Minutes – UK DM1 Registry Meeting

Friday 8th July 2011, 1200-1700, Newcastle University

Attendees:

Margaret Bowler (MDSG)
Amina Chaouch (Newcastle)
John Kelly (MDSG)
Hanns Lochmüller (Newcastle)
Cheryl Longman (Glasgow)
Georgie Mewing (London)
James Miller (Newcastle) (2nd half)
Darren Monckton (Glasgow)
Susan Musson (Newcastle)
Richard Orrell (London)
Margaret Philips (Nottingham)
Marita Pohlschmidt (MDC)
Ros Quinlivan (London)
Karen Rafferty (Newcastle)
Mark Roberts (Manchester)
Mark Rogers (Cardiff)
Michael Rose (London)
Rachel Thompson (Newcastle)
Chris Turner (London)
Tracey Willis (Newcastle) (1st half)

Session 1 – UK Myotonic Dystrophy Patient Registry

International developments

- Mark Rogers gave an overview of myotonic dystrophy (DM1 and 2) registries that are already running in other countries. He asked 13 contacts if the registries they run are national or regional databases, how the patients are registered, and what data is collected. The countries that have a registry up and running are listed below:
    - Quebec
    - Minnesota (John Day)
    - Rochester (James Hilbert)
    - Canada (Marigold) – CNDR (Canadian Neuromuscular Disease Registry)
    - Finland (Bjarne Udd)
    - Sweden (Christophe Lindberg)
    - France (Guillame Bassez)
    - Netherlands (Baziel van Engelen) - CRAMP (Computer Registry of All Myopathies and Polyneuropathies)
    - Italy (Giovanni Meola)
    - Germany (Benedikt Schoser)
- This was compared to the Naarden dataset (the core dataset that was agreed at the Naarden meeting on June 2009). Most registries use the Naarden core dataset with physician reporting only. There are some additional registries that are under construction: Poland, Serbia, Bulgaria and Australia.

Presentation:
www.treat-nmd.eu/downloads/file/DM1presentations/International_Status_MarkRogers.pdf

UK Registry Update

- Hanns Lochmüller used screen shots to outline what the UK registry would look like once it is launched – it is using a custom-made IT solution that the German registry is kindly sharing with the UK. Ethics have been submitted (including various consent forms and patient information sheets), and a meeting with the ethics committee is scheduled for September. Once the ethics committee has approved all forms, they will replace the current "place holders".
- There were some comments about the wording of some of the questions, in particular the one on sleepiness, and this was rationalised on the basis of being consistent with the international registry. It was thought that they might not generate the correct response due

to misunderstanding but the answers can be checked against the doctors' forms for any disparity. Problematic questions can be reviewed at the curators meeting - as part of a feedback loop one person from this group is invited to the curator's meeting.

- Pregnancy and male fertility were thought to be important and including them should be considered.
- Chris Turner mentioned that it may be beneficial to break the questions down into sections, e.g., heart, lungs, etc, to make it more structured.
- The data in the registry will be reviewed annually but it can be updated at any time by logging in for both patients and doctors. Doctors should update the patient records with a new date even if the new test result is the same as the previous.
- It was felt that a pilot phase would be useful but should not hinder the launch of the registry and could even be implemented now. MDC and MDSG will ask some of the patients on their contact list to participate in the pilot phase; an exact number of patients that should be asked to participate in the pilot is to be agreed upon.
- It was felt that each question should be answered and so alerts should be placed on all questions – this will not allow the next question to show unless the previous question is answered or the form cannot be submitted unless all questions are answered.
- Patients turning 16 should be re-consented as an adult – DOB is collected and so this can be flagged up on the system; login in details should be moved from the parent/guardian to the patient. Consent will be re-affirmed annually and patients can withdraw at any time.
- There will be a list of doctors that patients can select from; doctors here will be placed on the list. If a patient's doctor is not on the list then they can suggest someone – the curator will then contact the relevant doctor asking them to participate. All consultants present at the meeting were happy to be named on the list so that their patients can find them when signing up; those who could not attend the meeting will also be asked if they would like to participate.
- At present it is not possible to directly transfer hospital data into the registry and so will be double data entry – NHS data is difficult to transfer to another database that does not have the same restrictions. Patients would also need to consent to their data being entered into the registry, while patient consent is not obtained for holding patient data on an NHS system, so there could be no automatic transfer.
- The MDSG pointed out that many of the patients on their list are not computer literate or do not have access to a computer and/or internet connection. Paper forms can be made available for those who cannot register on line. It was also noted that due to the lack of drive within the DM1 patients they may not even register – clinicians will need to make patients and families aware of the importance of the registry at regular clinic visits and possibly offer a hand to register where possible (time permitting).
- CTG repeat is potentially useful for clinical trials and is at present not going to be collected in the registry. In most cases genetic reports for DM1 provided in the UK do not even contain the repeat count, as previous advice was that it was a potentially misleading item to tell patients owing to the difficulty precisely correlating repeat count with phenotype or risk of particular complications. This may progressively change in future and may be discussed at IDMC8, but would nevertheless take a while to filter through to general practice. It was thought that it would be useful to capture the consent to potentially measure CTG repeat from biomaterial that may already be stored in a biobank. Patients will not be excluded from any future trials without having a CTG repeat number available as this will be a part of the pre-trial screening process.

Presentation:
www.treat-nmd.eu/downloads/file/DM1presentations/DM_Registry_Screen_Shots_HannsLochmuller.pdf

Ethics

- Hanns Lochmüller gave an overview of the documents that have been submitted to ethics - the review will be held in September in Newcastle.
- Submitting R&D for each site was debated and no clear decision was reached – it is currently down to the individual clinician; Ros Quinlivan noted that she encountered no problems with the DMD Registry by not submitting R&D before a clinical trial was started.
- At a later point, when studies starting with the registry are launched, we will seek portfolio adoption and NIHR funding. At this point local R&D will be required.

Governance and Oversight

- Hanns Lochmüller gave an overview of how the TREAT-NMD Global Database functions and the Oversight Committee process and structure.
- Each national registry can send a curator and an oversight committee member to the annual curator meeting. It was asked who would represent the UK DM1 Registry on an international level but no decision was reached.
- Draft Terms of Reference were presented at the meeting – these were based on the DMD Registry documents; comments were asked for by end of the month.
- It was decided that the oversight committee should have a representative from the patient organisations (MDSG and MDC) and also a patient representative.
- Everyone present at the meeting were happy to participate on a steering/oversight committee (those who could not attend the meeting will also be asked if they would like to participate):

Margaret Bowler (MDSG)
John Kelly (MDSG)
Hanns Lochmüller (Newcastle)
Cheryl Longman (Glasgow)
Georgie Mewing (London)
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Mark Rogers (Cardiff)
Michael Rose (London)
Chris Turner (London)

Standard Operating Procedures

- Patients from Republic of Ireland are not eligible to participate in the Registry and so the SOPs need to be altered accordingly; Northern Ireland patients will be eligible but a clinical contact will need to be engaged (Alex McKee?)
- Draft Standard Operating Procedures and the relevant appendices were presented at the meeting – these were based on the DMD Registry documents; comments were asked for by end of the month.

Dissemination and funding

- Hanns pointed out that in the long-term it will be aspirational to have the registry adopted to the NIHR portfolio which will lead to further funding – at present this is not possible.
- The MRC centre grant is due for renewal in 2013 (second 5 year term) and DM1 may be considered a priority.
- Both the MDSG and MDC were interested to help with launching and promoting the registry plus funding a curator for at least 1 year (or when other funding is secured). Newcastle will draft a proposal that can be submitted to the MDSG board to review at their next meeting.
- MDSG noted that they are attending a GP conference and there will be a forum where the registry can be discussed. Margaret Bowler will establish whether there would be the opportunity to address the meeting to talk about the registry and will feed back.

Session 2 – Standards of Care for Myotonic Dystrophy

Results of Modafinil questionnaires

- Hanns Lochmüller provided an overview of the Modafinil questionnaires on behalf of David Hilton-Jones. Modafinil is currently licensed for treating Narcolepsy and so it is used off-label to treat DM1 patients' daytime sleepiness.
- Many PCTs will not pay for Modafinil to be prescribed for DM1 patients without a sleep study being carried out. It was asked if the US has the same problems prescribing Modafinil as the UK does – nobody had a definitive answer for this but it was thought that the US would have many of the same problems if not more.
- Overall there are 10-15% of patients on Modafinil across the different centres surveyed. Of those receiving Modafinil more than half claimed a dramatic benefit and headaches and insomnia as the most common side effects; EMA argued that Modafinil has side effects such as severe skin reactions, etc, which is not seen with this survey.
- More evidence is required about using Modafinil to treat daytime sleepiness in DM1 patients – the drug company that manufactures Modafinil have no plans to carry out a study (the company has just been bought over); it was noted that Multiple Sclerosis has NICE guidelines for Modafinil use.
- David Hilton-Jones has outlined a proposal for taking the data from the questionnaires forward to the EMA. He suggested preparing an outline for prescribing Modafinil – the meeting participants thought that overnight oximetry did not necessarily need to be present in this outline, a contact at EMA should be sought and a short letter/report could be published to provide weight to the results. Everyone agreed to the principles of the plan.

Presentation:
www.treat-nmd.eu/downloads/file/DM1presentations/Modafinil_Audit_Results_HannsLochmuller.pdf

Results of the London workshop and Standards of Care in DM1 Online Questionnaire

- Chris Turner gave an overview of the December 2010 Queen Square MRC neuromuscular centre DM workshop and an overview of the results from the Standards of Care in DM1 Online Questionnaire. The wording of some of the questions was noted to have caused some confusion amongst respondents but most questions were clearly understood and answered.
- Chris Turner highlighted the current published literature on standards of care in DM1 from Canada as part of the DM Expert Panel and Scotland as part of the Scottish Muscle Network.
- Cheryl Longman gave a brief overview of the Scottish guidelines. They were produced primarily for GPs and are an agreement on the minimum levels of care required, including referral triggers. The quality of the evidence for each recommendation was calculated based upon the Scottish Intercollegiate Guidelines Network (SIGN) – it was noted that most of the current recommendations have a poor evidence-base (Category D) and that they are based on professional experience rather than clinical trials.
- Chris Turner commented that nevertheless the Scottish Muscle Network guidelines provide an invaluable start to drawing up more formal practice.
- 11 out of 20 participants responded to the survey. As a whole there was significant disparity between the different centres with a relatively small number of areas with full agreement across all centres.

Presentation:
www.treat-nmd.eu/downloads/file/DM1presentations/Standards_of_Care_ChrisTurner.pdf

Proposal for areas of agreement

- Chris Turner suggested the following areas of agreement:
    1. Cardiorespiratory complications account for the majority of early mortalities in DM1 and there is an imperative to improve monitoring and treatment of these complications.

2. EDS is a disabling symptom for patients and families. Modafinil is effective at treating EDS in some patients and further clinical trials need to be performed to identify effective outcome measures for assessing excessive daytime sleepiness and therapeutic efficacy of Modafinil.
3. Further investigation is required into the poor tolerance of NIV in DM.
4. Improved acute admissions care planning especially for acute respiratory failure.
5. Randomised intervention studies to determine the efficacy and timing of pacemakers and implantable defibrillators in DM will be important especially with regard to "normal" electrophysiological parameters calculated with ECG and EPS monitoring. In the meantime a standardised national approach to monitoring cardiac complications should be configured and applied.
6. Improved access to specialist cardiology input with consideration of formation of a UK Cardiology DM network.
7. A better understanding of the role of dysphagia in causing aspiration pneumonia, malnutrition and early mortality in DM.
8. To improve management of lower GI symptoms.
9. To improve access and awareness of PGD/antenatal screening.
10. To improve access to therapy services in the community and access to advice from specialist centres.
11. The vital role of registry formation and charities in engaging clinicians, patients and families.
12. More open discussion and simplified pathways to obtain DM tissue for research need to be generated.

- 12 domains of care were proposed including 1) cardiology, 2) respiratory and EDS, 3) GI, 4) CNS, 5) muscle, 6) anaesthesia and sedation, 7) endocrine, 8) ocular, 9) diagnosis and pregnancy, 10) outpatient experience (including joint clinics), 11) community care, and 12) information for patients.
- Chris Turner asked for volunteers to lead on the care domains – he will send an email out to everyone, including those who could not attend the meeting.
- Chris will also set out a standardised procedure for reviewing the different care domains.
- It will be important to take advantage of the mechanisms for drafting consensus guidelines that have already been established internationally with the DMD, SMA and CMD international consensus guidelines: these used specific methods for establishing the consensus (RAND/Delphi) that may help the final guidelines gain credibility and ease the path towards NICE adoption.
- Mark Rogers noted that it will be useful to include Welsh and Scottish clinicians in all of the domains - this will hopefully allow the standards to be adopted in Wales and Scotland.
- The domains should include criteria that will trigger a referral pathway to a specialist.
- Patients and patient organisations should be involved in the process.
- Hanns Lochmüller suggested that everyone should have a draft of their care domain prepared by the end of October.
- It was agreed that a family guide will eventually be produced in a manner similar to the DMD standards of care.

Discussion on areas with further work required

- Chris Turner suggested that there are some areas where there is little consensus across DM1 experts, such as monitoring of diabetes mellitus, and a range of opinions will need to be drawn from to provide standardised guidelines .
- The standards of care are being developed as UK guidelines rather than international guidelines. This will be an iterative process and will require updating once completed.
- The focus will be on DM1 adult care initially.

Proposal and discussion for publication, dissemination and funding

- A consensus report on DM1 standards of care will be produced for publication.

- The standards of care document will be disseminated to the community, including patients and clinicians. The patient organisations will be instrumental in the dissemination process.
- Commissioners – a formal National DM1 Standards of Care document will enable better engagement with commissioners and improve funding of services for patients in the UK.
- NICE guidelines – in order for the standards of care to be adopted nationally, the process for generation of the standards needs to be outlined very clearly. A standardised method for reviewing the different domains of care is required.

Action Points

- All attendees and other invitees who could not attend will be given an opportunity to feed back on the Terms of Reference, SOPs and appendices for the DM registry by the end of July.
- Newcastle will provide a proposal for review at the MDSG board meeting by end of July.
- Newcastle will gather the names of the invitees who could not attend but would like to participate on a steering/oversight committee for the registry.
- Newcastle to gather the names of the invitees who could not attend but would be happy to be named on the doctors list for the registry so that their patients can find them when registering.
- Chris Turner will e-mail all members of the group (including those who could not attend the meeting) requesting volunteers to lead on each care domain.
- Once domain leaders have been agreed, Chris Turner will circulate a standardised method for the review of each domain.
- All care domain leads should have a draft completed for review by end of October.
- Registry front-end testing: pilot phase to be implemented as soon as possible – MDC and MDSG to recruit patients/carers that are willing to test out the registry.
- Launch of registry following full ethics approval– expected November 2010.