OPENBIOME

2019 ANNUAL REPORT

WELCOME LETTER

In 2011, my cousin developed a *C. difficile* infection. For the next year and a half, and after seven rounds of last-line antibiotics, he was still dangerously ill. Eventually, he was cured by a fecal transplant, in which bacteria from a healthy donor are infused into the patient's colon to outcompete the *C. difficile*. After many months of an all-consuming illness, within a day, he had his life back.

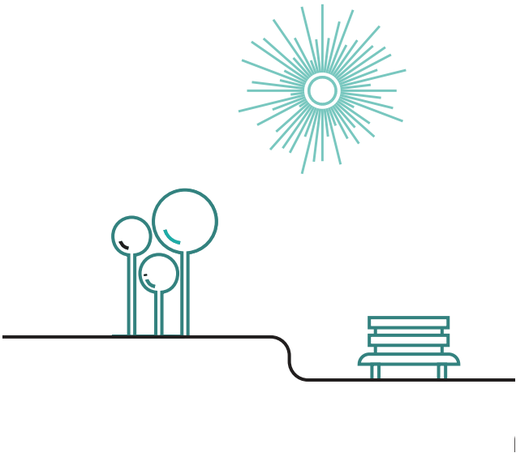
He was one of half a million people in the U.S. fighting C. *difficile* that year, one in five of whom found their infection returning after trying to beat it with antibiotics. However, he was most likely one of the very few who ultimately beat his infection with a fecal transplant.

These days, his story is less rare. In 2019, OpenBiome sent out its 50,000th treatment, a milestone that, to me, has a particularly salient point of reference: 50,000 is the population size that defines a small city. When I think about the fabric of people who comprise my own town, I appreciate not just the individual impact of each treatment, but the collective. A population the size of Niagara Falls, NY or Jefferson City, MO has had an opportunity to return to their lives, their loved ones, and their communities.

On the afternoon that we sent out the 50,000th treatment, it was one of 53 that we shipped, part of what our team makes happen every day. I marvel at not only what crossing this threshold means in terms of our overall impact, but also how, together, clinicians, researchers, patient advocates, and public health professionals have turned an extraordinary objective – the safe transference of stool into a patient's colon – into a matter of seamless routine. As we continue to work towards finding an ever more robust solution to treating *C. difficile*, and as we work to expand the frontiers of the microbiome field, the impact of these efforts is not only felt today, but it will continue to touch people in immeasurable ways in the future.

Thank you for engaging with us as we build new solutions.

Carolyn Edelstein



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MEETING AN URGENT MEDICAL NEED

OPENBIOME WAS FOUNDED TO HELP TREAT *C. DIFFICILE*— A BACTERIAL INFECTION CATEGORIZED AS AN "URGENT ANTIBIOTIC-RESISTANT THREAT" BY THE CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC).

Each year, *C. difficile* infects 500,000 people in the United States, leading to 30,000 deaths.

1 out of every 5 infections returns after antibiotics, leaving patients with few medical options other than a fecal microbiota transplant (FMT). Bacteria from the donor outcompetes the *C. difficile* bacteria, and cures 80-90% of infections.

PATIENT TESTIMONIAL

"I suffered with *C. difficile* for 4 and half months. I was finally cleared for a fecal transplant. By the next morning, it was like someone had lifted an evil curse off me. I never would have believed it would be possible to feel this good again. Thank you from the bottom of my heart. Thank you for giving me back my life."

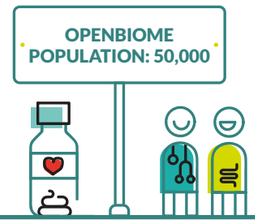
—An OpenBiome patient treated in 2019

THE ROAD TO 50K TREATMENTS

Our centralized manufacturing facility eliminates barriers to FMT.

Before OpenBiome, patients had to spend time, effort, and money finding a suitable stool donor—usually a family member or friend. It can cost a physician or patient over $15,00 dollars to find a healthy donor[1].

Like a blood bank, OpenBiome centralizes the donor screening and manufacturing process. While only 3% of candidates qualify to be OpenBiome stool donors, each donor contributes samples nearly daily for at least two months. Through this economy of scale, we offer affordable and rigorously screened FMT preparations that can be delivered overnight to patients in need.



IN 2019:

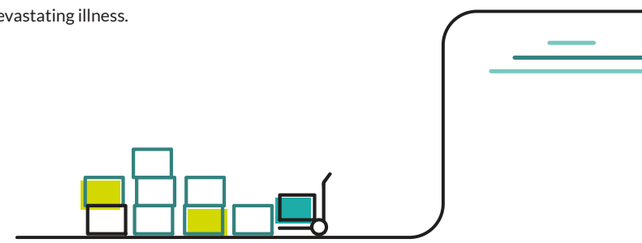
We shipped 10,818 stool preparations for FMT and partnered with 101 new hospitals and clinics.

In 2013:

We have shipped 53,461 FMT units to a network of 1,292 hospitals.

SPOTLIGHT ON 50K:

This August, OpenBiome processed our 50,000th FMT preparation—enough FMT units to treat a city's-worth of patients. This milestone highlights how OpenBiome, stool donors, doctors, and patient advocates have come together to treat a devastating illness.



1. Craven, L., Nair Parvathy, S., Tat-Ko, J., Burton, J., & Silverman, M. (2017). Extended Screening Costs Associated With Selecting Donors for Fecal Microbiota Transplantation for Treatment of Metabolic Syndrome-Associated Diseases. Open Forum Infectious Diseases, 4(4). doi: 10.1093/ofid/ofx243

SHAPING THE FUTURE OF FMT AND PATIENT CARE

AS THE COUNTRY'S LARGEST PROVIDER OF FMT MATERIAL, WE BELIEVE THAT ENFORCEMENT DISCRETION SHOULD CONTINUE AS LONG AS THERE IS A LACK OF AVAILABLE, APPROVED ALTERNATIVES TO ADDRESS THIS SERIOUS AND UNMET MEDICAL NEED.

Although it was first published in Western medical literature in 1958, fecal transplantation only emerged as a highly promising investigational treatment in the last decade. Balancing access to FMT in cases where benefit outweighs risk, while ensuring that more data is collected on the overall risk-benefit profile of FMT has been an area of active discussion.

HIGHLIGHTS FROM 2019

- OpenBiome presents to FDA on success of enforcement discretion, future of FMT regulation, and donor screening (Public meeting held by FDA seeking input on the future of FMT regulation)
- A Clarification About Fecal Microbiota Transplantation (Op-ed, Scientific American)
- Drug Companies and Doctors Battle Over the Future of Fecal Transplants (News article, The New York Times)

MAINTAINING ACCESS TO FMT

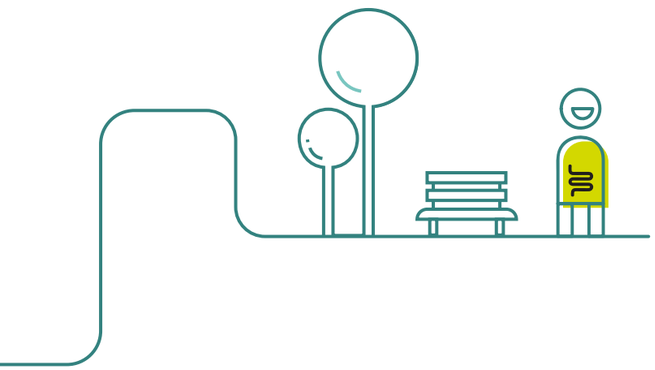
We support enforcement discretion—the FDA's interim policy since 2013 that allows patients with *C. difficile* that is not responsive to antibiotics to access FMT outside of clinical trials.

Although FMT is a promising treatment for recurrent *C. difficile*, additional well-controlled trials demonstrating safety and efficacy are needed before it gains FDA approval. Until then, enforcement discretion allows physicians to use FMT to treat antibiotic-resistant *C. difficile* infections and has enabled more than 50,000 people to access treatment in the last seven years.

OpenBiome's participation in public forums, media publications, and academic research shapes the national and global conversation on current and future FMT policy.

SHAPING THE FUTURE OF FMT AND PATIENT CARE

OpenBiome uses the data we have collected over the past six years across more than 50,000 FMT treatments to inform best practices for FMT.



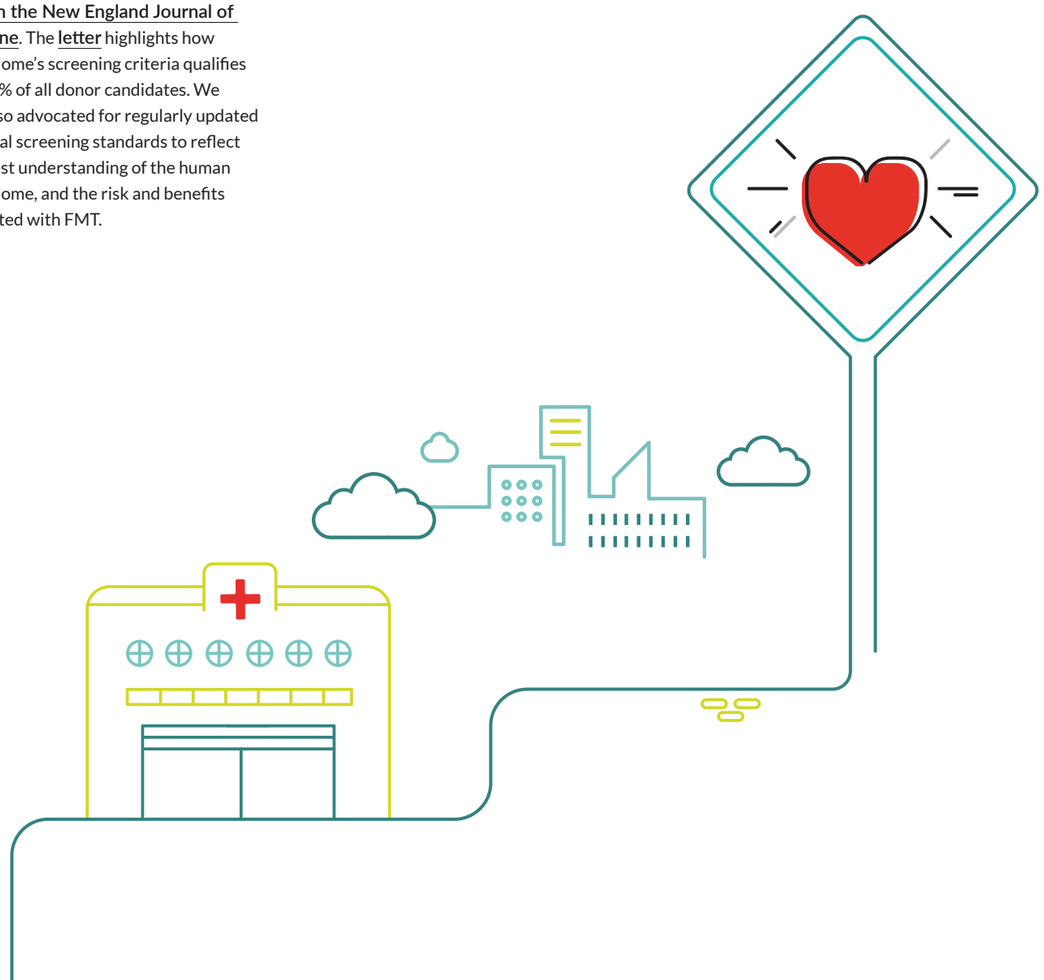
"SHARING OUR FINDINGS AND LEARNING FROM THE COLLECTIVE EXPERIENCE OF FMT IS HOW WE WILL ALL HELP ADVANCE SAFETY FOR EVERY PATIENT WHO FOLLOWS."

- CAROLYN EDELSTEIN, EXECUTIVE DIRECTOR OF OPENBIOME.

OPENBIOME HIGHLIGHTS DONOR SCREENING PROGRAM IN NEW ENGLAND JOURNAL OF MEDICINE

Screening donors for transmittable health risks to FMT recipients is one of the most important and challenging aspects of stool banking. Currently, there are no universal standards for screening human donor-derived microbiome-based products.

To share our model for producing standardized, rigorously screened FMT material, we published a research letter in the New England Journal of Medicine. The letter highlights how OpenBiome's screening criteria qualifies just 2.5% of all donor candidates. We have also advocated for regularly updated universal screening standards to reflect the latest understanding of the human microbiome, and the risk and benefits associated with FMT.

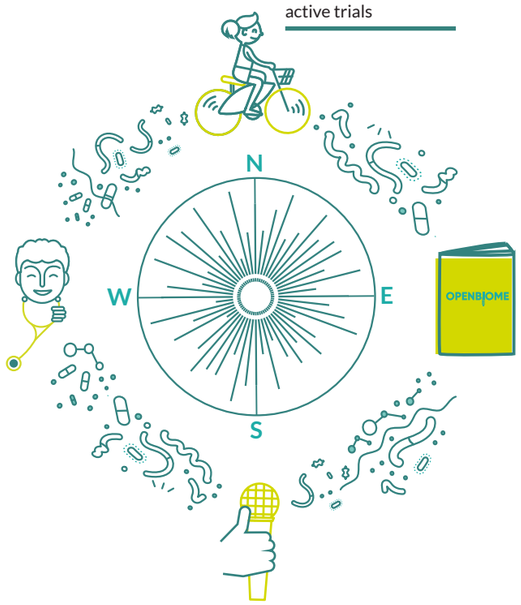


CATALYZING MICROBIOME RESEARCH

In 2019 OpenBiome and our research partners:

Enrolled 6 new clinical trials for a total of 23 active trials

Treated 10 single patient case reports



Published 27 peer-reviewed publications.

Presented 9 abstracts at scientific conferences including Digestive Disease Week, the annual meeting of the American Gastroenterological Association.

We are creating a new relationship between microbes and healthcare.

Through our partnerships with leading academic institutions, OpenBiome is exploring how bacteria can be engineered to prevent and treat disease. Our clinical trials portfolio spans autoimmune, infectious, metabolic, and neuropsychiatric diseases, and accounts for 36% of all active or completed FMT trials in the US.

University of Cape Town
Boston Children's Hospital
UNC School of Medicine
UHealth University of Miami Miller School of Medicine
VCU Medical Center
Brigham and Women's Hospital
UCSF School of Medicine
Memorial Sloan Kettering Cancer Center
University of Basel
NIH National Institutes of Health
Beth Israel Deaconess Medical Center

The human microbiome has emerged as a transformational new field of medicine. The bacteria in our gut are intimately connected to our health—they help digest our food, train our immune system, and may even modulate brain function.

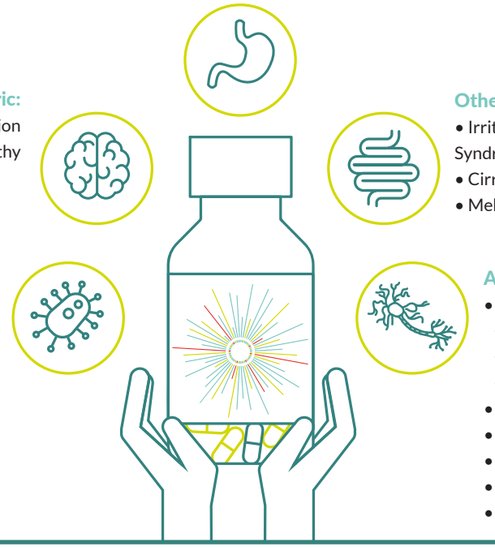
By transplanting bacteria from a healthy donor into a patient, OpenBiome and our collaborators are testing whether a variety of diseases can be treated by engineering the microbiome.

Nutrition:
- Obesity
- Severe Acute Malnutrition

Neuropsychiatric:
- Depression
- Hepatic Encephalopathy

Other:
- Irritable Bowel Syndrome (IBS)
- Cirrhosis
- Melanoma

Infectious Disease:
Vancomycin-resistant Enterococcus (VRE)
- Diarrheal Diseases:
  - C. difficile, S. typhi, NTS
- HIV/AIDS



Autoimmune:
- Inflammatory Bowel Disease
  - Ulcerative Colitis (UC)
  - Crohn's Disease
  - Pouchitis
- Allergies
- Multiple Sclerosis
- Graft vs Host Disease
- Primary Sclerosing Cholangitis
- Immune Mediated Colitis

RESEARCH SPOTLIGHTS

Highlights from our research portfolio

OPENBIOME AND THE NATIONAL FMT REGISTRY

To answer some of the most pressing questions about microbiome-based therapies, OpenBiome has partnered with the American Gastroenterological Association (AGA) and the American Gut Project on the FMT National Registry. The registry, a national data collection project, aims to track the health of 4,000 patients for 10 years after their FMT procedure and is planned to be the largest observational FMT study in history.

While FMT is a promising treatment for recurrent *C. difficile*, the potential long-term consequences of altering a patient's microbiome are not fully understood. The wealth of data generated from the registry will allow clinicians to evaluate the short-term and long-term effects of FMT, and better inform patients, clinicians, and researchers on the risks and benefits of the treatment.

Now entering our third year as a registry collaborator, OpenBiome has helped enroll an initial group of 260 patients. The AGA plans to share the first analyses of these patients in 2020.

ULCERATIVE COLITIS

OpenBiome is collaborating with researchers to enroll a pilot randomized clinical trial testing whether FMT can help treat ulcerative colitis—a chronic disease that causes inflammation in the digestive tract. This lifelong illness has a profound emotional and social impact on millions of people around the world.

Promising studies have suggested that FMT may help treat ulcerative colitis but the optimal regimen has yet to be determined.

Researchers at the University of California San Francisco are exploring whether administering antibiotics before FMT can help eliminate the patient's microbiome making it easier for donor microbes to engraft or grow into their new environment.

Preliminary results from 25 patients with mild to moderate ulcerative colitis showed that those who had received antibiotics pre FMT were significantly more likely to achieve steroid-free remission. The next step is to see if similar findings hold true in a larger patient population.

SJÖGREN'S SYNDROME (SS)

Sjögren's Syndrome (SS) is a systemic and serious autoimmune disease with no satisfactory long-term treatments. Symptoms vary but often include dry eyes and mouth as well as chronic pain, fatigue, and organ dysfunction. New treatment options are urgently needed to recover patient health and quality of life.

OpenBiome is partnering with a team of researchers from the University of Miami, who have previously shown that the microbiome of healthy individuals and those with SS differ. This observation, along with studies in mouse models of SS demonstrating that consumption of feces from healthy animals lessened symptoms, inspired us to collaborate on a phase 1 clinical trial to assess the feasibility and safety of performing FMT in patients with SS.

The study has completed enrollment and is currently in the data analysis phase preceding publication.

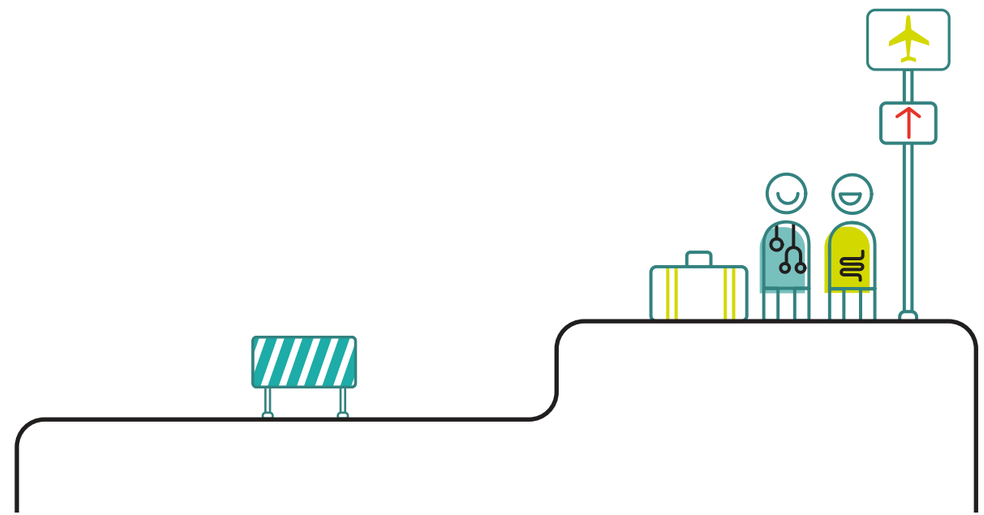
NARROWING GLOBAL DISPARITIES IN TRANSLATIONAL MICROBIOME RESEARCH

Research on the microbiome and FMT has focused predominantly on conditions that impact wealthy countries. Our Global Health program was founded to serve neglected patient populations in primarily low- and middle-income countries. We are excited to apply the lessons learned from treating patients with recurrent *C. difficile* to address some of the greatest global health challenges and build up local capacity for microbiome research.

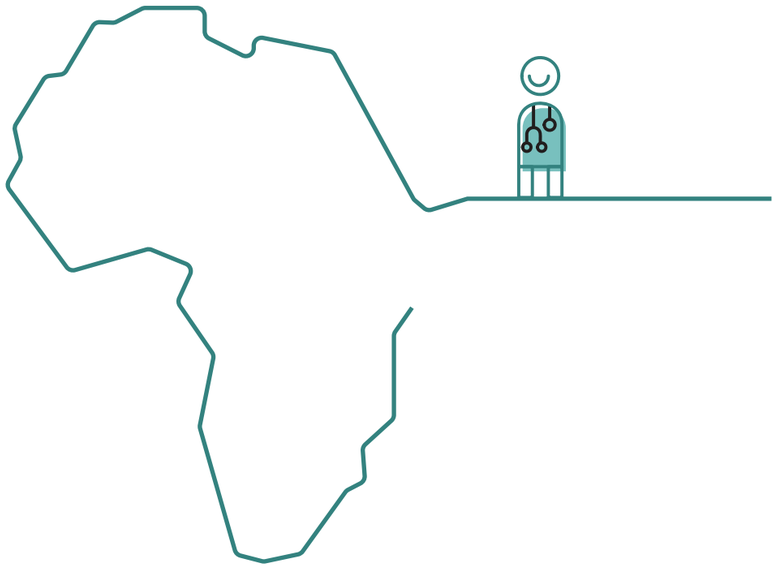
THRIVE

In 2019, OpenBiome and the University of Cape Town began enrolling **THRIVE—a clinical trial studying whether FMT can help treat children with Severe Acute Malnutrition (SAM)**. SAM, a life-threatening condition affecting over 20 million children worldwide, causes patients to be severely underweight, stunted in growth, or have swelling in their extremities. Over 35% of SAM patients do not respond to the standard treatment of nutrient-enhanced foods, and preclinical trials suggest that microbial-based therapies may aid in the absorption of nutrients.

THRIVE or Transfer of Healthy Gut Flora for Restoration of Intestinal Microbiota Via Enema is supported by the Bill and Melinda Gates Foundation, Children's Relief International, and the Thrasher Research Fund. Enrollment is taking place at our partner sites at the University of Cape Town and Red Cross War Memorial Hospital in Cape Town, South Africa.



OUR INAUGURAL GLOBAL HEALTH STUDY, THRIVE, IS THE FIRST FMT TRIAL TAKING PLACE ON THE AFRICAN CONTINENT



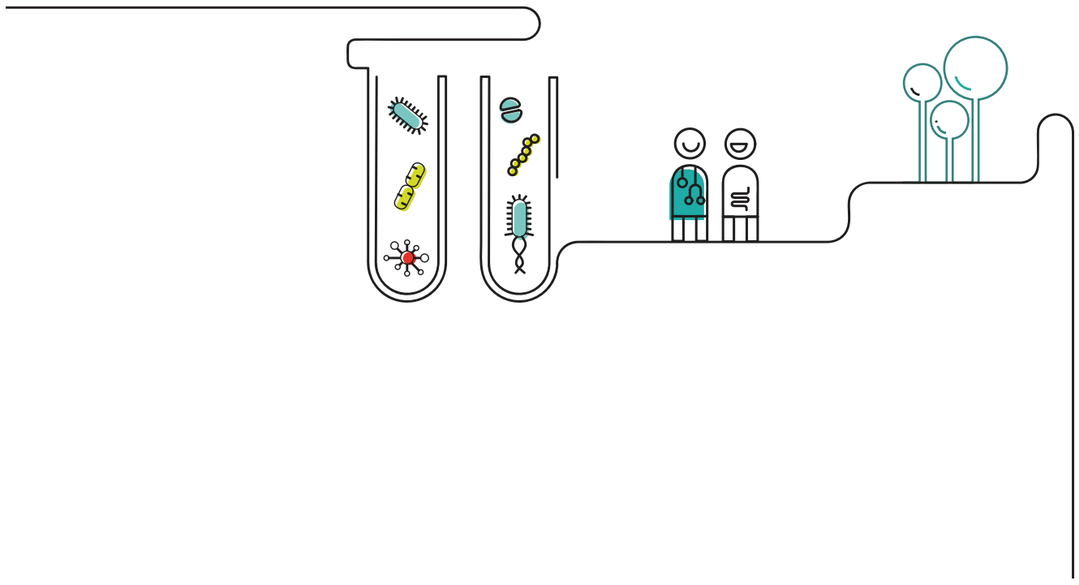
Beyond collaborating with our research partners, OpenBiome shapes research practice by sharing our expertise and experience.

NEW FRAMEWORKS FOR STUDY DESIGN

As the world's largest stool bank, we support 36% of all completed or ongoing FMT trials in the United States. Because OpenBiome is a central repository for stool and patient data, we are in a unique position to integrate findings across studies and discover hidden trends within the data.

One area of active investigation is donor selection—the idea that specific attributes of donors, such as their microbiome composition, may make their stool more effective at treating particular indications. Although donor selection does not seem to have an effect on the outcomes of *C. difficile* patients, it may be crucial for treating a wider range of illnesses.

In a PLOS ONE publication we describe different strategies researchers can follow to strategically select donors depending on how a disease of interest affects the body. To our knowledge, this is the first description of a comprehensive framework for donor selection in FMT clinical trials.



PUBLIC PRESENTATIONS

Aspen Ideas Festival: Carolyn Edelstein, OpenBiome's Executive Director, joined a panel of physicians and researchers to discuss the therapeutic potential of FMT.

Cure Accelerator: Dr. Majdi Osman, OpenBiome's Chief Medical Officer, delivered the winning presentation at CureAccelerator —a program that funds repurposing research to quickly and affordably improve patients' lives. Majdi pitched the THRIVE Study: Repurposing FMT for the treatment of severe acute malnutrition.

During the live philanthropic pitch event, audience members voted THRIVE as the winning presentation and awarded the study $50,000 of funding.

ABOUT US

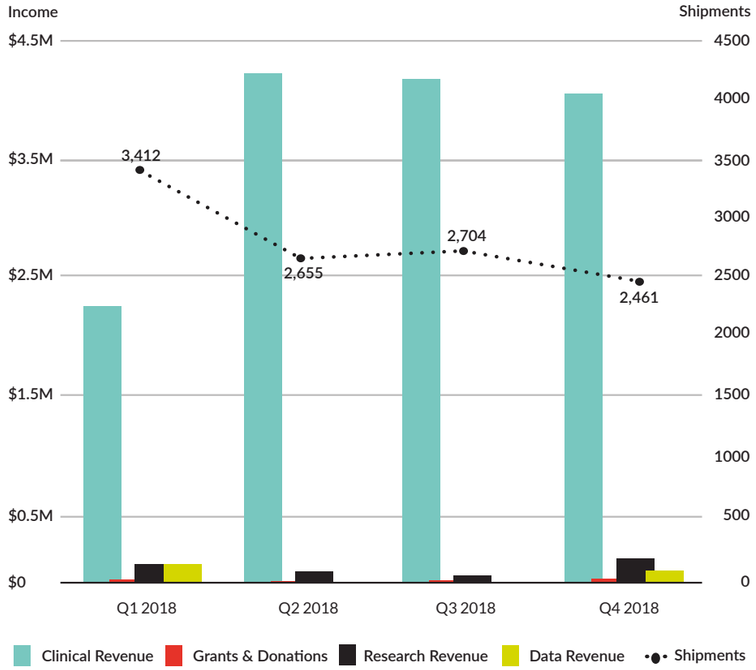
OpenBiome's mission is to expand safe access to fecal microbiota transplantation for patients with recurrent *C. difficile* and to catalyze research on the human microbiome.

Founded in 2012 in the Alm lab at MIT, OpenBiome aims to reduce the practical barriers to providing FMT and enable translational research investigating new applications of microbiome-based therapies.

BOARD OF DIRECTORS

Lisa Serwin—Chair of the Board
Eric Alm, PhD
Jim Bildner, JD
Neil Rasmussen
Jane Williams, MD MPH
Charles Hewett, PhD

QUARTERLY GROWTH



FINANCIAL STATEMENTS

BALANCE SHEET

ASSETS

Current Assets	2019	2018
Cash and equivalents	$4,460,778	$2,317,825
Accounts receivable, net	$2,114,339	$1,129,543
Inventory, net	$3,763,989	$188,080
Prepaid Expenses	$163,267	$72,534
Total Current Assets	$10,502,403	$3,707,982
Non-Current Assets		
Property and Equipment, net	$757,581	$313,069
Security Deposits	$84,782	$68,182
Total Assets	$11,344,766	$4,089,233

LIABILITIES AND NET ASSETS

Current Liabilities	2019	2018
Accounts Payable	$567,387	$34,435
Net Accounts Payable - Related Party	$3,259,488	$708,624
Accrued Expenses	$178,965	$205,503
Deferred revenue	$17,790	$253,276
Total Current Liabilities	$4,023,630	$1,201,838
Net assets		
Without donor restrictions	$7,215,813	$2,887,395
With donor restrictions	$105,323	-
Total Net Assets	$7,321,136	$2,887,395
Total Liabilities and Net Assets	$11,344,766	$4,089,233

INCOME STATEMENT

	2019			2018
	TOTAL WITHOUT DONOR RESTRICTIONS	WITH DONOR RESTRICTIONS	TOTAL	TOTAL WITHOUT DONOR RESTRICTIONS
Unrestricted Operating Revenues and Support				
Sales of Product (Net of Discounts)	$14,139,523	-	$14,139,523	$6,008,840
Research Sales				
General Research	$227,482	-	$227,482	$460,721
Federal contracts	$52,525	-	$52,525	$33,565
Grant revenue	$267,954	$105,323	$373,277	$51,000
Shipping and Handling Fees	$694,550	-	$694,550	$759,600
Less Cost of Clinical Program Sales	($5,224,052)	-	($5,224,052)	($3,688,014)
Gross Profit on Sales	$10,157,982	$105,323	$10,263,305	$3,625,712
Data Licenses and Royalties	$220,000	-	$220,000	$595,000
Other Income	$21,570	-	$21,570	$19,070
Other Donations	$37,314	-	$37,314	$3,085
Total Operating Revenues and Support	$10,436,866	$105,323	$10,542,189	$4,242,867
Operating Expenses				
Program				
Clinical	$3,266,448	-	$3,266,448	$840,270
Research	$2,091,052	-	$2,091,052	$2,474,766
Total Program Expenses	$5,357,500	-	$5,357,500	$3,315,036
General and Administrative	$609,232	-	$609,232	$697,509
Fundraising	$141,716	-	$141,716	$104,733
Total Operating Expenses	$6,108,448	-	$6,108,448	$4,117,278
Change in Net Assets	$4,328,418	$105,323	$4,433,741	$125,589
Net Assets, beginning of the year	$2,887,395	-	$2,887,395	$2,761,806
Net Assets, end of the year	$7,215,813	$105,323	$7,321,136	$2,887,395