The registry was launched just over two and a half years ago and **we now have 500 people registered**. This is an important milestone for us and we would like to give a huge thank you to everyone who has helped make the registry a success. The registry has already been used to help recruitment into a number of research studies with many more planned in 2015.

This is an exciting time for myotonic dystrophy research with the first pharmaceutical industry sponsored clinical trials starting in the USA, more information about this and other research updates are included on page 4. These developments mean that registries like ours will become increasingly important to help make trials move faster and more efficiently.

500 people have registered from across the UK!

The map above shows the location of the 500 people registered, can you spot yourself?
1. Registry Update

Over 100 people joined the UK Myotonic Dystrophy Patient Registry in 2014 and in February 2015 this total reached 500. The age of people on the registry ranges from 1 to 80 years old. Females makes up 52% of people registered, 48% males. The majority of people on the registry first experienced some symptoms in their adulthood. However 20% experienced symptoms before the age of 16 years old, 12% between 3 and 15 years, 8% before 3 years old. Fatigue and myotonia are the most commonly reported symptoms followed by swallowing difficulties. We will be continuing to analyse the data in the Registry in 2015 and hope to publish a scientific paper. This will help tell doctors and scientists about the information in the Registry and how it could be used for future trials and other research.

2. Update your details

Every year you will receive a reminder to login and update your details. This is so we have the most accurate information about you in the Registry.

You can log it any time www.dm-registry.org/uk, using your e-mail address and password.

Contact details: Check we have your most up to date contact details. If we want to contact you about a study we think you might be interested in then it is important your e-mail, postal address and telephone number are up to date. This is also important so that you can receive updates like this newsletter.

“Your Condition”: It is this information which will most likely inform researchers if you are eligible to take part in a trial. Knowing when things change e.g. if you start using a wheelchair or start experiencing fatigue is important for this. It may also be important for researchers wishing to look at how myotonic dystrophy progresses in different people.

“Your doctor”: It is very important you select a consultant to enter your clinical and genetic details on the Registry. Without your genetic diagnosis we cannot be sure if you are eligible to take part in a research study. If your doctor is not listed or you have any questions about this please contact the Registry curator, Libby Wood
3. What is myotonia?

One common question the Registry receives is about myotonia, a common symptom of myotonic dystrophy. Here we explain a little bit more about myotonia:

- Myotonia is a stiffness and tightness of muscles,
- Muscles can often be slow to relax after being used e.g. difficulty releasing grip from a handshake.
- The tightness often lasts around 20 seconds before relaxing fully,
- Myotonia is experienced most commonly in the finger and arm muscles,
- This stiffness can sometimes be experienced in the tongue and jaw muscles,
- In myotonic dystrophy type 2 (DM2/PROMM) myotonia can also occur in the leg, shoulder and back muscles. (There is more information about the different types of myotonic dystrophy in the last newsletter- which is available on the Registry website, www.dm-registry.org/uk)

There are currently no licensed therapies to treat myotonia in myotonic dystrophy. However some doctors in the UK prescribe mexiletine as a treatment for myotonia and 29 people on the registry report taking this drug. Mexiletine is currently licensed for the treatment of cardiac arrhythmias (a problem with the heart), but trials in other conditions have shown that it can also help to reduce myotonia. There is now a trial in the USA to show if the same is true in myotonic dystrophy. You can find out more about this study at www.clinicaltrials.gov, just search myotonic dystrophy.

Myotonia in the Registry

![Bar chart showing myotonia in the Registry]

Myotonia is one of the symptoms that most people in the Registry experience. Seventy five percent of people report myotonia to some extent, though in most cases this is mild.
4. Research Update

Throughout the research updates we might use some terms you have not heard before. There is a brief glossary on the Registry website (www.dm-registry.org/uk) and the Muscular Dystrophy Campaign has an excellent detailed glossary which you can access on their website www.muscular-dystrophy.org. Please don’t hesitate to get in touch if you have any questions.

ISIS/Biogen RNA therapy enters clinical trials in USA

We have previously reported that Isis Pharmaceuticals are working with Biogen-Idec (a biotechnology company) on a treatment for myotonic dystrophy. The treatment uses RNA anti sense technology and at the moment is called ISIS-DMPKRX.

Myotonic Dystrophy type 1 is caused by a mutation in the DMPK gene which carries the genetic instructions needed to make the DMPK protein. Cells translate these instructions into protein using a molecule called RNA. The mutation in the DMPK gene leads to RNA molecules that don’t work properly and are toxic to the cell. Biogen and Isis have used a technology called “RNA silencing” to develop a drug called ISIS-DMPKRX to destroy and remove the toxic RNA.

The start of the phase 1/2 trial means they are testing the treatment in people with myotonic dystrophy type 1 for the first time. The study is a randomised placebo controlled trial and the treatment is given via subcutaneous injections (similar to a vaccine). The treatment was tested in people without myotonic dystrophy first to make sure it is safe. The new study is a “dose-escalation” trial. This is to assess the response versus dose given, this prevents too much of the drug being given when it is not necessary or too little of the drug so that it doesn’t work.

The trial is taking place at a number of sites across the USA and people outside of the USA are not currently invited to participate. There are no plans for trials of this drug in Europe at the moment, but the Registry will keep you updated on any progress.

The Myotonic Dystrophy Foundation (MDF) in the USA has a clinical trial resource on their website (www.myotonic.org). This provides more details about clinical trials. This is a useful resource, but is aimed at people in the United States so some of the information may not be as relevant to people living in the UK. You can also find out more about this study www.clinicaltrials.gov, just search for myotonic dystrophy.
OPTIMSITC: European trial continues

OPTIMSITIC is a study testing the effect of a psychological treatment called Cognitive Behavioural Therapy (CBT) and exercise therapy. The study aims to find out if this unique treatment can help people with myotonic dystrophy type 1 to become more active, reduce fatigue and improve quality of life. Recruitment began in Newcastle upon Tyne in April 2014. The four sites across Europe (Paris, Nijmegen, Munich and Newcastle) are all now open and the 100th participant was randomised in October 2014. As of February 2015 we have 190 people included in the study, we hope this will increase to over 200 by April 2015.

There are still spaces available to take part in Newcastle if you meet the following criteria:
- Have genetically confirmed myotonic dystrophy type 1
- Experience fatigue and inactivity so that it has a negative impact on your daily life
- Are able to complete a six minute walk test (you can use a stick or splints to help)
- Are able to travel to Newcastle-upon-Tyne for at least five visits over the next 18 months.

Recruitment is expected to close April 2015 if you are interested in taking part please contact Cecilia Jimenez-Moreno, Email: a.c.jimenez-moreno@newcastle.ac.uk. Tel: 0191 208 8264.
There is also more information available on the website: www.optimistic-dm.eu

Registry Successfully helps recruitment for Nottingham natural history study

In the last Registry newsletter we discussed the study being carried out in Nottingham by Dr Saam Sedehizadeh. He has now recruited the 60 people the study needed. Twenty two of these people were recruited directly through the Registry. This is a great achievement for the Registry and shows how important the Registry is for research in myotonic dystrophy.
Dr Sedehizadeh is measuring lots of things (e.g. muscle strength, breathing, walking) in these 60 people with myotonic dystrophy type 1 once a year for three years. This will help doctors and researchers understand better how certain aspects of myotonic dystrophy change over time. If you would like to read more about Dr Sedehizadeh’s study visit the Muscular Dystrophy Campaign website.

Myotonic Dystrophy and Cancer Study

Researchers in the United States have been looking at an association between myotonic dystrophy type 1 and cancer. Dr Shahinaz Gadalla is leading this work. Dr Gadalla is an investigator with the National Cancer Institute at the National Institutes of Health. She has previously looked at population databases in Sweden and Denmark and which have shown that there may be a higher risk of Cancer in people with myotonic dystrophy (DM1 and DM2). They are now hoping to look into this in more detail and first need information from as many people with myotonic dystrophy (DM1 and DM2) as possible.

The study has begun by asking questionnaires about personal and family history of cancer, lifestyle factors and cancer screening strategies to people on the Rochester National Registry for Myotonic Dystrophy in the United States. They have approached us to help them ask the same questions of people living with myotonic dystrophy in the UK. The registry will be sending out these questionnaires via e-mail soon. Please look out for them and if you have any questions don’t hesitate to get in touch.
Everything you wanted to know about CTG repeats.

You may have been told when you were diagnosed with myotonic dystrophy that you have a mutation on chromosome 19 and that you have a high number of CTG repeats. There are lots of studies looking at these repeats, here we will try and explain what this means. For diagnosis a blood sample is normally taken, scientists are then able to extract DNA from this blood. DNA is often compared to a recipe, as it contains the instructions needed to construct other components of cells, such as proteins which allow our bodies to function. DNA is made up of just four molecules known as bases; these bases are represented by the letters A, C, T and G. These bases form genes which are sections of DNA that contain instructions on how to make a specific protein.

We know that the symptoms of myotonic dystrophy type 1 are caused by a change in DNA that occurs in a gene called DMPK. This change is an expansion made up of a series of CTG bases, a person without myotonic dystrophy has less than 50 of these repeats, in a person with myotonic dystrophy there could be hundreds or even thousands of these repeats. This triplet repeat expansion is not the same size in everyone with DM1 and it is not always the same in all cells in the body. The expansion can change throughout a person’s lifetime and throughout the generations. A child will often have a greater number of repeats than their parents or grandparents, this is known as anticipation. The variability of this expansion makes it difficult for doctors to know how myotonic dystrophy will progress in an individual.

Some recent research published by Darren Monckton at Glasgow and collaborators Fernando Morales from the University of Costa Rica has shown that the size of the repeat passed from parent to child can be affected by the age of the parent at the time of conception. In other words as people with DM1 age the size of the repeat in the eggs or sperm grows longer. Further research is being carried out to assess the relationship between the number of CTG repeats and the age of onset of the disease as well as the severity of the disease. This will increase the understanding of the genetic mechanism in myotonic dystrophy and how it relates to the symptoms people experience.

If you are interested in hearing more about the genetics of myotonic dystrophy Professor Darren Monckton recorded a webinar for the Myotonic Dystrophy Foundation which is available to listen to on their website. Either click the image above or follow the link; www.myotonic.org/webinar-everything-you-wanted-know-about-ctg-repeats
5. Muscular Dystrophy Campaign Information day

In November 2014 an information day for people living with myotonic dystrophy was held in Basingstoke. The day was organised by the Muscular Dystrophy Campaign in partnership with the National Centre for Neurology and Neurosurgery, part of the MRC Centre for Neuromuscular Diseases. The day was attended by over 160 people and some of the presentations from the day are now available on the Muscular Dystrophy Campaign YouTube channel:

- **Why should Myotonic dystrophy be monitored?** Dr Chris Turner, Consultant Neurologist, NMCCC, Queen Square, London
- **Management of excessive daytime sleepiness** Dr David Hilton-Jones, Consultant Neurologist, John Radcliffe Hospital, Oxford
- **Genetics and planning for a family** Dr Mark Rogers, Consultant in Clinical Genetics, University of Cardiff

You can find out more about the muscular dystrophy campaign and sign up to receive more information about events they hold on their website [www.muscular-dystrophy.org](http://www.muscular-dystrophy.org).

6. Myotonic Dystrophy Support Group Annual Conference

The 25th Myotonic Dystrophy Support Group Conference was held in Nottingham (East Midlands Conference Centre) June 7th 2014. The conference was a day of celebration to mark a milestone anniversary. A number of the presentations were filmed and are available to view online from the [MDSG Website](http://www.myotonicdystrophysupportgroup.org). Highlights include:

- **Research update** from David Brook, Professor of Human Genetics, University of Nottingham and Professor Mani Mahadevan, Professor of Pathology, University of Virginia.
- **Genetic advances in myotonic dystrophy over the last 25 years** by Dr Mark Rogers, Consultant in Clinical Genetics, University of Cardiff.

You can find out more about the Myotonic Dystrophy Support Group and sign up to become a member on their website [www.myotonicdystrophysupportgroup.org](http://www.myotonicdystrophysupportgroup.org).

Thank You!

Thank you for reading this newsletter and being part of the UK Myotonic Dystrophy Patient Registry. If you have any questions then please get in touch, Elizabeth.wood2@ncl.ac.uk.