



# Research matters

The latest developments, innovations and achievements in MS research

Spring 2019 • Issue 017

Hear from our experts  
on pain, fatigue and new treatments  
to stop disability and see...

Why the UK is a world  
leader in MS research



plus

The causes of MS, your questions answered, MS diets  
and what the UK MS Register can do for you

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# Welcome to Research matters

**L**ong term investment and some of the world's best minds have put the UK at the cutting edge of MS research. To date the MS Society has invested over £218 million in advancing MS science. And with your support we will continue to fund even more breakthroughs in 2019.

Our researchers are driving new trials into potential treatments and changing the way we understand MS. In this issue, our supporters speak with leading scientists about the advances being made in how we manage symptoms, stop disability progression and live better with MS in the UK.

Professor David Baker and Dr Klaus Schmierer talk us through their groundbreaking B cell research in London on **page 8**, including their efforts to make cladribine available to people with progressive MS. On **page 14**, Dr Sarah Thomas from Bournemouth explains how her work has spawned a worldwide change in the way we approach fatigue management. And you can get the latest on diet and nutrition on **page 18**.

Turn to **page 16** to learn more about clinical trials taking place across the UK. You'll also hear about a project I'm personally very excited about - our new clinical trial 'platform'. This is designed to speed up the way we test potential new treatments and find ones that work more quickly.

As always, we'd love to hear what you think about *Research matters* or if you'd like to be involved. You'll find contact details on the left hand side of this page.

**Dr Susan Kohlhaas**

Director of Research



**contribute**

The research network is a group of people affected by MS helping shape our research programme. They also help decide what 'Research matters' and write for the magazine. To find out more visit [mssociety.org.uk/researchnetwork](http://mssociety.org.uk/researchnetwork)

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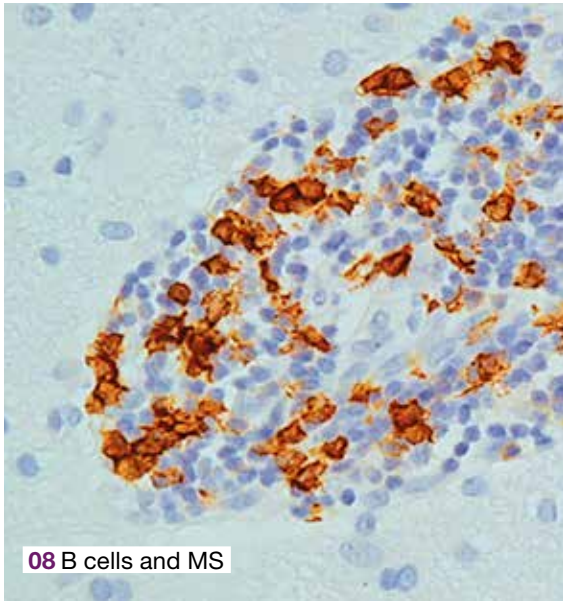
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### talk

If you'd like to talk to someone in confidence about any of the topics raised in the magazine, the MS Helpline is here for you. Call for free on **0808 800 8000**, or email **helpline@mssociety.org.uk**

**Research matters** is available as an audio download. For details, phone **0300 500 8084** or visit **mssociety.org.uk/Research-Matters**



# What actually causes MS?

We don't yet know for sure what causes MS, but it's likely to be a mix of genes, your environment and lifestyle. What we do know is that developing MS is no-one's fault

**U**nderstanding how we can prevent MS is one of our top research priorities. We know that many different factors are involved. Ultimately, we hope we can use this knowledge to make sure fewer people have to live with MS in the future.

## Genetics

There's no single gene that will definitely cause someone to develop MS, but we know that having certain gene mutations can make it more or less likely. Most people who carry these risk factor genes won't develop MS. They still need to be exposed to other environmental or lifestyle factors to trigger MS.

So far we've discovered over 200 genes that are linked to MS. Not surprisingly, as MS is considered an autoimmune condition, many of them play a role in the immune system.

## Other autoimmune conditions

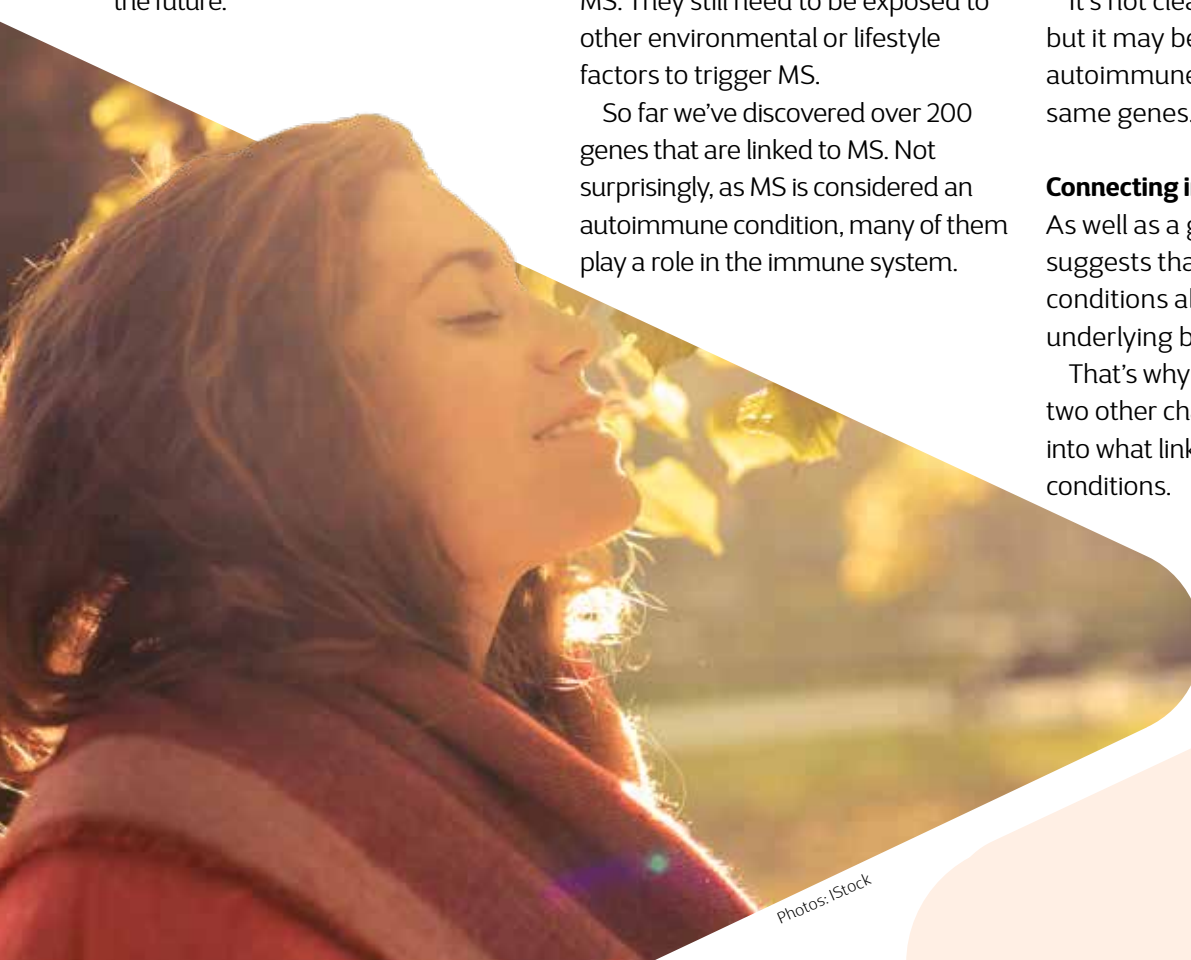
If you or a close family member has MS, you're more likely to develop another autoimmune condition, such as Crohn's disease, type 1 diabetes or rheumatoid arthritis, than people who don't.

It's not clear exactly why this is, but it may be because different autoimmune conditions involve the same genes.

## Connecting immune research

As well as a genetic link, research suggests that different autoimmune conditions also share common underlying biological mechanisms.

That's why we've joined forces with two other charities to fund research into what links different autoimmune conditions.



Photos: iStock

Our partnership with the type 1 diabetes charity JDRF and Versus Arthritis will fund Professor Yanick Crow, from the University of Edinburgh, to investigate immune proteins called interferons, and their role across autoimmune conditions.

His findings could help us unlock vital information not only about MS, but of benefit to everyone living with an autoimmune condition. Find out more at [mssociety.org.uk/connectimmune](https://mssociety.org.uk/connectimmune)

### Environmental factors

#### Vitamin D

We know there's a link between vitamin D levels and MS, though more research is needed to explain it. Vitamin D appears to play a protective role against MS, particularly during pregnancy and childhood.

In 2016, scientists found that children born with very low levels of vitamin D were more likely to develop MS in later life. Another study reported that month of birth also plays a role, suggesting levels of sunshine during pregnancy could be important.

And research shows that people who have moved to a new climate during childhood tend to adopt the risk level of the country they move to. But if people migrate later in life, they tend to keep the risk profile of their country of birth.

Despite these findings, we still don't know if vitamin D supplements could prevent or treat MS. To find out more about vitamin D, visit: [mssociety.org.uk/vitamin-d](https://mssociety.org.uk/vitamin-d)

#### Infections

It's long been thought that certain bacterial or viral infections may be a trigger for MS. Researchers haven't yet identified any infectious agent that definitely causes MS, but, there's growing evidence that certain infections could contribute to someone's risk of developing the condition.

The most well-studied of these infections is the Epstein-Barr virus (EBV), which causes glandular fever. Most people come into contact with EBV in their lifetime (though may never experience symptoms), and so

## A unique history



**Lyndsey's family has more experience than most of living with autoimmune conditions.**

'I have relapsing MS and autoimmune thyroiditis. Until my diagnosis, I hadn't heard of autoimmunity. I knew of other conditions in the family - my second cousin had rheumatoid arthritis and my great aunt had systemic lupus erythematosus. I studied biology at university and realised then that there could be a genetic link. Luckily, the thyroiditis is well controlled by medication, but it also causes fatigue, so I must be mindful that symptoms may not always be MS. I have a better understanding now, so when my daughter became unwell, I knew she was showing autoimmune symptoms and pushed to get her a diagnosis. She was then diagnosed with coeliac disease.'

### Chance of someone developing MS in their lifetime



**1 in 330**  
who grow up in the UK



**1 in 67**  
who have a parent with MS



**1 in 37**  
who have a brother or sister with MS



**1 in 5**  
who have an identical twin with MS

**That means 1 in every 600 people in the UK have MS**

### Autoimmune disorders

The immune system is your body's defence against infection. Autoimmunity is when the immune system attacks normal body tissues by mistake. In MS the immune systems treats the protective myelin coating around nerves like a disease.

will carry antibodies to it. A number of studies have shown that people with higher levels of antibodies to EBV are more likely to go on to develop MS. And practically everyone with MS has come into contact with EBV.

In 2018, a small phase 1 trial found that targeting cells infected with EBV in the brain could help people with progressive MS. A phase 2 study is being planned in Australia and the US. Find out more here: [mssociety.org.uk/immunotherapy](https://mssociety.org.uk/immunotherapy)

### Lifestyle

#### Smoking

Smoking can make you up to 50% more likely to develop MS compared with people who don't smoke.

Studies have also shown that smoking can speed up how fast your disability progresses. People with MS who smoke may see their MS develop from relapsing MS to secondary progressive MS earlier than people who don't smoke.

#### Obesity

In 2018, a study was published that found a link between obesity and MS. It showed that people who are genetically predisposed to having a higher body mass index (BMI) are more likely to develop MS. While the reasons for this aren't clear, we do know that people who are obese tend to have lower levels of vitamin D, and higher levels of tissue inflammation. Both of these are risk factors for developing MS.

Of course, not everyone who is obese will get MS, and only a fraction of people with MS are or have been very overweight.

#### Occupational hazards

There is some evidence that certain occupational hazards can also impact a person's risk of developing MS.

A study found that deaths from MS were much higher among people whose last job was in the armed forces. But the research was limited, as it only looked at someone's last job rather than their career. The study also didn't make any suggestions about why an increase in deaths was found.

Another study found that exposure to solvents, such as paint and varnish, could be a risk. People who had genetic risk factors plus a history of smoking and had been exposed to solvents were 30 times more likely to develop MS than people without any of these.



read

Read more about the causes of MS on our website: [mssociety.org.uk/causes](https://mssociety.org.uk/causes)

# MS data revolution

You can now use the UK MS Register to better track your MS



**B**y sharing their experiences of MS with the UK MS Register, thousands of people are helping us improve MS services and MS research for everyone.

By telling us what it's really like to live with MS in the UK, you're providing the evidence for us to campaign for better care and support and guide our research. You've done this by answering over 400,000 questions since it launched in 2011!

## Track your MS

We recently improved the register by making the website clearer and introducing a brand new 'My MS' hub. This allows members to get feedback



Photo: Amit Lennon

based on the questionnaires they completed. You can also track how your reported symptoms have changed over time. This information can be useful when talking with your GP or MS specialist, especially if you don't have frequent check-ups.

## What the experts don't know

The UK MS Register is also the first database in the world to combine information from people with MS with their clinical data. Over 40 NHS hospitals are currently taking part. That makes it a unique source of information for researchers around the world who want to understand how clinical data, collected by doctors, relate to your symptoms and experiences of MS. Only by bringing together scientific expertise and the real life experience of people with MS can we answer these questions.

## Share your experience today

My MS My Needs is one of the largest surveys of people affected by MS in the UK. It gives us a snapshot of people's experiences, and ask if you're getting the treatments, services and support you need.

The results are invaluable for our campaigning work – highlighting where services work well, and

most importantly, where improvement is needed.

The next survey is open until Friday 31 May, and we'd love for you to add your voice. You can give your answers online at [ukmsregister.org/landing/mymysmyneeds](https://ukmsregister.org/landing/mymysmyneeds) or get a paper copy from our Supporter Care team on **0300 500 8084**



Find out more about the UK MS Register at [ukmsregister.org](https://ukmsregister.org)



Photo: David Baker

B CELL LESIONS

# Why B-cells are on the A-list

Research network member **Lyndsey Shellard** interviewed **Professor David Baker** and **Dr Klaus Schmierer** from the Blizard Institute about their work on cladribine, a drug that targets B cells



## What are B cells?

The immune system is made up of many different cell types. These include B cells and T cells, which can 'talk' to each other and team up to fight infections.

B cells are a type of white blood cell formed in the bone marrow. They protect us by creating antibodies that can help kill off infection.

Not all B cells are the same. Some regulate the behaviour of other immune cells while others produce antibodies designed to recognise particular microbes. Another group act as 'memory cells', holding a

database of microbes that the immune system has previously encountered and destroyed.

## What is their role in MS?

B cells are not normally found in the central nervous system (the brain and spinal cord) except during infections. But in MS, something goes wrong and triggers them to enter the brain when they're not needed.

Initially it was thought that B cells were only causing damage by making antibodies that target the protective myelin coating around

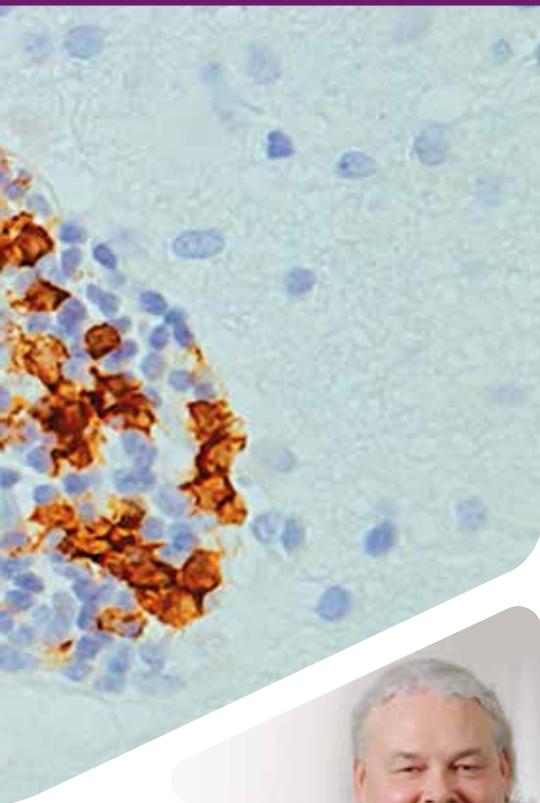
nerves. These antibodies then tell other immune cells to attack myelin.

But new research suggests that cells can also directly activate T cells in the brain or the blood, causing inflammation and further nerve cell damage.

## Are there disease modifying therapies (DMTs) that can stop B cell damage?

Historically, it was thought T cells were the major problem, because one of their jobs is to kill infected cells. But now we see that drugs that





target B cells are also effective (see information box).

So we've been looking again at the biology of MS and how DMTs work. It may be that the underlying problem is with B cells calling other immune cells into the brain, leading to inflammation and destruction.

We're personally excited about cladribine because it works on B cells and T cells directly in the brain, rather than just in the blood or immune tissues. That means we can target the 'memory' B cells that live in the brain, and hopefully reduce the cycle of inflammation.

## Do B cells also cause progression in MS?

We know that when B cells enter the brain, they can live there for a long time, making more antibodies and new 'memory' B cells. This can stimulate other cells in the brain to produce toxic substances, resulting in a cycle of damage seen in progressive MS.

## Can any DMTs help people with progressive MS?

Beta interferon is licensed to treat people with early secondary progressive MS, but only those who are still experiencing relapses. There is no evidence it can help with progression.

A B cell depleting drug called ocrelizumab (Ocrevus) has shown some benefit for early primary progressive MS, but it's not yet available on the NHS.

We're also keen to see if cladribine can help people who currently have no treatment options – those with primary and secondary progressive MS. In particular, we believe cladribine could slow progression and help arm and hand mobility for

people who use wheelchairs.

Cladribine is already licensed to stop relapses and slow disability progression in relapsing MS, but we need a proper clinical trial to demonstrate that it's safe and effective for people with advanced MS.

To see other drugs in the pipeline for progressive MS, turn to **page 16**.

## What are your hopes for the future?

The more specific we can make a drug to target different cell types, the fewer side effects we expect there to be.

One day we may be able to offer really targeted therapies, which are taken for just a short time. We could then add in other treatments, such as neuroprotective ones or drugs that boost myelin repair, as they become available.

**read**

Find out more about different immune cells and how they are controlled by DMTs at

[mssociety.org.uk/warriors](https://mssociety.org.uk/warriors)

## Disease Modifying Therapies (DMTs)

The following DMTs specifically target B cells in MS:

**Cladribine (Mavenclad)** directly targets B cells and T cells in the brain.

**Alemtuzumab (Lemtrada)** is an antibody that kills B cells and T cells to stop them entering the brain.

**Ocrelizumab (Ocrevus)** is an antibody that targets B cells for destruction, but doesn't enter the brain. **Rituximab (Rituxin)** is an older version of this treatment but is being used and tested in some countries where ocrelizumab isn't available.

# How exercise can help fight pain in MS

A lot of people with MS experience pain as a symptom at some point. Research Network member **Linda McGregor** spoke with neuro-physiotherapist **Rachel Flinn** to find out why exercise could help

**L**inda has always loved exercise. Before she was diagnosed, she was a keen runner and now likes to keep as active as possible with the help of her dogs and golf.

Rachel Flinn (pictured right) works at the MS Resource Centre in Belfast.



## Do we know what causes pain in MS?

A lot of people with MS experience pain at some time. Pain can be one of the most difficult symptoms to both describe and manage. It can be exhausting, impacting on your ability to do everyday activities.

Pain may be caused directly due to nerve damage (neuropathic pain), or indirectly, due to other MS symptoms (musculoskeletal pain) – see box opposite. Pain could also

be a side effect of drugs, linked to another health condition not related to MS, or caused by internal symptoms, such as a bladder infection.



## Can exercise reduce pain in MS?

There's less research around whether exercise can help with MS pain compared with other symptoms like fatigue, where the evidence is strong. But a recent review of previous clinical trials concluded that exercise may be able to help.

Researchers in Australia looked at the results of ten clinical trials involving 389 people in total. Different types of exercise were studied, including aqua aerobics, walking, and resistance exercise. Though it wasn't a huge effect, results



Photo: Colin Baldwin Photography Ltd



suggested that feelings of pain were lower in the exercise groups compared with the control group.

But the researchers did stress that the size of the studies made interpreting the results difficult, and that more investigation is needed.

### How do you think that exercise could help manage pain?

Exercise can help to relieve muscle stiffness and spasticity and the pain associated with this. It can also prevent deconditioning – the gradual loss of strength and fitness – which can make existing pain worse.

Recent research suggests that exercise might even change the wiring in your brain. Studies in mice have found that it promotes ‘neuroplasticity’ – where a brain signal finds a new route to avoid damaged nerves.

Excitingly, it’s now thought that exercise might increase the levels of chemicals in the brain that promote the repair and regeneration of damaged nerve cells. Studies are at an early stage, but it’s possible that exercise could be a promising way to reduce pain associated with MS-related nerve cell damage.

### What further research is needed?

As well as understanding more about what happens in the brain when we exercise, I think there needs to be more research into the

different types of MS pain.

Whether it’s neuropathic, musculoskeletal or something else, at the moment, trials don’t tend to differentiate and that could affect the results.

### What’s your advice to people living with MS?

Think of it as being more active rather than exercising – you don’t have to turn into a gym bunny or run 10 miles a day! Incorporating more movement into your daily life through gardening, stretching or going for walks is a good start.

The MS Society has worked with a

personal trainer to develop a series of videos designed to help you exercise whatever your level of mobility: [mssociety.org.uk/workout](https://mssociety.org.uk/workout). Your local MS Society group probably has classes too. It’s really important you find something you enjoy and can stick with.

#### watch

Take a look at Rachel’s videos, created to help you manage specific MS symptoms, including fatigue and spasms. [mssociety.org.uk/exercises](https://mssociety.org.uk/exercises)

## Causes of pain in MS

### Neurogenic pain

- The direct result of damage caused by MS to the nerves in the brain and spinal cord (neuropathic pain) or lesions.
- Nerve damage might cause a range of sensations, from minor irritations to intense sharp or burning pains.
- Examples include trigeminal neuralgia and the MS hug.



### Musculoskeletal pain

- The pain in muscles and joints that comes from living with the stresses and strains MS places on the body.
- For example, difficulties with balance could lead to problems with posture, putting a strain on joints, ligaments or other muscles.



Photo: Colin Baldwin Photography Ltd





# Your questions answered

Readers put our research team to the test with their latest MS science queries

## **Q** Do lesions in certain parts of the brain relate to specific symptoms?

We know that distinct parts of the brain usually perform specific functions, but there is some flexibility around this. Different regions can take over other roles if needed. And the brain has been shown to physically adapt to nerve damage, 'bypassing' the problem areas, in a process known as neuroplasticity.

Taken together, this means that although damage to nerves (lesions) in specific areas is more likely to cause certain symptoms, it's far from definite.

The largest part of the brain, the cerebrum, controls cognitive skills such as attention, memory and emotions. Lesions in this area can cause cognitive dysfunction, with the pattern of cognitive decline related to where the lesions are within the cerebrum. Certain lesion sites can also predict the type of bladder dysfunction someone with MS may experience, while others have been associated with depressive symptoms.

The spinal cord contains nerves that control movement, and so damage to this part of the central nervous system can result in loss of mobility.

## **Q** What are the long-term effects of disease modifying therapies (DMTs)? Can they stop MS progression?

Evidence from MRI scanning shows that even at the earliest stages of MS, nerve damage is happening in the brain. And once nerve cells are lost, they can't be replaced. So treating MS as early as possible is vital to improving long term outcomes.

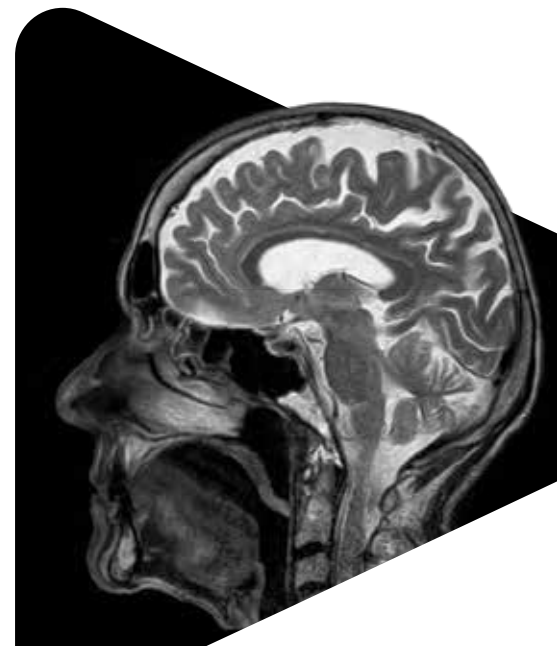
DMTs aren't a cure for MS, and they won't undo any permanent disability. But they are able to slow MS progression.

Long term studies found that people who took part in early trials of the first DMT lived longer, compared with people who started treatment later. And long-term follow up from the early natalizumab trials showed that after 5 years, people who were treated with the drug had a lower level of disability compared with those initially treated with the placebo.

As to whether DMTs can completely stop MS from progressing – there are still a lot of

unanswered questions. An 18 year-long study found that treatment with a DMT seemed to reduce the number of people who went on to develop secondary progressive MS. But there are other factors involved that could influence this, like age of MS onset, how early people started treatment and the type of treatments they had taken.

There remains a question as to how intensive early treatment should be. A cohort study published in 2018 suggests that the more



effective but higher risk the early treatment is, the lower the risk of developing secondary progressive MS over a minimum of four years. Turn to **page 16** to find out more about DELIVER-MS, a clinical trial hoping to give a definitive answer about early aggressive treatment.

**Q What's in the pipeline for secondary progressive MS?**

There currently aren't any treatments available for secondary progressive MS, but research is bringing us closer to finding drugs that can help.

Our UK-wide phase 3 trial, MS-STAT2, is currently recruiting (see **page 16** for details). This trial will give us the definitive answer about whether or not simvastatin can slow disability progression in secondary progressive MS. Results are due in 2023.

And excitingly, another drug called siponimod has been shown to reduce disability progression for some people. The drug is currently being considered for licensing – we should know the result by the end of the year.

Work is also underway to understand more about the underlying biology of progressive MS. Our research centres in Cambridge and Edinburgh are helping find treatments that can repair myelin and protect nerve cells from further damage.

Find out more about our work to stop progressive MS: [mssociety.org.uk/progressing](https://mssociety.org.uk/progressing)

**ask**

If you'd like to talk in confidence about any aspect of living with MS you can call our Helpline free on **0808 800 8000**, or email [helpline@mssociety.org.uk](mailto:helpline@mssociety.org.uk)

Photo: Simon Rawles

**Getting the right advice**

Our research staff are not medical professionals. This page is designed to provide general information. If you have specific health questions, please talk to your MS specialist.





DR SARAH THOMAS



Photo: Amit Lennon

# Tools to manage your fatigue

Research Network member **Sarah Rees** caught up with **Dr Sarah Thomas** about proven ways to handle MS fatigue



**F**or those of us living with MS, fatigue is often the most

debilitating symptom. It's invisible, difficult to treat, and can have a big impact on work. But life is about more than work, and fatigue can also greatly reduce quality of life by leaving little energy for fun.

Thank goodness then for people like Dr Sarah Thomas. She and her colleagues at Bournemouth University and Poole Hospital have spent almost a decade working on a

programme called FACETS, designed to help those with MS better manage their fatigue and get more out of life post-diagnosis.

### Developing FACETS

Sarah explains: 'When we started out, we saw there was a gap in the market for psychological interventions to help

with fatigue. There are drugs available, but they don't work for everyone and come with side effects.' 'There was some early evidence that cognitive behavioural therapy (CBT) could help, so we started developing what has now become FACETS.'

The FACETS (Fatigue: Applying Cognitive behavioural and Energy





effectiveness Techniques to lifeStyle) programme focuses on helping those with MS make lifestyle changes to optimise the energy they have.

It blends energy effectiveness techniques with cognitive behavioural strategies, getting you to think about how best to use your energy reserves, and what's stopping you from making changes.

Part of the process involves setting realistic expectations and recognising that it's better to manage fatigue than to fight it. 'It can be challenging for people, but we encourage them to start small and make little changes, such as understanding your triggers and recognising what your fatigue levels are,' says Sarah.

The programme has also been important in helping people accept their MS fatigue, and give themselves permission to approach things

differently: 'We've found the fact that FACETS is delivered in groups really helps people open up, and perhaps realise that the guilt they feel for taking a break is not needed – you're not being judged!'

### International success

FACETS is now being adapted and used across the world, while the MS Society is helping the course to be rolled out nationally.

There's also ongoing work to create a digital version of FACETS that people can use through the MS Society website (see information box).

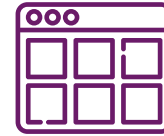
What was initially a small project exploring psychological interventions for fatigue has mushroomed, much to Sarah's delight: 'When we started, I really didn't envisage that this programme was going to get to where we are now. I think it's worked so well because we've involved people with MS right the way through the process. We're designing something that people want.'

### Making a difference

Sarah is thrilled to have helped create something that improves the lives of people with MS. 'People have described FACETS as life-changing, allowing them to get their lives back. That counts for so much.'

While she admits that there is 'no magic wand for fatigue', Sarah is confident that offering courses like FACETS right from diagnosis could make all the difference to those living with MS. But for those who can't yet access the programme, what advice

## Going digital: FACETS online



We're working with Sarah and her team to create an online

version of FACETS, giving everyone the chance to access this fatigue management tool.

Guided by people living with MS, we're creating six online modules that recreate the original programme, allowing users to understand their fatigue and uncover helpful ways to manage it. The online course will be launching later this year.

could she offer?

In addition to setting realistic expectations, Sarah stresses that 'it's important that people are kind to themselves and give themselves permission to rest.'

She also urges those with MS to make sure they aren't just using up their energy on work or chores. 'You must still leave energy for doing the things that matter to you, and that you enjoy. Life has to be rewarding too.'

learn

If you're interested in FACETS please ask your MS care team or local group, or email [education@mssociety.org.uk](mailto:education@mssociety.org.uk)

# Testing, testing ... phase 1,2,3

Bigger, faster and smarter clinical trials mean we're at the cusp of a revolution in testing new treatments that could help everyone with MS

## Research Pipeline

### Pre-clinical studies

Laboratory research using cells and animals

### Phase 1 clinical trial

Is it safe? What dosage?

### Phase 2 clinical trial

Is it safe for people with MS? Is there a benefit?

### Phase 3 clinical trial

Measure benefits and risks. Compare to current treatments.

### Phase 4 clinical trial

After licensing, check for long term effects and possible wider use.

It's a long journey getting a new treatment into the clinic. Ideas need to be proven in the lab, and clinical trials need to show a treatment is safe and effective, before a drug can be licensed for use.

The process can sometimes take up to 20 years from start to finish.

Our challenge is to speed this up: to identify the most promising treatments and test them as quickly and efficiently as possible. We're doing this through bigger, smarter and faster trials.

## Bigger trials

In 2018 people started joining the UK's largest academic clinical trial

## Taking part



**Stephen Ritchie has secondary progressive MS and is participating in the MS-STAT2 trial**

'Just being on the trial has changed my outlook and I feel I can take part in life again. It's made simple things like doing the dishes a possibility and whether that's down to a psychological boost or not, it can only be a good thing.'

for progressive MS. Over 1,000 people will take part in MS-STAT2, testing to see if simvastatin can slow disability progression for people with secondary progressive MS.

## Smarter trials

Last year, we got the disappointing news that none of the three drugs tested in our MS-SMART trial slowed MS progression.

But this 'multi-arm' trial showed

us we can effectively test many potential treatments for progressive MS at once. By doing so, we got the results up to ten years earlier than we would have done using a standard clinical trial set-up.

Find out more at [mssociety.org.uk/multidrug](https://www.mssociety.org.uk/multidrug)

### Faster trials

We need to find faster ways to see if a drug is working in a clinical trial.

By giving participants regular MRI scans, researchers hope to be able to detect early changes that give an indication of effectiveness before changes in disability are seen.

And by looking at ‘repurposed’ drugs that are already used to treat other conditions we can skip phase 1 safety trials, and move straight into looking at whether it’s effective for people with MS.

Our phase 2 trial to see if the cancer drug bexarotene can help repair myelin will be completed in autumn 2019.

### Inclusive trials

Disability progression is often measured using the Expanded Disability Status Scale (EDSS), which relies on changes in mobility to show how effective a treatment is. This means people with more advanced MS, who use a wheelchair, are often excluded from trials.

Using an alternative measure, called the 9-hole peg-test, researchers are now seeing if DMTs can preserve arm and hand function for people who use a wheelchair. The ORATORIO-HAND trial was announced last year.

### A mega-trial for MS

It’s now time to bring all these advances together. We think that the best way to find treatments for everyone living with MS is to set up a trial ‘platform’. We want to test many different drugs at the same time and involve as many people as possible, with all forms of MS.

So we’re working with the UK’s leading MS researchers, clinicians, and people with MS to make this happen.

Right now we’re funding underpinning studies to work out the best way to choose the drugs to be tested, what infrastructure is needed and how to get the answers we need quickly. These studies will finish in the late summer and then we’ll begin establishing a UK clinical trials platform for MS.

Find out more at: [mssociety.org.uk/trialconsortium](https://www.mssociety.org.uk/trialconsortium)

## Current Trials

### MS-STAT2 trial

**Phase:3 | Status: recruiting**

An earlier trial showed that the cholesterol-busting drug simvastatin can reduce brain shrinkage in secondary progressive MS. This trial will test if it can also slow disability progression and will take six years to give a definitive answer. Visit [ms-stat2.info](https://www.ms-stat2.info) to find out more about taking part.

### Bexarotene trial

**Phase: 2 | Status: recruitment complete**

Bexarotene is already used to treat cancer, but researchers think it could also boost myelin repair in MS. The trial is looking at people with relapsing MS who are taking a DMT, but we believe repairing myelin will help with both relapsing and progressive MS.

### ORATORIO-HAND trial

**Phase: 3 | Status: recruiting**

Researchers think that ocrelizumab, which is currently licensed for relapsing and early primary progressive MS, could also help people with advanced primary progressive MS. The trial will involve 1,000 people from multiple countries, including the UK. Visit [roche.com/media/releases/med-cor-2018-06-14htm](https://www.roche.com/media/releases/med-cor-2018-06-14htm) to find out more.

### DELIVER-MS

**Phase: 4 | Status: recruiting**

We know that DMTs work for relapsing MS, but this trial involving 800 people in the UK and US will tell us whether it is better to start with more aggressive treatments early or whether to go more cautiously to avoid potential side effects of stronger medicines. Visit [deliver-ms.com/](https://www.deliver-ms.com/) to find out more.



# The hunt for an MS diet

Research Network member **Ghazia Ahmed** asks dietitian **Dr Conor Kerley** from the Dublin Institute of Technology if the food we eat can help manage MS

**W**e know that healthy eating is important, but have you ever wondered if following a specific diet might actually help your MS symptoms?

## How important is nutrition for MS?

Recent statistics suggest that poor nutrition probably contributes more to death and disability in the general population than smoking or lack of exercise. And it's starting to play a bigger role in treating and preventing chronic conditions like diabetes, obesity and some cancers.

There currently isn't much data on whether nutrition is a problem in people with MS. But we know nutrition is important and a healthy diet is beneficial for everybody.

## Why is research into diets for MS so tricky?

Nutrition is notoriously difficult to study as it's hard to accurately track what people eat. There are many online anecdotes

claiming benefits, but we generally only hear from those feeling well, not the negative experiences.

To get a better understanding of the long-term effects on health – both good and bad – of a change in diet, we need clinical trials that last a long time. There is at least one study in the US comparing the Swank and Wahls diet (see box right), which is exciting, but it's only looking at the effect on MS fatigue.

## Should I be following a specific MS diet?

There's no evidence that following a specific diet is best for MS. But some people find that following a special diet makes a difference to how they feel, and can offer a sense of control over an often unpredictable condition. Most experts advise on reducing saturated fats and increasing vegetables, fruit and healthy fats. Before considering a special diet, you should talk to your GP about a referral to a dietitian. Approach any change with care to make sure that your diet isn't too restrictive and that you're still getting all the nutrients needed. An unbalanced



diet can make symptoms, such as fatigue, worse.

### What is 'leaky gut syndrome', and is it important in MS?

The theory behind 'leaky gut syndrome' is that the cells in our intestines become 'loose'. These gaps let large molecules of food, including gluten, legumes and dairy, which should be kept in the digestive system, enter the blood.

Studies have suggested MS is associated with a leaky gut. It's not known if this is a cause or an effect of the condition, but having a leaky gut can increase levels of inflammation in the body.

The Wahls and the Best Bet diets were developed with leaky gut syndrome in mind. It's an interesting area of research but the evidence around it is still quite weak.

You can hear more from Conor on **twitter @ConorKerley**.

**read**

Learn more about healthy eating and MS: [mssociety.org.uk/dietbooklet](https://mssociety.org.uk/dietbooklet)



Photos: iStock

## Popular diets

### Swank



The most well-known diet associated with MS was designed by neurologist Dr Roy Swank in 1940. It is based on a low fat, red meat free diet.

**Evidence** There have been a number of small studies carried out but these haven't all been well designed and had high drop-out rates, making results hard to interpret.

### Paleolithic



This diet involves only eating foods we think our Palaeolithic (cavemen) ancestors had. That means no processed food or meat from domesticated animals.

**Evidence** There's little research into whether this diet affects the course of MS.

### Best Bet



It focuses on removing "problem foods" associated with leaky gut syndrome, and eating a variety of fish, fruit and vegetables, nuts, seeds, and poultry. It also recommends having allergy tests to discover other foods that should be avoided.

**Evidence** There is very little research to back completely avoiding food types like legumes and gluten.

**What the evidence says:** there's lots more to discover, but you should be able to cover all your nutrient needs from a well balanced diet, with some specific supplements if necessary.

### Wahls



This is a modified version of the Paleolithic diet, with the addition of more vegetables like cabbage, mushrooms and onions.

**Evidence** A small study reported an improvement in fatigue with this diet, but the study also included other lifestyle changes and had no comparison diet.

### Ketogenic



This is a high fat, low carbohydrate, moderate protein diet.

The body burns fat instead of carbohydrates as fuel source in a chemical state called ketosis, which is not without risk.

**Evidence** The evidence is inconsistent and at an early stage in the context of MS.

### Overcoming MS



This was designed in 1999, by Professor George Jelinek. It suggests cutting out dairy and meat, and reducing fat intake – particularly saturated fat. It also recommends taking supplements, particularly of omega 3 and vitamin D.

**Evidence** Research into this diet has not provided conclusive evidence of its benefits. In Melbourne, there is ongoing research into people following the diet and whether it's effective.

# Uncovering the mysteries of myelin repair

We visited **Dr Veronique Miron** at the University of Edinburgh to find out more about her ground-breaking research

## How did you get involved in MS research?

I've always been interested in the brain and how it can change – particularly in the context of conditions like MS. Growing up in Canada, a place where MS is very prevalent, I was aware of the impact it can have on people's lives. I wanted to help. So I chose to focus my PhD on understanding more about regeneration in MS. I've carried this forward to my own lab.

## What does a typical day in the lab look like for you?

Every day is different, stimulating and challenging! My work involves guiding my team to design experiments and analyse the results. I also spend time meeting with fellow researchers to discuss ideas, and reading published studies to learn about new research. It's also important to share our work with the public and other researchers, so I often get out of the lab to attend talks and present our work at conferences.

## What exciting MS research projects are you working on at the moment?

My lab is really interested in finding out more about how we can repair myelin. Our bodies have an amazing capacity to repair myelin, but we know that as MS progresses, the myelin repair process becomes less efficient and damage accumulates. In order to stop MS, we need to be able to repair this damaged myelin.

A few years ago we found that a protein called activin-A plays a role in myelin repair. Since then we've been finding out more about how it works, by identifying the receptors it affects. Now, we'd like to test whether existing drugs can also target activin-A receptors to

improve myelin repair. We hope that any drugs we find could be used as treatments for MS in the future.

You can read more about Veronique's myelin research project here: [mssociety.org.uk/activin](https://mssociety.org.uk/activin)

Photo: Joe McGorty





I'm also currently supervising a really talented PhD student. She's investigating proteins that are released by immune cells in the brain called microglia. We've seen that these proteins can also support myelin repair, which is really exciting.

Find out more about microglia here: [mssociety.org.uk/myelintarget](https://mssociety.org.uk/myelintarget)

### What does being a PhD supervisor involve?

It's my job to guide my students to carry out a research project, while helping them to become independent and skilled scientists. The most rewarding part of being a PhD supervisor is seeing my students develop into confident, motivated, and skilled researchers.

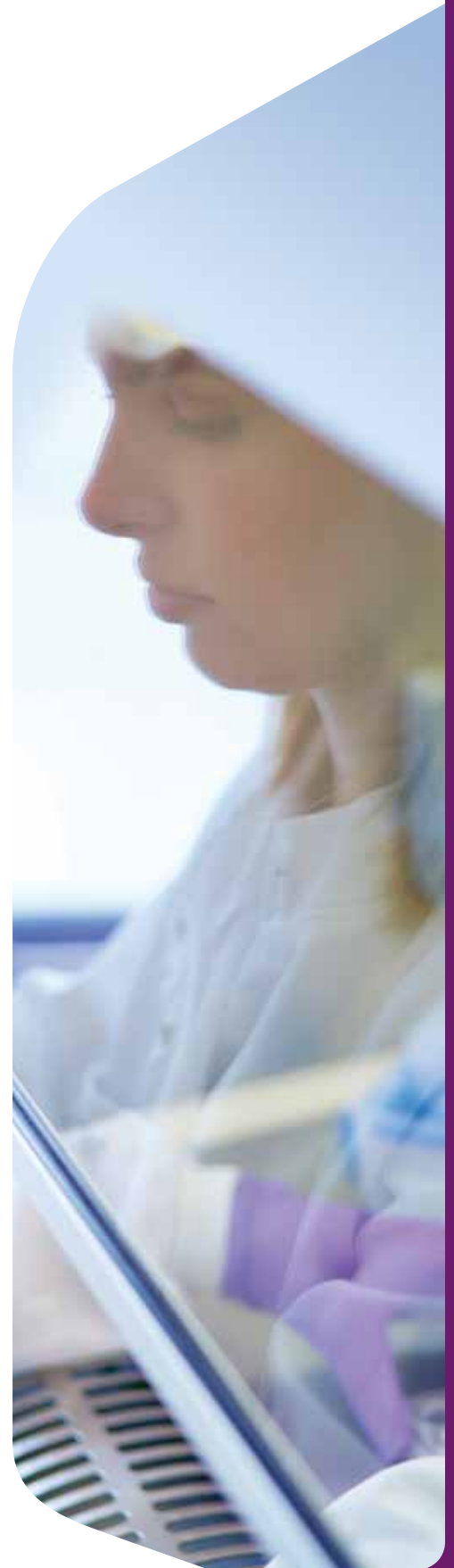
Many breakthroughs in MS research and treatment come from young researchers carrying out projects in the lab. My goal is that at the end of a PhD, the student has contributed to our understanding of MS, is motivated by research and has the skills and confidence to pursue a successful career.

watch

Meet our researchers and find out more about the cutting edge research that we fund on our YouTube channel [mssociety.org.uk/veronique](https://mssociety.org.uk/veronique)

MYELIN

Photo: Ally Dillenburg



# Coming to you



## Hear about research at events all around the UK

**E**very year, members of our research team pack their bags and head off around the UK to talk to the MS community about MS research.

From evening talks led by a local group, to all-day events attended by hundreds of people, there's an event

to suit your needs.

With more than one event a fortnight across the four nations, we hope to see you at one in 2019.

We'll be adding more dates over the coming weeks. Enter your postcode at [mssociety.org.uk/local](https://mssociety.org.uk/local) to find events happening near you.

### watch

This year's **Stop MS Annual Lecture** is at 7pm on Wednesday 1 May. Hear from some of the UK's world leading MS researchers about their plans to stop MS. You can watch live or catch up later at [mssociety.org.uk/stopMSlecture](https://mssociety.org.uk/stopMSlecture)

**"It put a friendly face to the MS thing! The event had a good atmosphere about it."**

**"The whole event gave me hope for the future"**

**"It was good to see that people with MS haven't been forgotten."**

**"We were a little nervous about going but we both had a really positive day"**

**"A truthful factual report about MS research: the good and the bad results"**





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