

# Research Blog

## “RESTORE-ME: restoring gut microbiota to treat ME/CFS”

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My name is Rik Haagmans, and I am a Dutch PhD student at the Quadram Institute in Norwich.

My research project, which is funded by Invest in ME Research and the University of East Anglia, focuses on the relationship between gut viruses and ME/CFS.

During the project I will be working on the RESTORE-ME clinical trial, which will investigate treatment of ME/CFS through faecal microbiota transplants (FMT). Many ME/CFS patients, report experiencing gastrointestinal symptoms and conditions like irritable bowel syndrome (IBS).

Also, populations of gut microbes (the microbiota) in ME/CFS patients are often disrupted and abnormal (dysbiosis). This can increase inflammation in the gut and potentially lead to ME/CFS. With FMT, the whole collection of gut microbes from a healthy person is transplanted into a patient's gut and replaces existing microbes. The treatment has proven to be very effective in treating recurrent *Clostridium difficile* infection, which is associated with severe dysbiosis. Patients with other gut disorders associated with dysbiosis, like Crohn's disease and Irritable Bowel Syndrome (IBS), can also benefit from FMT. One clinic in Australia has reported positive long-term outcomes in ME/CFS patients who had been administered a mixture of gut-derived bacteria.

Since gut dysbiosis might be a contributing factor in ME/CFS, particularly in those with IBS, replacing the gut microbiota could be an effective treatment. This is the hypothesis behind the RESTORE-ME clinical trial – a phase 2b, double blind and placebo controlled – which focuses on establishing safety and efficacy. During the trial, ME/CFS patients with a diagnosis of IBS will receive an FMT or a placebo (mock) treatment. Over the course of 6 months,



the benefits of the treatment will be assessed by measuring physical activity and cognitive improvements. Since half of the participants will be given a mock treatment, the study will give us the ability to objectively measure if FMT improves ME/CFS patients symptomatology. We will also analyse blood and faecal samples from the participants. This will help us gain insight in the mechanism at play in FMT.

My project is in virology and gut viruses, a field that has gained a lot of public attention in the past year. With the outbreak of SARS-CoV-2, it has become obvious to all of us how quickly viruses can spread. They can have a massive impact on our daily lives, even outside of a pandemic. We are usually able to recover from most viral infections, but recovery from an infection does not always mean a rapid and full return to health. For example, many COVID-19 patients suffer for a long time after the initial infection from what is sometimes called “Long COVID”. This is something that many ME/CFS patients are familiar with. Leading up to the development of ME/CFS, many patients experience a viral infection. Various viruses are associated with ME/CFS and some of these viruses are also associated with gastrointestinal diseases and dysbiosis. This suggests that, at least in a subgroup of ME/CFS patients, gut viruses could play an important role.

To investigate this, I aim to:

- Identify viruses in faecal samples DNA through sequencing technologies
- Define the collection of viruses in the gut of ME/CFS patients
- Determine if ME/CFS patients have unique viruses in their gut
- Determine whether FMT leads to a change in gut viruses and how this relates to improvement of symptoms

In the past year I have been preparing experiments that allow us to optimise this process and ensure we can obtain high quality data. In the meantime, colleagues involved in the trial are working with the Health Research Authority (HRA) and the Medicines and Healthcare Products Regulatory Agency (MHRA) to obtain ethical approval for the study, which is expected to be finalised soon. Once the HRA and MHRA approve our study, eligible patients will be recruited. I am very excited to be part of this study, because it could finally offer a treatment option for many ME/CFS patients. And on top of that, it can give us valuable information about the mechanism underlying ME/CFS and the role of gut viruses in human health. I can't wait for the study to get started!

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