



National Commissioning Group
For Highly Specialised Services

Diagnostic and Advisory Service for Neuromyelitis Optica (NMO)

Oxford University Hospitals NHS Trust

Annual Report October 2013

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Outcomes that can't be quantified.....



JS: I owe a lot to Oscar



N&N: Patients forming friendships

"I just wanted to thank all of you for being so incredibly caring, thorough and thoughtful. My return to oxford has been much easier because of your team – I'm forever grateful" – **ST in December 2012**



DA: "Just thought I would share my news - I am now a proud daddy!"

"When I first fell ill 5 years ago there was a total lack of information and support. I am really impressed with the help, energy and support that is now occurring and feel it is a great benefit to the JR that the team are now available. They are fantastic. Well done!" **(From anonymous "patient experience questionnaire" feedback, 2012 - 2013)**

"Really appreciate the time and effort being invested in research and support for NMO. The NMO team is very dedicated. Excellent progress made in the service since it was first formed e.g. Production of booklets, website etc."
(From anonymous "patient experience questionnaire" feedback, 2012 - 2013)

1. Service Overview

The Diagnostic and Advisory Service for NMO at the Oxford Radcliffe Hospital (Herein referred to as the “NMO Service”) combines a specialist laboratory with a dedicated clinical service to offer a multidisciplinary service for patients across the south of the country.

The NMO team comprises of:

Clinical team

Dr Jackie Palace	Consultant Neurologist (service lead)
Dr M Isabel Leite	Honorary Consultant Neurologist, Senior Clinical Research Fellow
Dr Saleel Chandratre	Consultant Paediatric Neurologist
Mr John Elston	Consultant Ophthalmic Surgeon
Dr George Tackley	NMO Clinical Fellow
Jon Revis	NMO Specialist Nurse
Kay Day	Occupational Therapist
Kate Browne	NMO Physiotherapist
Julia Goodgame	Clinical Service Manager, NMO/CMS
Annaliza Rye	NMO Service Coordinator

Laboratory Team

Prof Angela Vincent	Honorary Consultant in Immunology
Dr Patrick Waters	Senior Postdoctoral Scientist
Dr Mark Woodhall	Postdoctoral Scientist

The service performs around 320 patient activities per year, in a combination of outpatient, inpatient and day case episodes, depending on clinical need. Patients are offered a full multidisciplinary experience when they come to clinic, with assessments from neurologists, ophthalmologists, specialist nurse and a team of therapists. For patients who are unable to attend (possibly due to disability) remote advice from the relevant team specialist is offered to local neurologists and GPs, as well as an advice email and phone line for patients to call with any queries.

To ensure ease of access, the service aims to ensure all appointments and investigations are completed within one visit. All patients are discussed within a multi-disciplinary meeting attended not only by clinicians, but also by laboratory and administrative staff to ensure a holistic and thorough assessment as well as a good communication to patients about appointments.

The service has the ability to admit patients who require urgent review to a dedicated neurosciences unit, with access to specialist therapies such as plasma exchange. A “relapse” (or exacerbation) of NMO can be a medical emergency, so the team liaise closely with bed managers to ensure rapid admission and treatment.

Most patients are on long term oral medication, but the few who need intravenous medication can be admitted as a day case to the neurology

investigations unit, where trained nurses can administer medication such as Rituximab. Education links have been developed between the NMO team and the ward staff to ensure continuity of care.

An important part of developing a truly national service is closely linking with our sister NMO team in Liverpool. This is done through a combination of face to face meetings, teleconferences and jointly hosting and attending conferences relevant to the field of NMO. At these meetings, collaboration can be fostered in a supported environment to ensure continual developments in standardised care and evidence based practice for NMO patients.

2. Service Objectives, Outcomes and Performance measures

The purpose and goals of the service are set out in the service specification.

- To make a definitive clinical and laboratory based diagnosis of patients with suspected Neuromyelitis Optica Spectrum Disorder (NMOSD).
- To optimise NMO assay reporting time, this in turn speeds up the diagnostic process.
- To ensure that NMO patients are quickly started on the correct long term immunotherapy to reduce the likelihood of having further relapses. Preventing a relapse is associated with a much better outcome than treating a relapse after it has occurred.
- To involve patients in their own care and allow them to feedback on their own experiences.
- Develop patient / health care professional information.

These are measured using the following outcomes:

Activity levels

- Number of new and follow up outpatient episodes, day cases and inpatient stays.
- Number of AQP4 antibody tests performed in the laboratory.

Performance indicators

- Certainty of diagnosis
- Time to report NMO assay
- Annual relapse rates
- Mortality rate
- ↓ 20% unsatisfactory replies in patient feedback questionnaires

Miscellaneous

- Geographical access to the service
- Time from the service receiving the referral to being offered a clinical consultation by the service.

Activity Figures

The service activity is monitored and recorded on a monthly basis so that the centre can meet the demands of a shifting patient demographic and case load.

Laboratory Update:

For the period April 2012 to March 2013 the Laboratory team for the Diagnostic and Advisory Service for NMO (Oxford John Radcliffe Hospital) tested a total of 4849 samples (this is the total of all samples received from eligible and non-eligible countries worldwide) of which 4437 samples were received from the United Kingdom and other NHS eligible overseas EEA member countries under the testing remit of the service. Of these 4437 samples, 3929 were new patient serum/CSF samples from which 104 (2.6%) were reported positive for AQP4 antibodies see **[Appendix 3]**.

The activity figures for each country for the period April 2012 to March 2013 are summarised in **[Appendix 1a-c]**. Comparing the activity figures for April 2012 to March 2013 with the same service period in 2011-2012, the service has seen a 6.5% increase in the number of NMO assay tests being performed (3371 in Apr-11 to Mar-12; 3593 in Apr-12 to Mar-13; refer to **[Appendix 2a-c]**). During the period April 2012 to March 2013, 93.7% of all assays completed were reported within 5 days of receiving the sample **[Appendix 3a-c]** with the remaining being reported within 11 days. This compares with the previous service year where 95.9% were completed in 5 days with the remainder being reported in 11 days.

A summary of the activity for the first quarter of this year (April 2013 to July 2013) compared with the same service period for the last two years is shown in Tables 1, 2 and 3. In the first quarter of this year 1251 new patient samples **[Appendix 1d]** have been tested by the service with 28 (2.24%) of these being reported positive for AQP4 antibodies **[Appendix 2d]**. During this period 93.7% of all assays completed were reported within 5 days of receiving the sample **[Appendix 3d]** with the remaining reported within 10 days.

In addition to testing routine samples for NMO the Laboratory team also provide AQP4 titrations on request for individual patients and have now completed titrations on 177 patient samples in 2012 compared with 86 patient samples in 2011 **[Appendix 4a-c]**. The team have currently completed titrations on over 60 patients either known or on remote advice to the NMO service **[Appendix 4a]**. Although titrations are labour intensive the benefits of being able to follow a patient's AQP4 titres over the course of their disease can be invaluable for assessing the effectiveness of treatment regimes, for example.

Clinical Services Update:

In the April 2012-March 2013 period the service received 61 new patients referrals from eligible areas **[Appendix 5]**. A large proportion of the patients seen in an outpatient setting are followed up at the centre on an annual or bi-annual basis whilst also visiting their local neurologist.

Since 2013, the service has increased the number of outpatient clinics per year from 28 to 46 per year, to cope with increased demand. This equates to roughly 90 extra patient appointments.

The clinical service activity for 2012-13 was 2% over annual plan on new patients seen, 9% over annual plan on follow up patients seen, 37% under

annual plan for day case admissions and inpatient events were 48% under annual plan.

See **[Appendix 5]**

The clinical service activity for 2013-14 is 27% over annual plan on new patients seen, 49% over annual plan on follow up patients seen, 13% under annual plan for day case admissions and inpatient events were 35% under annual plan. Since August 2013 we have not been using straight line forecasting we now calculate than actual patients seen within the last 12 months to give us a more accurate yearly forecast.

See **[Appendix 6 & 6a]**

This equates to an increase in new patients seen by 25%, follow up patients seen by 40%, 24% patients seen in the day case unit and 13% of patients admitted to the ward.

Remote advice for patients and clinicians is incredibly important, especially for those unable to attend clinic due to disability or current illness. An audit of remote advice provided by the NMO Nurse in one month is summarised in Table 4 below.

	Pt call r.e. Treatment/Relapse	Call with HCP	Admin Call	Email Trail complete with pt	Email with HCP	Lab related
Number	68	42	30	55	13	8
Time(mins)	540	230	115			

Table 1:

Certainty of diagnosis

The NMO service has access to highly specialist investigations (including the laboratory test for AQP4 antibodies, highly specific for the diagnosis of NMO) as well as review with experienced clinicians to ensure that patients receive an accurate diagnosis of their condition.

Due to the difficulties in differentiating NMO from other demyelinating and inflammatory disorders, many patients will come to the service with an unclear diagnosis, or in some cases an incorrect diagnosis. In 2013, 57% of patients seen by the NMO service have their diagnosis altered which has a huge implication on treatment choice and prognosis for the patient. Only 8% of patients leave the clinic with an uncertain diagnosis.

The service saw 61 new referrals between April 2012 and March 2013. Many of these patients were assessed to have a different diagnosis to the one they had been given at their local hospital. The impact of an incorrect diagnosis can be devastating, for example, work by doctors Palace and Leite in 2008 suggested that treating NMO patients with interferon- β , used in relapsing remitting multiple sclerosis can increase the number of relapses a patient may have.

Service discharge

The service has an overall discharge rate of 24.5%. Approximately half of these patients have MS and were discharged back to their referring

neurologist. The remaining discharged patients had other demyelinating conditions, such as ADEM or idiopathic transverse myelitis. These have a significantly lower risk of relapses and often do not require long term immunosuppression or review from the NMO service. In any case, we ensure that the referring clinician can re-refer the patient if there are any further problems.

Speed of reporting results of NMO antibody test

NMO can be a devastating disease if left undiagnosed and untreated. This can be compounded further by incorrect diagnosis. Therefore the service aims to assess and diagnose patients as rapidly as possible.

Since the last service year (Apr-11 to Mar-12) the service has seen a 6.5% increase in the number of NMO assay tests being performed (3371 in Apr-11 to Mar-12; 3593 in Apr-12 to Mar-13; refer to **[Appendix 2]**). However even with an increase in samples received and with the additional AQP4 titrations factored in during this period (April 2012-March 2013), 93.7% of all assays completed were reported within 5 days of receiving the sample **[Appendix 3]** with the remaining being reported within 10 days. This compares with the previous service year where 95.9% were completed in 5 days with the remainder being reported in 11 days **[Appendix 3]**.

To ensure that all relevant correspondence and imaging from the referring centre has been transferred to the NMO service, a figure of 8 weeks from receiving referral to assessing the patient was agreed. From April 2012 to March 2013 patients were seen on average in 51 days (7.2 weeks) from receiving a referral.

Annualised relapse rate

Of the 160 patients that have been seen since the clinical service was commissioned, 76 patients are AQP4+. To ensure accuracy, patients without this diagnosis (e.g. monophasic diseases or MS) were not included in this analysis

The annualised relapse rate was 2.83 relapses pre-service and 0.09 relapses post service. This corresponds to a 97% decrease in the relapse rate.

This significant reduction could be mostly due to:

- Reaching a correct diagnosis.
- Ensuring that the treatment is the most appropriate.
- Providing patient education to increase compliance with treatments and prevention of associated complications.
- Facilitating good communication links between the service, patient, GP and other healthcare professionals.
- Educating other neurology teams by visiting clinics, talks and email advice.

This 13% reduction in relapse rate over the last year (from 86% in Sept 2012) is very encouraging when considering the service tends to see the most severely affected patients for long term follow up and the relapse rates may rise in the future due to rationing of the service.

Mortality rate

Since the service commenced in April 2010, 3 patients seen within the service have died. A meeting was held on 6th December 2012 between Oxford and Liverpool NMO services to discuss mortality and morbidity in NMO patients, with another meeting planned for December 2013.

Patient feedback

The service should be geared towards the needs of the patients and should be sensitive to any suggestions or complaints that are made. To ensure that patients feel they are free to speak freely, they are provided with anonymous questionnaires which focus on their experiences from receiving an appointment through to being seen. This also looks at any remote contact (emails, phone calls) that the patient may have had. An example of this questionnaire is in **[Appendix 7]**.

Patient Experience

April 2012 – March 2013 – data from 60 questionnaires

March 2013 – September 2013 – data from 30 questionnaires

The service continues to improve with information regarding appointments and location. There have not been any concerns raised by patients with regard to their appointments, timings location. Patient choice is adhered to with regard to rescheduling when necessary.

Informing patients of their condition has improved; with all patients who have completed the questionnaire stating they have an understanding of the disease.

The information given to the patients (new booklets) has resulted in 100% positive feedback. The booklets will very soon be available in audio format.

Please see **[Appendix 7a]** for further outcomes from the questionnaire in **[Appendix 7]**.

Patient Geographic's

As a national service for NMO Oxford aims to offer equal access to the diagnostic and management expertise at the centre to patients from across the South of England. However, many patients cite transport costs as a limiting factor in their decision to attend the Oxford clinic. In cases where the patients are physically unable to attend outpatient clinic a remote advice service is offered to their local clinician regarding diagnosis and management. Please see **[Appendix 8 and 8a]** for a breakdown of patient geographic's for Lab assays and patient appointments.

3. Financial Update

To be presented by the ORH Financial team lead by Rachael Raven, NTSS – Assistant Business Partner, Oxford.

4. Service Developments

An important part of developing a truly national service is closely linking with our sister NMO team in Liverpool. This is done through a combination of face to face meetings, teleconferences (an example of the minutes are in **[Appendix 9]**) and jointly hosting and attending conferences relevant to the field of NMO. At these meetings, collaboration can be fostered in a supported environment to ensure continual developments in standardised care and evidence based practice for NMO patients. **A meeting is scheduled with the NMO team on 19th December 2013 in line with 2013- 2014 CQUIN guidance. (Appendix 10)**

Joint/Outreach Clinics

Joint clinics were held in GOSH London, Norwich, Southampton, and Plymouth. Earlier this year with Dr Cheryl Hemmingway at Great Ormond Street Hospital (GOSH), members of the National NMO Service and paediatric neurologists with an interest in NMO.

QIDIS

Dr Isabel Leite has worked with Jon Revis to develop a database to capture clinical and non-clinical information. This is a new QIDIS project, and still at the data input stage. Analysis of this data will be available in 2014.

Both specialist centres have worked together in the development of written and web based patient info, which has been very well received.

The Oxford outpatient experience improvement scheme

- This involves developing a document library in outpatients for the use of patients who come to clinic. Our OT, Kay Day, has spent the past few months collecting the relevant patient info sheets from external support groups and charities and other relevant HCP's. signs;

Patient info library

For the last year patients have had access to a library section in the OPD with information as picked by our nurse and therapist team from charities, healthcare organisations and other support agencies for our patients. Alongside this are reference books that patients can read and decide to purchase.

Feedback has been incredibly positive:

L.H, patient "been able to grab leaflets at appointments is so useful – Neurosupport (a charity in Liverpool looking at the after effects of disability) have guided me on employment rights and helped me get back to work."

Expertise in NMO is developed by seeing as many patients in our catchment area as possible. It is imperative to share they experiences and observations that are made on this cohort not only with service users, but also referring clinicians, healthcare professionals and researchers interested in NMO. As NMO is a rare condition, the upmost effort has been made to promote

knowledge of NMO and the service provided to healthcare professionals who may come into contact with a patient who may have NMO.

This engagement is carried out in a number of ways

Research Developments.

Teams (both clinical and laboratory teams) have demonstrated that the assays used in the UK are the most sensitive assays available (Waters *et al* 2012) and they remain highly specific. Although not in routine use the Laboratory team have also used quantitative flow cytometry (FACS) on transiently transfected HEK cells to confirm low positive results in a quantitative manner every few months. However, there are still patients classified as NMO by clinical criteria that are AQP4 antibody negative. In order to further examine this group of patients the Laboratory team have set up an assay to detect antibodies against myelin oligodendrocyte glycoprotein (MOG) as others groups had previously shown that patients with similar inflammatory diseases have these antibodies transiently. The NMO team thought that this would be important to determine if any of the patients diagnosed as NMO had another antibody that could exclude a diagnosis of NMO and perhaps indicates a milder disease requiring less severe treatment. The NMO team identified 4 patients out of 27 diagnosed as NMO or NMOSD who were positive for MOG antibodies (Kitley *et al* Neurology 2012). The Laboratory team are continuing to improve this assay and use it routinely to identify new patients in order to gain a better understanding of them clinically.

As we have discovered more about the conditions we see through the NMO service, we have highlighted a number of symptoms which seem to be very specific to NMO, one of the most interesting and difficult for the patients being neuropathic pain. Whilst neuropathic pain is not unique to NMO (it is commonly recognised in MS and other spinal cord conditions), the exquisite severity and nature of the pain appeared to be very different. We began thinking about the nature of the pain in 2011/12 and have since completed a project looking at the pain characteristics in NMO (presented at ECTRIMS 2012). This led to a much larger project for 2013 in conjunction with the pain services within the hospital to better understand the psychological aspects, impact on quality of life and potentially interventional techniques to improve our patients pain. As a team, we provide opportunity to medical and scientific trainees to undertake these projects on our behalf with our supervision, which provides them with a unique training experience and us with the manpower to undertake study without a cost implication to the service. More importantly we have now engaged with a pain specialist who has clinically taken interest in our patients and is offering advice on individual cases where all traditional methods have failed.

Meetings/Conferences

NMO Patient information day, June 2013.

To follow on from last year's patient information day in Birmingham, the Oxford and Liverpool NMO services jointly organised two day of talks which changed the dynamics of the meeting and interactive sessions for patients, friend and families of those affected by NMO. The feedback from the meeting was excellent. Although the majority of attendees were known to the 2 services, a few patients and families who were unknown also came along,

after seeing advertising on the MS society, and other websites. This led to new referrals to the NMO service at the John Radcliffe Hospital. Please see **[Appendix 11]** for the programme of day two this meeting.

People attending were encouraged to network, which led to patients setting up support groups on social sites, such as Face book as well as a section on the NMO UK website for web forums and local support groups.

NMO patient and healthcare professional information

Patient information

The information booklets which were developed by our team have now been made available in Audio. These are available on CD or via the NMO website.

Namely:

- Living with NMO – Independence in daily life X2 CD's,
- Living with NMO – Movement, mobility and travel X2 CD's,
- Living with NMO – Work and money.

NMO scientific/medical publications and presentations

One of the best ways to inform other healthcare providers about work going on within the field of NMO is to publish journal articles. These articles often form the basis of a presentation to other HCP and scientists at various meetings. See **[Appendix 12]** for a full list of publications, presentations and posters produced by the team.

Web based information

To ensure information is available on as many mediums as possible, The NMO Service has developed a website designed mainly for patients, but with sections for healthcare professionals. This website will hold PDF copies as well as audio files of all written info, up to date news and information about relevant events, trials and research updates as well as an area for patients to use as a forum. It has been set up in association with the RNIB to ensure easy access for all.

This website is hosted by The Walton Centre NMO Team.

5. Future Development Plans

Paediatric relapse treatment trial

Dr Jacob, alongside a group of paediatric neurologists has applied for funding to set up a study looking at the best management for relapses. This will compare a standard treatment (IV Steroids) against a dual therapy approach (IV steroids + IVIg).

Relapse prevention trial

Dr Palace has been closely liaising with pharmaceutical companies interested in relapse prevention; however a study would need to be organised at international level to ensure reliability.

6. Appendices

- Appendix 1a. b. c. d. Monthly activity summary for assay service 2010-2013
- Appendix 2a. b. c. d. Yearly activity summary for assay service
- Appendix 3a. b. c. d. Turnaround summary for assay service
- Appendix 4a. b. c. d. Yearly activity summary for Titres done by assay service.
- Appendix 5. Copy of NMO Monthly stats Mar 12 to Apr 13
- Appendix 6. Copy of NMO monthly stats 1st two quarters 2013
- Appendix 7. NMO Patient Survey Final version
- Appendix 7a. Patient feedback compariston from 2012 to 2013 and 2013 to date.
- Appendix 8. Neuromyelitis Optica Oxford Patient Demographics April 2013 to September 2013
- Appendix 8a. Patient demographics for Patients and Assay service for April 2013 to date.
- Appendix 9. NMO Teleconference Agenda 14th March 2013
- Appendix 10. Guidance on the implementation of the highly specialised services 2013/14 CQUIN
- Appendix 11. 2013 NMO Patient day agenda
- Appendix 12. Publications and presentations of NMO service