National Commissioning Group
For Highly Specialised Services

Diagnostic and Advisory Service for Neuromyelitis Optica (NMO)

Oxford University Hospitals NHS Trust

Annual Report September 2017

Outcomes that can't be quantified……

NMO Patient Day 2017 – NMO Team photo

May 2016

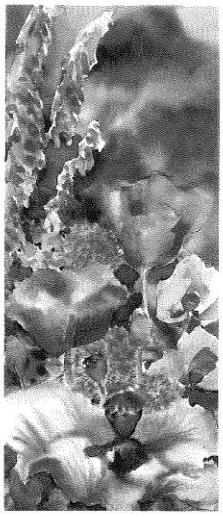
To Annaliza and the N.M.O Team.

Please accept our grateful thanks for all the hard work that went into the N.M.O Conference. We feel so much better being well informed and thankful for all the research being done. Meeting other patients and their families was inspiring and moving.

We are your biggest fans!

With best regards

and [redacted]



Dear Rose, Sandra & the team,

Thankyou for all your help and advice recently when [redacted] was relapsing at Bristol.

A fantastic service!

Thankyou again!

[redacted]

xxx

Thank you cards from patients in 2016

Positive feedback from patients seen in 2016

1. All staff were notably efficient, courteous and highly professional. Excellent impression that Dr Palace and her team were keen to provide a total service, requiring utmost detail + immediate retests of previous spurious results.
2. I look forward to my visits. Afterwards, I have information to follow up and positive suggestions. I feel that I am the focus of the team, and it makes me feel good & encouraged. Thank you!
3. Staff are wonderful. At what can be a very scary time for new patients I was put completely at ease. Staff are warm, friendly, knowledgeable & caring. I have never before experienced care like I have in the NMO clinic in Oxford.

1. Service Overview

The Diagnostic and Advisory Service for NMO at the Oxford Radcliffe Hospital (herein referred to as the "NMO Service") with the Walton Centre in Liverpool, combines a specialist laboratory with a dedicated clinical service to offer a multidisciplinary service for patients across England and Scotland [funded by highly specialised services] and the rest of the UK [directly charged].

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
Miss Srilakshmi Sharma	Consultant Medical Ophthalmologist
Dr Silvia Messina	NMO Clinical Fellow
Rosie Everett	NMO Specialist Nurse
Sandra Reeve	NMO Specialist Nurse
Annaliza Rye	NMO Service Coordinator
James Moore	NMO Admin Assistant
Kay Day	NMO Occupational Therapist
Nina Eagle	NMO Physiotherapist
Julia Goodgame	Clinical Service Manager

Laboratory Team

Dr Patrick Waters	Senior Postdoctoral Scientist/Co-director of the Laboratory
Dr Sarosh Irani	Associate Professor/Co-director of the Laboratory
Dr Mark Woodhall	Postdoctoral Scientist

The service performs around 557 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.

Our service has an international reputation which means we frequently have doctors from abroad working and learning with us, which directly improves the service offered to patients at no extra cost.

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 about the condition.

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

- Remote Support
- Time to report NMO assay
- Certainty of diagnosis
- Annual relapse rates
- Mortality rate
- Patient feedback questionnaires

Miscellaneous

- Geographical access to the service
- Time from the service receiving the referral to being offered a clinical consultation
- Outreach clinics
- Service discharge
- CQUIN

Activity Levels

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.

Clinical Services Activity:

Basic activities are demonstrated in ***[Appendix 1].***

From 1st April 2016 to 31st March 2017 the service received 133 new patient referrals from eligible areas*.* A large proportion of the patients seen in an outpatient setting are followed up at the centre on an annual basis whilst visiting their local neurologist in between.

For financial year 01/04/2016 to 31/03/2017, the service has increased the number of outpatient clinic slots per year from 353 to 371 per year, to cope with increased demand. This means we now have out-patient clinics every week, which often extend into the afternoon.

The clinical service activity for 2016-17 was 48% over annual plan for new patients seen, 24% over annual plan for follow up patients seen, 5% under annual plan for day case admissions and inpatient events were 167% over annual plan.

The annual plan for inpatient spells was reduced from 40 to 12 in 2016/17 because there had been fewer admissions in previous years. 32 inpatient spells this year meant we were much over plan. It is difficult to predict in-patient spells and we expect to be closer to plan next year.

Remote support

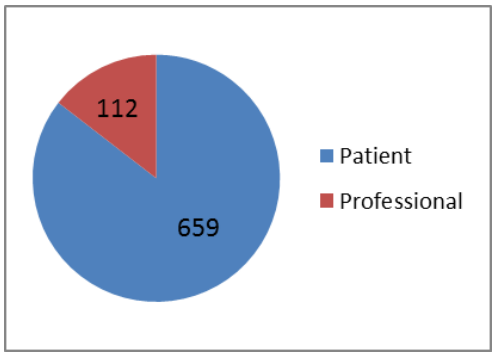


Fig. 1 Calls to nurse advice line 01.04.16 – 31.03.17: call numbers from patients and professionals

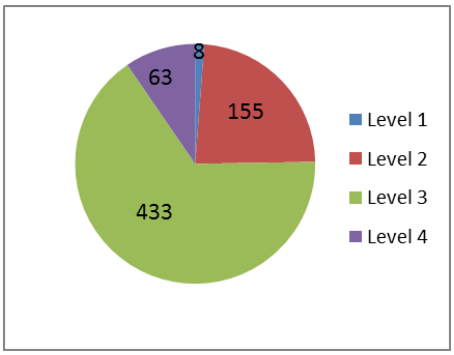


Fig. 2 Calls to nurse advice line 01.04.16 – 31.03.17: call complexity grading

1. Calls to nurse advice line 01.04.16 – 31.03.17: call numbers from patients and professionals

Remote advice	Calls 2016 /17 01.04.16 - 31.03.17	Calls 2015 /16 01.04.15 – 31.03.16	Percentage change 2015/16 – 2016/17
Patient/carers	659	341	+93.3%
Professionals	112	29	+286.2%
Total	771	370	+108.4%

There was 93.3% increase in patient calls from 2015/16 to 2016/17.
There 286.2% increase in calls with professionals from 2015/16 to 2016/17.
Total increase in calls was108.4%.

2. Calls to nurse advice line 01.04.16 – 31.03.17: call complexity grading

	Calls 2016/17 01.04.16 - 31.03.17	Calls 2015/16 01.04.15 – 31.03.2016	Percentage change 2015/16 – 2016/17
Level 1	8	19	-57.9%
Level 2	155	59	+162.7%
Level 3	433	179	+141.9%
Level 4	63	84	-25%
Total	659	341	+93.3%

Call grading:
Level 1 = simple admin
Level 2 = simple patient contact/discussion
Level 3 = more complex discussion, e.g. medication or investigations, follow-up required
Level 4 = relapse management, urgent response required, complex care/planning.

There was 57.9% decrease in calls at Level 1 from 2015/16 to 2016/17.
Level 2 calls increased by 162.7% in 2016/17.
There was 141.9% increase in Level 3 calls in 2016/17
Level 4 calls reduced by 25%.

Being able to contact the NMO nurses is greatly valued by our patients, who receive prompt response and follow-up. The numbers of calls has been steadily increasing each year.

3. Emails 01.04.16 - 31.03.17

	Emails 2016/17 01.04.16 - 31.03.17	Emails 2015/16 01.04.15 – 31.03.2016	Percentage change 2015/16 – 2016/17
Existing Patients	238	183	+30.1%
Potential Patients	62	44	+40.9%
Professional Queries	177	135	+31.1%
Total Emails	477	362	+31.8%

There was 30.1% increase in emails from patients already known to the service from 2015/16 to 2016/17.
We received 40.9% more emails from patients not previously known to the service.
These included emails from European countries Poland & Malta and internationally from Chile, USA, India and Malaysia.
Email queries from professionals increased by 31.1%.
There was an overall increase in emails of 31.8%.

Laboratory Activity:
A more detailed breakdown of the laboratory activity is shown in ***[Appendix 2.]***

For the period April 2016 to March 2017 the Autoimmune Neurology Laboratory team for the NMO Service tested a total of 7754 samples (this is the total of all samples received from eligible and non-eligible countries worldwide) of which 7542 samples were received from the United Kingdom (7364 samples) and other NHS eligible overseas EEA member countries (178 samples) under the testing remit of the service. Of these 7754 samples, 6332 were new patient serum/CSF samples from which 115 (1.8%) were reported positive for AQP4 antibodies ***[Appendix 3]***.

Turnaround times
We aim to report all samples within 5 days and even though the number of samples tested has increased by 20.6% this year our turnaround times have reduced. During April 2016 to March 2017, 99.7% of all assays were reported within 5 days with the remaining (21/6332) being reported within 16 days ***[Appendix 3]***. This year the current turnaround time is 89.5% of assays reported within 5 days ***[Appendix 3]*** and 84.7% reported within 2 days from April 2017 to August 2017.

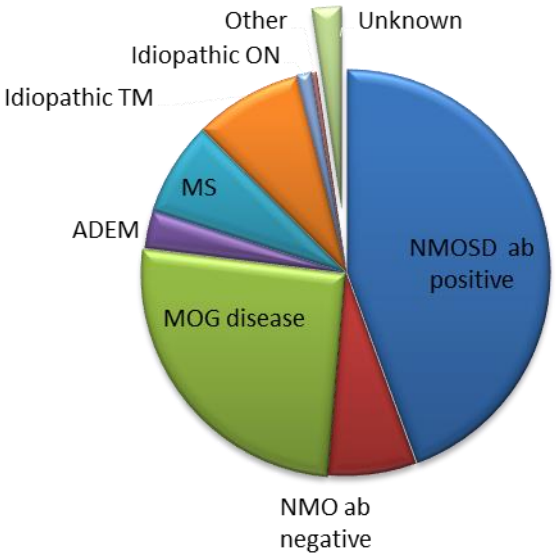
End-point titres to follow serum antibody levels
As well as providing the routine AQP4 antibody test we also provide AQP4 titrations on request for individual patients. Dr. Woodhall has completed serial AQP4 titrations on over 300 patients who are either seen within the service or are receiving remote advice from the service. Refer to ***[Appendix 4]*** for a summary of the AQP4 titrations completed over the last service year. Although titrations are labour intensive [6-12 assays for 1 titration], 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 regimens for example. An important use of the AQP4 titres was highlighted earlier this year when a patient accidentally stopped taking their medication. This resulted in an increase in their AQP4 titres that alerted the Oxford medical team to investigate.

Diagnosis

% definitive diagnosis made

Of our follow-up NMO patients and of the recently seen mimics, only 3.3% remain with an uncertain diagnosis.

Diagnosis	No (%)
NMOSD (Ab positive)	113 (44.3)
NMO (Ab negative)	18 (7)
MOGAb Disease	65 (25.5)
ADEM	8 (3)
MS	19 (7.5)
Idiopathic TM	22 (8.6)
Idiopathic ON	3 (1.2)
Other, e.g. Sarcoid	1 (0.4)
Unknown	6 (2.3)



Relapse rates

Relapse rates pre & post treatment:

Note: Patients are more likely to be kept under our care if their disease is active.

The annualised relapse rate was 2.83 relapses pre-service (ARR calculated on a group of 160 patients seen since the service was commissioned).

In the last year we saw a total of 63 new patients. The average annualized relapse rate pre service was 2.74, while it is 0.19 after they have been seen in the service. This corresponds to a decrease of 93% in the relapse rate.

Table 1. *Pre- and post- NMO service relapse rates for new patients*

	No of patients	*63*
Post NMO Service	*Follow-up, yrs.*	*0.5*
	No Relapses	*7*
	Average relapse n (per pt.)	*0.1*
	Average Annualized Relapse Rate	*0.19*
Pre NMO Service	*Follow-up, yrs.*	*4.7*
	No Relapses	*110*
	Average relapse n (per pt.)	*1.746*
	Average Annualized Relapse Rate	*2.74*

Table 2*. Number of relapses over last financial year*

For 01/04/2016 - 31/03/2017	
Total Active Patients:	264
Total Relapses:	24
n pts who relapsed:	21
Overall ARR:	0.1
Overall % who relapsed:	8%
n AQP4:	113
AQP4 Relapses:	11
n AQP4 pts who relapsed:	11
AQP4 ARR:	0.1
AQP4 % who relapsed:	10%
n MOG:	65
MOG Relapses:	6
n MOG pts who relapsed:	6
MOG ARR:	0.1
MOG % who relapsed:	9.2%

Mortality rate

One death in year 01.04.2016 – 31.03.2017

July 2016: MM – 55 y/o, AQP4Ab positive NMO (on cyclosporine and prednisolone), cause of death: sepsis. Disease onset in 2003, 2 attacks of ON and 4 attacks of TM by 2010 resulted in severe disability, one further attack of TM in 2012.

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. Patients are asked to complete anonymous questionnaires focussing on their experiences of receiving an appointment through to being seen in clinic. The questionnaire also asks about their experience of remote contact (emails, phone calls), privacy and dignity and if they would recommend the service to family and friends. An example of this questionnaire can be seen in ***[Appendix 5].***

The results from completed questionnaires for the last financial year April 2016 – March 2017 can be seen in ***[Appendix 6]*****.**

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 or location. Patient choice is adhered to with regard to rescheduling when this is 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 (all booklets) has resulted in 100% positive feedback. The booklets are available in audio format, all blind patients are informed of this and audio discs are sent to patients on request.

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 an outpatient clinic, a remote advice service is offered to their local clinician regarding diagnosis and management. The expansion of outreach clinics has also helped with this.

Please see ***[Appendix 7]*** for a breakdown of Patient Geographic's for patients seen by the NMO Service in clinics and / or given remote advice from April 2016 to March 2017.

In addition to this we also deal with international enquiries as well. This year we have had emails or phone calls from South America, North America, South Africa, Japan and many European countries.

Referral to consultation time

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. This is more important in AQP4 antibody positive patients, particularly those not on a stable therapeutic dose of immunosuppressant medication.

To ensure that all relevant correspondence and imaging from the referring centre has been transferred to the NMO service, a timeframe of approximately 8 weeks from receiving referral to assessing the patient was agreed.

Since the 1st April 2016 to date all new patients that have been referred to the service have been offered appointments within 8-10 weeks of their referral being received by the service. Some of the patients however have chosen to be seen at a later date. Urgent appointments are also offered when patients are untreated and immunosuppression is indicated and the team also liaises with the referring clinician in the interim.

Joint/Outreach Clinics

Current:

- Joint clinic with Dr Cheryl Hemmingway at Great Ormond Street Hospital (GOSH) twice per year.
- Joint clinic with Dr Peter Brex at Kings College Hospital four times per year.
- Joint clinic with Dr Christopher Halfpenny at Southampton General Hospital every year.
- Joint clinic with Dr Arani Nitkunan at St Georges Hospital twice per year.
- Joint clinic with Dr Leonora Fisniku at the Princess Royal Hospital, Brighton twice per year.

Planned:

- Joint clinic with Dr Martin at Gloucestershire Royal Hospital, Gloucester
- Joint clinic with Dr Hobart at Derriford Hospital, Plymouth

Service discharge

After NMO clinic assessment and review, those with other demyelinating conditions, such as MS, ADEM or idiopathic transverse myelitis are discharged for local neurology management.

CQUIN

Annual CQUIN meetings are held with our sister NMO team in Liverpool. 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 was held this year on 23rd June 2017 and the next one is scheduled for 29th June 2018 in line with 2013- 2014 CQUIN guidance. Minutes from the meeting held on the 23rd June 2017, please see *[Appendix 8]* and copy of the National CQUIN guidance *[Appendix 9]*.**

3. Financial Update

To be presented by the OUH Financial team lead by Carol Ann Gourlay, Neurosciences Finance Manager.

4. Service Developments current and future

a) Review of Clinical Outcome Measures

Oxford continue to use:

- Quality of Life – Euroqol EQ-5D
- Anxiety and Depression – Hospital Anxiety and Depression Scale (HADS)
- Pain – Brief Pain Inventory (BPI)
- Fatigue – Modified Fatigue Impact Scale (MFIS)

Started August 2016:

- Eyesight questionnaire
- Visual Functioning Questionnaire (VFQ-25)

Completed for all patients for 10 months (using those with no eye involvement as control). Sent to patients prior to clinic and reviewed in clinic. 22 pages (large print) but some patients have found this too lengthy.
Plan: review completed questionnaires and ask patients to complete specific questionnaires; if clinically relevant and not completed in past year. Complete during clinic visit where possible.

We have started to analyse patient reported outcome measures.

b) Diet Project:

Monitor the weight of patients at diagnosis before or within few weeks of starting steroid medications (Prednisolone).

Aim:
To provide nutritional and exercise support and information for patients starting long term steroid medication (Prednisolone) as a prevention to becoming obese and compare to weight gain prior to preventative support.

Why:
Patients diagnosed with NMO are treated with steroids which is a long term treatment to reduce the risk of NMO relapses. Some of the associated side effects of Prednisolone are weight gain, osteoporosis, high blood sugar, mood and behaviour changes.
Monitoring and helping patients to minimise some of these side effects can also contribute to improving their sense of well-being and general health.
Supporting people to self -manage their weight and exercise may also contribute to reducing other associated symptoms of NMO such as pain, fatigue, loss of movement and muscle tone and risk of diabetes.

Intention:
To prevent weight gain by implementing an active prevention plan when starting steroids; tapping into local services such as slimming world and weight watchers and local gyms.

c) Actual / potential relapses

Aim: To review all actual and potential relapses (June 16 - June 17) to find out if there are key indicators which may help to identify relapses.

Plan: Record details of all potential and actual relapses reported to team. Relapse data includes: symptoms, medication, recent changes to meds, recent infection, antibody levels, previous pseudo relapse, MRI and electrophysiology findings. Review findings comparing actual relapses

to ones identified as alternative causes. Identify which factors more commonly occur in actual relapses.

d) NMOSD and atypical or opportunistic infections

Prospective record of infections and vaccinations Jan – Dec 2017

Aim: Explore whether being on immunosuppression increases the risk of developing infections and understand which patients are at greater risk, which infections are most common, their severity and impact on their neurological condition and general health

Plan: Ask patients to complete 'prospective record of infections and vaccinations' (given to patients in clinic and send via post) and nurses to complete when infections are reported. Review completed forms.

e) Regional Patient Events

The NMO teams at Liverpool and Oxford are organising regional patient events (similar to our annual patient day but on a much smaller scale), with the aims:

- To update patients/carers re: NMO treatment & research.
- Provide opportunity to meet other people with the condition and share experiences.

The Oxford team are organising an event for patients and carers in the Southampton/Portsmouth area on Wednesday 4th October 2017.
Event will include:

- Presentation/talk about an aspect of NMO.
- Buffet & social time.

The NMO patient charity is funding these events (venue & refreshments).
Oxford team are planning to organise a similar event in London.

f) Patient Information

1. MOG booklet written and in use in draft format. Diagrams with medical illustrations to allow NMO service to reproduce diagrams.
2. Exercise booklet written by Nina Eagle; in review.
3. Fatigue booklet updated by Kay Day; with printers.
4. Newly Diagnosed; practical help and advice by Kay Day.
5. NMO condition booklet under review and being updated to reflect diagnostic criteria and NMOSD (Rosie Everett).
6. Plan for pain, mood and pregnancy booklets.
7. Liverpool have produced healthy eating and continence booklets.

Please see ***[Appendix 10]*** NMO New patient introduction booklet and ***[Appendix 11]*** for the NMO Advice line pamphlet.

g) Web based information

1. NMO Website www.nmouk.nhs.uk
Approximately 800-1000 hits per month.

2. Charity NMO-UK research foundation
Website: www.nmo-ukresearchfoundation.org

The NMO charity NMO-UK is a non-profit charitable organisation which aims to raise awareness of NMO, support people living with the condition, provide financial support and legal advice. This was set up from the annual patient days, and the NMO services work closely with the charity to raise awareness of the condition, run fundraising events, to set the program for the patient days and to distribute NMO patient publications.

h) Research Developments

In 2012 we developed an assay to detect antibodies to MOG in patients with clinically-definite AQP4-seronegative NMO and not in patients with multiple sclerosis. We found that these patients initially present with equally severe optic neuritis and/or transverse myelitis, but that they recovered much better than the AQP4 seropositive patients. These patients require less long term immunosuppression.

We have further developed this assay and confirmed a more than 60% increase in sensitivity, while maintaining specificity (i.e. no multiple sclerosis patients identified) based on adult patient cohorts from Oxford, Japan, and two separate cohorts from Korea; and a paediatric cohort from London. The papers have now been published and further advanced world-wide understanding of the clinical features of MOG disease (Sato et al 2014; Kitley et al 2014). A world-wide study led by Patrick Waters and Markus Reindl (Innsbruck, Austria) to compare MOG assays is planned for 2017.

We also followed up the initial publication on MOG antibodies to further elucidate the clinical features of these AQP4 seronegative NMO patients (Kim et al 2015; Symmonds et al 2015; Piccolo et al 2016; Woodhall et al 2015), pediatric patients (Hacohen et al 2014, 2015) and the biology of the disease (Horellou et al 2015; Saadoun et al 2015; Kaneko et al 2015) in several publications. These publications show that patients with MOG antibodies predominantly have optic nerve involvement. When they have myelitis it often involves the conus (lower extremity of the spinal cord); they are mostly oligoclonal band negative (whereas most MS patients are OCB positive), and lack co-existing autoimmunity. Although these MOG positive patients presented with equally, if not more severe disease when compared to AQP4 positive NMO patients, they seem to recover much better and require less long term treatment.

In line with these clinical observations we developed a second animal model to compare CNS lesions recovery over 2 weeks in animals that were injected with either AQP4 or MOG antibodies. The animals injected with MOG antibodies recover from the antibody insult much faster than those injected with AQP4 antibodies. They do not fix complement in the same manner or to the same degree and do not have vast lymphocytic cellular infiltrates as is seen in the AQP4 animal model. They do get some alteration in myelin structure and temporary loss of nodal proteins, which recover after 2 weeks (Saadoun et al 2015).
In addition AQP1 antibodies have hit the headlines in NMO after two publications from groups in Greece and Turkey suggesting that some NMO patients also have antibodies to AQP1, another aquaporin present in the brain. Dr. Markus Reindl (Innsbruck, Austria) developed an AQP1 cell based assay in collaboration with Patrick Waters and demonstrated that NMO patients do not have AQP1 antibodies (Schanda et al 2015). As AQP1 contains the Colton blood group antigen present on the surface of red blood cells, one might expect patients to suffer from severe anaemia. We don't see this in NMO patients.
Clinically we have demonstrated that pregnant individuals with NMO miscarry more often after disease onset than before (Nour et al. 2016). Miscarriages are more common in patients who demonstrate active disease in the 3 months pre-pregnancy and during pregnancy than those in remission. Based on these observations by Dr. Leite we developed an animal model to show that peripheral injection of NMO-IgG and complement can induce placental inflammation and fetal death in mice, with inflammatory features identical to those seen in human spinal cord and brain lesions. This demonstrates possible AQP4 antibody mediated disease outside the CNS (Saadoun et al 2015).

Clinical research progresses alongside laboratory research. Pain in NMO sufferers is increasingly recognised to be highly prevalent and particularly severe, and in this way distinct from pain in MS. A project in 2011/12 looking at pain characteristics in NMO (presented at ECTRIMS 2012)

spearheaded a much larger venture now underway investigating psychological aspects, impact on quality of life and non-conventional MRI imaging correlates of pain descriptors with the hope of exposing novel treatment targets for NMO related pain. The research has prompted engagement with a pain specialist, who has subsequently developed a clinical interest in NMO, and now regularly reviews patients, offering advice on a case-by-case basis.
Another symptom, fatigue, has also emerged as highly relevant and frequently problematic. We now routinely collect fatigue questionnaires to stratify its characteristics in NMO. Our occupational therapist has created an updated booklet on managing fatigue that has already received much positive feedback. Initial analysis has identified a significant burden of fatigue within our AQP4 antibody positive cohort with the physical-fatigue component coming out as most important. Concurrent depression, anxiety, pain and disability were strong independent predictors of fatigue in NMO.
Through our tissue- and data-bank consent, we have collected a huge body of information on our NMO patients, a process that is on-going. A recent analysis (submitted for publication) has added to existing evidence that immunosuppression reduces relapse rates, but also provided (for the first time) evidence that being on established immunosuppresion likely reduces the disabling impact of an individual relapse.

AQP4Ab negative NMO remains poorly defined and consequently difficult to treat. An externally funded member of our team has begun a multi-modal research project looking into better defining AQP4 negative disease, looking for clinical and investigative differences (including non-conventional MRI) from AQP4 positive NMO, MS and other related conditions, working towards guiding best therapeutic and clinical management.

As a team, we provide the opportunity for 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.

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i) **NMO Drug Trials**

Abide study
Assessing the safety and efficacy of a new therapy administered orally in patients with pain associated with neuromyelitis optica spectrum disorders (NMOSD).
Plan: Recruit approximately 30 patients with myelitis-related neuropathic pain.
Rationale: Current pain medications have not produced satisfactory relief and living with this pain can have dramatic negative effect on quality of life.

Chugai Trial
A multicentre, randomized, addition to baseline treatment, double-blind, placebo-controlled, phase 3 study to evaluate the efficacy and safety of SA237 in patients with Neuromyelitis optica (NMO) and NMO spectrum disorder (NMOSD). Dr Palace is the lead investigator in the UK and we have one patient taking part.

We are closed to recruitment for the Alexion trial: a randomized, double-blind, placebo-controlled, multi-centre trial to evaluate the safety and efficacy of eculizumab in patients with relapsing NMO.

Full list of research projects at Oxford – see ***[Appendix 12]***
Hand-out given to patients regarding research at Oxford – see ***[Appendix 13]***

j) Meetings/Conferences

NMO Patient Information Day, 7th April 2017 & 8th April 2017.
This year's patient information day was held over two days in Birmingham. The first day was more informal with a social event in the evening for patients and carers who wished to stay overnight. The second day consisted of talks by members of the NMO teams and interactive workshops. There was lots of opportunity for participants to meet other people living with NMO as well as discussions with the Oxford and Liverpool teams. The venue was the same this year as the previous two years because the feedback about the venue has been consistently positive. The patient charity NMO-UK research foundation attended the event again and presented awards to fundraisers for their contributions.
Please see ***[Appendix 14a]*** for the event programme and ***[Appendix 14b]*** for the feedback from the patient information day.

k) **NMO scientific/medical publications**
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. For publications please see ***[Appendix 15]***

l) <u>NMO Team Presentations for 2016/2017:</u>

Dr Jackie Palace:
27.05.2016 - St Georges Neurology Grand Round "MOG antibodies".
10.06.2016 - NMO Talk, NOK meeting Arkus, Denmark "Optic Neuritis".
June 2016 - ATLAS meeting, Sydney "Aqp4-Ab Negative NMO"
26.06.2016 - ECTRIMS summer school "NMO Spectrum Disorders"
13.09.2016 - ECTRIMS: MRI teaching course: "MOG is clinically important".
14.09.2016 – ECTRIMS: 'Improving the differential diagnosis of MS using MRI'.
16.09.2016 - ECTRIMS: MRI teaching course 'MOG antibodies and inflammatory CNS disease'.
06.10.2016 - Brighton and Sussex University Hospitals, Grand round presentation."NMOSD"
15.10.2016 - Annual Scientific Meeting of Hong Kong Multiple Sclerosis Society. "AQP4 antibody negative NMO"
28.10.2016 – PACTRIMS "Measurement and interpretation of AQP4 and MOG antibodies" and MAGNIMS: "Differentiating the imaging features of MS from NMOSD and ADEM"
11.11.2016 - Charring Cross Hospital, London, "NMO Spectrum Disorders".
25.11.2016 - Charcot "10 year prospective observational UK study".
02.02.2017 Imperial college: Neuropathology of MS workshop "Assessing the value to patients of the No Evidence of Disease Activity (NEDA) criteria for clinical practice."
17.02.2017 – Grand Round presentation at Oxford Radcliffe Hospital on NMO
16.03.2017 – NDCN Teaching on NMO
13.03.2017 – Presentation at Guthy Jackson meeting on Definition of NMO Relapse & Severity Project - Treatment of NMOSD

Dr Isabel Leite:

Dr Patrick Waters:
21.05.2016 - National NMO Day
13.10.2016 - MOG talk in French Embassy London 11th November 2016: FRC Talks on antibody assays

Dr Mark Woodhall:
21.05.2016 - National NMO Day - Patient Video presentation (Journey from your blood to your antibody result)
08.07.2016 - Work Experience Programme - Sixth Form Students - NMO practical class

Rosie Everett:
09.03.2017 – RCN Nurse Awards 'NMO Nurse Service'
09.12.2016 – JR Neuroimmunology Training Day 'Clinical Questionnaire Platform'
09.09.2016 – Regional MS nurse meeting at Kings College Hospital 'NMO'
29.05.2016 – JR Neuroimmunology group 'Health-related quality of life in NMO'

Sandra Reeve:
16.03.2017 – Guthy Jackson Foundation Patient Day 'Neuropathic Pain'
30.09.2016 – JR Neuroimmunology group 'Early indicators of relapses vs pseudo relapses in NMOSD'

3. Appendices

Appendix 1.	Service activity April 2016 to March 2017.
Appendix 2.	Monthly activity summary for assay service April 2016 to March 2017.
Appendix 3.	Turnaround summary for assay service April 2016 to March 2017.
Appendix 4.	Activity summary for AQP4 titrations completed by assay service April 2016 to March 2017.
Appendix 5.	NMO Patient Survey Form.
Appendix 6.	Patient feedback from April 2016 to March 2017.
Appendix 7.	NMO Oxford Patient Demographics breakdown including clinics and email advice April 2016 to Mar 2017.
Appendix 8.	Minutes from CQUIN meeting held on 23rd June 2017.
Appendix 9.	Guidance on the implementation of the highly specialised services 2013/14 CQUIN.
Appendix 10.	NMO New patient introduction booklet.
Appendix 11.	Advice line pamphlet.
Appendix 12.	Full list of research projects being done in Oxford.
Appendix 13.	Hand-out given to patients regarding research being done in Oxford.
Appendix 14a.	NMO Patient Information Day programme 7th- 8th April 2017.
Appendix 14b.	NMO Patient Information Day feedback
Appendix 15.	Publications of NMO service April 2016 to March 2017.