

Novel Biome



The use of FMT to treat
Clostridium difficile (c.Diff) infections

Where is the research headed?

**Unlocking Gut Health :
A Guide to Fecal Microbiota
Transplantation (FMT)**

Novel Biome

Your Health, Our Mission

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INTRODUCTION

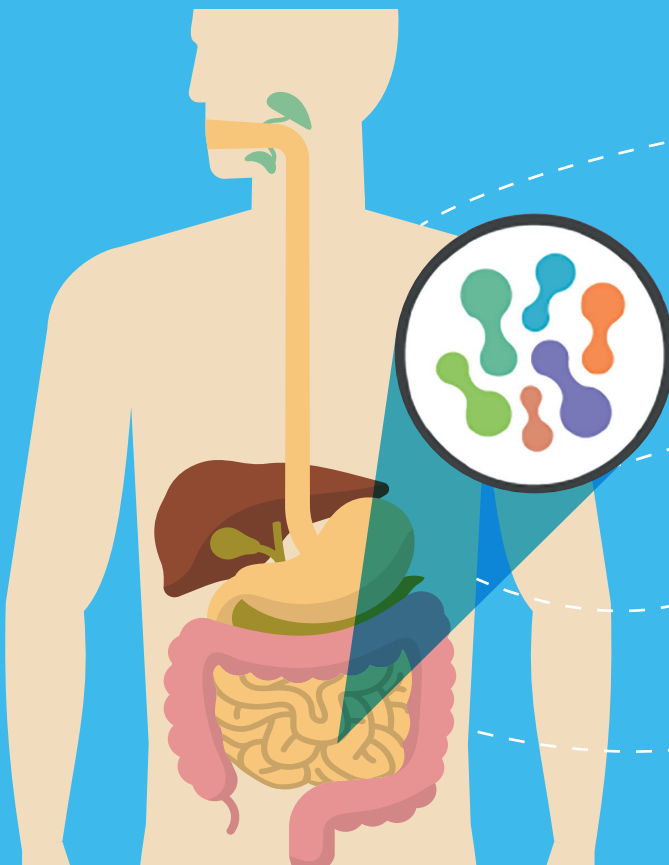
The research is clear: a healthy microbiome is essential for overall health and well-being¹⁻⁴. While modification of one's lifestyle⁵⁻¹⁴ (e.g. diet, exercise, sleep, etc.) or use of probiotics¹⁵⁻¹⁹ can help to improve the health of our gut microbiome. In some cases, the damage to the gut microbiome is severe, and changes in diet or supplementation cannot restore the gut microbiome to a healthy state. In extreme cases like this, manipulating the gut microbiome from an unhealthy state to a healthy state through a procedure called Fecal Microbiota Transplants (FMT) to help restore lost or depleted bacteria that are essential to human health and well-being is required^{4,20-24}. While science is still trying to understand whether changes in the gut microbiome are a cause, consequence or unrelated to disease, research shows that restoring the gut microbiome to a healthy state with FMT is a therapeutic approach with significant potential²⁵.



WHAT IS THE GUT MICROBIOME?

Our gut microbiome is as unique as our fingerprint, shaped by genetics and environmental influences, and fluctuates throughout our life ^{4,26-29}. The gut microbiome is formed during birth (possibly in utero) and is comprised of a complex community of microorganisms, including trillions of bacteria, quadrillions of viruses, fungi, parasites, and archaea, coming together to create one's gut microbiome ^{4,28,30-32}.

THE GUT MICROBIOME



Included the small and large intestine



Most Bacteria is in the large intestine



Approx. 100 trillion bacteria



Critical to our health and wellbeing



Linked to many acute and chronic health conditions

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WHAT DISEASES ARE LINKED TO A DYSFUNCTIONAL GUT?

Dysfunction of the gut microbiome (termed gut dysbiosis) can trigger infections and has been associated with the development of diseases like ^{5,6,9-13,30,33-40}.

- inflammatory bowel disease
- irritable bowel syndrome
- neurological disorders including neuropsychiatric, neurodegenerative and neurodevelopmental disorders
- metabolic conditions
- cardiovascular diseases
- immune-related disease
- cancer

The list of diseases which show gut dysfunction continues to grow with more clinical research into the role the gut microbiome plays in overall health ²⁵.

**An unhealthy gut
has been link to
many disease
such as:**



INFLAMMATORY BOWEL DISEASE



METABOLIC CONDITIONS



IRRITABLE BOWEL SYNDROME



CARDIOVASCULAR DISEASES



NEUROPSYCHIATRIC-RELATED DISEASES



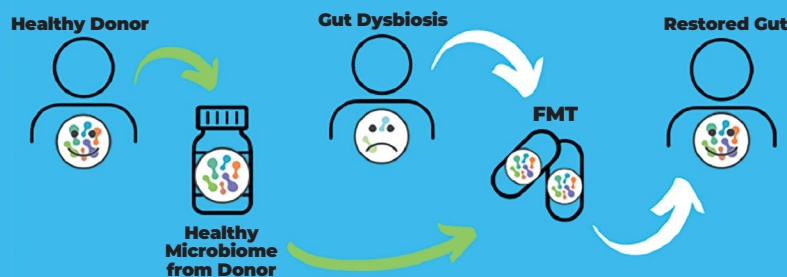
AGE-RELATED CONDITIONS

What defines gut dysbiosis varies between different disorders but is commonly characterized by low microbial diversity and environmental factors such as diet, lifestyle, and antibiotics ^{4,26,30,32,41-43}. Specifically, antibiotics have been shown to affect both the gut bacterial community's overall size and the community's composition ^{30,44}.

WHAT IS FECAL MICROBIOTA TRANSPLANTATION (FMT)?

Fecal microbiota transplantation (FMT) is the infusion of specially prepared stool material from a healthy, well-screened donor(s) into the gut (intestinal tract) of a recipient to restore a healthy and stable microbial community and confer health benefits and/or treat a specific disease or symptom(s) ^{30,36,38,45}.

Fecal Microbiota Transplantation (FMT)



The idea here is that FMT will help re-educate the recipient's gut microbiome, inducing the re-colonization of the gut and restoring microbial diversity to donor-like proportions ^{4,20-24}. FMT success is often defined by a shift in the gut microbiome profile towards that of the donor ⁴. The efficacy of FMT may depend on the donors' high diversity and composition of the gut microbiota and the ability to provide the necessary microbiota capable of overcoming the gut dysbiosis of the recipient ^{4,46}.

THE HISTORY OF FMT

FMT isn't anything new; it has been around for over 1,700 years in some way, shape or form ^{36,47}, but in the last 15 years, there has been increased scientific and clinical research into how modifications of the gut microbiome using FMT can improve health and tackle areas of unmet medical need. The promising outcomes of FMT treatment in patients with CDI have led to the expansion of research evaluating the efficacy of FMT for a wide variety of GI and non-GI disorders ^{25,30,38,48,49}. In 2022, both the United States (FDA) and Australia (TGA) provided regulatory approvals for the use of FMT for recurrent cDiff. Yet, FMT research is still in its infancy, particularly regarding how and why it works, so much is still to be understood.

DID YOU KNOW?

FMT isn't anything new; it has been around for over 1,700 years and in the last 10 years, there has been increased clinical research into using FMT to improve health and tackle many areas of unmet medical need.

While we know there is a lack of large randomized controlled clinic trials, the number of clinical trials is growing, with more than 300 publicly registered trials exploring FMT in May 2020, compared to less than 30 in 2013 in ^{25,36,57}.

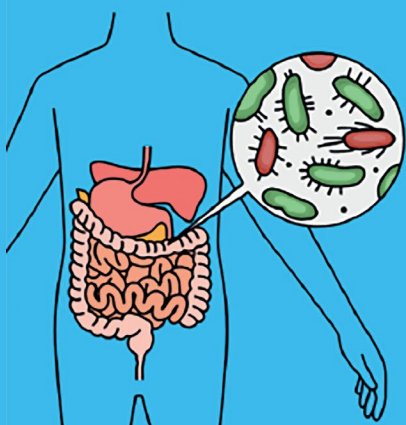
FMT TIMELINE

- **4th-century China**
first documented use for FMT called "yellow soup" to treat severe diarrhea
- **World War II**
Camel stool was used by German soldiers to treat bacterial dysentery
- **1959: Dr. Ben Eliseman**
published results of the use of FMT for antibiotic-associated diarrhea
- **1988: Dr. Thomas Borody**
performed his first FMT
- **Early 2010's**
Increased use of FMT for cDiff with clinical trials indication a 90% cure rate
- **Late 2010's**
Early studies published in non-GI diseases (i.e. ASD, MS, PD, Obesity)
- **2020: Novel Biome**
established their state-of-the-art FMT manufacturing lab, exporting FMT products to FMT treatment centres
- **2022: Regulatory Approval**
FDA and TGA approvals for FMT therapy for recurrent cDiff

WHERE IS FMT BEING USED TODAY?

THE USE OF FMT TO TREAT CLOSTRIDIUM DIFFICILE (C.DIFF) INFECTIONS

Currently, FMT has been most widely approved and studied as a very effective treatment for patients with recurrent *Clostridium difficile* infections (c.Diff) who are non-responsive to antibiotic therapy ^{25,50-54}, though there is a steady growth of clinical research in the use of FMT in a growing list of conditions. FMT has demonstrated success in the treatment, decolonization and prevention of the recurrence of c.Diff with high success rates and favourable safety profiles ^{20,49,55-59}. A recent analysis found a 92% clinical resolution rate compared to the first-choice antibiotics against c.Diff, vancomycin ^{56,60}. In addition, another small-scale study showed that FMT leads to higher rates of overall survival, shorter hospital stays, and lower rates of bloodstream infection in patients with recurrent c.Diff than receiving antibiotics alone ^{57,61}. Overall, FMT has been shown to be effective and has superior long-term efficacy compared to other medical treatments in c.Diff ^{36,62,63}.



FMT has been Effective in treating cDiff with:

- **Success rate over 90%**
- **Favourable safety profiles**
- **Superior long-term efficacy compared to other medical treatments**

FMT outside of cDiff:

Where is the research headed?

In the last ten years, there has been increased scientific and clinical research into how modifications of the gut microbiome using FMT can improve health and tackle areas of unmet medical need. The promising outcomes of FMT to improve symptoms and alter the gut microbiota in patients with recurrent c.Diff has led to the expansion of research on the use of FMT for a wide variety of both gastrointestinal (GI) and non-GI disorders ^{25,30,38,48,49}.

A growing body of clinical research indicates that FMT may be a useful treatment option for many GI disorders:

- inflammatory bowel disease (IBD) ⁶⁴⁻⁶⁶,
- irritable bowel syndrome (IBS) ^{61,67,68}, and
- other GI disorders including cancer and constipation, ^{25,38,48}.

In addition, the therapeutic use of FMT may not be confined to GI diseases, with a growing number of studies looking at the use of FMT in treating a wide range of non-GI disorders, including:

- metabolic disorders ^{49,69-73}
- autism spectrum disorder ⁷⁴⁻⁷⁶
- Parkinson's disease ⁷⁷⁻⁷⁹
- multiple sclerosis ^{80,49}
- among others including cancer, arthritis, and autoimmune disorders ^{25,38,48}.

Overall, there is a lack of large randomized controlled clinical trials, but the number of clinical trials is growing, with more than 300 publicly registered trials exploring FMT in May 2020, compared to less than 30 in 2013 ^{25,36,57}.

Embracing our commitment to advancing our understanding of FMT, Novel Biome is open to collaborating with researchers and clinicians seeking to explore the potential of FMT across a diverse spectrum of conditions. Together, we can broaden the horizons of FMT's therapeutic applications, and enhance our understanding of this life-saving treatment. If you are interested in collaborating with Novel Biome, please reach out at support@novelbiome.com.

HOW CAN FMT BE PERFORMED?

METHODS OF FMT

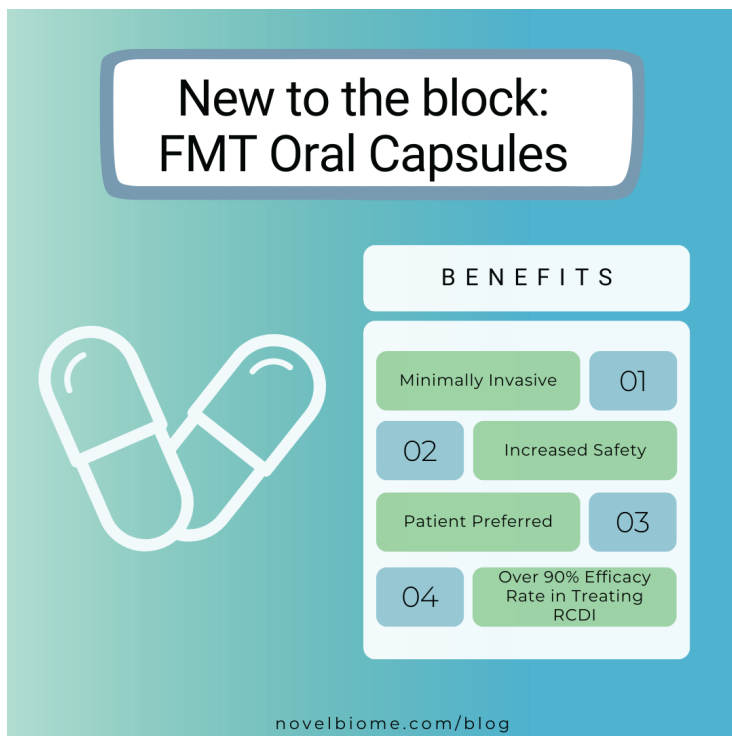
FMT administration can generally be categorized into either upper or lower GI routes ^{4,30,81}.

- Upper routes include: nasogastric tube (NGT), nasoduodenal tube (NDT), nasojejunal tube (NJT), and FMT capsules
- Lower routes include: colonoscopy and retention enemas

COLONOSCOPY: THE GOLD STANDARD VS CAPSULE: PATIENT PREFERRED

Currently, colonoscopy is still considered the gold standard for FMT administration, as it is still the most common administration method and has a wealth of data and efficacy rates reported over 90% ⁸²⁻⁹⁰. But, with the comparable success rates of oral FMT capsules, there has been a shift towards capsule-based approaches ^{51,81,91}. Oral FMT capsules have created a more patient-friendly alternative with increased convenience, safety and a more tolerable and preferred mode of delivery, making them an attractive option for many patients ^{4,51,51,59,81,91-94}.

At Novel Biome, we offer a choice of FMT delivery methods tailored to one's needs and preferences, including enema, oral capsules, and oral dry powder. Our oral preparations are colourless, tasteless, and odourless and allow a treatment option for those who cannot swallow capsules.



The infographic features a teal background. At the top, a white rounded rectangle contains the title 'New to the block: FMT Oral Capsules'. Below the title, on the left, is a white line-art illustration of two capsules. On the right, a white box titled 'BENEFITS' contains four items, each with a numbered blue circle and a green text box:

- 01 Minimally Invasive
- 02 Increased Safety
- 03 Patient Preferred
- 04 Over 90% Efficacy Rate in Treating RCDI

At the bottom right, the URL novelbiome.com/blog is displayed.

IS FMT SAFE?

Most adverse effects reported within the public domain are mild transient symptoms, including mild fever, diarrhea, nausea, abdominal discomfort, and bloating, which resolve quickly without intervention ^{25,38,48}. The most critical safety component for FMT involves appropriate donor screening and high-quality manufacturing.

At Novel Biome, safety is our top priority! We apply extensive donor screening criteria to our high-quality donors and utilize our new, state-of-the-art microbiome lab to ensure the highest quality and consistency of our end product for FMT.



WHAT TO LOOK FOR IN YOUR FMT PRODUCT

As the efficacy of FMT becomes evident in treating a range of conditions extending beyond recurrent cDiff, safety, standardization, and efficacy are paramount. Donor screening protocols, universal stool banks, and adherence to manufacturing standards are integral to ensuring FMT treatment success. When looking to utilize FMT products, there are two pivotal components for ensuring the safety of FMT; donor screening and high-quality manufacturing standards. Ensuring these two factors are met, allows for the knowledge that the FMT products utilized are screened to reduce the transfer of unwanted factors from the donor, which may impact a patient, and are consistent and processed like any other pharmaceutical, under strict manufacturing standards with checks and balances in place to ensure quality.

What are the **Key Factors** to quality FMT products?



DONOR SCREENING

HIGH-QUALITY PRODUCT MANUFACTURING



At Novel Biome, we leverage years of experience in FMT to manufacture high-quality FMT products utilizing our highly screened donors and stringent manufacturing standards.

Learn more: www.novelbiome.com

THE IMPORTANCE OF DONOR SCREENING

Donor screening serves as the initial line of defence against potential risks associated with FMT. The primary objective is to exclude donors carrying known pathogens, minimizing the risk of transmitting infectious diseases and other undesirable traits ¹⁰⁴⁻¹⁰⁷. To determine a donor's health and eligibility, comprehensive screening must be implemented, including health and wellness questionnaires and blood and stool testing ^{103-105,108-113}.

The significance of a donor's medical background cannot be overstated. This information is pivotal in determining a donor's suitability and identifying potential issues not detectable through routine blood and stool screening ^{103,108,109}. This initial screening examines the risk of infectious diseases, the history of disorders potentially associated with dysfunction of the gut microbiota and the use of treatments and/or medications that can affect the gut microbiota ^{108,109,111} which excludes a substantial percentage of potential donors, between 50% and 90% ¹¹⁴⁻¹¹⁷.

Those who pass the initial health and wellness screening undergo extensive laboratory analysis of blood and stool samples ^{108,109}. Comprehensive laboratory analysis is paramount to the safety of FMT and helps to identify potential pathogens possibly transmissible during FMT to reduce risks to patients ^{103,108,109}. The regular repetition of these tests further underscores the commitment to ongoing safety evaluation.

At Novel Biome, our donor screening program is notably stringent, with initial donor screening exceeding industry standards ^{103-105,108-113} and over 120 testing parameters to evaluate blood and stool. Donors meet specific criteria, including being vaginally born, breastfed, adhering to a diverse omnivorous diet, and undergo rigorous regular evaluation to ensure only the highest quality donor pool.

DONOR SCREENING INVOLVES SEVERAL STEPS



INITIAL DONOR SCREEN

Evaluates medical and health history to minimize the risk of transferring infections or adverse gut “traits”

DAY OF DONATION SCREENING

Donors are screened to check of any changes in health that could be potentially harmful

BLOOD AND STOOL SCREENING

Extensive laboratory analysis of blood and stool are performed to identify potential pathogens transmissible by FMT

WHY HIGH-QUALITY MANUFACTURING MATTERS

The safety of FMT is equally contingent on the quality of manufacturing processes. Incorporating pharmaceutical-grade laboratory spaces, equipment, and production standards is imperative but often expensive ^{104,108,110,111}. The challenges include finding suitable laboratory spaces, securing high-quality personnel, and establishing stringent and consistent manufacturing processes ^{104,108,110,111}.

In FMT manufacturing, upholding the highest standards of Good Laboratory Practices (GLP) and Good Manufacturing Practices (GMP) is non-negotiable. This commitment extends across various facets, including personnel quality, facility and laboratory equipment, test systems processes optimization, manufacturing processes, quality assurance, standard operating procedures, and stringent donor screening protocols, ensuring all products are processed and meet the same standards as other pharmaceuticals. While these are high barriers to overcome, expertise in FMT manufacturing techniques and the use of proper equipment are critical ^{104,108,110,111}.

At Novel Biome, we understand the importance of manufacturing under stringent standards to create consistent, safe and scalable high-quality FMT products. Our commitment to producing high-quality products is reflected in our Health Canada Drug Establishment Licence (DEL), our Good Manufacturing Practices (GMP) certified pharmaceutical-grade laboratory facility and our adherence to Good Laboratory Practices (GLP).



AT NOVEL BIOME, WE'VE DEDICATED YEARS TO PERFECTING OUR FMT MANUFACTURING PROCESS. OUR FOCUS IS SOLELY ON PRODUCING THE MOST EFFECTIVE AND CONVENIENT FMT PRODUCTS POSSIBLE



WHAT DOES FMT TREATMENT LOOK LIKE?

Role of pre-treatment

While the commonly held belief is that the better the donor, the better the success of FMT, there has been some new exciting research highlighting that the recipient's microbiome and not only that of the donor, determines the outcomes of FMT ¹¹⁸. New research suggests that pre-treatment before FMT to prepare the recipient's gut microbiome can help improve FMT success ^{74,76,118}.

The infographic features a blue background with a central white text box. Above the box is a search bar with a magnifying glass icon and a close button. The text box contains a definition of pre-treatment. Below the box is a disclaimer. The background also features a large, colorful, abstract shape resembling a stylized 'S' or a path, composed of green, yellow, orange, and red segments.

Q What are pre-treatments for FMT? X

Pre-treatment (or microbiome prep) helps to prepare the gut microbiome by reducing species richness and which microbiota are dominant before FMT, which can then allow for better engraftment of the donor microbiome and, therefore, better outcomes post-FMT

Disclaimer: The information provided should not be considered medical advice and is based on research.

SO WHAT IS PRE-TREATMENT

Pre-treatment (or microbiome prep) helps to prepare the gut microbiome by reducing species richness and which microbiota are dominant before FMT, which can then allow for better engraftment of the donor microbiome and, therefore, better outcomes post-FMT and help improve the magnitude and duration of improvements after FMT.

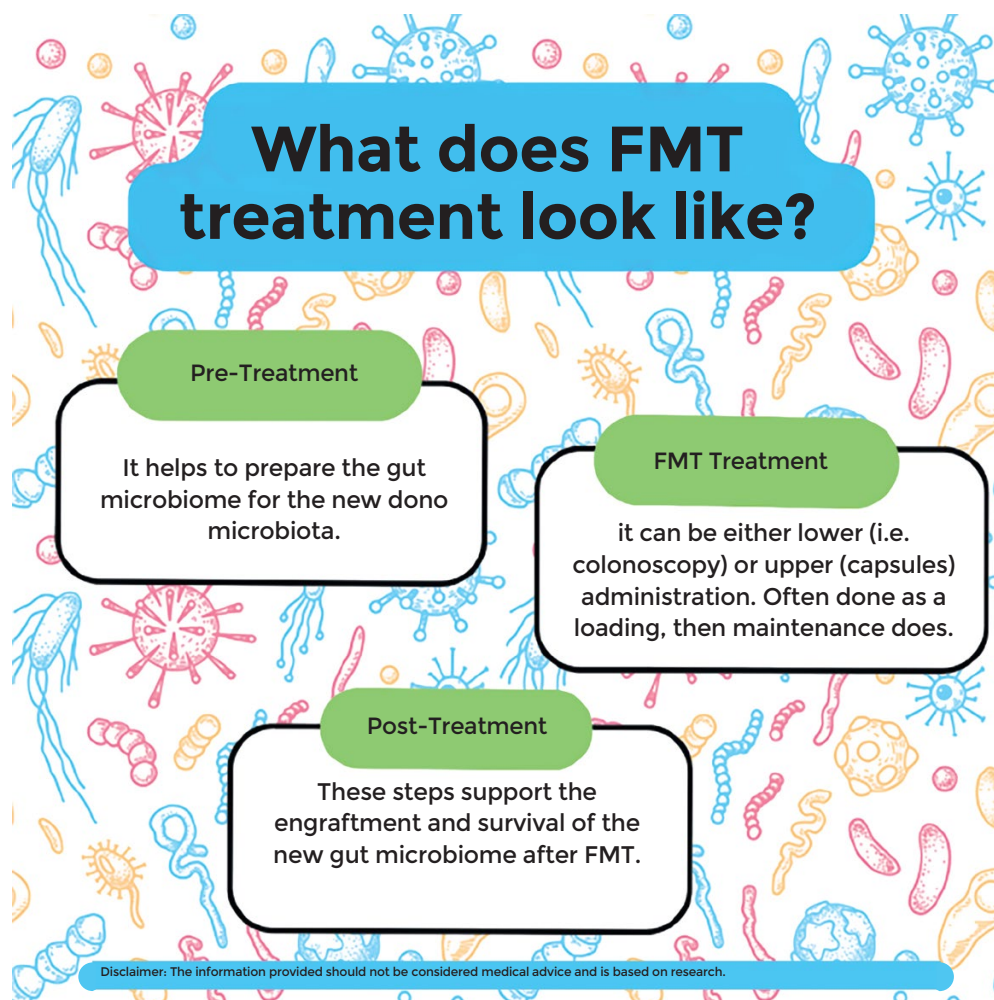
Some types of pre-treatments include:

- Treatment with antibiotics, antifungals and antiparasitics
- Review of supplements and removal of any containing antimicrobial ingredients
- Bowel cleanse to help “wash out” the digestive tract
- Fasting before FMT treatment

HOW TO PLAN OUT FMT TREATMENT: LOOKING AT THE RESEARCH

FMT treatment is often divided into a loading dose and, if needed, a maintenance dose. Loading doses are normally larger FMT doses over 1-2 days and take place following pre-treatment. The implementation of a maintenance dose, which is a smaller dose over a period of days/weeks/months, is affected by several things, the main being if the condition is chronic or acute and the decision of the doctor.

As a general statement, many chronic conditions have involved clinical treatment plans, including multiple rounds of FMT ^{74-76,121,122}, but this is not always the case and often varies within the same condition ^{77,123-129}, which highlights further the need for more clinical research. At Novel Biome, we have many great resources to help understand the ever-changing landscape of FMT research, including a database of research protocols and ongoing clinical trials.



ROLE OF LIFESTYLE CHANGES POST-FMT.

Encouraging patients to make lifestyle changes after FMT can help enhance the survival and composition of the new gut microbiota. While there are a lot of ways to approach altering lifestyle after (and often before) FMT to increase success and further improve gut health, here we include 4 areas that are shown in the literature to have big impacts on the gut microbiome.

1. **Diet:** Diet is the most potent way to shape the gut microbiome ^{7,130-134}. A diverse diet helps to nourish the beneficial microbes, promoting their growth and diversity ¹³⁵⁻¹³⁸. So, it is important to prioritize a balanced diet, including a wide variety of whole foods, including vegetables, fruits, nuts and seeds, with a healthy amount of fats and proteins ^{137,139-141}, aiming to add 50 different foods a week to ensure diet diversity.

2. **Physical Activity:** Physical activity has been shown to increase the diversity of the gut microbiome, and people who exercise regularly have a more diverse gut microbiome than those who are sedentary ¹⁴²⁻¹⁵¹. While any type of physical activity will positively impact health and the gut microbiome, research does suggest that aerobic exercise may be more effective at improving gut health ^{148,152-154}.

3. **Sleep:** Sleep can directly impact the makeup of our gut microbiome ¹⁵⁵⁻¹⁶². Poor sleep quality, reduced sleep hours, and inconsistent sleep schedules can lead to imbalances in the gut microbiome, potentially contributing to various health issues ^{156,159,163-165}. By adopting good sleep practices, managing stress levels, and establishing consistent sleep routines, one can support the health of the gut microbiome and promote overall wellness.

4. **Environmental toxins:** One way to support the gut microbiome is to remove any harmful sources of environmental toxins with your environment, such as heavy metals and pesticides, which are known to damage the gut microbiome ^{13,40,166}.

THE NOVEL BIOME MISSION

Novel Biome is a contract manufacturer of FMT products, leveraging years of experience in FMT treatment, manufacturing and a deep knowledge of the human microbiome, to provide high-quality FMT products safe, effective and consistent.

Our sole focus is to provide the best FMT products possible utilizing highly screened donors, a state-of-the-art microbiota lab, and stringent manufacturing standards. Our goal is to expand access to microbiome-based treatment and educate on the importance of the gut microbiome in many chronic conditions.

Learn more about us: <https://novelbiome.com/about-us>

HOW DO I ORDER FMT PRODUCTS?

Novel Biome does not offer products directly to patients, we are a contract drug manufacturer and sell directly to hospitals/clinics, doctors, and researchers. We recommend discussing your interest in our product with your healthcare provider. They can provide you with more information and guidance on its potential suitability for your specific needs. You can reach out to our team (support@novelbiome.com) to learn more.

Why? Based on regulators, we must understand how FMT products are used and that only trained professionals are utilizing these products.

If your healthcare provider is interesting in becoming a clinical partner, they can register on our website: <https://novelbiome.com/user/account/register>

DISCLAIMER:

Novel Biome is a contract manufacturer of FMT products, providing high-quality FMT products to physicians. The information provided in this document should not be considered medical advice and is based on Novel Biome's understanding of their FMT products and past experience treating patients with FMT. Our hope is that this information helps as a starting point for physicians.

If you have more questions, comments or concerns, please email us at support@novelbiome.com.

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