

General Octopus FAQs:

What is the aim of the Octopus trial?

The main aim of Octopus is to find treatments that can slow down, and ultimately stop, the progression of disability in people with progressive MS.

How does the trial work?

Octopus uses a multi-arm multi-stage (MAMS) trial design. MAMS trials make it possible to test new treatments faster by:

- Testing more than one at once – and then comparing them with a single control (placebo) group.
- Using an early marker of effectiveness (in this case MRI scans) to get an idea of whether a drug looks like it has potential, many months before we'd be able to see an effect of the drug on disability progression.
- Promising-looking drugs stay in the trial at this point and drugs that don't look promising can be dropped, with new drugs slotted into the trial in their place as they are discovered.
- Patients will not have to withdraw if the treatment they are on is deemed to be not showing benefit, they will stop and then if they would like to screen again to see if they can be randomised again to a different arm instead.

Who can take part?

- Adults with primary or secondary progressive MS who meet the trial's eligibility criteria. Not everyone is able to take part in Octopus, so please fill out the Registration of Interest form to see whether it may be suitable for you.

How many people will take part?

- For Analysis Stage 1, there will be two treatment groups, or 'arms', and one control arm. Each group will have 125 participants - so 375 people in total will be taking part at this stage.
- At the end of Analysis Stage 1, researchers will review magnetic resonance imaging (MRI) data from participants' scans. The results will help researchers decide whether the treatments under investigation are showing enough benefit for them to continue being tested in the trial.
- Each arm continuing after this point into Analysis Stage 2 will continue recruiting until there are 600 participants per arm. The total number across Octopus will depend on whether two, one, or no arms continue after MRI analysis.
- New arms can also be added to Octopus in the future to test other new and promising drugs. If this happens then each new arm will, again, have 125 participants in the first stage and grow to 600 if it continues into the second.

How long will it take?

The first stage, Analysis Stage 1, will last for 18 months. In this time, participants will have four MRI scans to look for treatment effects on the brain. After that, the researchers will examine the MRI scan data and decide if the treatments show enough promise to continue to be tested in the second stage of the trial.

The second stage, Analysis Stage 2, will last at least another 3 years. Participants will continue to take medication, but no longer need to do MRIs.

Why has it taken so long to open Octopus?

The Octopus team understand the frustration about how long it takes to open trials. We understand that for many people with progressive MS, these trials give hope and an opportunity to take part in something that may help people with MS.

The process of planning and gaining approval for a new clinical trial is highly rigorous, to ensure the safety of participants and to give the trial the greatest chance of success. This is even the case for medications that are already available for other conditions. While the medications for Octopus have been selected based on some positive signals seen in earlier work, there is no guarantee that ordering them online would be either safe or effective. A clinical trial is needed to tell us whether a particular type and dose of a medication (as this may vary over the counter) is safe and effective, and people must be monitored carefully, which requires careful planning.

In trials of progressive MS treatments, we need to see whether the drug slows down how quickly disability gets worse. Progression generally happens gradually, so it can take several years to be able to say for sure whether a treatment has effectively slowed it down.

The aim of the MAMS Octopus design should still mean that answers will come more quickly than in traditional trials, since we won't need to set up new, separate trials every time we want to test a different drug.

What treatments will be tested in Octopus?

In Octopus, at the moment, there are 3 arms being tested. This means that to begin with there is a 2 in 3 (67%) chance of being on an active treatment arm and a 1 in 3 (33%) chance of being on the control arm, which is called placebo.

All participants will also continue to have their current treatment or standard of care that they are already receiving before joining the trial.

The drugs currently being tested in Octopus are Metformin and R/S Alpha Lipoic Acid, plus a control arm, called placebo.

Treatments are chosen for the trial on the grounds that:

- They've shown promise in the laboratory that they may have the ability to protect nerves from damage and/or repair myelin.
- They are already used to treat other conditions – see 'What are repurposed treatments' below.

Any potential side effects will be clearly explained to people thinking about joining Octopus.

Will these drugs just slow disease progression or could they stop or even reverse it?

We don't yet know exactly what the effect of the first drugs will be in MS. But if they're effective, it's likely they'll slow down disability progression. This is a real unmet need for people living with MS, many of whom have no treatments to slow disability progression at the moment.

The Octopus trial is designed to slot in new drugs as they're discovered. We hope that Octopus will test more drugs – or combinations of drugs – that can stop progression of the disease altogether, and even one day reverse it. Our Treatment Advisory Committee is monitoring new scientific evidence to help identify more drugs that could be added as treatment arms in Octopus.

How are potential drugs selected?

Octopus has a Treatment Advisory Committee that reviews scientific evidence available about potential drugs and advises the Octopus investigators on which show the most promise.

What are repurposed treatments?

Repurposed treatments are medicines or therapies already used to treat other conditions. This means there is already an understanding of their safety and possible side effects, and so the usual early safety tests for a brand new medicine are not required. Therefore, it will be faster to test them for progressive MS.

Will the participants know what drugs they are on?

No. This is a double-blinded trial meaning the treating doctors and nurses, nor the participants, will be aware of what drug they are on. Only the trial statisticians will know what treatment you will receive.

However, if you have a medical emergency, there are details on your participant card that your treating doctor can use if they need to know what treatment you are taking.

What is randomisation?

This is the random allocation of participants to each group in a trial, to ensure groups receiving each treatment are as similar as possible at the start of the study.

It allows a fair comparison between the new treatment and the existing treatment group to see which one works best.

What does standard of care mean?

Standard of care means exactly what it sounds like. This means your regular standard of care should not change due when you join the trial. It will be specific to each participant. This means if your NHS neurologist or MS team think you would benefit from a treatment, this will not affect you joining the trial.

Examples of current SOC include (but are not limited to) are like ocrelizumab and symptomatic treatments such as baclofen, and physiotherapy. But this may change throughout the course of the trial.

Who do I contact about the trial?

To indicate your interest in taking part in Octopus, please sign up via the Registration of Interest form. This will provide an initial indication of the suitability of the trial for you. If suitable, you will be contacted in due course once your chosen site opens to recruitment.

We apologise that the Medical Research Council Clinical Trials Unit at University College London Octopus trial team who oversee the website cannot advise on clinical or eligibility queries.

Please contact the MS Society for further information about MS research and practical support for MS.

Why Octopus?

The name was chosen after people in the MS community voted for their favourite in a social media poll in 2020. It comes from the long title of the trial, which is Optimal Clinical Trials Platform for Progressive Multiple Sclerosis.

I cannot join Octopus. Are there other studies that may be suitable for me?

If you would like to look for other studies or other ways to get involved in research, you can find out more on the MS Society website.