

NEWS OF THE ME RESEARCH YOU ARE HELPING TO FUND

# breakthrough

## SCIENCE SUPERTEAMS

in Alabama & Newcastle



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Welcoming our new CEO  
Immune cells and the brain  
Muscle function abnormalities

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## Welcome

*Breakthrough* magazine is published by ME Research UK, a Scottish Charitable Incorporated Organisation that funds research into Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (also known as ME/CFS). The charity has an international remit, and its principal aim is to commission and fund high-quality scientific (biomedical) investigation into the causes, consequences and treatment of ME/CFS. It also aims to energise ME research by identifying potentially important areas for future biomedical research, producing high quality professional reviews and reports, and presenting research at meetings and conferences. *Breakthrough* is an open access publication and, with the exception of images and illustrations, the content may be reproduced free of charge, subject to the terms and conditions found at:

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# In the spotlight

What's happening in the world of ME research and funding



Hello everyone, I would like to take this opportunity to introduce myself. I am Simon Phillips, the new Chief Executive Officer (CEO) of ME Research UK. I am extremely proud to have been invited to take up this role and I very much look forward to helping the organisation deliver its continuing mission of energising ME research.

The charity has a long track record of providing funding for research into the causes, diagnostics and possible treatments of ME. I wish to continue that tradition as well as find ways to increase funding for future research.

I have worked in the charity sector since 2006 and prior to that, in the private sector for many years. There is a huge amount of scientific knowledge within this organisation and I hope that my own background and experience will complement those skills and enable us to

develop and deliver our ambitious goals over the next few years.

ME is clearly a complex, challenging and debilitating condition. ME Research UK funds vital biomedical research across the world and this must remain at the heart of our work. The Board of Trustees, the staff and I are committed to ensuring that focused biomedical research continues in order to find ways to understand, diagnose and treat this condition, which can only happen with your support.

I look forward to talking with and meeting as many of you as possible as we progress together and am contactable through the office in Perth. I am also on Twitter via @MERUKCEO.

I hope you enjoy this issue of *Breakthrough*.

Simon Phillips, CEO  
ME Research UK

## Recycle 4 Charity

Did you know that most makes of inkjet cartridges are recyclable? HP, Dell, Lexmark, Canon, Samsung, Neopost and Brother, but not Epson or Kodak.

Just pop eligible cartridges into the freepost envelope provided and post directly to Recycle 4 Charity. We'll receive a donation for every inkjet cartridge recycled, and you'll be helping the environment too. You don't even need a stamp!

It is cartridges that have circuit boards that have a recycling value when empty. However, cartridges that are damaged, have been refilled previously, have been labelled for another brand like Tesco, PC World or Office Depot, or have labels removed or extra holes cannot be recycled and so please don't send them.



## Shopping at Amazon

There are a number of ways to support ME Research UK when shopping at [amazon.co.uk](https://amazon.co.uk).

But the best thing is that it doesn't cost you a penny more!

There are three ways to help:

- Go to [amazon.co.uk](https://amazon.co.uk) via the button on our website,
- Go through [easyfundraising.org.uk](https://easyfundraising.org.uk), or
- Login to Amazon Smile via the link [meres.uk/smile](https://meres.uk/smile), and select ME Research UK as your charity.

When you shop - they'll donate!



## A thoroughly decent man

### *Farewell to Sir Alex Fergusson*

It is with great sadness that ME Research UK learned of the death of Sir Alex Fergusson on 31st July 2018. Sir Alex represented the Galloway area from the inception of the Scottish Parliament in 1999 until his retirement at the 2016 election, firstly as a regional list MSP for the South of Scotland and then as a constituency MSP for Galloway and Upper Nithsdale (latterly Galloway and West Dumfries).

Such was his standing amongst his fellow MSPs that he was elected as Presiding Officer – a role he discharged with honour, good humour and the utmost integrity – but only once he was assured that he could continue to serve his constituents' interests.

Unlike either of his predecessors, Sir Alex returned to the backbenches after four years as Presiding Officer, and continued to represent his constituency, and its farmers in particular, with great skill and passion until his retirement. He was knighted in the 2016 Birthday Honours – stating in typically self-effacing manner that the honour resulted in 'an ecstatically proud, happy and excited 96-year-old mother'.

Sir Alex's involvement with ME began when his son became bedridden after three years of increasing ill health. As part of his duties as a parliamentarian, Alex attended a meeting on ME at the Scottish Parliament and, after listening to the speakers, recognised that ME might





© Scottish Parliamentary Corporate Body

be the cause of his son's illness. Afterwards, he spoke to Dr Vance Spence, Chairman of ME Research UK, who gave advice and suggested that his son see a paediatric consultant with experience working with children with ME.

This was the start of a long journey for Sir Alex and his family – a journey detailed in his wife Lady Merryn's book *What Is Wrong With ME*. Fortunately, over the following years, Alex's son began to recover gradually, and he is now living a successful adult life.

Thereafter, Sir Alex became a stalwart advocate and influential ally in the creation of the Scottish Parliament's Cross Party Group on ME in 2001, a group of which he was deputy convenor until 2003 and convenor until 2007. Dr Vance Spence worked closely with Sir Alex throughout this time, and their de-

termination and input culminated in the establishment of the Short Life Working Group on ME/CFS.

At Kirkcudbright Parish Church, the congregation attending his memorial service included parliamentarians such as Deputy First Minister John Swinney, Scottish Conservative leader Ruth Davidson, current Presiding Officer Ken Macintosh, and all former Presiding Officers Lord David Steel, Sir George Reid and Tricia Marwick. As a further mark of respect, flags were flown at half-mast at the Scottish Parliament, as they had been on 31st July.

In delivering the parliamentary eulogy, Scottish Secretary David Mundell highlighted Sir Alex's political achievements and gave a flavour of his other work, including ME campaigner and even Parliamentary Slimmer of the Year. Perhaps his comment that Sir Alex was 'Quite simply the most thoroughly decent man I've ever known' is the most deserved epitaph to a great man.

We extend our sympathies to Lady Merryn; their children Iain, Dougal and Christopher and their families; and to his mother, siblings and Sir Alex's many, many friends.



Scottish Parliament Debating Chamber





## 'Time to transform ME/CFS research'

*CMRC conference brings together UK researchers*

On the 19th and 20th of September, scientists, physicians, patients and carers, and many others with an interest in ME/CFS made their way to Bristol for the fifth annual science conference of the UK CFS/ME Research Collaborative (CMRC).

ME Research UK's Research Director, Dr David Newton, attended the conference on our behalf. He experienced 'a positive, optimistic atmosphere, and a well organised programme of high-quality presentations covering a range of relevant topics, and delivered by enthusiastic participants.'

The CMRC was established in 2013, bringing together researchers,

charities, funders and patients with the aim of driving interest and funding in ME/CFS research, and the Collaborative has recently undergone a change in its charter and the appointment of a new Deputy Chair, Prof. Chris Ponting from the University of Edinburgh.

The 2018 conference was opened by Prof. Stephen Holgate from the University of Southampton, who is the Chair of the CMRC. He emphasised the aim of the collaborative which is to represent ME/CFS organisations with a single voice and to influence change.

The varied programme included presentations from Prof. Cathie Sudlow on the use of big health data and open

science, Cara Tomas on cellular bioenergetics, Dr Nina Muirhead on the education of doctors and medical students, and Dr Mark Jones on engagement of the pharmaceutical industry in ME/CFS drug discovery. Two talks looked at the role of microRNAs in the pathogenesis of ME/CFS, and there was intriguing work from Poland describing the use of whole-body cryotherapy to treat the condition.

The event also included three workshops on activity, nutrition and research priorities, as well as a number of poster presentations. Most of the talks are now available to watch for free on Action for ME's YouTube channel ([bit.ly/2yBIydp](https://bit.ly/2yBIydp)).





## Forward – ME

### *Anniversary celebration*

Members of the Forward – ME Group marked the 10th anniversary of its foundation at the House of Lords on 23rd October 2018. Those who attended wished to thank the founder and moving force behind the Group for all her efforts on behalf of those affected by ME/CFS.

The dedication and work of the Countess of Mar in creating and leading the Group cannot be overstated and, with the end of the All Party Parliamentary Group on ME/CFS, Forward-ME's role in political circles is of vital importance.

Thanks to the Countess of Mar's parliamentary questions and contributions to debates, the profile of ME/CFS has been raised considerably amongst legislators. Having such an influential Chair has also meant that many important decision-makers have accepted invitations to speak to the Group, and have left the meetings more informed about the realities of the illness.

ME Research UK's Vice-Chair, Mrs Sue Waddle, and Secretary, Jonathan Davies, joined other Group members in thanking the Countess of Mar for her work and looking forward to the next 10 years of action.



Easyfundraising is the UK's biggest charity shopping fundraising site. It's simple to use, and it's free. It doesn't cost you a penny extra. When you shop online with one of their 3,328 shops and sites they donate as you shop. Easy!

Retailers cover everything from entertainment to travel – it's

a high street on the Internet! Visit [easyfundraising.org.uk](http://easyfundraising.org.uk) to create an account, register to support ME Research UK, and shop as usual.

You can find your chosen shop via the website, or install a browser plugin. The retailers donate as you buy, and every penny helps our work.









# crosstown traffic



A new study at the University of Alabama plans to investigate **whether immune cells are infiltrating the brain** of ME/CFS patients

Our bodies have two distinct immune systems helping to defend us from invaders such as viruses and bacteria.

One immune system protects the brain, while the other, the peripheral immune system, protects the rest of the body. The two employ different kinds of cells (microglia in the brain; T cells, B cells and NK cells in the rest of the body; see Box on page 11) which are separated by what is known as the blood–brain barrier.

But what happens when the blood–brain barrier is damaged, allowing cells from the peripheral immune system

to infiltrate the brain? And might this situation be happening in people with ME/CFS, so driving their symptoms.

These are the questions addressed by a project led by Prof. Jarred Younger at the University of Alabama, that ME Research UK has offered to fund.

## Activated immune system

Many of the characteristic symptoms of ME/CFS suggest that the immune system is activated in the brains of people with the illness. Fatigue, pain sensitivity, cognitive problems and sleep disturbances are all common in people with ME/CFS, and all can be caused by the inflammatory chemicals that are released when the

immune cells in the brain are activated, a process called neuroinflammation.

During neuroinflammation, the blood–brain barrier can become damaged allowing peripheral immune cells to infiltrate the brain, and this has been observed in other neuroinflammatory disorders such as multiple sclerosis. These infiltrating T cells can then push the native microglia of the brain into an activated and inflammatory state.

To investigate whether this is happening in ME/CFS, Prof. Younger and his team plan to track peripheral immune cells and see whether they do indeed break the blood–brain barrier and infiltrate the brain.





*‘What happens when the blood–brain barrier is damaged, allowing peripheral immune cells to infiltrate the brain?’*

This is quite a challenge, and the team has developed a new technique where they will take a sample of the patients’ own peripheral immune cells, label them with a radioisotope called zirconium-89, and inject them back into the patients. The investigators will then use positron emission scanning to track the cells and detect whether they enter the brain.

The plan is to study 15 women with ME/CFS and 10 age-matched healthy control women, and to scan them

at 24 hours and then 96 hours following the injection. This should allow enough time for the cells to cross the blood–brain barrier (if they are going to).

As well as advancing our understanding of the pathogenesis of ME/CFS and the role of the immune system, the results of this study may indicate that neuroinflammation is a worthwhile target for treatment of the illness, and even help in establishing a diagnostic test that can distinguish between patients and healthy control subjects. ●



## A guide to some of the terms used

**B cells** – A type of white blood cell, and part of the central immune system. When B cells encounter a foreign body, they secrete antibodies to attack the invader.

**Blood-brain barrier** – This is a semipermeable membrane that prevents cells, particles and large molecules from moving from the blood into the brain or spinal cord.

**Microglia** – These small cells are found in the brain and spinal cord, and act as the main immune defence of the central nervous system.

**NK cell** – Natural killer cells are also white blood cells. As their name suggests, they are involved in the destruction of tumours and cells that are infected by viruses.

**Positron emission tomography** – An imaging technique which detects gamma rays emitted by radioactive tracers that have been introduced into the body.

**T cells** – Another kind of white blood cell involved in the central immune system. There are several types of T cells which all have different functions.

**Zirconium-89** – A radioactive tracer used in positron emission tomography.

## Prof. Jarred Younger

Although this is the first time Prof. Younger has been offered a research grant from ME Research UK, he has a considerable track record working in ME/CFS, fibromyalgia and other chronic pain conditions.

He currently heads up the Neuroinflammation, Pain and Fatigue Laboratory at the University of Birmingham in Alabama, and is also involved with the ME/CFS Collaborative Research Centre at Stanford University.

The stated aim of his laboratory is 'to end chronic pain and fatigue for millions of people across the world'; and to accomplish this the team uses a variety of neuroimaging, pharmaceutical and immunological methods.

Prof. Younger is very keen to communicate his ideas and findings, and has a number of very informative videos posted on YouTube ([bit.ly/2NHDOOT](https://bit.ly/2NHDOOT)), and he was interviewed recently by Joe Cohen on SelfHacked Radio ([bit.ly/2DZznly](https://bit.ly/2DZznly)).



**Jonathan McConathy**, MD, PhD – Chief Radiologist, **Jarred Younger**, PhD – Principal Investigator, **Suzanne Lapi**, PhD – Chief Radiochemist, **Denise Jeffers** – Project Coordinator, **Jennifer Burkemper**, PhD – Radiochemistry Research Associate, **Christina Mueller**, MS – Investigator





# muscle *bound*

Preliminary results from Newcastle are starting to narrow down **the source of muscle function abnormalities** in ME/CFS

**I**t has been only a year since we announced funding for a new research project for Prof. Julia Newton's team at Newcastle University, continuing their investigations of the abnormalities in muscle function experienced by people with ME/CFS. But the work is already bearing fruit, and the group published their first results earlier this year.

For a more detailed discussion of the background to this research, have a read of the article on pages 12 to 15 of the Autumn 2017 issue of *Breakthrough* (available on our website). But here it is in a nutshell.

In their exploration of the mechanisms underlying the abnormal muscle fatigue commonly reported by people with ME/CFS, the Newcastle team has previously obtained muscle biopsies from patients, from which muscle cells were cultured and examined in standardised laboratory conditions. Electrical pulses were applied to these cells to simulate the muscle contraction that occurs during exercise.

## Impaired AMPK activation

AMP-activated protein kinase (AMPK) has an important role in regulating energy in the cell and is normally activated

during muscle contraction. The researchers found that this was impaired in the cultured muscle cells, and that the uptake of glucose was reduced.

Although AMPK was not activated by simulated muscle contraction in these cells from ME/CFS patients, later experiments suggested that it could be activated by treatment with metformin. This raises the possibility of whether a drug such as this could improve muscle function in patients.

To look at these abnormalities in more detail, and to trace where they occur in the signalling pathway, ME Research UK awarded further funding to





Prof. Mark Walker, Dr Audrey Brown, Prof. Julia Newton and Cara Tomas at Newcastle University

***‘AMPK was not activated by electrical stimulation but could be activated pharmacologically’***

Dr Audrey Brown, Prof. Newton and colleagues to continue their investigations.

The first part of this work, published in *Bioscience Reports*, used a similar methodology to that in their previous study to investigate whether AMPK and glucose uptake in muscle cells from ME/CFS patients could be activated by treatment with pharmacological agents.

**Metformin and compound 991**

Skeletal muscle cells were obtained from eight patients with ME/CFS and seven healthy control subjects. The cultured cells were then treated with metformin or with compound 991. Metformin is a drug commonly used to treat diabetes, and is known to activate AMPK indirectly via other mechanisms. Compound 991, on the other hand, was designed specifically as a direct activator of AMPK.

Treatment with metformin increased both AMPK activation and glucose uptake, and this was true for muscle cells from ME/CFS patients and from healthy control subjects. Similarly, compound 991 treatment also significantly

increased both parameters in patient and control cells, and the effect on glucose uptake was similar to that expected following treatment with insulin.

Therefore, while AMPK from ME/CFS patients was not activated by electrical stimulation of the cells, it could be activated pharmacologically, and there are two important conclusions that might be drawn from these findings.

Firstly, this abnormality in signalling can potentially be bypassed by pharmacological treatment, and the investigators suggest that this adds further support to the idea of conducting a clinical trial of an AMPK activator in ME/CFS patients. Secondly, their results indicate that the signalling defect lies further up the molecular chain, possibly involving upstream enzymes such as LKB1 or CaMKK.

These findings represent the fascinating first step of this project, which will continue to look more closely at the mechanisms underlying muscle fatigue in ME/CFS, and hopefully to identify potential targets for therapy. ●

# Research bites

A brief round-up of recent research from around the world



## Epstein-Barr virus infection

*Pedersen et al., Brain, Behavior, and Immunity, 2018*

Epstein-Barr virus (EBV) infection may be a trigger of ME/CFS, but which infected individuals will later develop the condition? A study from Norway has attempted to answer this by recording possible predictors in 200 adolescents with EBV infection, and then documenting who had chronic fatigue six months later. Baseline factors associated with the development of fatigue included sensory sensitivity, pain severity, functional impairment, plasma C-reactive protein and vitamin B12 levels. So, fatigue in these individuals appears to be predicted by baseline symptoms and function rather than immune factors.



## Altered oral microbiome

*Wang et al., PLOS ONE, 2018*

The microorganisms comprising the microbiome of the gut are known to be altered in ME/CFS, but the oral microbiome may also be important, particularly because oral mucosal inflammation is commonly reported in the illness. To investigate this further, Chinese researchers took saliva samples from 46 patients and 45 control subjects, and analysed them for a range of oral bacteria. While the microbial diversity was similar in these two groups, ME/CFS patients had a higher abundance of some bacterial genera and were deficient in others. These bacteria were typically involved in amino acid and energy metabolism.



## Exercise testing

*Stevens et al., Frontiers in Pediatrics, 2018*

Cardiopulmonary exercise testing (CPET) is used to assess an individual's physiological response to exertion, through the measurement of cardiovascular, respiratory and metabolic parameters. A new article by researchers in California describes a two-day CPET procedure for patients with ME/CFS, in which the test is performed twice, 24 hours apart, to examine the effects of post-exertional malaise on physiological function and energy production. The authors discuss how the technique can help reveal abnormalities in function and could potentially be used to provide an objective endpoint measure in clinical trials.



## Brain glial activation in fibromyalgia

*Albrecht et al., Brain, Behavior, and Immunity, 2018*

On page 9 of this issue, we describe a new ME Research UK-funded study investigating whether immune cells are activating the microglia of the brain in individuals with ME/CFS. Researchers from the USA and Sweden have been looking at a similar thing in patients with fibromyalgia. Using positron emission tomography, they found increased levels of a protein known to be upregulated in activated microglia (possibly to a greater extent in those with higher ratings of fatigue). These findings provide evidence that glial activation may play a role in the pathophysiology of fibromyalgia.





# Friends united

Some of our supporters' fundraising activities. If you would like to support ME Research UK and raise funds for ME research, visit our website for a range of ideas.

## Channel crossing

Swimming the English Channel has become an iconic challenge of endurance ever since Matthew Webb first completed the feat in 1875. In August this year, a team of six adventurous athletes from Jump Trading joined the channel crossing club when they made their own 21-mile crossing, swimming in relay from Dover to Calais. The event has so far raised a truly staggering amount in this year's challenge, which the swimmers chose to share between two charities

that are close to the hearts of the team members, including ME Research UK. What an incredible achievement! Many thanks to all those in team Jump X and to all those who sponsored them.

## Marathon triumph

The Brighton Marathon, which this year was held on 15th April, is currently the UK's second largest marathon. With a stunning backdrop of the sea, and in one of the country's most vibrant cities, it now forms part of a whole weekend

of running events which attracts more than 15,000 participants and more than 150,000 spectators. ME Research UK is really proud to have had Marice Lunny and Rachel Harris running the course in aid of our work, and we'd like to say a huge thank you to them.

## Movie night

We would like to thank everyone involved in the very successful screening of the award-winning documentary *Unrest*, at Perth Theatre in May. This moving



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**01 Robert and Rachel Craig** celebrate completing the London Marathon

**02** The dynamic Celtic Wisemen Perpetual team embark on their ride.

**03 Marice Lunny** proudly shows her medal for completing the Brighton Marathon

**04 Jennifer Brea** of *Unrest* fame

film explores Jennifer Brea's experiences as her health deteriorates and she struggles to find answers, and as she connects with sufferers around the world. The event was organised by Sheena Hewitt, and the film was screened by Perth Film Society, with financial support from The National Lottery Awards for All Scotland, BFI Film Audience Network and Film Hub Scotland. Attendees included Deputy Lord-Lieutenant Alistair Cruickshank and Provost Dennis Melloy

## Running hot

This year's Virgin Money London Marathon was apparently the hottest ever,

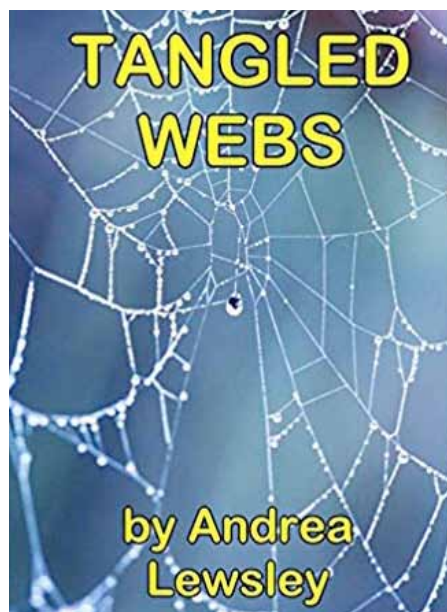
with temperatures of 24.1°C recorded in St James's Park. Despite the heat, we were delighted to have four runners in the race raising funds for ME Research UK. Rachel and Robert Craig, Rob Copley, and Chris Aylett all completed the event, and we are very grateful for all their efforts. Chris's sister, Rachel, summed it up beautifully: '[Chris] did amazingly well, and I am so proud and so thankful on behalf of myself and other ME sufferers for his massive achievement.'

## In the loop

The Celtic Wisemen Perpetual is described as a gruelling 75-mile cycle

ride across Devon and Cornwall. In May, a team of five cyclists set off to complete the course to highlight their friend, Martin Wiseman, who has been bedbound with ME/CFS for the last ten years. Their objective was also to raise funds for ME Research UK so that more research on the illness can be conducted. The team has shared their circular route online in the hope of encouraging other cyclists to tackle it and make a donation to ME research, so if you are interested please visit [justgiving.com/fundraising/celticwiseman](http://justgiving.com/fundraising/celticwiseman). Many thanks to the team for their fantastic and inspiring ride, and their valuable support for ME research.





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### True blue

This year's ME Awareness Week in May certainly turned a few heads in Portsmouth where the 560-foot-high Emirates Spinnaker tower was bathed in blue for a day to mark the occasion and to highlight the experiences of ME/CFS sufferers. This popular tourist attraction frequently changes colour in support of various causes, and enjoying the spectacle on this occasion was supporter Abbie Grant. Awareness of ME/CFS was given a further boost by mentions in the local newspapers.



**05 Andrea Lewsley's** book *Tangled Webs* is out now at Amazon

**06 Abbie Grant** enjoys a visit to the Emirates Spinnaker tower

### Reading list

The latest book from Andrea Lewsley is *Tangled Webs*, which follows the love affair of divorcees Lorna and Cameron whose romance is complicated by Cameron's ex-wife's illness. It is available as a Kindle book ([amzn.to/1Wk2Lf1](https://amzn.to/1Wk2Lf1)), and Andrea will donate a portion of her royalties to ME Research UK. Her earlier book *Mikah the Meerkat Gets Lost* is still available ([amzn.to/2JL8CqA](https://amzn.to/2JL8CqA)), and she joins a number of other authors donating part of their proceeds or royalties to ME Research UK.

Robert McMullan's *Stranger and Stranger* is the true story of an unlikely encounter in the life of a young man with ME ([amzn.to/1ks8CO2](https://amzn.to/1ks8CO2)). Hayley Green's *101 Tips for coping with ME* is a guide offering tips on coping with the condition ([amzn.to/2PGEu5q](https://amzn.to/2PGEu5q)). Mer-ryn Fergusson's *What is wrong with ME* is a story through the eyes of her son Chris and the experiences of his family ([amzn.to/1GLbFLR](https://amzn.to/1GLbFLR)). And Jack Croxall has released a short story about his experience with ME/CFS, which is available free to read ([bit.ly/2yU3fBk](https://bit.ly/2yU3fBk)).

# Standing Order Form

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