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INTRODUCTION

Friends,

Welcome to Issue 2 of MS Research! We have a very exciting issue for you this time, starting with an interview with leading MS researcher Dr. Denise Fitzgerald on **pages 3-5**. Dr. Fitzgerald and her team at Queen's University Belfast have secured £2 million in funding for various research projects looking at potential ways to reverse the effects of MS. It was a great pleasure to meet her and ask about her work. We hope you enjoy reading about what she and her team are hoping to achieve.

ECTRIMS, the largest international MS research conference, took place in September and we have a report on some of the highlights for you on **pages 9-11**. We also have some further developments from the International Progressive MS Alliance on **pages 12-13**. Several of MS Ireland's voluntary Branches have donated to the Alliance in the last couple of years and it is fantastic to see the range of exciting projects that this money is helping to fund.

Lab-based research is vital for finding new ways to treat MS, but it takes a long time and sometimes it can seem very remote from the reality of living with MS every day. Therefore, we also want to make sure we report on research that looks at the day-to-day ways of managing MS and its symptoms, so on **pages 14-18** we look at the latest Irish MS research into mindfulness, physiotherapy and swallowing difficulties.

We hope you enjoy these and the many other articles we have for you. A major thank-you to all our contributors!

See you in June 2017 for Issue 3.



Harriet Doig

Information, Advocacy and Research Officer

Editor of MS Research and MS News



Professor Susan Coote

Chair of MS Ireland's Research Committee

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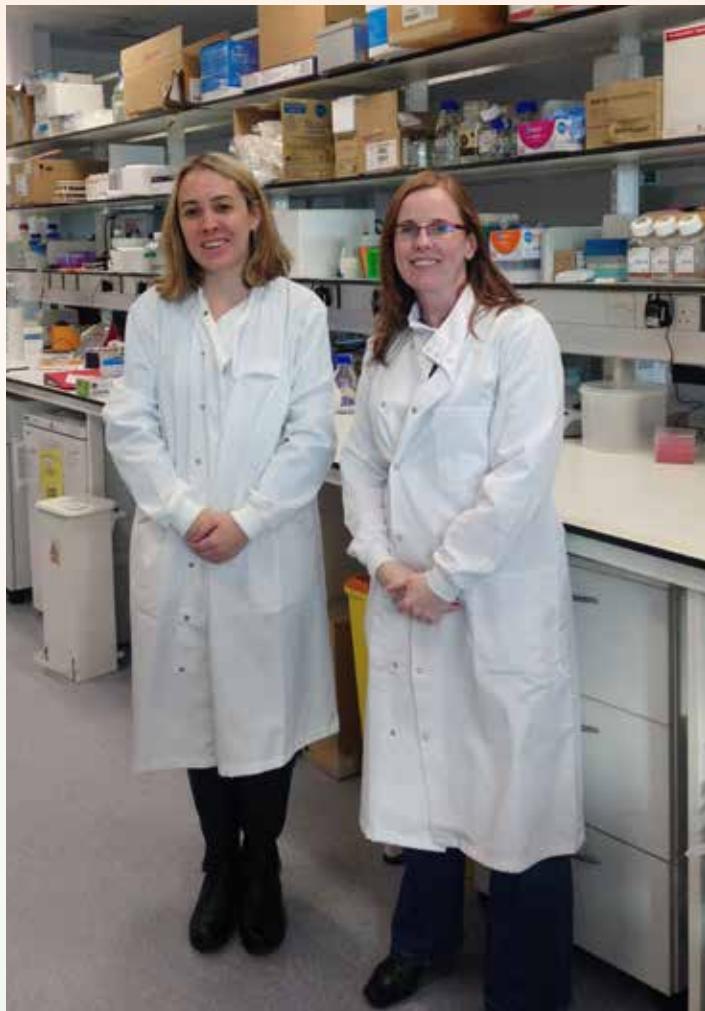
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Research into reversing the effects of MS



Harriet Doig, Information, Advocacy & Research Officer, MS Ireland (left) with **Dr. Denise Fitzgerald** from Queen's University Belfast.

Researchers at Queen's University Belfast have begun a £2 million research programme to investigate reversing the damage caused by multiple sclerosis.

The research programme, which is funded by the **Wellcome Trust** and **BBSRC**, aims to understand how myelin, the insulating layer that surrounds nerves in the central nervous system, can be repaired.

Harriet Doig, MS Ireland's Information, Advocacy and Research Officer, met with Dr. Denise Fitzgerald who is leading the team of researchers at Queen's to get some further information on the projects and what they will be investigating.

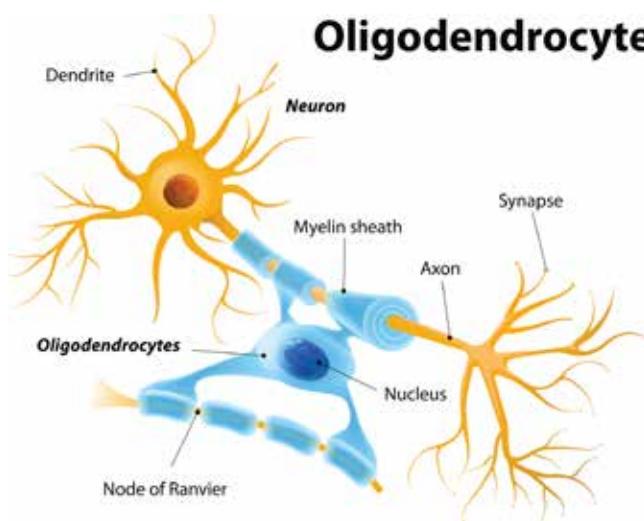
Can you explain a bit about your background and how you came to be involved in MS research?

I did my degree in University College Dublin and pursued a Ph.D there studying how the immune system is involved in inflammation. During my Ph.D, when I was 21, I developed a very rare condition called transverse myelitis, which is somewhat similar to multiple sclerosis. I suffered demyelination in my spinal cord, similar to what can happen in MS but in my case it was a single attack. The consequence for me was that I was very rapidly paralysed and I had to learn to walk again. Once I had recovered I decided that I wanted to research myelin damage and inflammation, and the most prominent disease in which that occurs is multiple sclerosis. So that took me to Philadelphia to pursue a post-doctoral fellowship there.

Your team has recently secured funding of £2 million to look at repairing the damage caused by MS. Can you tell us about the projects that you are hoping to fund with this money?

We are really delighted with these two grants, one from the Biotechnology and Biological Sciences Research Council (BBSRC) and the other from the Wellcome Trust. The grant from the BBSRC is to understand the fundamental biology of the cells that make myelin in the central nervous system. These cells are called oligodendrocytes. Work from my team over the last few years has discovered a new way that the immune system can trigger these cells to switch on myelin production. So the first project that we're going to be doing over the coming three years is to understand what changes occur inside the oligodendrocyte that trigger it to start making myelin. The goal is to use that new knowledge to potentially make treatments that can trigger the same effect. This would be very relevant for MS, because a lot of the cells that make myelin become stuck in an immature stage in MS lesions and so the myelin cannot be repaired.

Oligodendrocyte



The grant from the **Wellcome Trust** is a five year Investigator award; it has three main parts. The first part is to understand how the immune system is sending signals into the oligodendrocytes to trigger them to mature. We've discovered one of the signals which are involved; it is a new protein that hasn't been known to be produced by these immune cells before. So, we are really going to interrogate the biology of that protein to determine whether it could be a potential lead into a new therapeutic agent for patients.

The second part of that programme is to really link our research projects in the lab with MS clinics. Some of our work involves animal models and some of our work involves human cells. This second part is completely focused on human cells. So we will be comparing these beneficial immune cells from people who have MS, of different types, and people who don't have MS. We'll also be looking at whether treatments change the immune cells in these patients and if we could potentially affect them in a way that alters how the immune system helps to repair the brain.

The third part is a very exploratory area. The project is looking at lots of other types of immune cells, and we're really going to mine the immune system for effects on oligodendrocytes (the cells that make myelin). So from our initial discoveries we know at least one immune cell type that can trigger oligodendrocytes to start making myelin and we want to know about lots of other cell types. That type of research is fundamental basic discovery research; it's to provide new biological knowledge that then feeds into future projects to again translate into potential new therapeutic targets to improve the lives of patients.

Why do you think that there has been so little research to date investigating reversing the effects of MS?

I think there has been quite a bit in the last 10 years or so, and prior to that there was very little. One of the reasons is we don't have as much understanding about how the brain functions, compared to how the immune system functions. So all our current disease-modifying therapies target the immune system. As it is easier to study, it is easier to make new drugs that act on the immune system. It is also easier to get at the immune system. Our immune system has cells in our blood, in our spleen, in our lymph nodes, and drugs can get to those parts of the body much more easily than the brain. So if we want to reverse damage in the central nervous system, most likely we need to get the drug to the central nervous system. So there are a couple of reasons, one, we don't understand the brain as well, and secondly we can't access the cells in the brain quite as easily.

You mentioned in another recent interview the possibility of developing an entirely new class of treatments for MS – this is obviously a long way off in the future, but can you explain a bit more about what you mean by a new class of treatments?

We classify these as remyelinating therapies, therapies that will regenerate the myelin in the central nervous system. We might not be as far off as we think, clinical trials have already started treating patients with agents that can promote remyelination in the laboratory, and there's some very exciting results emerging, particularly in the last two years or so. What we are not seeing yet is huge changes. We're not seeing huge clinical benefits, but we're certainly seeing positive indicators in these trials that some of the neurological impairment that has been caused by MS has been improved with these agents. So we'll be watching very closely over the next two years or so as to whether or not any of these agents make it to market. If they do, that would be an entirely new class of treatments, 'remyelinating' or 'regenerative' treatments.

Depending on the outcomes of the research projects, what further developments would you like to see in this area of MS research in the future, including other potential future projects for you and your team?

Certainly from the work that we're doing, we want to determine whether this particular protein coming from immune cells can be used as a drug. Most likely, what we'll be investigating is which parts of that protein have the action of triggering oligodendrocytes to make myelin, because if we can narrow it down to a small portion of the protein we can potentially make a small drug that can get into the central nervous system and trigger re-myelination. So that would certainly be an exciting area. Overall, what we would like to establish with this research programme over the next five years is in-depth understanding of how the immune system and in particular cells called T-cells participate in remyelination. Many groups have researched T-cells in multiple sclerosis over many decades and most of those studies look at whether the T-cells are involved in causing the damage, or blocking the inflammation. But there is very little known about whether these T-cells participate in the repair of myelin. So that's really what we seek to find over the next five years. There are lots of different types of T-cells, and my prediction is that some will promote remyelination and some will inhibit remyelination. If we can understand how that is happening, we may have druggable targets to help make the next generation of therapies for MS.

Aside from your own area of research, what do you think has been the most exciting development in MS research in recent years, and how optimistic are you for the future?

I'll start by saying I'm very optimistic for the future, while being cognisant of just how long it takes to translate some of these discoveries into a benefit for patients, which is a frustration. Certainly in my opinion, the most exciting results that we have had in the last couple of years are the clinical trials in progressive MS. For so many years, we were hearing about failed clinical trials for disease modifying therapies in primary progressive MS and secondary progressive MS. These agents that were working for relapsing remitting MS were not having an effect in patients with progressive MS. I think that has been extremely frustrating for patients who have progressive MS because they are seeing the benefits patients with relapsing remitting MS are gaining from these new therapies but they

do not work for them. The fact that we've now had two phase 3 trials showing slowing down of disability progression in the past year is incredibly encouraging. I think the first of those, ocrelizumab, is likely to be approved within the next six months in the US, maybe 12 months in other countries. The fact that there will now be a treatment available to people with progressive MS I think is so incredibly hopeful and exciting. The effects are modest - the risk of disability progression is reduced by around 25% with this drug, so we absolutely have to do much better. What's exciting about the results of the phase 3 trials in progressive MS is really the proof of principle, that we can slow down progression in MS.

How do you do the research?

We choose our experimental models based on the scientific question we want to answer. Some of those questions can't be answered using the human brain because we can't access that tissue easily. There aren't too many people rolling up to have a brain biopsy! So we use a range of models - both mouse and human cells. Sometimes we work with cells in a dish, in some cases we work with larger pieces of tissue in a dish or from archives. In some cases we are asking healthy volunteers as well as people with MS to provide blood samples, and in the future saliva samples, and we also study cells from mice. It is this variety of experimental models that allows us to perform in-depth, cutting-edge studies .

MS Ireland will be keeping a close eye on developments in these research projects and will keep our stakeholders updated on progress.



The use of Neurofilament in monitoring disease activity in Multiple Sclerosis (MS)

By Dr. Nonnie McNicholas
Winner of the 2015 Dean Medal
Travel Bursary



Karolinska Institutet is a large university hospital situated near the centre of Stockholm; it has a culture of having a high emphasis on research in clinical care as part of an academic health care system. They have a large MS service, with more than 1,500 people attending for treatment. I spent two weeks based in the MS department there, with the intention to learn about the use of neurofilament (a cerebrospinal fluid marker), in clinical practice in MS. This is measured by lumbar puncture, which is not

an uncommon procedure to have done when you are attending for a routine annual outpatient appointment there!

Neurofilament chains form the backbone of the neuronal cytoskeleton in the central nervous system; they maintain axonal calibre and therefore healthy propagation of impulses along it. When the axon is damaged, neurofilament leaks out into the surrounding cerebrospinal fluid. In MS, the level of axonal injury and axonal loss has been shown to be associated with the degree of neuroinflammation. Neurofilament light (NfL) chain corresponds with acute axonal injury, i.e. ongoing inflammatory activity. Neurofilament heavy chain correlates more with established disability. Thus NfL chain is a more valuable marker in treatment decisions for subsequent disability prevention; and it is what is used for treatment guidance at Karolinska.

NfL is measured at the Karolinska in the laboratory using enzymatic immunoassay, known as ELISA. An antibody which binds neurofilament light is coated on a surface containing cerebrospinal fluid (CSF). Detection is then done by adding a second conjugated antibody; enzymatic turnover leads to change from a colourless substrate to a coloured one – and this colour corresponds to the amount of neurofilament light chain in the sample - measured by a technique called optical absorbance.

For relapsing-remitting MS, NfL is measured at many different time points. At diagnosis, higher NfL levels may be associated with more severe subsequent disease course, therefore in conjunction with clinical presentation and MRI findings, it might help the clinician in selecting more highly active disease modifying treatments (DMT). Following initiation of treatment, NfL may be measured again to ensure it has decreased adequately in response to treatment. During clinical relapse, NfL is measured and the relative increase in its level can give further prognostic value of the outcome following relapse.

In secondary progressive MS, NfL is used to guide if ongoing treatment is required or not. If a person with MS notices gradual decline in their symptoms without superimposed relapses suggesting a more progressive course, and there is an associated normal level of neurofilament for age seen in CSF, we know the patient will not benefit greatly from any immunomodulatory DMT. If this same person has similar symptoms associated with much higher levels of NfL in the CSF, this indicates that there is ongoing neuroinflammatory activity, so we can deduce that there is still a role for immunomodulatory treatment. In future following further research, an anti-CD20 monoclonal antibody may be most beneficial in this scenario (for example, ocrelizumab).

My time in Karolinska has shown me the helpful role for NfL in both research and clinical practice, and we hope to begin incorporating the measurement of this molecule in some of our research studies now commencing at St. Vincent's Hospital in Dublin. I am very grateful to MS Ireland for giving me the opportunity to visit Karolinska Hospital and further my understanding of these different practices in MS management.

Public and Patient Involvement in Health Research in Ireland Conference Report



Keynote speaker **Mark Pollock** (left) with MRCG Chairperson **Philip Watt**.

The Medical Research Charities Group (MRCG) held a conference on public patient involvement in medical research on 27th September at the Irish Aviation Authority, Dublin. Below is a report of the day (reproduced with kind permission from the MRCG).

Philip Watt, MRCG Chairperson and CEO of Cystic Fibrosis Ireland, opened the event. "It's heartening to see how much PPI has come on in recent years in Ireland" he told the attendees. "But it remains clear that we still lag far behind many other countries and more work still has to be done".

Philip then introduced the keynote speaker, Mark Pollock. Mark provided a poignant, moving and inspiring overview of his experiences of disability, as someone living with both a visual impairment and a spinal cord injury, and his determination to improve the outlook for spinal injury patients in the years ahead. Mark has participated in a number of research projects including a project looking at a form of spinal electrocution borrowed from old USSR athlete camps. Mark has been working to facilitate collaboration between different specialists so as to "get the concept out of research and into the clinic".

Next up was Katie Scott, Senior Patient Involvement Manager with Cancer Research UK. Katie provided an overview of current PPI in cancer research in the UK, explaining that in recent years there has been a trend towards increasing PPI in medical research, and this includes a 'consumer forum' for patient representation and patient involvement in clinical studies groups.

Next to address the conference was Professor Anne McFarlane of the University of Limerick (UL) who discussed the topic 'Public Patient Involvement: Meaningful Participation'. She talked about the concept of partnerships in health research and the dialogue necessary to make this happen.

Next to take to the podium was Beccy Maeso of the James Lind Alliance. Beccy explained that the Alliance is based on bringing patients, carers and clinicians together into priority-setting partnerships (PSPs) designed to eliminate uncertainties on the effects of treatments. She said "Research on the effects of treatment is usually led by researchers or funders. Sometimes, this doesn't address the real concerns the patients themselves may have about their treatments."

Anne Cody of the Health Research Board (HRB) spoke on the topic of 'Supporting PPI Across the System: A Research Funder's Journey'. She reinforced the Board's commitment to promoting PPI within HRB-funded projects and outlined the contents of the HRB's strategy document Research, Evidence, Action. She also outlined findings from HRB surveys of both researchers and the general public, which showed strong appetite for PPI among both groups.

The final part of the conference featured a panel discussion involving both patients and researchers. The panel included person with MS and qualified researcher Alexis Donnelly, and Consultant Neurologist Professor Michael Hutchinson. Alexis said "I feel that my journey with PPI is just beginning.... The problem with MS is that while there are about 15 new medications for it, there hasn't really been an awful lot of research done. We don't really know what kicks MS off and it is very hard to measure whether a medication is really making any difference in progressive MS, because you need to wait a long time to see if your disability is progressing or not". He also described his work with the International Progressive MS Alliance Scientific Steering Committee. Professor Hutchinson added "We have a relatively low level of basic research into MS in Ireland.... Clearly, the need for people with progressive MS was there and the most significant event in MS in the past five years has been the Progressive MS Alliance....The future looks good for advancements in progressive MS and that's down to involvement between researchers and people with MS."

Philip Watt concluded the conference by thanking all the speakers and those who attended.

PUBLIC PATIENT INVOLVEMENT

Report from European Patient Innovation Summit

By Joan Jordan

European Patients Academy on Therapeutic Innovation (EUPATI) Participant



When you have been living with MS for a while, I think that it's good to look around and engage with other chronic disease communities. To focus on what we have in common and how we can collaborate to make our individual positions stronger. It's called the umbrella principle. The European Patient Innovation Summit was an opportunity to do just this. The theme for this year's conference was to learn how digital technologies are revolutionising patients' lives and increasing the reach and effectiveness of patient organisations, and discuss how patient groups can make the best use of available technologies in order to address common problems.

The Summit took place in Milan on October 4th-5th and there was a strong Irish contingent there-including representatives from MS Ireland, Croí, the European Headaches Alliance, COPD Support Ireland, Fighting Blindness, Retina International and the European Organisation for Rare Diseases. I gave

a workshop called "Giving Patients a Voice in Drug Development" with Jan Geissler and Caitriona Dunne from EUPATI. The main message is that patients need to get meaningfully involved in the process as early as possible to avoid "Rubbish In – Rubbish Out" outcomes. The availability of digital technologies like patient registries, surveys and websites can help capture what patients as a whole actually want and provide hard data to the pharmaceutical industry. The full potential of patients in drug development has yet to be realised and there is a huge challenge to de-mystify the process and give us an equal "seat at the table".

It takes over 12 years and on average costs over €1 billion to perform all research and development before a new medicine can be made available to patients. Only about 2% of substances evaluated in research make it to the market as new medicines. Prior to learning this, I didn't really think too much about where my medication came from and why it takes so long for new, life-changing drugs to get on the market. I also didn't consider other chronic disease communities and how they are fighting a very similar fight to those living with MS.

The conference gave me an opportunity to share experiences from the MS world and learn from the experiences of others. I want to share what I learned with you and say that we as customers need to clearly express our needs in the drug development process. You can learn more about the life-cycle in the European Patients Academy toolkit www.EUPATI.eu



Report from European Federation of Neurological Associations (EFNA) conference

By Laura Lee



The European Federation of Neurological Associations recently hosted a two-day training event held in Trinity College Dublin, which I was fortunate to attend. The aim of the event was to discuss ways in which the perspective of the neurology patient can form an integral part of research and practice. A number of speakers from varying backgrounds (e.g. medicine, psychology, health policy and research) presented over the course of the two days, with each offering a unique perspective on how patients can and should have central roles in the management of their illnesses.

Indeed, throughout several of the presentations there was a clear emphasis on the ownership and leadership role that the person living with neurological illness can have in the grand scheme of their treatment. Professor Orla Hardiman, Professor of Neurology and Consultant

Neurologist, spoke about the "Citizen Patient". The Citizen Patient is characterised by a number of features:

- They are an integral member of the team managing treatment and care.
- They understand their condition(s) and are knowledgeable about it/them.
- They are aware of the societal implications of their illness.
- They have the ability to question and adjust treatments in a rational and evidence based manner.

To achieve all of this is no doubt a big ask of those living with any neurological illness, and becomes an even bigger ask when there are multiple illnesses at play. Naturally, it involves the collaboration of several parties, not just the person affected by illness, and such collaboration can be more or less difficult to achieve in certain contexts. However, the potential power that being a Citizen Patient brings is both inspiring and exciting. Many people living with neurological illnesses receive our diagnoses at an early age. Hence, we often live with lifelong illnesses, and the plans we make for our treatment and disease management are vital in the promotion and maintenance of our wellbeing. Although challenging, we may identify opportunities where we can gain more knowledge about our illnesses, and become more actively involved in our care. Instead of letting our GPs, neurologists and nurses take the lead, should we view ourselves as equally important stakeholders in the management of our care? There are many who argue that we should. Indeed, as Professor Charles Normand noted, it is an incredibly powerful experience for the person living with illness to know that we are receiving the best care possible. Arguably, the knowledge that we ourselves are contributing to and influencing that care is an even more powerful experience. With this theme in mind, The European Patients Forum is currently running a year-long campaign on patient empowerment, with the organisation offering lots of useful resources for those interested in making informed decisions around their health. I, for one, will certainly be making use of them!



EUROPEAN COMMITTEE FOR TREATMENT
AND RESEARCH IN MULTIPLE SCLEROSIS

What happened at ECTRIMS 2016?

Written by Arman Eshaghi, winner of the ECTRIMS Young Investigator Award 2016.

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MS researchers from around the globe gathered in London, UK, in September for the annual congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS). ECTRIMS is the largest global MS conference, bringing together over 9,000 researchers and health professionals for the latest updates and research findings on treatment, care and management of MS.

During ECTRIMS, we saw significant progress in the field of MS and new studies on progressive MS. Below are some of the highlights.

Positive results for a fingolimod-like drug for people with secondary progressive MS

Siponimod is a similar drug to fingolimod, but it has a more targeted effect on white blood cells and therefore may have fewer side effects compared to fingolimod while maintaining similar beneficial effects.

In a phase III trial called EXPAND (the biggest clinical trial on people with secondary progressive MS with 1,651 people from 31 countries) participants received either a daily placebo or siponimod tablet. Further results from the trial were presented at ECTRIMS showing that, after three and six months, people with MS who received siponimod had slower progression as assessed by Expanded-Disability Status Scale (EDSS). Novartis, the producer of siponimod, will apply for the regulatory approval to formally include this drug as a treatment for secondary progressive MS. The results

of this study have been submitted for publication. You can read more about this trial on the International Progressive MS Alliance website, www.progressivemsalliance.org

Negative results for fluoxetine in progressive multiple sclerosis

Fluox-PMS is a multi-centre study performed in Belgium and Netherlands. Fluoxetine is mainly used for the treatment of depression, but may be useful to protect brain cells from dying (degeneration). In this study investigators asked whether fluoxetine could slow the progression of MS. This drug trial included both people with primary progressive MS and secondary progressive MS. Participants were divided in two groups of placebo (68 participants) and fluoxetine (69 participants). After 108 weeks, there was no significant difference between the two groups of participants in terms of the rate of progression. Therefore, this study failed to show significant improvement in people with progressive MS who took fluoxetine. Although the trial showed a trend towards a reduction in disability progression, a larger and longer trial would be needed to show if this trend was statistically significant.

MS-SMART: Reports on the recruitment phase

Three research abstracts were presented, which reported the recruitment phase for a promising drug trial for people with secondary progressive MS, called MS-SMART. MS-SMART stands for Multiple Sclerosis –Secondary progressive Multiple Arm Randomisation Trial. This trial for secondary progressive MS is testing three drugs at once:

- amiloride – licensed to treat heart disease
- fluoxetine – licensed to treat depression
- riluzole – licensed to treat motor neurone disease (MND)

This is an ongoing study in 13 different sites across the UK. A total of 440 participants with worsening secondary progressive MS have been recruited in four groups: (1) placebo, (2) riluzole, (3) fluoxetine, and (4) amiloride. Investigators plan to follow participants for 96 weeks and assess the effects of each drug on clinical, disability and MRI outcomes. We look forward to seeing the results over the coming years.

Lipoic acid: Is it useful for people with secondary progressive MS?

Lipoic acid is a tablet with antioxidant effects. In a study from Portland, Oregon, USA, investigators ran a clinical trial on 54 participants with secondary progressive MS. Participants were divided into two groups who either received placebo or lipoic acid. The results of this trial after 96 weeks of follow up showed that the group who received the lipoic acid treatment had lower rate of brain shrinkage. However, there was no significant effect of the treatment on disability and clinical measures in people who received the treatment. Authors stressed the need for trials with more participants in order to prove the effectiveness of lipoic acid.

ORATORIO trial: New promising information on Ocrelizumab, a treatment for people with primary progressive MS

Last year, Ocrelizumab showed positive results for people with primary progressive MS (ORATORIO trial). The ORATORIO trial is a multi-center and multi-national drug trial. This year several groups presented new data on the trial from around the world. Ocrelizumab treatment showed consistent positive effects on walking and slowing disability progression. The most common adverse event was the reaction at the site of infusions.

MS risk factors: Smoking, vitamin D and obesity

In a proportion of people with MS, the disease starts without fulfilling all the criteria for MS (clinically isolated syndrome). People with clinically isolated syndrome may (or may not) develop MS over time. The factors that can affect conversion from clinically isolated syndrome to MS are of high interest if they can be modified and reduce the conversion rate to MS.

Investigators from the MS Centre of Barcelona (CEMCAT) reported their findings on the relationship between vitamin D and smoking at the time of the diagnosis of clinically isolated syndrome on the

risk of developing MS and disability progression in participants, followed for many years.

Investigators looked at the vitamin D levels in 503 people with clinically isolated syndrome. They also looked at a blood marker of smoking (cotinine) in 464 people with clinically isolated syndrome. This study started in 1995 and followed participants for an average of eight years (up to 15 years). Investigators did not find any significant increase for the conversion to MS in people with low vitamin D or those who were smokers. However, low levels of vitamin D, and cigarette smoking were both significantly associated with development of higher disability in the study participants. Therefore, both these risk factors, if modified, can slow the progression of disability in people with clinically isolated syndrome.

People with relapsing remitting MS are often treated by injectable interferons. A study from the Danish MS centre on 1,145 people with relapsing remitting MS showed that smoking has significant effects on the response to treatment with interferon. Investigators observed that people with MS who smoked more were less likely to respond to interferon treatment.

In another study from University of California in Berkeley and San Francisco Lisa Barcellos and colleagues asked whether body mass index (an index to define normal weights) has any effect on the risk of developing MS. Investigators looked at a huge population of people with MS and healthy volunteers from USA and Sweden (close to 20,000). They found a causal association between abnormal increase in weight (overweight or obese people) and the risk of MS. Authors suggested that this observation might be due to the effect of obesity on the immune system.

Comparing alemtuzumab, natalizumab or fingolimod

There was great interest in a presentation by Dr. Tomas Kalincik and his colleagues who had conducted a major analysis comparing the clinical data of people receiving alemtuzumab, natalizumab or fingolimod, using the extensive international data gathered in the MSBase database. The results suggest that natalizumab and alemtuzumab are better able to suppress relapses in comparison with fingolimod. Alemtuzumab and natalizumab appear to be similar in suppressing

relapses and disability progression, with natalizumab more often showing an early improvement in disability levels. Of course, these effects represent the overall effects across a large population and may vary considerably for each individual. Treatment decisions also need to be based on other factors including general health, family planning, and other work and life related factors for each individual.

ECTRIMS 2016 Poster display highlights

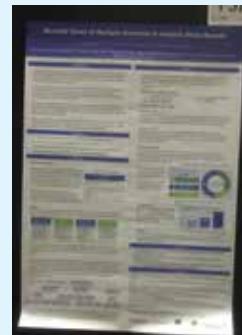
By Harriet Doig, Information, Advocacy & Research Officer, MS Ireland

On Thursday 15th September 'The Societal Cost of MS in Ireland' poster was displayed during the afternoon session. Dr. Christopher McGuigan (below right) and Dr. Killian O'Rourke (below left), the Consultant Neurologists who were involved in the study, were present at the poster as was Peter Carney, Health Economist from Novartis (below centre). MS Ireland steered this project to completion and were delighted to see the poster presented at such a prestigious meeting.

On Friday 22nd September there was a very unusual poster on display. A cardboard, handmade poster was produced by the authors – but why? The authors of the poster wanted to emphasise the importance of upper limb function in MS so they handmade their poster – on recycled paper.

This unusual poster attracted a lot of interest – you can read about it on the Barts MS blog

multiple-sclerosis-research.blogspot.com/2016/09/gimmickdatagenius.html



ECTRIMS 2016 'Burning Debate' report

By Harriet Doig, Information, Advocacy & Research Officer, MS Ireland

On Thursday 15th September a Burning Debate was held. The topic of the debate was :

"People in wheelchairs should be included in progressive MS trials".

Dr. Klaus Schmierer from Barts Hospital London argued in favour of the motion and Dr. Patricia Coyle from Stonybrook Hospital in US argued against.

Main arguments in favour of the motion were:

1. Pathology: MS is a length dependent pathology (hypothesis)
2. Pharmacology – some trials of DMTs have failed their primary endpoints but still improved upper limb function
3. Current trials – in some current trials EDSS (measure of disability) is quite high
4. Patient perspective: in a survey carried out by Barts Hospital, 95% of people with MS said people in wheelchairs should not be excluded from clinical trials.

The main argument against the motion was:

In general it's good to include people in wheelchairs in clinical trials, however in PIVOTAL trials (large registration trials) it is not. This is because in these pivotal trials of new drugs you are trying to show progression (or lack of it) and you need to include people with LOW levels of disability to prove this.

Questions were taken by Twitter to #burningdebate, and as this was a social media session voting took place by Twitter too! Two statements were put up on Twitter corresponding to the two sides of the debate and the one with the most retweets won.

The motion was passed by 29 in favour versus only four against.

For more information from ECTRIMS including a highlights video, webcasts and abstracts, visit www.ectrims-congress.eu/2016.html

International Progressive MS Alliance

Project funding update



The International Progressive MS Alliance continues to fund the most promising research that will seek the solutions so urgently needed by people with progressive forms of MS. The Alliance's Collaborative Network Award initiative began with 52 original network applications in response to the initial call. From these, 11 were selected for network planning awards. These planning awards were further developed over the past year and submitted to compete for one of the three multi-year €4.2 million Alliance Collaborative Network Awards. The proposals were submitted in one of three priority areas identified by some of the world's leading experts in progressive MS namely:

- Drug Discovery
- Biological and Imaging Biomarker Development
- Faster and Smaller Treatment Trials

The Alliance Scientific Steering Committee of leading MS experts, chaired by Prof. Alan Thompson and including three persons directly affected by MS (Caroline Sincock[UK], Jon Strum[USA] and Alexis Donnelly [Ireland]), conducted a thorough review process. This process sought independent external expert opinion and included many probing questions and much thoughtful debate. Discussions covered, among other things, the game-changing potential of each proposal, each team's track record and likelihood of success, the downstream impact on the lives of people with progressive MS together with each proposal's attention to the wishes of people with progressive MS.

The Scientific Steering Committee provided scientific recommendation to the Executive Committee, which considered these recommendations and approved funding in support of three particular proposals for the Alliance's Collaborative Network Awards. The quality, breadth, innovation, and focus of these proposals have the potential to generate some of the most important

and potentially transformative work in the area of progressive MS.

The three successful network proposals are described in more detail below. They centre on the following areas:

- Using advanced MRI techniques to identify and track progression (Douglas Arnold, McGill University, Canada)
- Identifying neuro-protective molecules using advanced bio-informatics and cell re-programming techniques (Gianvito Martino, San Raffaele Scientific Institute, Milan, Italy)
- Clarifying further details of the innate immune response in progressive MS and thereby identifying candidate drugs for progressive MS, some already approved by the FDA for human use in other diseases. (Francisco Quintana, Brigham and Women's Hospital, Boston, USA)

An MRI biomarker for disability progression for use in clinical trials

Principal Investigator: Douglas Arnold, M.D., McGill University (Canada)

Douglas Arnold, M.D., of McGill University and his team are pioneering the development of magnetic resonance imaging (MRI) markers that signal disease progression, and adapting these for use in early (phase 2) clinical trials of treatments for progressive MS. Dr. Arnold's research examines the underlying idea that brain injury-associated disease progression in MS is detectable by MRI prior to its identification by physicians in a clinic visit. This may be due to the ability of the brain to compensate for injury, but only up to a point. Thus the advanced MRI techniques may be able to reveal damage due to progression before the brain's own compensation techniques have been exhausted at which point the damage becomes clinically evident. The innovative tools being developed by Dr. Arnold and his team are essential for planning the larger scale phase III clinical trials required for approval of new treatments. The study also has extraordinary potential to inform proactive treatment for people with progressive MS which has not become clinically evident.

INTERNATIONAL RESEARCH

Dr. Arnold's novel research will investigate features of the MRI that:

1. Change measurably over the short time intervals used in phase II trials for progressive MS;
2. Relate to progression over the same period of time; and,
3. Are predictive of the effect of treatments on future progression.

To identify MRI patterns with the above characteristics, Dr. Arnold and his multidisciplinary team will combine their expertise in computer science, image processing, and statistics to:

- Access existing data from more than 2,000 patients and 40,000 MRI scans in order to enable efficient, automated computer analysis and application of advanced information technology techniques.
- Apply cutting-edge computer science tools with demonstrated potential in other fields that have not yet been used in MS research.
- Use advanced imaging analysis tools to measure the size, shape, and appearance of the main structures of the brain, and statistical approaches to identify patterns of changes in the brain structures that have the required association with disease progression.
- Combine this approach with advanced machine learning techniques, such as those used for facial recognition, to detect features of the image that may not be recognized by humans, but are related to disease progression.

Dr. Arnold believes this research can directly facilitate testing new drugs for progressive MS in trials that are smaller and less expensive, which therefore encourage pharmaceutical companies to develop new therapies for progressive MS. He and his team will create an interactive tool to share their innovative new methods with the scientific community.

Project Title: Bioinformatics and cell reprogramming to develop an in vitro platform to discover new drugs for progressive multiple sclerosis (BRAVEinMS)

Principal Investigator: Gianvito Martino, San Raffaele Scientific Institute, Milan (Italy)

The BRAVEinMS team is working to identify molecules that may have a protective role in nerve cells or neurons and/or the capacity to promote myelin repair. The project has three phases:

1. Identifying potential drugs or compounds using sophisticated bioinformatics tools specifically developed to virtually reproduce pathogenic mechanisms of MS;
2. Screening these compounds for their ability to protect nerve cells or promote myelin repair in laboratory tests using both rodent and human neurons and myelin-forming cells; and,
3. Evaluating in animal models of progressive MS the therapeutic potential of the 'candidate' compounds previously identified through the in vitro screening.

In the first phase of the study, the researchers will leverage their leading IT expertise to comb through large data sets of biological and chemical information. This data will help identify biological pathways and treatment targets, possibly useful chemical compounds, and drugs already approved by the Food and Drug Administration or the European Medicines Agency that can be repurposed to promote remyelination and neuroprotection.

In the study's second phase, the research team will test compounds for their neuroprotective and/or myelin repair potential in laboratory tests using rodent cells, and then attempt to reproduce these results using human neuro-glia cells. They will further validate their screening system by harnessing stem cell technology to generate neural cells from the skin cells from MS patients - the so called 'disease in a Petri dish' technology.

Compounds that pass the different in vitro screenings in laboratory tests will be extensively evaluated in vivo in animal models, each representing a key aspect of the degenerative process occurring in MS.

The BRAVEinMS research team believes that their work can pinpoint a limited number of previously unidentified molecules with a high chance of therapeutic efficacy in progressive MS patients. They expect that within four years of the start of the project they will identify one or two human grade compounds that can be used in phase I/II clinical trials in patients with progressive MS. The team therefore hopes to have a clinical trial underway by the end of 2020.

Development of a drug discovery pipeline for progressive MS

Principal Investigator: Francisco Quintana, Ph.D., Brigham and Women's Hospital (U.S.)

The goal of Dr. Quintana's project is to identify drug candidates that may be effective therapies for progressive MS, and that will be ready for evaluation in patients within four years of the initiation of this research. The project's central idea is that targeting the damage done by the innate immune system to the central nervous system will uncover effective therapeutic approaches for progressive MS. The innate immune system normally functions to protect the body from infections. Dr. Quintana and others have found that innate immune cells in the central nervous system actually promote disease activity in MS and other diseases. Dr. Quintana's team recently identified the biological pathways that control the innate immune response. They also found that genetic manipulation of the pathways can arrest nerve damage and alter disease progression in preclinical MS animal models. However no candidate drugs are available to modulate the activity of innate immune cells in MS.

Dr. Quintana's study will:

1. Identify the biological processes that control the innate immune response in the central nervous system;

2. Evaluate the activity of candidate drugs on the innate immune system in experimental models of progressive MS;
3. Analyze how the candidate drugs exert their beneficial effect; and,
4. Identify additional candidate targets and therapeutic drugs that impact the innate immune system in progressive MS.

The project uses cutting-edge tools and approaches to understand how the brain is damaged in progressive MS and to identify targets for treatment. The research team has access to unique collections of central nervous system-active compounds including FDA approved drugs for human use in other diseases, patient sample collections, genetically-engineered mice, and advanced methods for conducting detailed genetic analysis of individual cells.

Dr. Quintana has assembled a novel multidisciplinary team that integrates the expertise of Sanofi Genzyme Corporation with leading research groups focused on basic and clinical MS research and drug development including the Brigham and Women's Hospital, The Broad Institute, The Montreal Neurological Institute, Université de Montréal, and The Weizmann Institute of Science.

Many thanks to all MS Ireland Branches who have contributed funds to the International Progressive MS Alliance in 2015 and 2016.

Thank you also to Alexis Donnelly for his assistance in preparing this article.



MINDFULNESS

Online mindfulness programme for adults living with MS



Research Aim: Researchers at the School of Psychology and Centre for Pain Research at NUI Galway are evaluating a new internet-delivered, eight week mindfulness programme for people living with MS. The goal is to help people manage their psychological and emotional well-being as they live with MS.

About the research: Living with MS can impact a person's life in many different and complex ways, for example, social and family relationships can be affected and there may be financial strain when one is unable to work. Not surprisingly, it is quite common that people living with MS report feeling depressed, anxious, distressed, tired and in pain. Thus, helping people with MS to manage their psychological well-being is of great importance. Previous research in the UK has shown that mindfulness can help alleviate MS-related distress and assist people as they manage their day-to-day lives. Mindfulness has been defined as 'paying attention, in a particular way; on purpose, in the present moment and non-judgmentally' and thus, can encourage more positive coping responses.

MS Ireland is supporting the new research at NUI Galway, led by Professor Brian McGuire and Dr. Brian Slattery, that aims to develop an online version of a mindfulness programme for people living with MS. The programme is based on previous work in the UK by Dr. Angeliki Bogosian and Prof. Rona Moss-Morris who showed that the mindfulness programme was effective when delivered using Skype. Working with their colleagues in the UK, the team at NUI Galway will develop a version of the programme that will be

delivered over the internet, so that people can access the programme whenever they want and can work at their own pace. The eight session programme will be delivered over eight weeks; one session per week. During the programme, participants will be educated about mindfulness, trained in various mindfulness techniques and given mindfulness homework so that they can practice and hone their skills.

To assess the impact of the programme, the researchers will ask participants some questions at the start and at the end of the study. Two main questions are of interest: 1) Does the online mindfulness programme improve people's psychological well-being following their participation (i.e. do people feel emotionally more able to deal with their health difficulties and the other consequences that arise from them) and 2) How cost effective is the program? (i.e. is it financially worthwhile to run this programme and keep it going in the long term?).

It is hoped that the results of this research will improve the quality of life and emotional well-being of people living with MS. Indeed, if the programme proves to be successful, the research team aims to make it free for people to use into the future.

Anyone interested to find out more about the study can contact Dr. Brian Slattery, School of Psychology, NUI Galway (Tel. **091 495 832** or email brian.slattery@nuigalway.ie).



Professor Brian McGuire



Dr. Brian Slattery

Physiotherapy updates from the University of Limerick



The MS Research Team at University of Limerick aims to reduce symptom severity and improve quality of life for people with MS through exercise and physiotherapy treatments. The team has four strands of research: physiotherapy, falls prevention, physical activity and technology enhanced rehabilitation treatments.

In this e-zine the team members funded by MS Ireland present information on some of the studies that contribute to these programmes of work. If you would be interested in taking part in any of our studies or would like to be added to our research e-mail database to learn about our studies please e-mail

susan.coote@ul.ie

Why are people with Multiple Sclerosis not physically active?

By Bláthín Casey

The MS research team at UL aims to develop a web-based resource to encourage people with MS to become more active, namely, 'Activity Matters'. Research suggests that before developing such a resource, we should attempt to understand any behaviour we are trying to change. In this instance, we are aiming to change physical activity behaviour. Therefore, we must seek to understand why people with MS are not engaging in physical activity behaviour. This knowledge will help guide the development and implementation of 'Activity Matters' to ultimately ensure its success.

We conducted a review of research papers in the area of physical activity for people with MS. We wanted to

understand what factors contribute to people with MS being active or not. In particular, we focused specifically on the psychosocial factors. Psychosocial factors can be thought of as factors that are either psychological (e.g confidence) or social (e.g peer support) in nature. 26 papers were included in the final review. The results showed that self-efficacy, goal-setting and outcome expectancies (explained below) were all associated with being active in a large sample of people with MS (over 3,300 people). So what do these results mean?

Self-efficacy is the belief/confidence a person has in their ability to do something. In this example, the belief/confidence a person with MS has in their ability to engage in physical activity behaviour. This study suggests that those people with reduced exercise confidence are less likely to be active. If this is something you struggle with, it is suggested that you can improve self-efficacy through vicarious experience (seeing other people with MS exercise, joining an exercise class and seeing the benefits) and self-regulatory techniques (keeping an exercise log, setting an exercise plan, using tracking devices such as pedometers).

Goal-setting was also shown in this review to be associated with physical activity behaviour. Those people with MS who do not set realistic goals have a tendency to be less active. This excellent resource will help you set your exercise goals and make an action plan, if setting goals is an issue for you:

[www.csep.ca/cmfiles/Guidelines/
MSToolkitEnglishInsert.pdf](http://www.csep.ca/cmfiles/Guidelines/MSToolkitEnglishInsert.pdf)

Finally, outcome expectancies may also be an important psychosocial factor. Outcome expectancies can be defined as the knowledge a person with MS has on the benefits and barriers to exercise, which can ultimately have an effect on their physical activity participation. Remember that exercise is not harmful. Also, being physically active is associated with improvements in many symptoms of MS including, fatigue, strength, mobility and quality of life.

The results of this review will help inform the development of 'Activity Matters'. However, this review did only include psychosocial factors. It must be investigated if MS specific symptoms or other unknown factors also play a role in physical activity behaviour of people with MS. This is a future aim of Bláthín Casey's research.

Falls prevention

By Laura Comber

Currently the MS Research Team at the University of Limerick, led by Professor Susan Coote, is developing a falls prevention intervention for people with MS. Recent evidence shows that in excess of 50% of people with MS will fall in any three-month period. Despite this high rate of falling there is very little research around falls prevention interventions for this population currently. In order for any intervention to be well formulated there should be three key opinions considered, namely; the existing research evidence, the people who will utilise the intervention and the clinicians who will deliver it.

Participant Survey:

In order to gather the opinion of people with MS who will utilise the decisive intervention, we recruited people with MS who had fallen in the last three months and who could walk for 10 metres with or without an aid to take part in a phone survey. The survey took 60 minutes to complete and 136 people took part. The survey asked questions about what the participants felt should be included in the developing intervention and how it should be delivered. The majority of participants were concerned about the prospect of future falls and only 8% had ever taken part in a programme that focused on reducing their falls. In terms of what should be included in the future intervention participants expressed a large degree of interest in the majority of presented topics. Exercises, multitasking, preventing falls in new situations and the influence of MS symptoms on fall risk were the topics rated with the highest level of interest by participants. One-to-one was identified as the preferred method of intervention delivery followed by group settings and participants also expressed a high level of interest in the inclusion of role-playing to learn skills such as how to get up safely from a fall. Participants were most interested in a physiotherapist or an occupational therapist leading the intervention and the majority felt it should be approximately six weeks in duration with sessions lasting 1-2 hours and taking place on a weekday in the morning time.

Clinicians' Opinion:

To gain the insight of practicing clinicians we conducted semi-structured interviews over the phone. We recruited five expert physiotherapists who work

predominantly with people with MS and seven novice clinicians who work in areas where people with MS would present for treatment but would not be the primary population seen, for example in primary care. The clinicians were asked about three main areas, namely; what they currently do with people with MS who are at risk of falling, barriers and facilitators to treating this population and what they think should be included in the future falls prevention intervention to make it successful. From these interviews we gained very valuable information about areas such as assessment of falls risk, treatment of these risk factors, methods of implementing the intervention and practical ways of taking the developed intervention from a research setting into everyday practice.

We are currently writing research papers from the findings of these two studies which we hope to publish in the near future. These findings will be combined with the meta-analysis we have already published relating to walking deficits in people with MS and a meta-analysis we are currently conducting on postural balance deficits. In this way we will have collected information on the three integral elements of intervention development, these will then be combined to inform the development of a decisive falls prevention intervention for people with MS.

Functional Electrical Stimulation for the correction of foot drop and thigh muscle weakness in people with MS

By Marcin Uszynski PhD. MISCP

Walking is our everyday activity. We get up every morning and we walk to the bathroom and then downstairs to our kitchen to have a lovely "healthy" fry. We walk with our children to school, we walk to work, we walk our dogs, we generally walk a lot in this country. People with MS consider walking as the most valuable bodily function (Heesen et al 2008) and we know that walking limitations lead to long-term changes in their quality of life. Walking limitation is a common health problem in MS (Coote et al. 2014) and up to 75% of people with MS experience mobility impairments (LaRocca et al. 2011). Walking

problems in MS are caused by a variety of factors such as muscle weakness in lower legs, poor balance, numbness or spasticity. We know that regular exercise can improve the symptoms of MS (Platta et al. 2016, Kjolhede et al. 2012, Snook and Motl 2009), however these improvements are not maintained if exercise is discontinued and these exercise interventions require the regular support of a physiotherapist which may not be feasible. Technology may offer great potential in this area.

Functional Electrical Stimulation (FES) is defined as the application of a surface neuromuscular electrical stimulation (NMES) in real-time in order to facilitate purposeful tasks such as walking. When FES is applied for the correction of a foot drop, it delivers improved lifting of the foot during gait. FES is used to improve mobility in people who have problems with walking as a consequence of damage in their brain or spinal cord. An FES system (BIONESS L300plus), consists of four small components that communicate with each other wirelessly: two ergonomic leg cuffs (sheen and thigh components), gait sensor (heel switch that detects pressure changes as the foot start to move) and wireless control unit (about the size of a pack of cards).



An FES system

Several authors have reported the positive effects of FES in people with MS (pwMS). Current evidence suggests that using FES in pwMS leads to increases in walking speed (Street et al. 2015, van der Linden et al. 2014) a reduction in falls (Taylor et al. 2014) and an improvement in activities of daily living (Taylor et al. 2014, Esnouf et al. 2010). A recent study by Gervasoni et al. 2016 suggested that the use of FES had an impact on gait, specifically reducing the number of falls and improving walking in people with MS and stroke patients.

MS Ireland Western Regional Office in Galway has currently two full sets of FES devices (BIONESS I300) which have been purchased by the Galway Branch via funding from the Saturday Hospital Fund. We are conducting a couple of case studies to establish FES efficacy in people with MS. First results are available and are very promising.

Case Study

Person one is a female, age 65, diagnosed with MS in 2003, currently walking with a four wheel-rollator and with a history of falls. In 2013 she was advised by a community physiotherapist to start using a dictus splint due to left foot weakness and left foot drop. She reported that since wearing a splint her left foot was not sticking to the ground that much - however apart from this the improvements were minimal. Her muscle endurance (measured by six minute walk test) was poor prior to the FES treatment. She was able to walk a distance of 149 meters within six minutes. After two months of using FES device (twice weekly for one hour) she has improved significantly and is now able to walk a distance of 260 meters within six minutes. That is an improvement of 110 meters. The most interesting finding is that she carried out these tests without the FES device on her leg which means that she had a significant therapeutic effect from using the FES treatment. She also noticed significant improvements in relation to muscle strength in her left lower leg. She feels that her walk is more stable now and she can easily cross the street or step up on the pavement. She had an initial assessment and device fitting by our chartered neurophysiotherapist here in the MS Office in Galway. An exercise programme was designed for her and she continued exercises with the assistance of a trained physiotherapy assistant. Her exercises consisted of walking indoors and outdoors, a stairs routine and functional activities such as kicking a ball, stepping on an aerobic step or stepping over various obstacles. She was asked to walk slowly then fast, to change walking direction, to stop and turn around -the activities that we all do every day without thinking.

An assessment by a chartered physiotherapist trained in the use of FES is required to ensure that the treatment will be suitable for people with MS as this device is not beneficial to everyone. A trained physiotherapist in FES treatment will check suitability and contraindications for FES with you during your first assessment. MS Ireland Western Regional Office in Galway has a trained chartered neurophysiotherapist who can carry out an assessment and provide recommendations regarding FES and other treatments.

Exploring the Experiences of Swallowing Difficulties in People with Multiple Sclerosis.

Authors: Anne Barrett, Alex Carey & Dr. Margaret Walshe.

Research carried out in the Department of Clinical Speech and Language Studies, Trinity College Dublin.



The objective of this study was to examine the experiences of dysphagia (swallowing problems) for individuals with Multiple Sclerosis (MS). The prevalence of dysphagia in people with MS is believed to be between 34.3% and 43%. However, little is known about the impact and experience of dysphagia on this population. A mixed methods methodology was used to explore this impact of dysphagia.

Six individuals with dysphagia due to MS were recruited. The Dysphagia Handicap Index, the Dysphagia in Multiple Sclerosis Questionnaire and the Functional Oral Intake Scale were completed. Qualitative data was obtained using individual unstructured interviews. Data from quantitative measures and qualitative interviews were triangulated. The results revealed that all participants were homogenous in terms of oral intake, while self-reported or perceived dysphagia severity varied between participants.

The qualitative data provided an in-depth understanding of life with dysphagia due to MS. Challenges included functional limitations and dietary changes, in addition to significant psycho-emotional and psychosocial concerns. Emerging themes were "Dynamic adjustment to the eating and drinking process", "Evolving roles and relationships", "Quotidian participation", "Dysphagia in the context of other disabilities" and "Reaching acceptance".

This study provides an insight into the challenges faced by individuals with MS and dysphagia. It also raises a number of clinical implications, primarily, that dysphagia can have a significant impact on the individual with MS. This study highlights that the impact of dysphagia on quality of life should be an important consideration for healthcare professionals and service providers.

Acknowledgments: We wish to thank the participants who shared their experiences and the staff at the MS Care Centre for facilitating the research.



An Exploration of Family Caregivers' Lived Experience of Oropharyngeal Dysphagia as a Primary Result of Multiple Sclerosis

Completed by Kate Bree (MSc. Student), Supervised by Dr. Margaret Walshe

Background:

Oropharyngeal dysphagia, (OD), is a life changing and common symptom in Multiple Sclerosis, (MS), (Poorjavad et al., 2010; Alali et al., 2016), associated with aspiration pneumonia, dehydration, malnutrition and weight loss, (Walshe, 2014). Additionally, choking, social isolation, depression and anxiety, are also possible consequences of OD (Leow et al. 2010). Due to advances in medical treatment there is increasing recognition of home based care and people with progressive neurological conditions such as MS receive the majority of their care from home, (Altschuler, 1997; Cheung & Hocking, 2004). Family caregivers are key stakeholders in carrying out various interventions of care, namely, diet modifications for family members with OD. Caregivers report OD as a source of perceived burden, (Choi Kwon et al., 2005), yet there is a paucity of research on caregivers' experiences of managing OD in the home nor their experiences of services related to OD in an MS context. Thus, a qualitative methodology is warranted to underpin the foundational knowledge of this phenomena of caregivers' experiences of OD to inform the research base, direct services and clinical practice.

Methods:

Purposive sampling was employed in recruiting five family caregivers of people with MS (PwMS) with OD as a primary result of MS, through a respite centre in Dublin. Data was collected through unstructured interviews exploring caregivers' day to day management of OD and also any recommendations caregivers had for healthcare professionals working with people with OD and their families in the context of MS. Interviews lasted between 60 and 90 minutes. At the end of the interviews, the researcher provided the main interpretations from the interview, and the participant had the opportunity to add to or retract any details of their interview. All participants were happy with the researcher's feedback of their lived experience of OD.

Major Findings:

The analysed data revealed 5 superordinate themes with the corresponding emerging themes, as shown below in **Figure 1**.

Figure 1: Superordinate Themes



It appeared that family caregivers perceived many challenges in the day to day management of OD in the context of MS in the home. Challenges included perceived guilt, grief, fear of choking on food or secretions and a lack of training to deal with such an emergency. Further, the presence of non-oral feeding represented two identities for caregivers; non-oral feeding as relief but evoked guilt. Caregivers perceived many positive and negative experiences with health services and provided recommendations for the improvement of care to people with OD as a primary result of MS and their families.

Care Alliance Ireland Discussion Paper Series

By Zoe Hughes, Policy & Research Officer,
Care Alliance Ireland

In 2015, Care Alliance Ireland was pleased to launch the "Discussion Paper Series". The primary purpose of this series is to stimulate discussion and debate within the family carer sector and beyond, in particular of minority/niche issues, or issues which are sensitive in nature. The purpose of the series is not to provide in-depth, original research on a topic, nor to espouse a particular viewpoint or position, but to get people talking and thinking.

These topics have been identified through various methods, including (but not limited to):

- Consultation with member organisations (including MS Ireland) and with Family Carers
- Discussion at Board and Care Alliance Ireland staff team level
- Inspiration from attendance at national and international events
- Literature reviews undertaken throughout the course of the everyday duties of the Policy & Research Officer.

To date (November 2016) there have been four Discussion Papers published on the following topics:

Discussion Paper 1: Defining Carers (October 2015)

Key points:

- The language used to describe Family Carers can be quite contentious
- In some sectors, such as the disability and mental health sectors, it's vital that organisations are aware of the connotation of the language used, and how this can contribute to overly paternalistic approaches to care
- Some of those providing care to family members are insistent that they do not wish to be recognised as anything other than as a father, daughter, husband or other relationship and resist identifying with the term Family Carer.

Discussion Paper 2: Intellectual Disability, Caring and Role Reversal (December 2015)

Key points:

- It is often assumed that people with intellectual disabilities are solely the recipient of care
- As the population ages, it is becoming more likely that older people with intellectual disabilities will be part of a co-caring relationship with their aging parents, which increasingly impacts on supports which organisations can provide

Discussion Paper 3: Online Supports for Family Carer - Options & Experiences (June 2016)

Key points:

- Although Ireland has one of the highest levels of web connectedness, relatively few organisations are providing online supports to Family Carers
- There are many opportunities to reach out to younger and more isolated Family Carers through the use of web-based supports and training
- Providing these supports does come with challenges such as how to moderate online fora, creating safe environments for Family Carers to share their experience, and how to ensure quality information is available

Discussion Paper 4: The Wisdom of Family Carers (October 2016)

Key Points:

- Family Carers across Ireland were asked to share the advice they would pass on to those new to the role
- Key piece of advice include to make sure, ask for, and accept help; stay positive when times get tough; and to trust yourself and your knowledge and skills.
- It's clear that Family Carers have a huge wealth of knowledge to pass on - it's important that organisations recognise that in their daily work.

All papers in this series are available on the Care Alliance Ireland website
www.carealliance.ie/discussionpapers

Iron in the Brain

Iron is known to be a vital element for human health but, in recent years, there has been much media attention on the idea that iron overload in the brain may be an important factor in developing MS. While some of these claims are wildly speculative, and indeed some of the suggested "cures" have no scientific basis whatsoever, there is clear evidence that abnormal iron deposition can occur in neurological diseases such as MS, Alzheimer's Disease and Parkinson's Disease. What scientists still don't know is whether this aberrant handling of iron by brain cells is due to or is the result of the disease.



Sinead Healy (left) is a doctoral candidate in the MS Research Group at NUI Galway. Supervised by Dr. Una FitzGerald and Dr. Jill McMahon, she has spent the last four years studying this very topic. Along with another PhD student in the group, Michelle

Naughton, Sinead has developed a means of studying the interactions and responses of brain cells when subjected to iron overload. The model system, known as organotypic brain slice culture, allows small pieces of brain to be grown and maintained in the lab in dishes, with the help of added nutrients, growth factors and a plentiful supply of oxygen. The brain slice cultures allow the study of how brain cells respond, not just individually, but in the context of their interactions with other cells within the central nervous system, which is a distinct advantage over *in vitro* studies, where individual cell types such as neurones are grown and tested in isolation. In such an environment, where the brain milieu is being mimicked, scientists can study the effects of iron overload and even loss of myelin.

Sinead has developed a very useful and life-like system where iron can be added to the brain slices at levels corresponding to recorded MS brain iron levels. This then allowed her to investigate the cellular responses by using 3D imaging and molecular techniques to reveal components of the brain tissue, such as numbers of the different individual cell-types, levels of the messenger RNA encoding vital cellular proteins and molecules known to be involved in handling iron within the brain.

Her findings show that iron overload can result in loss of oligodendrocytes, the cells that are responsible for producing myelin and which are vital in recovery from the demyelination that causes relapses. She also found iron caused an increase in the number of "immune" cells of the brain, the microglia, as well as an activation of these cells to an inflammatory type.

This model will be of great use to the NUIG researchers who plan to use it for future projects studying the mechanisms of neurological disease. Sinead's work was recently published in the prestigious journal, *Scientific Reports* [1], and she is currently in San Diego presenting her work at the Society for Neuroscience International Meeting. Sinead's research has been part-funded by the Foundation Office NUIG and the Thomas Crawford Hayes Fund.

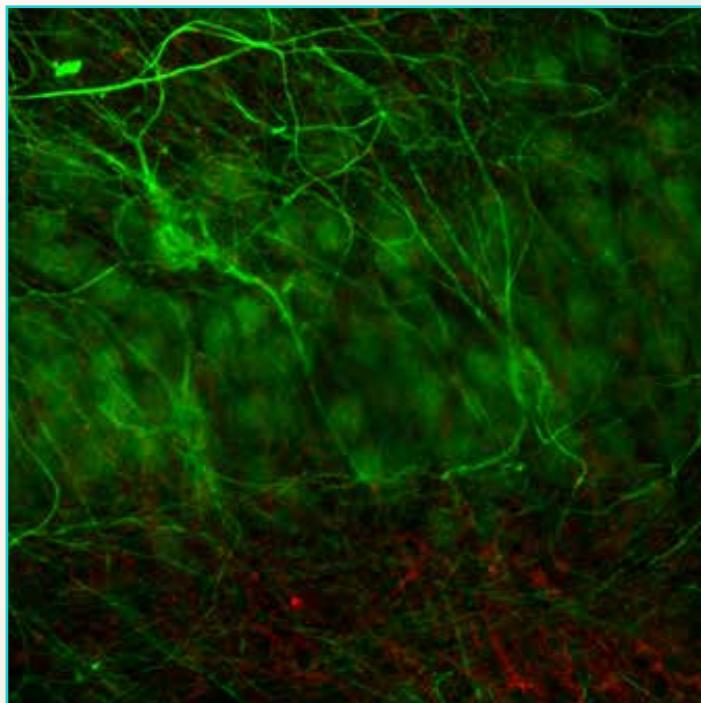


Image of neurones in a brain slice. The green highlights neurones and the red marks the location of iron in the brain slice. Fluorescent immunohistochemistry was done to detect these and the images were taken using a confocal microscope.

1. Healy S, McMahon J, Owens P, FitzGerald U. Significant glial alterations in response to iron loading in a novel organotypic hippocampal slice culture model. *Sci Rep*. 2016 Nov 3;6:364

HEALTHCARE EXPERIENCES

Healthcare Experiences of People with Multiple Sclerosis in Ireland

By Matthew McCarthy

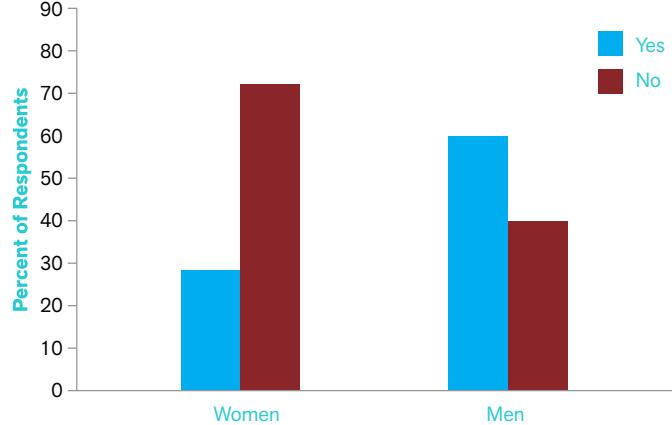


MS Ireland hosted an undergraduate medical student as part of UCD's Student Summer Research Initiative. The student, Matthew McCarthy (left), carried out a research project on people with MS's experiences of interacting with medical services. A total of 197 people took part in the study. Below is a summary and selection of some of Matthew's findings. A copy of the full report can be obtained by emailing harrietz@ms-society.ie

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The question asking whether the healthcare system had prepared the respondent adequately for the future resulted in 38.8% (n=69) of respondents uncertain and 39.9% (n=71) expressing they weren't. A statistically significant result ($p=0.003$, X^2) was found between gender and preparation for the future (Figure 2). The majority of female respondents did not feel that they had been adequately prepared for the future with MS (72.6%, n 23) whereas only the minority of men did (40%, n 10).

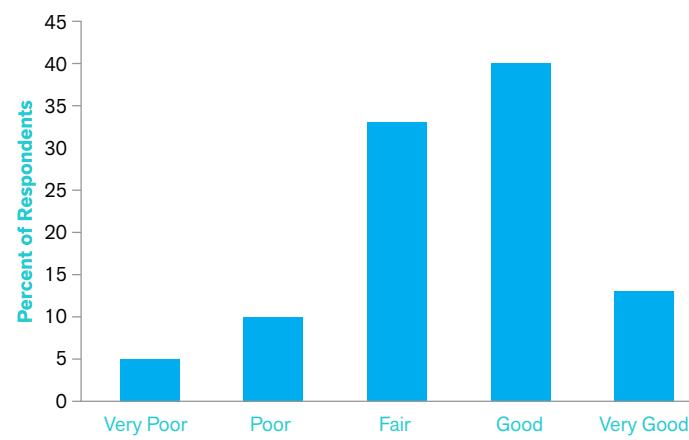
Fig 02: Healthcare Preparation for the Future Differences for Women and Men



Quality of Healthcare

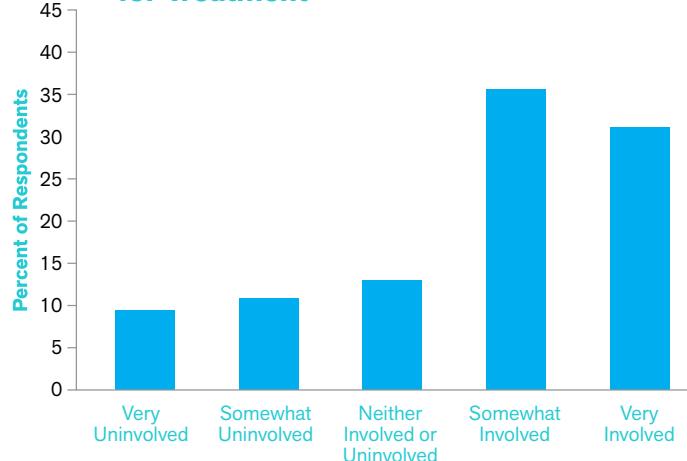
In general the majority of people were favourable towards the quality of healthcare they had received for their MS (Figure 1).

Fig 01: Quality of Healthcare Overall



Over half (67.2%, n 119) of respondents felt involved in their treatment decision making stating 'Somewhat Involved' or 'Very Involved'. (Figure 3).

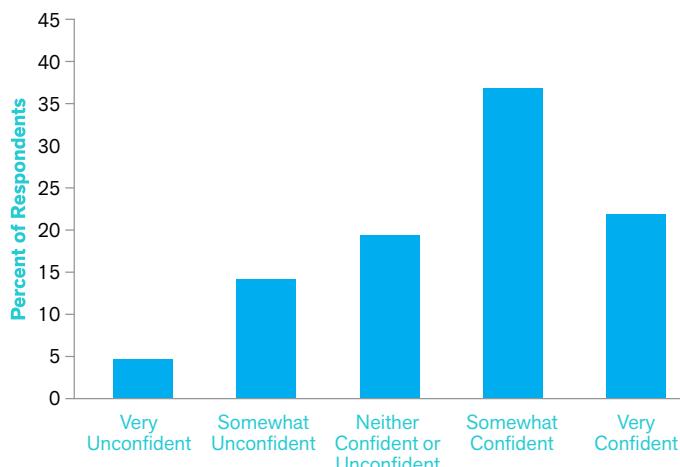
Fig 03: Involvement in Decision-making for Treatment



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63.5% (n 113) expressed confidence in healthcare professionals choosing the 'somewhat confident' or 'very confident' options. (**Figure 4**).

Fig 04: Confidence in Healthcare Professionals

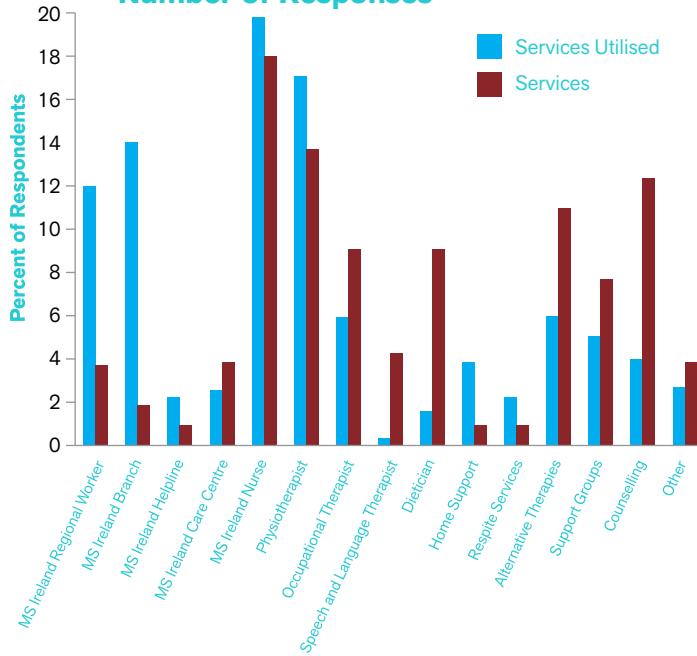


Twenty people gave a qualitative statement on their safety concerns in the healthcare system. Two major themes emerged; one of **hospital safety** and the second of **medication safety**. Six people (30%) expressed hospital safety concerns, mainly concerning issues regarding A & E and included complaints of complacency on the part of staff, short-staffing concerns, and a notable case where one respondent had a lumbar puncture "done in the ward during visiting hours with a lot of people around." Another six people (30%) expressed medication concerns, including three complaints of adverse reactions. One medication complaint was due to poor communication between the hospital and the GP regarding medication.

Access to Additional Services

The service most utilised was the MS Nurse at 19.9% (n 72) followed by Physiotherapist at 16.9% (n 61). 43.8% (n 71) of respondents felt they had access to services they needed, however 23.5% (n 38) didn't and 32.7% (n 53) were uncertain. 'Other' services that were expressed included MS group physiotherapy and hydrotherapy, a psychotherapist and psychiatrist, swimming group and Aquafit, wheelchair assistance, seating assistance, and drug assistance nurses (Rebif and Copaxone). Of those who did not have access to the services needed the MS Nurse and Physiotherapist were once again the top two results at 18.7% (n 20) and 14% (n 15) respectively, however counselling and alternative therapies also scored highly at 13.1% (n 14) and 11.2% (n 12).

Fig 05: Services Utilised and Desired by Number of Responses



Access to Healthcare

Out of 176 people who answered, 116 (67.1%) of people saw a neurologist publicly, and 36 (20.8%) saw a neurologist privately. 46.2% (n 80) of respondents did not feel that they saw the neurologist as much as they needed, 11.6% (n 20) were uncertain.

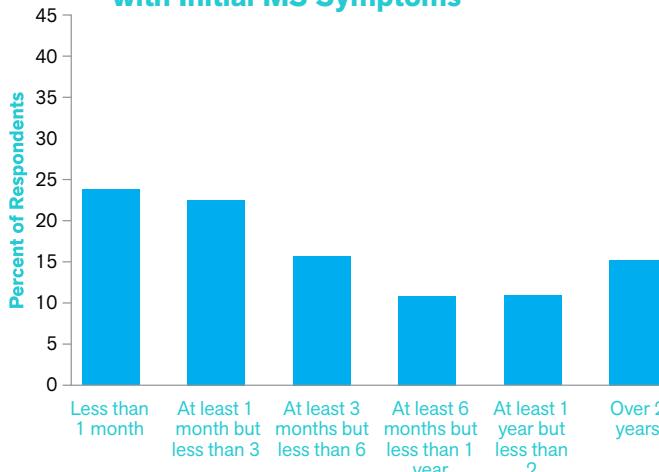
(SU- 145 respondents, SD- 44 respondents)

Diagnosis

Following the first visit to the GP, 23.9% (n 38) of respondents were diagnosed in less than a month, and over half of respondents (62.3%, n 99) by six months. However it took over two years for 15.1% (n 24) of respondents to be diagnosed (**Figure 6**).

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Fig 06: Time to Diagnosis Following visit to GP with Initial MS Symptoms

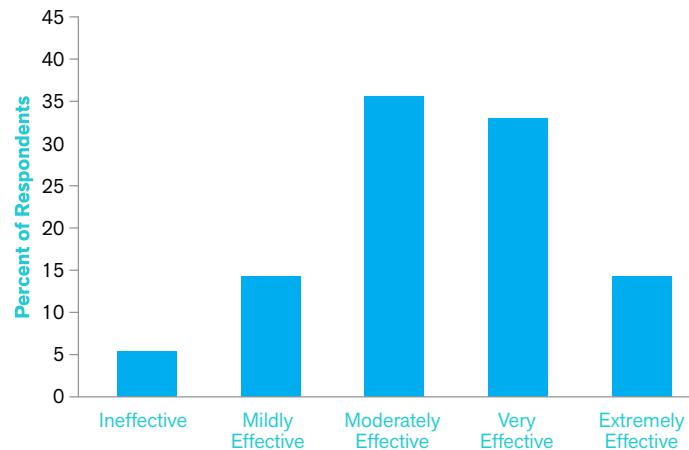


75.5% (n 111) of people understood the explanation of MS given at diagnosis. Only 28.2% (n 40) thought their diagnosis was oversimplified, and only 18.8% (n 27) thought it was over-complicated. A statistical difference was found between men and women, with 22.7% (n 25) of women feeling it was over-complicated compared to only 5.9% (n 2) of men.

Over half of respondents, 55.6% (n 79) felt that they were not given enough information about MS at diagnosis, 32.8% (n 44) felt information was being withheld at diagnosis, and 30.4% (n 42) did not understand the treatment plan at diagnosis. There was no statistical significance found between these questions and the independent variables

In general, respondents weren't negative about the manner of their doctor at diagnosis.

Fig 07: Medication Effectiveness



Most respondents felt their medication was having some effect with only 5.2% (n 8) stating they were ineffective. The median and mode responses fell into the 'moderately effective' category (**Figure 07**).

Fig 08: Effect of Healthcare Treatment on Quality of Life



Only 12.4% (n 17) of respondents felt that the healthcare treatment they had received had negatively affected their quality of life with 50.3% (n 69) expressing a positive effect on their quality of life.

67 people responded qualitatively to describe what beyond their healthcare had improved their quality of life. Four major themes emerged.

1. Family, friends and support services
2. Diet
3. Exercise
4. Maintenance of mental well-being encompassing mindfulness, meditation and positive thinking

MS Ireland will use the data from Matthew's study to identify areas of interest for future research projects and advocacy work.

A Cognitive Occupation-Based Programme for People with Multiple Sclerosis (COB-MS)

By Sean Reilly



Background

Cognitive rehabilitation is a treatment that has been integrated into numerous health professions, including occupational therapy. Cognition is a term used to describe the mental processes involved in understanding and gaining knowledge. This includes things like thinking, concentrating, remembering, judging and problem-solving. Difficulties with cognition are present in 43-70% of people with MS. Cognitive rehabilitation can be described as a way to improve cognitive difficulties through the use of strategies and tools that can be applied to everyday life.

What does the study involve?

This study aims to test a cognitive rehabilitation intervention called the COB-MS (a Cognitive Occupation-Based Programme for People with Multiple Sclerosis), which will address cognitive difficulties in an occupation-focused way in order to be of most benefit to the person. This means that the strategies and tools will be applied to all the activities a person does in their daily life, such as taking a shower, cooking, shopping, or meeting a friend for coffee. The COB-MS is an eight session programme which includes two individual sessions, six group sessions and homework activities. The group sessions will contain

5-8 people who are experiencing similar difficulties. The sessions will take place in Áras Moyola, which is located in NUI Galway.

A preliminary version of the COB-MS has been previously trialed with both people with MS and health care providers to identify both positives and negatives of the programme. The overall response was positive, and all feedback was taken on board when developing the current version of the COB-MS. This study aims to determine if the COB-MS can improve a person's cognition, daily life, mood, and quality of life. This will be determined by using questionnaires and tests. All participants will have three assessment sessions where they will carry out a number of different questionnaires and tests with a researcher. We carry these out in order to see if there is any change in the assessments before and after taking part in the programme. These three sessions will be at the beginning, at week 11 and week 18.

What are the benefits?

The COB-MS would enable people with MS to identify, understand and learn new strategies to deal with their cognitive difficulties.

Where can I find out more information?

If you are interested in participating or have any questions, please contact Dr. Sinéad Hynes on **091 495 624** or by email to sinead.hynes@nuigalway.ie



Diet and MS

Interview with Conor Kerley



Conor Kerley (above), a post-doctoral nutrition researcher with Dublin City University and HeartBeat Trust, recently spoke at MS Ireland's MS Research Explored evening. Here we ask him a few questions about his research into the role of diet in MS.

Can you tell us a bit about yourself and what inspired your research interest in MS?

Not long after my Junior Certificate exams and after three episodes in eight months, I was diagnosed with MS. It was a scary time for my family and I but my biggest concern was playing sport and chasing girls! The doctors and nurses told me all about medications but nobody advised me about diet or lifestyle in general. I reasoned that lifestyle had to be important and started to read as much as I could.

Can you tell us about the research project(s) you are working on at the moment?

At the moment, my research does not actively involve MS but has some crossover. For example, some of my work relates to nitrate containing vegetables. Examples of these vegetables include rocket, lettuce, betroot and rhubarb. We know these foods seem to increase the size of our blood vessels. We also know that these foods increase blood flow to the brain which would be a good thing in MS. I also do some research on vitamin D which seems to be very important in MS also.

Can you describe what research is saying about how diet and other lifestyle factors impact on the management of MS?

Proof is very hard to come by in science and therefore scientists and clinicians (doctors, dietitians) need to look for the best information available. The research in MS is quite consistent that fats from animal sources (meats, eggs, dairy) is associated with harm in MS whereas a diet based on plants such as grains, legumes, nuts, seeds, fruits and vegetables is beneficial in MS. Regarding exercise, some really interesting work has shown that being physically active can prevent, delay and even reduce some impairments caused by MS. It would be important to know what types of activities and for how long are appropriate for each individual. Sunshine and vitamin D do seem important but are only one piece of the puzzle and certainly not a cure-all!

What areas do you think researchers should focus on in the future regarding lifestyle factors and MS?

Scientists often conduct research with one component, for example, is vitamin D beneficial compared to a placebo? I think because MS is such a serious condition, a big focus should be on multiple components, so called 'complex interventions'. This might involve research based on the current evidence that decreasing animal fats while increasing plants, maintaining good vitamin D levels as well as exercise and stress reduction is likely beneficial. If these statements are true it is likely that adding these actions together would be more beneficial than each component alone. Indeed, this is what I do!

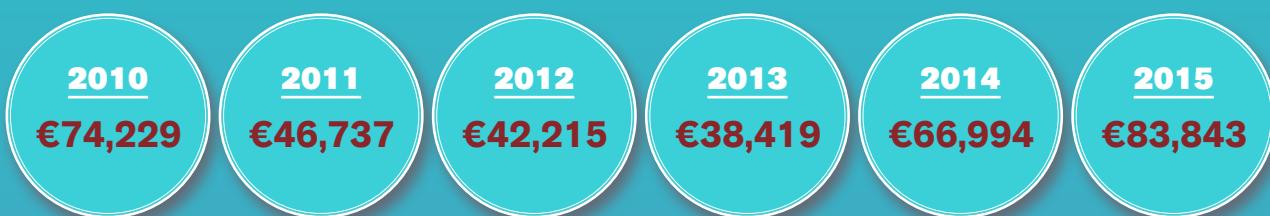
Conor Kerley (*PhD, BSc, H. Dip*)

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