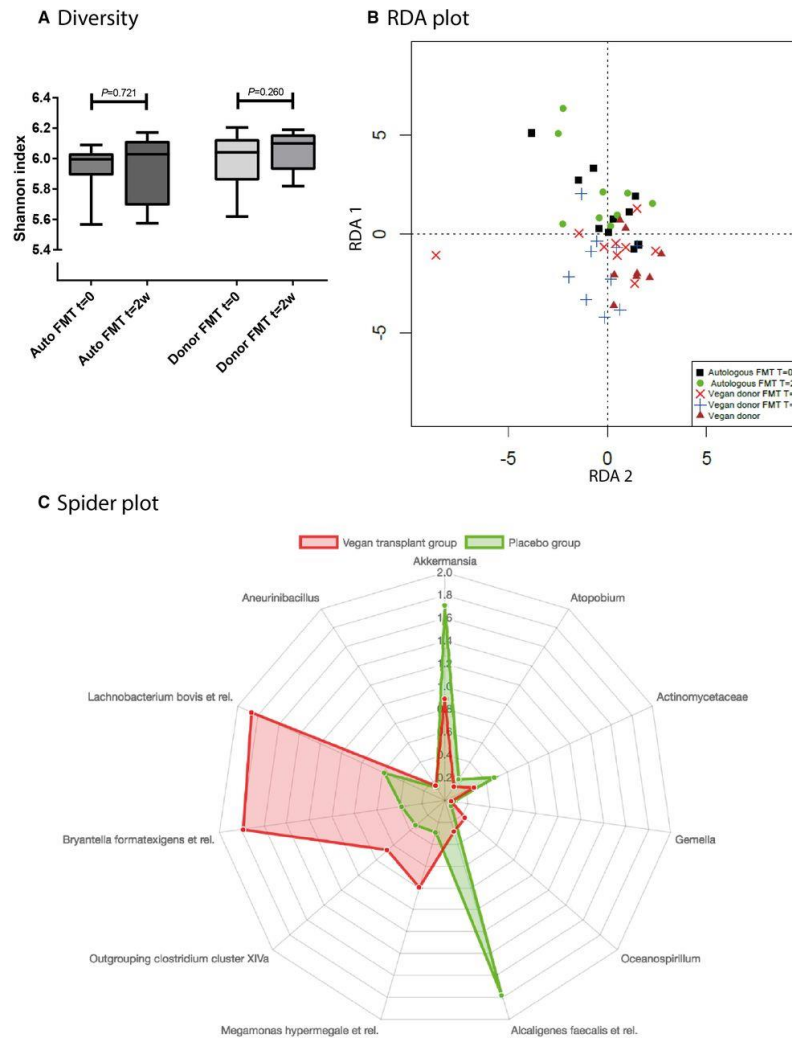
Loek P. Smits, Ruud S. Kootte, Evgeni Levin, Andrei Prodan, Susana Fuentes, Erwin G. Zoetendal, Zeneng Wang, Bruce S. Levison, Maartje C. P. Cleophas, E. Marleen Kemper, Geesje M. Dallinga-Thie, Albert K. Groen, Leo A. B. Joosten, Mihai G. Netea, Erik S. G. Stroes, Willem M. de Vos, Stanley L. Hazen, Max Nieuwdorp

**Table.** Baseline Characteristics

|                        | Metabolic Syndrome Patients, All (n=20) | Vegan Donors (n=9) | P Value | Metabolic Syndrome Patients, Autologous FMT (n=10) | Metabolic Syndrome Patients, Vegan-Donor FMT (n=10) | P Value |
|------------------------|---|--------------------|---------|--|---|---------|
| Age, y                 | 55.0±8.2                                | 33.4±14.8          | 0.002   | 57.7±8.5   | 52.3±7.4  | 0.15    |
| BMI, kg/m <sup>2</sup> | 33.9±3.8                                | 22.9±1.7           | <0.001  | 33.8±4.0   | 33.9±3.9  | 0.94    |
| Pulse, bpm             | 65.9±12.5                               | 70.7±9.9           | 0.32    | 67.8±13.2  | 63.9±12.2   | 0.50    |
| SBP, mm Hg             | 150.2±12.3                              | 130.6±6.2          | <0.001  | 152.2±12.5   | 148.2±12.4  | 0.48    |
| DBP, mm Hg             | 93.1±9.0                                | 78.9±6.6           | 0.001   | 93.3±8.3   | 92.8±10.1   | 0.91    |
| Glucose, mmol/L        | 6.0±0.8                                 | 5.1±0.3            | <0.001  | 6.18±0.9   | 5.8±0.5   | 0.25    |
| Insulin, mIU/L         | 126.1±55.3                              | 50.9±31.2          | 0.001   | 107.7±45.5   | 144.5±60.3  | 0.14    |
| HbA1c, mmol/mol        | 37.8±4.4                                | 34.0±3.4           | 0.03    | 38.7±3.6   | 36.9±5.1  | 0.37    |
| Cholesterol, mmol/L    | 5.3±0.8                                 | 4.1±1.2            | 0.02    | 5.3±0.8  | 5.3±0.9   | 0.90    |
| HDL-C, mmol/L          | 1.1±0.2                                 | 1.3±0.3            | 0.28    | 1.2±0.2  | 1.1±0.2   | 0.74    |
| LDL-C, mmol/L          | 3.3±1.0                                 | 2.5±1.0            | 0.1     | 3.1±1.3  | 3.5±0.7   | 0.37    |
| Triglycerides, mmol/L  | 1.30 (1.05–1.53)                        | 0.82 (0.53–0.90)   | 0.006   | 1.30 (1.06–1.57)                                   | 1.27 (1.01–1.56)                                    | 0.82    |
| CRP, mg/mL             | 1.50 (0.88–4.38)                        | 0.50 (0.40–0.80)   | 0.005   | 1.90 (1.15–4.50)                                   | 1.45 (0.80–4.25)                                    | 0.65    |

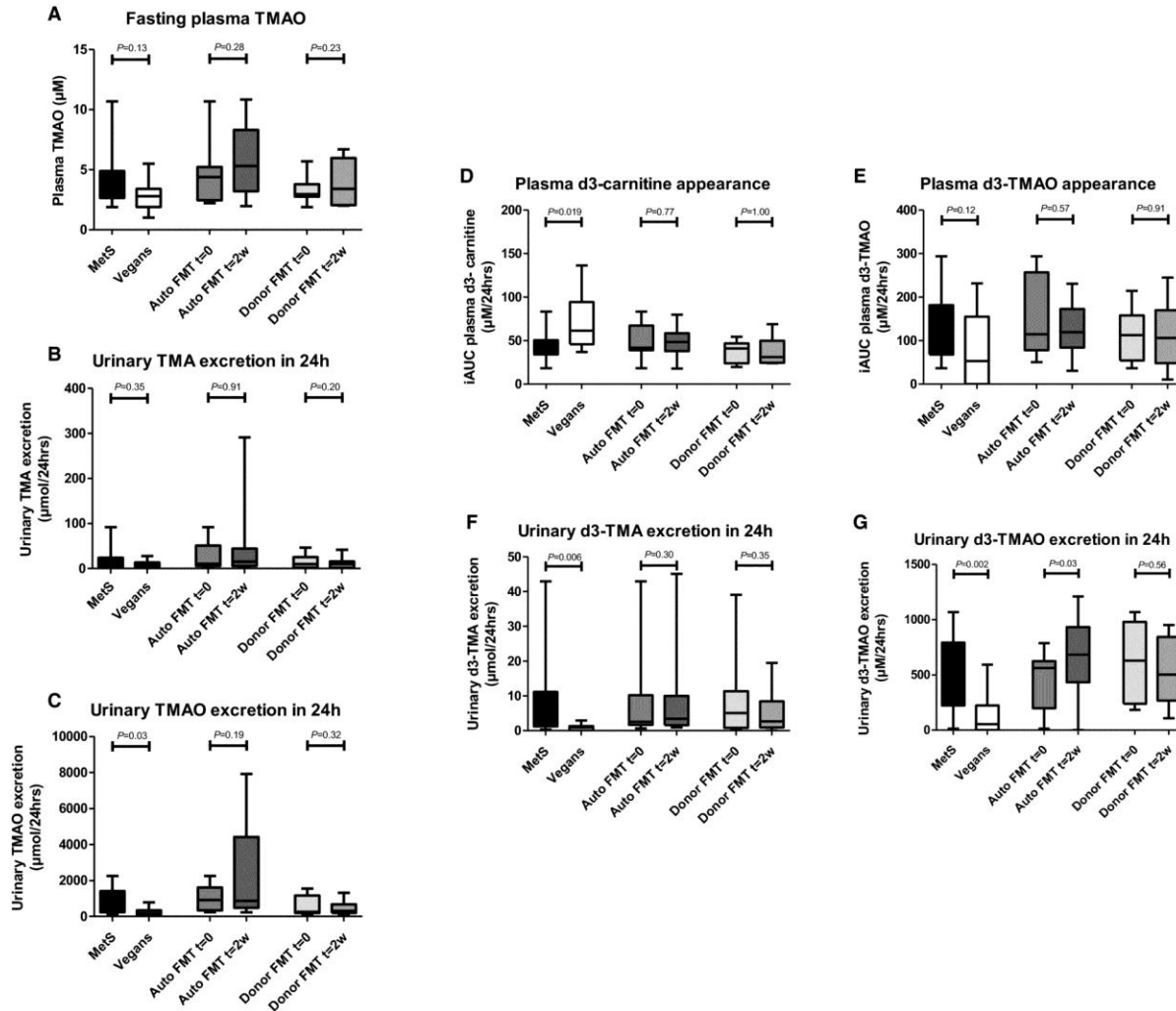
Data are depicted as mean±SD or median (interquartile range), depending on their distribution.  $P<0.05$  was considered significant. BMI indicates body mass index; CRP, C-reactive protein; DBP, diastolic blood pressure; FMT, fecal microbiota transplantation; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

# The effect of lean vegan-donor FMT in fecal microbiota diversity and composition.



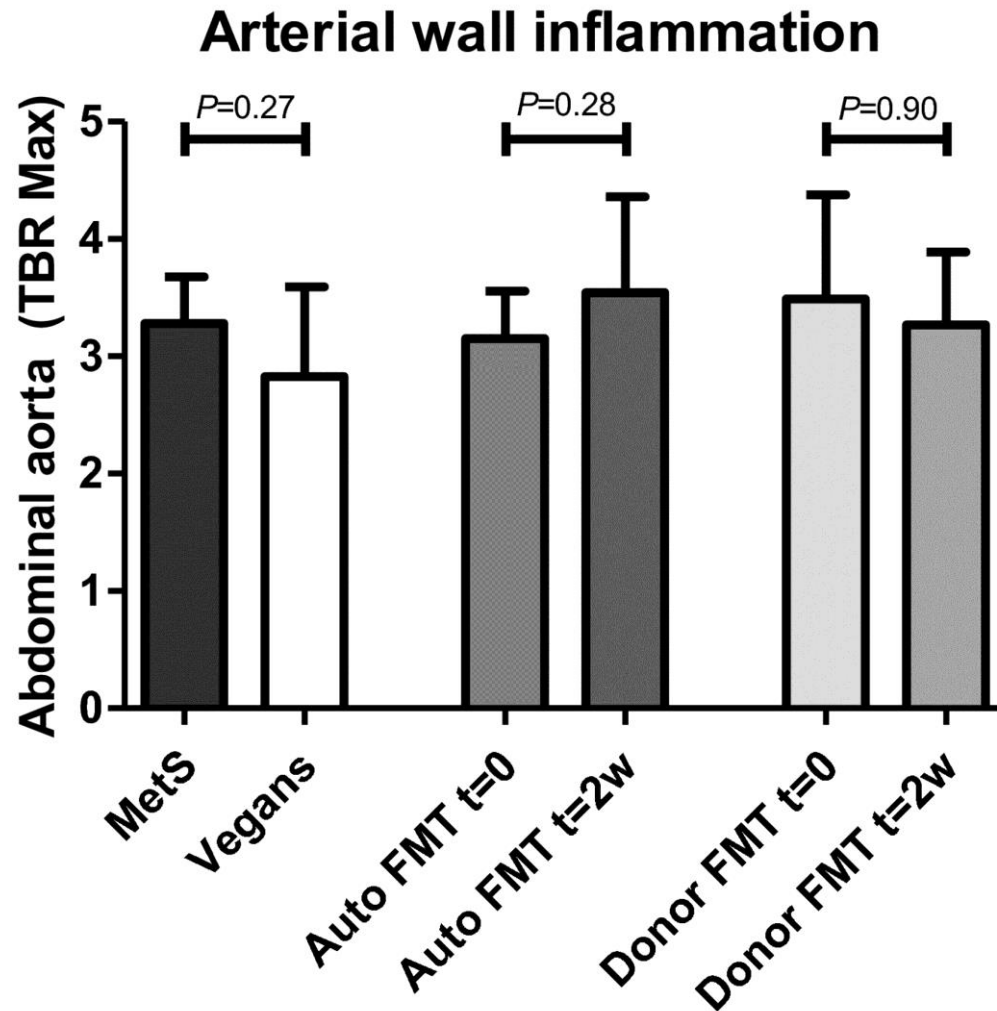
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# Unlabeled plasma and urine TMA/TMAO- and d3-carnitine-derived plasma and urine metabolites: metabolic syndrome patients vs lean vegan FMT donors, and the effect of lean vegan donor FMT. A through C, Unlabeled plasma and urine TMA/TMAO data compari...



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# 18F-FDG PET/CT results of lean vegan donors vs obese metabolic syndrome patients and posttreatment changes.



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RESEARCH NOTE

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# Fecal microbiota transplantation against intestinal colonization by extended spectrum beta-lactamase producing *Enterobacteriaceae*: a proof of principle study

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Ekstended spektrum beta laktamaz (ESBL) üreten Enterobacteriaceae dekolonizasyonu için 15 hastaya FMT uygulanmış.

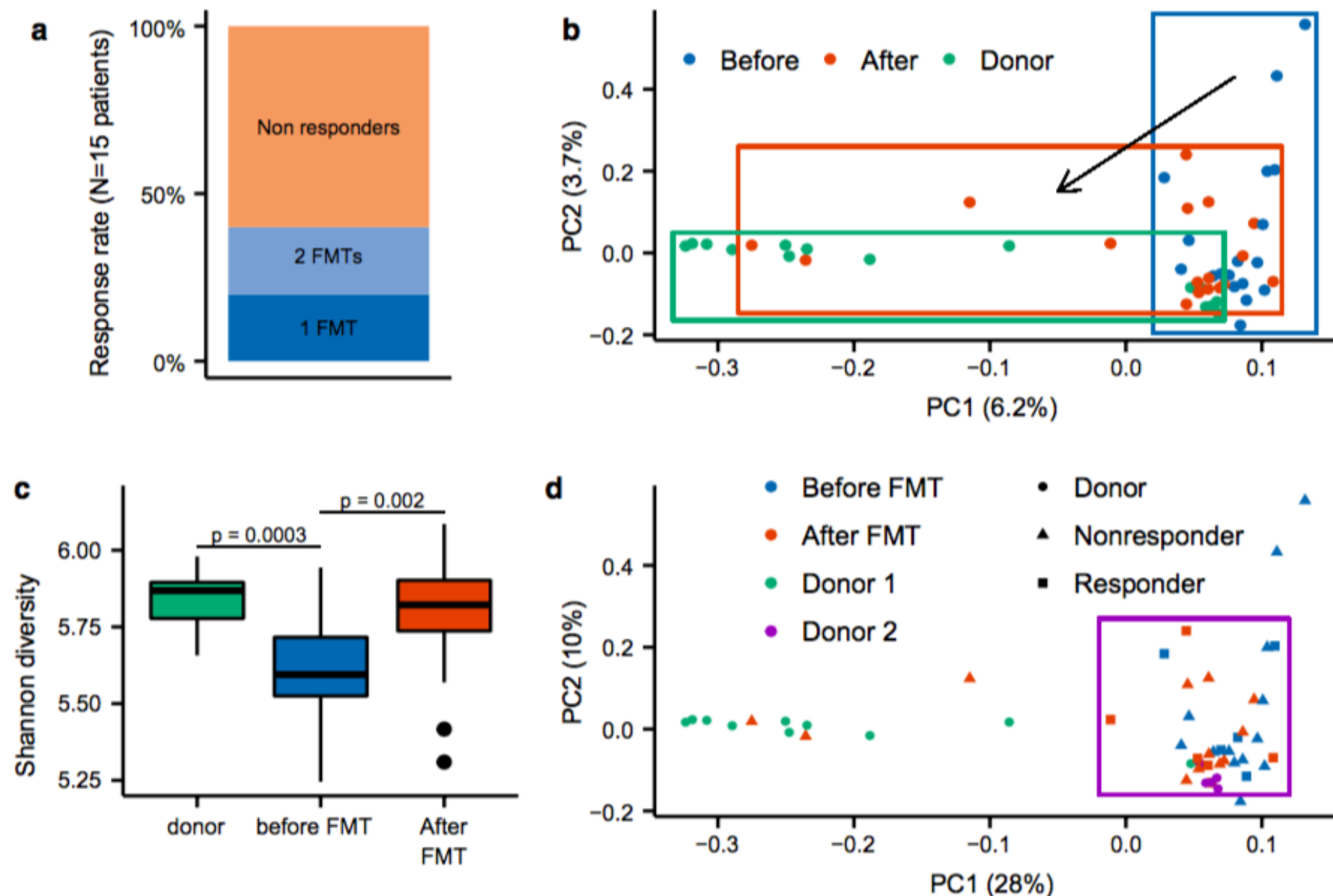
Birinci seans sonrası 3/15 (%20) 4 hafta sonrası ikinci FMT uygulanmış, bundan sonra 6/15 (%40) negatif bulunmuş.

**Table 1 Patient characteristics**

| #  | Age | Sex | BMI (kg/m <sup>2</sup> ) <sup>a</sup> | Comorbidity  | ESBL-Producer                | ESBL-neg. <sup>b</sup><br>after 1st FMT <sup>c</sup> | ESBL-neg.<br>after 2nd FMT | Donor FMT 1 | Donor FMT 2 |
|----|-----|-----|---------------------------------------|--|------------------------------|--|----------------------------|-------------|-------------|
| 1  | 58  | M   | 19                                    | ESRD <sup>d</sup> , PD <sup>e</sup> , CVD <sup>f</sup> | <i>E. coli</i> <sup>g</sup>  | Y  | –                          | 1           | –           |
| 2  | 47  | M   | 27                                    | Tetraplegia, rUTI <sup>h</sup>                         | <i>E. coli</i>               | N  | –                          | 1           | –           |
| 3  | 65  | M   | 25                                    | Renal Tx <sup>i</sup> , rUTI                           | <i>E. coli</i>               | N  | N                          | 1           | 1           |
| 4  | 61  | M   | 24                                    | rUTI   | <i>K. p</i> <sup>j</sup>     | N  | –                          | 1           | –           |
| 5  | 29  | F   | 35                                    | rUTI   | <i>E. coli</i>               | N  | Y                          | 1           | 2           |
| 6  | 56  | F   | 28                                    | RUTI   | <i>E. coli</i>               | N  | N                          | 1           | 2           |
| 7  | 70  | F   | 28                                    | Renal Tx, rUTI   | <i>K. p</i> , <i>E. coli</i> | N  | N                          | 1           | 2           |
| 8  | 59  | F   | 20                                    | Renal Tx, rUTI, HBV <sup>k</sup>                       | <i>E. coli</i>               | Y  | –                          | 1           | –           |
| 9  | 61  | F   | 28                                    | rUTI   | <i>E. coli</i>               | N  | Y                          | 1           | 1           |
| 10 | 57  | F   | 26                                    | ESRD, rUTI   | <i>E. coli</i>               | N  | –                          | 2           | –           |
| 11 | 76  | F   | 23                                    | rUTI   | <i>E. coli</i>               | Y  | –                          | 2           | –           |
| 12 | 70  | M   | 24                                    | Renal Tx, rUTI, T2D <sup>l</sup>                       | <i>E. coli</i>               | N  | –                          | 1           | –           |
| 13 | 59  | F   | 29                                    | Renal Tx   | <i>K. p</i>                  | N  | N                          | 1           | 1           |
| 14 | 58  | F   | 36                                    | rUTI   | <i>E. coli</i>               | N  | Y                          | 1           | 2           |
| 15 | 21  | F   | 24                                    | rUTI   | <i>E. coli</i>               | N  | –                          | 1           | –           |

<sup>a</sup> Body mass index, <sup>b</sup> extended-spectrum beta lactamase producer-negative, <sup>c</sup> fecal microbiota transplantation, <sup>d</sup> end-stage renal disease, <sup>e</sup> peritoneal dialysis, <sup>f</sup> cardiovascular disease, <sup>g</sup> *Escherichia coli*, <sup>h</sup> recurring urinary tract infections, <sup>i</sup> transplant, <sup>j</sup> *Klebsiella pneumoniae*, <sup>k</sup> Hepatitis B virus, <sup>l</sup> type 2 diabetes. Patient 7 had (only) *K. pneumoniae* before the 1st FMT and (only) *E. coli* before the second FMT





**Fig. 1** **a** Percentage of responders after one and two FMTs. **b** PCA-plot showing microbiota composition of donors and recipients before and after FMT. **c** Microbial diversity **d** Microbiota of responders and non-responders. The black square encloses all responders

# Sonuç

- FMT CDI için başarısı kabul edilmiş bir tedavidir
- Diğer alanlarda sonuçlar değişken olup, henüz geniş ölçekli çalışmalar yok denecek kadar az
- Sorun muhtemelen kişiye özgü mikrobiyota ve bunun tedaviyle nasıl değiştiğini gösterecek tanı yöntemlerinin yaygın olmaması
- Ancak gelecekte etkili bir tedavi olması muhtemel.