MS Society

Research matters

The latest developments, innovations and achievements in MS research

Autumn/Winter 2020 · Issue 020

Lifestyle and MS

Can a healthy lifestyle, alongside effective medications, help us live our best lives with MS?

plus Answers to your burning questions on myelin repair and clinical trials for advanced MS

Welcome to Research matters

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Designers
Redactive

This has been a really challenging year for everyone. Research hasn't escaped the crisis unscathed. But we've done everything we can to keep MS research moving and there continues to be lots of exciting discoveries. You can read about some of the latest developments on **page 4**.

There are still so many things we don't know about coronavirus and researchers around the world are working hard to understand more about how it affects people with MS. Read about some of these studies on **page 5**.

We do know maintaining a healthy lifestyle is good for everyone, with or without MS. So this issue of Research Matters is devoted to the question – can a healthy lifestyle, alongside effective medications, help us live our best lives with MS?

Turn to **page 8** to hear the latest evidence on diet and MS. On **page 14** we hear from a leading health psychologist on the importance of looking after our minds as well as our bodies. And on **page 18** you can hear from the researcher who believes exercise could have even more benefits than we thought.

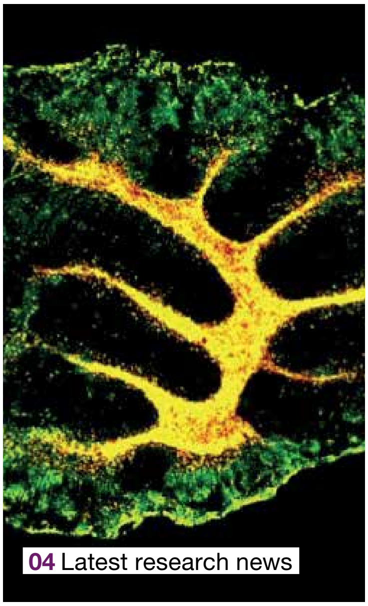
And finally, I'd like to add my welcome to Dr Sarah Rawlings, who will be starting as our new Executive Director of Research and External Affairs in November. Find out more about Sarah on **page 43** of MS Matters.

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

Dr Emma Gray
Assistant Director of Research

contribute

Our Research Network are a group of people affected by MS who help to shape our research programme. Turn to **page 22** to find out how you can get involved.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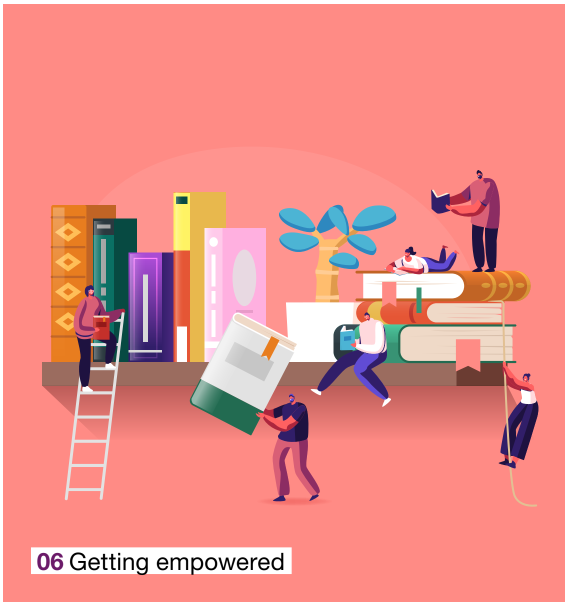
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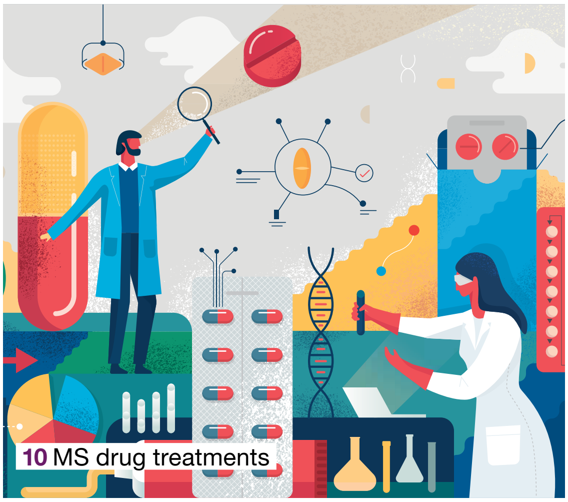
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talk If you'd like to talk to someone in confidence about any of the topics raised in the magazine, the MS Society Helpline is here for you – call free on **0808 800 8000**, or email **helpline@mssociety.org.uk**

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

Research roundup

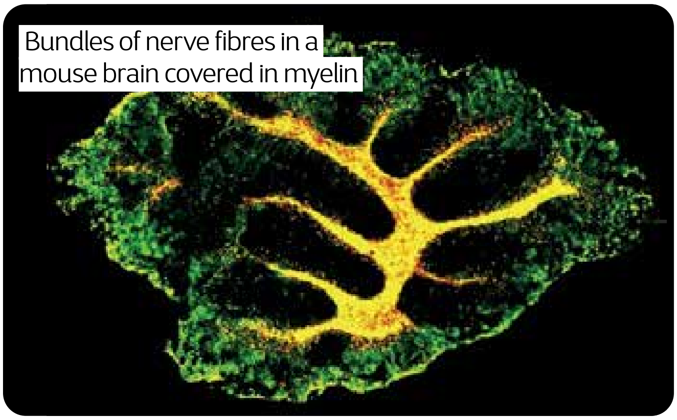
We take a look at some of the latest discoveries from our inspiring MS Society-funded researchers

Clinical trial results take us a step closer to myelin repair

A clinical trial led by researchers at our centres at Cambridge and Edinburgh universities has shown that myelin repair in humans is possible – taking us one step closer to our goal of stopping MS. The trial showed bexarotene (a drug initially developed to treat cancer) is capable of repairing damage to myelin – the protective coating that surrounds nerve fibres, which is damaged in MS.

Unfortunately, participants in the trial experienced severe side effects, which means bexarotene will not be taken forward. But this trial has given us strong evidence that myelin can be repaired in humans.

And we're excited to be funding a new clinical trial at our Cambridge centre to see whether a combination treatment of the drugs metformin and clemastine are able to promote myelin repair. This new research will build on the lessons learned from the bexarotene trial. The trial will kick off in 2021 with 50 participants with relapsing MS.



Bundles of nerve fibres in a mouse brain covered in myelin

Credit: Francesca Pieropan

New trial for people with advanced progressive MS

A new trial called ChariotMS* will test whether cladribine, a drug developed for cancer and already being used to treat relapsing MS, can slow down the worsening of hand and arm function for people with advanced MS.

There are currently no disease modifying therapies available for people with MS who aren't able to use their lower limbs. Traditionally, walking ability has been the key measurement of whether a drug is effective, so many people who use wheelchairs have been unable to take part in MS trials.

This ground-breaking trial will be led by Professor Klaus Schmierer at Queen Mary University of London and Barts NHS Trust.

*ChariotMS is funded by the Efficacy & Evaluation Mechanism Programme - a Medical Research Council & National Institute for Health Research partnership, along with Merck Serono, Barts Charity, the National MS Society in the US and ourselves.

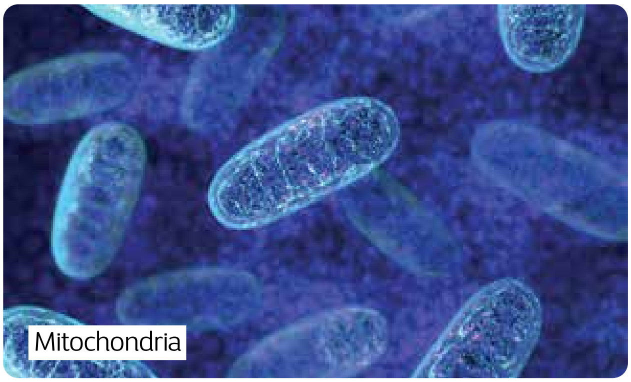
Photos: iStock, Shutterstock

Nerves may get an energy boost from diabetes drug

In MS, nerves carry messages less efficiently than they should. And they need more energy to compensate for this.

Researchers at the University of Edinburgh have shown, for the first time, nerves have the natural ability to boost their energy supplies after being damaged. They do this by moving mitochondria (the energy powerhouse of cells) to the damaged part of the nerve fibre.

This process alone isn't able to provide enough energy to meet the increased energy demand caused by myelin damage. But the researchers also discovered pioglitazone, an existing diabetes drug, could further increase the number of mitochondria in the nerve fibre. This produces more energy and protects the nerve fibres in mice from additional damage. The next step would now be to find out whether we can see the same effect in human brains.


Mitochondria

read

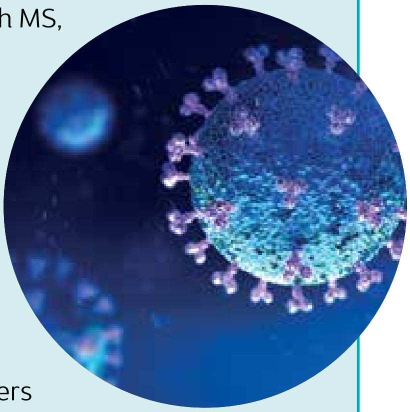
You can catch up on all the latest MS research news on our website: **mssociety.org.uk/research/latest-research**

Coronavirus and MS

Many factors affect our individual risk of COVID-19. Researchers around the world, including some funded by the MS Society, have been working hard to understand more about how COVID-19 is affecting people with MS.

For example, findings from a survey by the UK MS Register showed that during the early phase of the pandemic, when strict lockdown measures were taken, people with MS had a similar chance of getting COVID-19 as the general population.

Researchers in China observed that 1,804 people with MS, of whom about half were taking a DMT, did not have an increased risk of getting COVID-19, regardless of whether they were on a DMT.



And in a study of 347 people, researchers in France found that those with more severe MS were more likely to get more serious forms of COVID-19. Older people and those who were obese were also more likely to get more serious forms of COVID-19. But people on DMTs were not more likely to get more severe COVID-19 symptoms than people not taking them.

What does this mean for me?

Our medical advisors are closely following what's happening with MS treatments and COVID-19. Visit our webpages on COVID-19 to find out what we know right now: **mssociety.org.uk/covid19**

Getting empowered

Katherine Bliss, whose daughter lives with MS, asks whether getting actively engaged in our healthcare can empower us to make informed choices about our MS, from lifestyle changes to medication

For some people, their natural reaction on receiving an MS diagnosis is to learn as much as possible about the condition. They Google different treatment options, ask their doctor lots of questions and read about other people's experiences on internet forums. Other people may not want or be able to do much of this at all.

MS neurologist Professor Gavin Giovannoni is part of an international group of experts who've been exploring the impact of this difference.

Professor Gavin Giovannoni

Katherine Bliss

Engagement improves quality of life

Gavin says research across lots of different diseases shows the positive effects of getting people actively involved in their own healthcare.

He tells me about a colleague from Germany who found that people with MS who completed a programme where they learnt about MS science, reported improved quality of life.

They don't know if you'd see the same effect on MS-specific outcomes such as reduced relapses, but Gavin suggests having a good quality of life is arguably the most important outcome of all.

Challenging assumptions

Gavin says some healthcare professionals still make all the decisions about people's treatment without involving patients themselves. He believes if people with MS had better understanding of how different treatments could impact their MS, they may get more involved in decision-making.

For example, he says, research shows more intensive treatment can delay MS progression. If you know about this research, you're able to proactively ask your doctor about it.

"The engaged patient shops around," Gavin says. If people with MS are encouraged to learn about all the options available, they're more able to challenge what they're told, and clinicians are more likely to involve patients in their own care.

Making healthy choices

Engagement isn't just about medication.

He tells me most people are aware of the value of healthy lifestyle choices in relation to overall health, MS symptoms, and increasingly, MS itself. But, he says, in general the rate at which people in the UK actually adopt a healthy lifestyle is "pretty shocking".

He believes part of the issue is you might not feel tangible benefits of lifestyle changes for a few decades. That's why engagement is "all about helping people educate themselves about their condition – the more knowledge you have, the more likely you are to adopt helpful changes".

The barriers to engagement

Unfortunately, Gavin says, it can be difficult for people to actively engage with their healthcare if

Photos: iStock

they're worried about other things in life.

Poverty, poor housing, other health conditions can all make simple survival the main priority. He says "you might blame some people for, say, drinking or smoking, but actually they might live extremely stressful lives and that's part of the stress response".

Even if you put programmes in place to help people get engaged, you're likely to miss a chunk of the MS population. If you don't have a smart phone or internet access for instance, he says, you might get left behind.

Improving engagement

Gavin is trying to find ways to help people get better acquainted with their MS. He and his colleagues run programmes such as Digesting Science, which encourages families to learn about the science of MS.

Recently, they've noticed signs of an extra benefit of these programmes - when people get involved, they start socialising together and making new friends.

He says it's already well-known that in the general population, there's a strong link between loneliness and poor health.

So to find out whether the data supports their observations, they've obtained funding for a PhD student to research whether increasing the amount someone engages in activities to learn more about their MS leads to increased "social capital" (the number and quality of real supportive relationships you have with other people).

Evidence is key

Gavin ends on a note of caution. He says it's possible to go "overboard" with doing your own research. There's always the risk that you become persuaded by ideas that aren't evidence-based.

Some may be harmless, as long as they don't replace the treatment offered by a healthcare professional. Others may be counter-productive or even damaging.

Turn the page to start reading about some of the latest reliable evidence on both lifestyle and disease modifying treatments.

Can my diet make a difference to my MS?

Our Research Network member **Sarah Rees** talks to two researchers about one of the most hotly-debated topics in MS research: the impact of diet.

“Is there anything I should be eating – or avoiding?” This may have been one of the first questions you asked following your MS diagnosis.

There have long been claims around diet and MS. Back in the 1940s, Dr Roy Swank developed a diet that he suggested could help MS. Anecdotally, many people with MS report feeling better when they follow a specific diet.

But still no consensus on the effect of diet on MS exists.

Dr Shelly Coe, a senior lecturer in nutrition from Oxford Brookes University says: “It’s important we have solid research into MS and diet, otherwise people search on the internet and may find diets or foods that don’t have evidence behind them.”

So what reliable evidence is available?

read

Learn more about healthy eating and MS: **mssociety.org.uk/diet-booklet.**

Over 2,000 diet studies

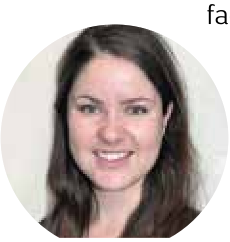
One specialist often asked this question is Canadian neurologist Dr Natalie Parks. “I felt I needed to have accurate and comprehensive information to give people,” she says, “but there’s wasn’t a current resource available”.

So she took on the mammoth task of completing a Cochrane Review - the gold-standard in the academic world for gathering evidence on a topic.

She reviewed over 2,000 completed studies in different areas of diet, from eating different types of fats to cutting out whole food-groups. “I was surprised at how much research we found,” she says.

Dr Natalie Parks

Sarah Rees



Dr Shelly Coe

Sadly, Natalie reports, “after a rigorous review of the evidence, we did not find high-quality evidence to support a particular diet having an effect on MS outcomes”.

Part of the problem was a lack of studies meeting their criteria for ‘high-quality’ evidence. Often the studies only included a few people or didn’t check if other factors, such as medications, were affecting results.

So for now, medication remains the only means of treating this idiosyncratic

condition (although page 18 has some exciting new data on the effect of exercise on MS).

Momentum in diet research is building

Recently though, momentum has been building, as more researchers become interested in the interplay between what we put into our body and what happens inside it. “Things are very different now to when I started in the field six years ago” says Shelly.

She approaches MS research from a different angle, as a nutritionist.

She is particularly interested in flavonoids, which are compounds found in various plant-based foods including – wonderfully – chocolate. Last year, she found that drinking flavonoid-rich hot chocolate daily could potentially have an impact on MS fatigue. It was a great first step, but now she needs to discover what’s actually happening inside the body that means we see this effect.

Shelly’s following other developments closely, including on nutrients like omega 3s or vitamin B12, although research so far hasn’t been conclusive.

Photos: iStock

“Vitamin D is the one supplement I personally take,” she says. “Although there is conflicting evidence about whether it can impact the symptoms of MS, we know having adequate levels is good for everyone in the UK, and there’s evidence of a link between vitamin D deficiencies and an increased risk of developing MS.”

What’s the answer?

The million dollar question remains: what can I eat to give me the best chance of improving my quality of life?

Unfortunately, research so far offers us little certainty. Neurologist and nutritionist alike remain cautious, advising that a healthy, balanced diet is always the best choice.

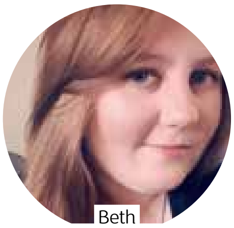
That said, Natalie says: “if there is potential that something might be of benefit with little or no associated risk, then it may be reasonable to try.” Indeed, trial and error is often the way people with MS find an optimal quality of life, such as varying our daily exertions to manage our energy levels.

“MS is unpredictable and different for everyone,” says Shelly, “and we are still in the early stages of understanding diet and MS.”

So we must continue to be ‘experts of our own MS’ while talented researchers explore this promising area of complementary treatment.

What can I do?

- Aim for a healthy, balanced diet with a variety of different foods, so you get enough of all the main nutrients: proteins, carbohydrates, fats, vitamins and minerals.
- Make sure your diet meets your own personal needs, like foods to help with fatigue, the bladder or bowel, swallowing difficulties or keeping a healthy weight.
- Consider regular vitamin D supplements as recommended by the NHS – you could speak to your neurologist at your regular appointment about your vitamin D levels.
- Keep an eye on emerging areas of research, like the possible influence of bacteria and other organisms in our guts (known as the ‘gut microbiome’)


Beth Shorthouse-Ullah


Dr Emma Tallantyre

The evolving world of MS medication

Disease modifying therapies (or DMTs) are the drugs used to alter the underlying biological mechanisms in MS. **Beth Shorthouse-Ullah** lives with MS. She asks **Dr Emma Tallantyre**, a neurologist from Cardiff University, about this constantly evolving world.

What DMTs are available?

Relapsing MS

There are now over a dozen DMTs available for people with relapsing MS.

Primary Progressive MS

For people with primary progressive MS, the first treatment – ocrelizumab – became available in the UK last year. But to be eligible for ocrelizumab, you need to be showing active signs of inflammation on an MRI scan.

Secondary Progressive MS

Earlier this year, the first new DMT for secondary progressive MS in over a decade became available in the UK – siponimod. Siponimod is only licensed for people who have 'active' secondary progressive MS (i.e. they are experiencing relapses or showing new lesions on an MRI scan).

For more information on available DMTs go to **mssociety.org.uk/DMTs**

For many people with MS, taking a DMT is their main tool for protecting their quality of life from the effects of MS.

The lowdown on current DMTs

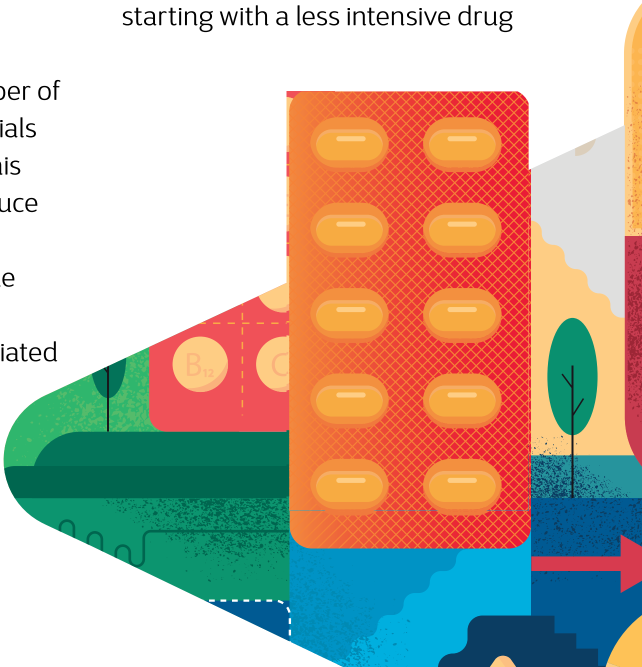
All currently-licensed DMTs work by stopping the immune system from attacking the myelin coat that protects our nerves.

Since the 1990s, a huge number of robust peer-reviewed clinical trials have consistently shown that this type of DMT can effectively reduce MS relapses.

There is also now considerable evidence to show that early intervention with DMTs is associated with a slower build-up of MS disability in the long term. There is even evidence to suggest taking a DMT could increase life expectancy.

But Emma says there is still work to be done in several areas, including:

- Reducing unpleasant or dangerous side-effects
- Deciding whether to start with the highest intensity drugs as soon as you're diagnosed versus starting with a less intensive drug



and only switching to a more intensive one if it is not controlling your relapses

- Personalising the way we give treatments. For example, finding ways to predict which treatment will be most effective given someone's genetics, their MS lesions, their personal circumstance etc.

The future of DMTs and progression

Of course, not everyone with MS has relapses.

Emma tells me: "Research is branching out to look at other treatments that work differently, by protecting nerves from damage or promoting myelin repair". There are now lots of clinical trials exploring potential drugs that work in these areas.

She believes "in the future we could be using a combination of approaches, such as a treatment that works on the immune system in parallel with treatments to repair myelin and protect nerves, which is a really exciting prospect".

read Find out more about the three steps to Stop MS: **mssociety.org.uk/three-steps**

This is exactly what the MS Society's Stop MS Appeal is trying to do. Researchers believe we could have treatments to slow progression for everyone with MS in late-stage clinical trials by 2025.

Lifestyle choices and DMTs

This issue of Research Matters focuses on how a healthy lifestyle can help you live well with MS. And Emma agrees "many lifestyle factors have been linked to brain health and are certainly worthy of further investigation for managing MS."

"When weighing up lifestyle changes it's important to consider three things", Emma says.

"1) What evidence is there that it works in MS?

2) Are there any potential harms? And that includes financial harm. If something is very expensive but there isn't much evidence it works then I'd be inclined to steer away from it.

3) What is the evidence that it can boost general health? Things like exercise and stopping smoking have clear general health benefits for example."

Everyone's MS is different

There's no one-size-fits-all answer. Emma says "some people have changed their lifestyle and their MS has remained stable, but we don't know if that's coincidental. It could be that their MS would have remained stable anyway.

"We need more robust evidence to know for sure," she continues. "As a neurologist I make sure I tell people with MS what we know about different treatments. But I also explain that there's still a lot we don't know."

Illustration: iStock

How do we know if a treatment or lifestyle change is working?

People often talk about a new treatment or lifestyle change 'having a positive effect on MS' or 'helping their MS'. But what does that actually mean?

The confusing thing is, 'a positive effect on MS' can mean a few different things. Whether we're discussing a treatment, a specific diet, or giving up smoking, we need to know what kind of impact it's having on our health.

On the surface

Sometimes, when a healthcare choice - such as starting a new treatment - affects your MS, the change happens on the surface.

Maybe you no longer have the sudden flare-up of symptoms that constitutes a relapse. Or the gradual worsening of disability over time is slowed. These are visible signs that the processes causing the damage in MS are being successfully targeted.

Some approaches to living well with MS are about making a specific symptom feel more bearable, rather than targeting the biological processes underlying your MS. For example, botox injections can reduce bladder problems.

Under the surface

Sometimes, a treatment or lifestyle choice might lead to change that only happens under the surface at first. There might be no obvious difference in your symptoms, but you could have more or fewer lesions on an MRI scan.

And researchers have other ways of detecting change you might not be aware of. Like measuring the volume of your brain.

Our brains all shrink as we get older, but it can happen faster if nerves are being damaged in MS. One way of testing if a new treatment is effective might be to see whether it slows down that shrinkage.

Sometimes progression is 'silent' - it can't even be detected using our standard tests. So researchers are developing special tests to know whether it's happening. You can read more about why this is important on the page opposite.

Turning up the volume on silent progression


Dr Sharmilee Gnanapavan


Jamie Cartwright

Dr Sharmilee Gnanapavan is a Consultant Neurologist and researcher based at Queen Mary University of London. **Jamie Cartwright**, a member of our Research Network, spoke to her about silent progression in MS.

What is silent progression in MS?

"Some people with MS show no evidence of disease activity or 'NEDA'. This means they are not experiencing any MS symptoms and you don't see any lesions on an MRI scan.

But, we're now beginning to believe that even for these people, MS can still be progressing.

Silent progression is something some of us neurologists and MS researchers have suspected for a long time."

Why is this progression 'silent'?

"It's 'silent' because it isn't being captured using existing ways of measuring MS progression.

Normally we ask patients if they have had a relapse in the last year. Often the symptoms they've experienced may not be an obvious relapse in their mind. But minor symptoms could be signs of silent disease progression.

And traditionally, we've used the presence of lesions on MRI scans to track progression in relapsing MS. But when MS is progressing silently there might not be any visible changes on an MRI scan. So we need new ways to track MS."

How can we detect silent progression?

"To help monitor how someone's MS is progressing we can look for biological signals created during the disease process called biomarkers.

Recently, we published work that showed 20% of our patients had high levels of neurofilaments (which indicate nerve damage) in the protective fluid around the brain and spinal cord. Yet they had no recordable clinical or MRI scan activity. These results could help us turn up the volume on silent progression."

How will this help people with MS?

"We need to know if someone's MS is progressing to ensure we can target it with effective treatments. If they have no physical symptoms at the time of testing but something else can show silent disease progression, their treatment can be modified.

As a neurologist, I understand that the idea of MS progressing silently is frightening. I want to help people with MS understand more about their condition and make informed decisions about treatment."

Photos: iStock

The mind and body as equal partners

Research Network member **Caroline Howlett** finds out why mental health is just as important in MS as physical health.

I've always struggled with anxiety, constantly weighing up all the possible outcomes of any action, imagining the worst-possible-case scenario. MS has only made this worse. But I still tend to think of my mental health as something completely separate from my MS.


Caroline Howlett


Professor Rona Moss-Morris

I spoke with Professor Rona Moss-Morris, a health psychologist at Kings College London, about how mental and physical health go hand-in-hand when it comes to living well with MS.

Finding your condition overwhelming

Rona tells me she's seen time and again the effects living with the uncertainty of a long-term health condition can have on well-being.

Of course, feeling distressed is a normal part of life. And sometimes, she says, "it's about accepting something distressing is happening and allowing yourself to feel that."

But distress can become overwhelming and stop you enjoying or even just doing things. That's when Rona believes more support should be available.

I know only too well what it's like when the different bits of MS – pain, fatigue, managing your medicines – get on top of you. "In those really critical times" Rona says, "people may need help to find their illness less overwhelming".

Looking at the whole picture

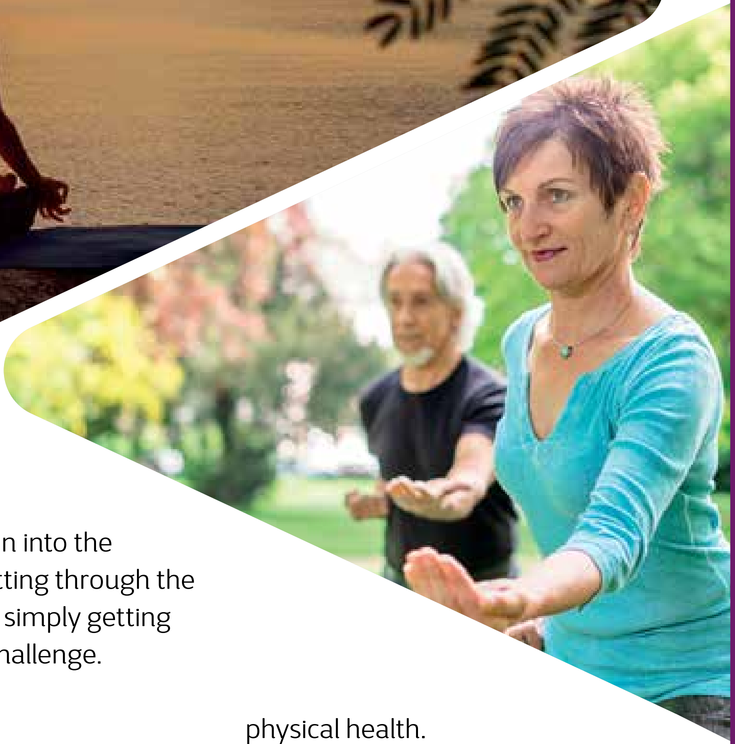
But accessing mental health support services in the UK can be incredibly hard. Often it depends on where you live, or even how pushy you are at doctors appointments.

Part of the problem, Rona says, is "sometimes people think solutions are purely biological and once we've nailed the biological problem, everything else is solved."

Rona believes while it's vital to support people to take the right medications (for both their physical and mental health), we should be doing so alongside taking into account their beliefs, their behaviours and their goals.

Be kind to yourself

Rona wants to support people to get their bodies and minds as healthy as possible. We know there's all sorts of



health benefits of keeping physically active, eating a balanced diet, practicing mindfulness etc.

But she's keen to point out no-one should feel guilty for not doing these things. "We certainly don't want to give the message that if you do all this your MS will go away" she says. "It'll hopefully help you manage your MS better and keep you stronger, but we absolutely aren't suggesting you're a failure if you can't do it".

This will come as a relief to those of us who like enjoying a glass of wine or a day in front of Netflix. Especially given the difficulty of fitting things like a tai chi or mindfulness session into the business of just getting through the day with MS, when simply getting dressed can be a challenge.

An ideal world

So what would Rona like to see in an ideal world?

For her, the key change would be that helping people look after their mental health is seen as equally valid as managing their physical health.

"When we're thinking about routine treatment" she says, "not just the condition itself, but its impact on your whole life, your relationships, your emotions, should be seen as equally important."

What is your subconscious paying attention to?

Rona's research explores how psychological and behavioural therapies can help people with long-term health conditions like MS. She told me about one of the exciting projects in the pipeline.

The work involves trying to understand how people process information subconsciously. Rona and her colleagues hope this will lead to new ways of supporting people with their mental health.

We all know everyone's MS is different. Some of us are much more anxious, some get more fatigued. Rona tells me the standard approach to understanding these differences is by asking people to reflect on their thoughts and behaviours. Now they're also doing experiments to figure out how our brains process information subconsciously.

They want to find out what our brains pay attention to without us noticing, because some people may have more of a tendency to interpret things negatively. And one of her colleagues is already thinking about ways for people with high levels of anxiety to train their brains to focus away from always being captured by more threatening information and towards more realistic interpretations.

Photos: Shutterstock

Over to you

We answer your burning questions on myelin repair and clinical trials

Myelin repair

Q Why is everyone suddenly talking about myelin repair?

In short, because researchers think it might be one of the key ways to slow or stop MS progression, alongside protecting nerves and preventing immune attacks.

In MS, the protective coating around our nerve cells, called myelin, gets damaged. Messages from the brain to the rest of the body find it harder to get through – or can't get through at all. And without myelin, nerve cells are vulnerable to damage. Once a nerve cell is lost it can't be replaced. This is what causes disability progression.

Our bodies have an amazing natural ability to repair myelin. But this repair becomes less effective over time and doesn't work as well as it should in MS. If we can understand why the repair process breaks down and find ways to kick-start it, we could get messages moving again.

Q Who could myelin repair treatments help?

Finding ways to boost myelin repair could slow or stop disability progression for people who have damaged myelin but the nerve cells underneath are still intact. This is most likely to be people with relapsing MS or less advanced progressive MS.

Unfortunately, you can't put myelin back onto nerves that have already been lost. So myelin repair won't be able to reverse permanent disability caused by lost nerves. This is more likely to be an issue for people with more advanced MS.

Q Can I start taking a myelin repair treatment?

Currently there are no myelin repair treatments licensed for people with MS. The treatments in trials – like metformin and clemastine – are only licensed for other conditions. We need to know they are safe and effective for people with MS before they can be prescribed.

read Keep up-to-date on the latest myelin repair developments **mssociety.org.uk/myelin-repair**

Getting the right advice

Our research staff are not medical professionals. This page provides general information. For specific health questions talk to your healthcare professional.

Photo: iStock

Clinical trials

Q Why are people with advanced progressive MS often not eligible for clinical trials?

Traditionally, the regulators have required clinical trials in MS to focus on walking as a measure of how effective a drug is. This means wheelchair users often aren't eligible to take part in trials. It also means we don't have evidence of whether these drugs could help people with more advanced disability.

At the moment, if your score on the Expanded Disability Status Scale (EDSS) is above 6.5 you don't qualify for access to disease modifying therapies. The EDSS measures how much someone is affected by their MS. A score of above 6.5 means you use a wheelchair most of the time.

Q Are there any trials for people with advanced progressive MS?

There is some emerging evidence to suggest that treatments that target the immune system may slow down the worsening of hand and arm function.

The new ChariotMS trial will test whether cladribine (a drug already licensed for relapsing MS) could preserve hand and arm function for people with an EDSS of 6.5-8.5. And the ORATORIO-HAND trial is seeing whether ocrelizumab could help people keep using their upper limbs.

Showing that it is possible to run trials in advanced MS will also enable more people to take part in future trials and help the development of treatments for all forms of MS.

Q How do I find out about trials to take part in?

If you're interested in taking part in a trial, ask your MS specialist to find out about a referral. The NHS Be Part of Research website lists all clinical trials currently recruiting in the UK. You can use this tool to see whether there are trials you may be eligble for – so you know which ones to discuss with your doctor.

ask

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

Exercise and MS: more than symptom management?

Becky Perry

Dr Ulrik Dalgas

Research Network member **Becky Perry** caught up with **Dr Ulrik Dalgas** to hear the latest on what we know about exercise and MS.

When I was diagnosed with MS over twenty years ago I was advised to avoid high-intensity exercise, as it was believed to increase fatigue, and overheating could make symptoms worse. There has been lots of new research since then though! So I was interested to hear from exercise physiologist Dr Ulrik Dalgas from Aarhus University in Denmark.

Ulrik pointed out that exercise benefits the body in many ways and we need to let go of past ideas that people with MS should avoid exercise. “Although there might be temporary flare-ups in symptoms like fatigue or heat sensitivity, those effects usually subside,” he said.

Different types of exercise

- Aerobic, or endurance, exercise is an activity involving many muscle contractions over time, like swimming.
- Anaerobic, or resistance, exercise involves few muscle contractions against heavy load, such as weight-lifting.

Could exercise change my MS?

It’s already been shown that exercise can reduce stress, and improve self-esteem, mood and sleep quality, as well as some specific MS ymptoms like balance problems, fatigue and pain. Now, Ulrik’s team are exploring whether certain forms of exercise could actually have disease modifying effects as well. “We think high-intensity exercise started as early as possible after diagnosis could prevent damage,” he told me.

The team is halfway through a study to determine if they see this effect with people newly diagnosed with MS. They’re measuring whether highly intensive aerobic exercise reduces the number of relapses participants have. If they find that it does, this opens up an exciting new avenue for exercise as another way to actually treat the underlying biology of MS.

Promising results so far...

Recent research has suggested exercise may reduce relapses by around 30%. Ulrik also spoke of one recent study where a control group who continued with their normal lifestyle had seven relapses between them, while people doing very intense aerobic training had no relapses during the intervention.

“These effects are similar to what you see with some DMTs,” said Ulrik, “but although these findings are really interesting they weren’t the focus of the research, so need to be studied further.”

We know that MS affects

brain structure by damaging nerves. But small studies in people with relapsing MS have shown that exercise might actually change that too.

"Resistance training could reduce brain shrinkage, and aerobic fitness can preserve a part of the brain important for cognition," he told me.

Studying exercise

Studying exercise can be challenging! Ulrik's team tries to design studies that are easy to do anywhere, but most studies involve exercising twice a week for about an hour. This could be challenging for many people with MS, but Ulrik hopes it's reasonable for some people to achieve in real life.

"Everyone who signs up for a study on exercise expects to be exercising," he says. "However, researchers need to compare these participants with others who don't exercise."

To help gather information from the wider MS population, Ulrik uses the Danish MS Registry – a database of information about life with MS similar to the UK's MS Register.

Moving forward

So far evidence suggests certain forms of exercise could play an important role alongside disease modifying drugs in helping people live well with MS.

That's why Ulrik feels that everyone should be given information about the importance of a healthy lifestyle, including exercise, when they're first diagnosed.

Another big plus is the lack of side effects: "The side effects are essentially that you are getting in better shape!" said Ulrik.

Ulrik told me many types of exercise can help MS, from yoga to kick-boxing or even climbing. "The key is to find exercise you enjoy or people you enjoy exercising with, so you maintain the activity and its benefits."

So, fortunately, we don't all have to go out and start running marathons. It's more about trying to increase your heart rate and build up your muscles in a way that works for you. That can include anything from sitting-down yoga to wheelchair Zumba.

Making exercise work for you

My chat with Ulrik reminded me how important staying active is for people with MS. I've been recovering from tendinitis this year so have struggled to get around and have also fought with relapses.

Hearing about benefits such as strength and sharper focus, as well as the possibility of disease modifying effects, has helped me find the motivation to start exercising.

Even if I might have a spike in some symptoms, I learnt that this effect would typically go away. And there could potentially be longer-term benefits for my MS as well.

read See our tips for staying active with **mssociety.org.uk/staying-active**

Photo: iStock

Overcoming the challenges of lifestyle research

Professor Richard Nicholas

Ben Marshall

We keep hearing that we need more research on the impact of lifestyle on MS. So what's been holding researchers back? Research Network member **Ben Marshall**, spoke with **Professor Richard Nicholas**, a consultant neurologist, about the challenges of researching lifestyle and MS.

Why is it so difficult to do research into lifestyle changes?

"In order to get robust evidence to support a new drug treatment or lifestyle change that could help people with MS, we need sound scientific studies. There are several reasons why this can be more challenging in lifestyle research than drug trials.

For example, people given a set diet or exercise regime will know they are being watched closely by the researchers and may adapt their behavior, which can make the results less reliable.

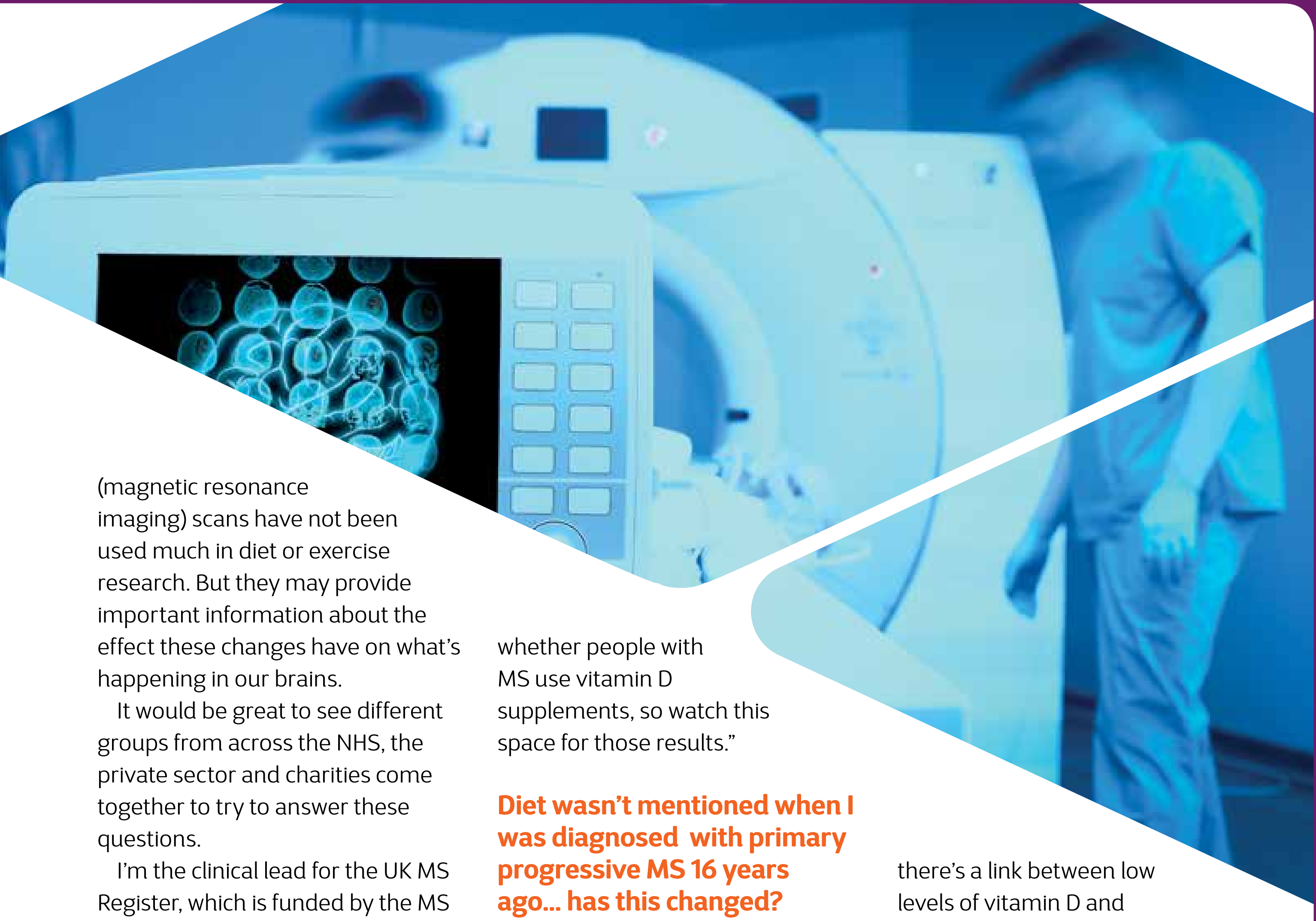
People who take part in these studies may also have better results anyway. Someone who's already interested in living healthily may be more likely to take part in research into lifestyle interventions. So we don't get data from people who aren't already interested in healthy living.

In clinical trials, you control what treatment people are taking, because we give them the pills or injections. But diet research often relies on people providing their own details about their diet. People may not be able to recall what they've eaten accurately. And people will often tell you what they think you want to hear, which can introduce bias.

And lastly, when people change one aspect of their lifestyle, like diet, it can often be part of an bigger change. For example they may use this chance to exercise more. Many people will also be taking DMTs. This can make it difficult to see exactly which change has had an effect."

How can we tackle these challenges?

"I think we need to look at using different ways to measure outcomes. For example, MRI



(magnetic resonance imaging) scans have not been used much in diet or exercise research. But they may provide important information about the effect these changes have on what's happening in our brains.

It would be great to see different groups from across the NHS, the private sector and charities come together to try to answer these questions.

I'm the clinical lead for the UK MS Register, which is funded by the MS Society and provides a huge database of information from people with MS. It connects survey data from people with their clinical data, so we get an overall picture of someone's condition.

By using the MS Register, we're now able to ask large numbers of people about their lifestyle over a long period of time. This solves problems in some previous studies, such as having small numbers of participants or only looking at data from a few weeks or months. The Register has been going for over a decade and has over 17,000 people signed up.

Researchers have already used the MS Register to gather data on whether people with MS use vitamin D supplements, so watch this space for those results."

Photos: iStock / Shutterstock

Diet wasn't mentioned when I was diagnosed with primary progressive MS 16 years ago… has this changed?

"Yes, things have moved on. I encourage all my patients to adopt a healthy lifestyle, including a sensible diet, regular physical activity and only drinking in moderation.

Changes of this nature will have a positive impact on everybody, whether or not they have MS.

Giving up smoking is the one lifestyle change we are certain will have a positive effect on both MS symptoms and progression. So if someone with MS smokes, I strongly advise them to give up.

I also suggest people take vitamin D supplements, which is recommended by the NHS for everyone in the UK. We know there's a link between low levels of vitamin D and increased risk of MS, although we don't yet know whether vitamin D could be an effective treatment.

I see lifestyle changes as another tool in the MS toolbox and part of an overall approach including taking disease modifying therapies, and other support like physiotherapy.

These changes don't need to be too extreme. Step up slowly – a healthy lifestyle is just a part of a life worth living."

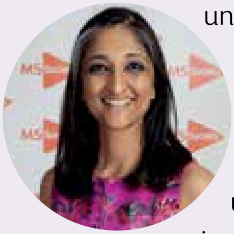
read

Read our page on vitamin D research **mssociety.org.uk/vitamind**

Join the Research Network

The MS Society Research Network is a group of people affected by MS who help shape our research programme. We hear from **Jenny Robertson**, who runs the Network, and **Trishna Bharadia**, who joined the Network to help shape MS research.

Trishna says:



"Being part of the MS Society Research Network has been invaluable in helping me to better understand what goes into MS research. It's enabled me to develop new skills, get to know researchers, scientists and clinicians, and keeps me updated about the latest happenings in the MS world.

You can take on as much or as little as you like and the MS Society is always there to help you if you're unsure. If you're interested in taking an active role in the way MS research is developed and undertaken then this is a great way to get involved.

It's particularly important to me because traditionally there has been a lack of diverse representation of people within clinical research, and MS is no exception. So for me it's also about making sure that, as an Asian woman with MS, my views are being represented to help shape MS research."

Jenny says:

"The Research Network makes sure all the research we fund reflects the needs and interests of people living with MS. And they help us talk about it in a way that's accessible to everyone.

Anyone who lives with a diagnosis of MS or is a non-professional carer for someone with MS can get involved. It doesn't matter where in the UK you live or how much research experience you have.

If you want to help to shape our research programme and learn more about medical research, and you're happy to discuss your views and work with researchers and other people with MS, we want to hear from you!

There's lots of ways to get involved. Recently, members of our Research Network have shared their thoughts on using virtual reality games as a form of rehabilitation, worked with researchers on a funding application to investigate childhood MS, and interviewed neurologists for Research Matters articles.

We'll provide all the training you need and support you in any way we can."

info

To find out more about how to join our Research Network, simply get in touch with Jenny for a chat on **0208 438 0844** or email **researchnetwork@mssociety.org.uk**

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