NHS National Commissioning Group - Highly Specialised Services

Chronic Pulmonary Aspergillosis National Service

The National Aspergillosis Centre

Annual Report 2015-2016
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Cover photo shows a PET scan and CT transverse image of one patient with chronic pulmonary aspergillosis. The colour image shows high intensity radio-labelled glucose uptake at the apex of the left lung indicating high metabolic activity, which may be seen in lung cancer or infection, in this case CPA. The CT scan shows the left apex replaced by a cavity with highly irregular interior walls representing fungal growth on the interior of the thick-walled cavity, and some additional material within the cavity, which is also fungal growth that has detached from the cavity wall. There is marked pleural thickening as well. The right apex shows some fibrosis which is not illuminated on the PET scan.
1 General Overview and highlights
This report covers the seventh full year of this nationally commissioned service. The number of new patients with chronic pulmonary aspergillosis (CPA) increased annually to 2012/13 and has now levelled off; 66 in 2009/10, 58 in 2010/11, 74 in 2011/12 and 89 in 2012/13, 125 in 2013/14 and 119 in 2014/15, and 111 in 2015/16. Sixty seven patients died and 20 were discharged from service, leaving a total of 398 on service from England and Scotland and an additional 13 patients from Wales on April 1st 2016. This represents an 8.8% growth (9.4% growth in prior year). Non-CPA patients with aspergillosis are also being referred in larger numbers, a total of 346 in 2015/16.

The plan to utilise n-of-1 trials of posaconazole (and now isavuconazole) has been successful in that 34 of 78 patients trialled remained on the therapy and the remainder did not benefit and/or were intolerant. One application was made to NHSE for long term therapy but this was declined. Two patients that were on long term therapy have now come off and one remains on treatment.

The Mycology Reference Centre continues to process increasing numbers of samples, notably for aspergillus PCR (87% increase). Antifungal resistant rates in *A. fumigatus* remain above 10%.

In March 2016, the 7th Advances Against Aspergillosis international meeting was held in Manchester, with 350 attendees. News of the meeting reached 8 million viewers via BBC Breakfast Time, BBC NW Tonight, BBC News, BBC local radio throughout the north west of England and ex-pat communities in Spain. Stories were also run in the Guardian, The Sun, The Mirror and Good Housekeeping magazine. A greater emphasis on reaching out to the public is bearing fruit in terms of general awareness.

UK guidelines on the investigation and diagnostic testing of patients with fungal diseases were published in Lancet Infectious Diseases. In January 2016, clinical guidelines for the diagnosis and management of CPA were published jointly by the European Society for Clinical Microbiology and Infectious Diseases and the European Respiratory Society. This is the first ever set of management guidelines for CPA.

The whole Manchester research group (fungi@manchester) published 57 papers and book chapters including some key observations including extremely high levels of the neutrophil chomattractant PPBP found in monocytes in CPA patients. In 2015, estimated country burdens of serious fungal diseases including chronic and allergic aspergillosis were published for 20 countries. A call for all populations to have access to fungal disease diagnostics and antifungal treatments was issued by the Global Action Fund for Fungal Infections in May 2015, an NGO closely linked to the National Aspergillosis Centre.
2 Activity
The total referrals, inpatient stays, procedures, death and caseload in 2015/16 were as follows:

* The NCG fund patients from England and Scotland only
# Appendix 1 shows the Banding criteria used

Of the 457 new ‘aspergillosis’ referrals from England and Scotland (increase of 27.3%) during the year 2015/16, 111 (24.2%) had CPA, very similar to the previous 2 years (125 and 119 patients). Among the outpatient referrals, the mean time from referral to being seen was 6 weeks (Appendix 2), including 10 patients who rescheduled their appointments or did not attend initially. This is similar to the previous year. Appendix 2 shows the area of residence, date of referral and date of appointment. These numbers include 2 referrals and care for 16 patients from Scotland. In addition the service had 3 referrals from Wales and cared for 16 Welsh patients. There were no patients referred from Northern Ireland. Twelve referred patients died within the year.

There has been a growth in Band 1 numbers from 150 to 173 patients, Band 2 patient numbers have grown from 175 to 190, and Band 3 was steady at 25 patients (see banding at Appendix 1). These shifts include 67 deaths (49 the previous year) and 16 discharges from service (21 the previous year). At the end of year, 398 patients were on service from England and Scotland, compared with 363 in the previous year (8.8% growth). Four patients were presumptively cured with surgery and 5 underwent bronchial artery embolization.

Admission days were increased on the prior year – from 814 to 981, with 49 patient days at home on IV therapy.

We have plotted the outpatient activity over the 7 years of the National Aspergillosis Centre operations in the figure below. The green line represents gradually increasing numbers of aspergillosis referrals, and the gap between that line and the actual CPA patients indicates that many alternative diagnoses are made, such as allergic
bronchopulmonary aspergillosis, *Aspergillus* bronchitis, various forms of *Aspergillus* rhinosinusitis and invasive aspergillosis.

**3 Mycology Reference Centre, Manchester (Director Prof Malcolm Richardson)**

The Mycology Reference Centre Manchester (MRCM) has completed its sixth year of operations. There have been numerous developments and continued growth in its portfolio of tests and activities, and as well as major contributions to the University of Manchester taught Masters level degrees in Medical Mycology and Medical Microbiology.

1) Primary activities and developments:
   1. Ongoing validation and familiarisation of new tests in portfolio
   2. Expansion of training and educational activities, including short training courses, and hosting university work placement students who have successfully completed their IBMS Registration portfolios.
   3. Highly successful completion of the third year of a Masters degree in Medical Mycology, in collaboration with the University of Manchester. This Masters is accredited by the Institute of Biomedical Sciences, and individual units are offered as three-week CPD courses accredited by the Royal College of Pathologists.
   4. Marked increase (87%) in requests for Aspergillus PCR tests on NAC patients
   5. Income: internal and external: increase of 4.3% compared to 2013-2014
   6. Income: environmental monitoring business unit: income in excess of £30,000
7. Environmental surveillance services: projects commissioned by UHSM Estates Department/UHSM Infection Control unit: complying with the UHSM policy: “Prevention of Nosocomial Invasive Aspergillosis During Demolition/Construction and Renovation Activities”
   - Heart Biopsy Suite
   - Department of Microbiology, Clinical Sciences Building
   - ENT Theatres: ventilation system upgrade
   - Catheter Laboratories
   - Completion of Paediatric OPD Courtyard Project
   - New Bronchoscopy Unit
   - Burns Unit
   - Cardiac MRI Scanner Building
   - Endoscopy drying cabinets and environment
   - Fire Detector Upgrade works
   - Fire stopping works
   - Hybrid Theatre Project: 12 months
     - CF/Pearce Ward
     - Doyle Ward
     - TDC/Endoscopy Recovery Suite

8. Establishment of a Mould Surveillance Service for assessing the homes of NAC and Respiratory Medicine patients, UHSM

9. Other services for non-CPA patients:
   - Real-time PCR for Pneumocystis DNA
   - Sustained demand for the β-1,3-D-glucan ELISA test (Fungitell): a pan fungal assay for fungal cell wall glucan, including Aspergillus and Candida, offered nationwide
   - Environmental monitoring (air sampling and dust analysis) of patients' houses, schools and workplaces for indoor moulds, including Aspergillus.

2) Representation on national and international committees:
   - EUCAST Antifungal Susceptibility Testing Committee as a Collaborating Laboratory
   - Public Health England Standards for Microbiology Investigations Steering Committee
   - British Society for Medical Mycology
   - International Society for Human and Animal Mycology

3) Research activities:
   - Consolidation of test portfolio offered for the benefit of CPA patients:
     - Ongoing evaluation of a lateral flow device (ISCA Diagnostics/OLM Medical) for the detection of an Aspergillus exoantigen in sputum from CPA patients
     - Ongoing experience regarding sensitivity testing on Aspergillus isolates to include terbinafine, anidulafungin, caspofungin, micafungin and a new azole antifungal, isavuconazole
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- Real-time PCR for Aspergillus in respiratory secretions and blood
- Molecular identification of fungi, including unusual *Aspergillus* species. This is a nation-wide service
- Ongoing evaluation of automated DNA extraction robots in order to respond to the dramatic increase in PCR assay requests
- Completed evaluation of improved methods for detection of anti-Aspergillus antibodies: ELISA for *Aspergillus* IgG and indirect haemagglutination for *Aspergillus* precipitating antibodies
- Methods development and validation of pyrosequencing for detection of azole antifungal resistance mutations in *Aspergillus fumigatus* in respiratory samples
- Monitoring of NAC/CPA patients' houses, workplaces for Aspergillus
- Publications 2013: 15 (Appendix 5) including treatment and diagnostic guidelines commissioned by the European Society for Clinical Microbiology and Infectious Diseases.

4) Training:

- Completion of four year training programmes for two trainee Clinical Scientists funded by NHS NW SLA. One has been appointed as a Band 7 Clinical Scientist in Edinburgh Royal Infirmary. One appointed to a five-year Higher Specialist Scientific Training post at Manchester Royal Infirmary
- Completion of a three-year Healthcare Scientist training programme under the Department of Health’s Modernisation of Scientific Careers scheme.
- UCL/BSMM distance learning Masters in Medical Mycology: one staff member enrolled
- Individual CPD modules of University of Manchester Masters in Medical Mycology, in collaboration with MRCM approved by Royal College of Pathologists and each awarded 25-27 credits
- Contributions to the development of an on-line histopathology of fungal infections training course, in collaboration with the University of Manchester, Leading International Fungal Education ([www.LIFE-Worldwide.org](http://www.LIFE-Worldwide.org) - UK charity).
- Host to four University of Manchester PhD students
- Award of two IBMS registration portfolios. The MRCM is a designated IBMS training laboratory.
- Enrolment of one of the laboratory’s Medical Laboratory Assistants on a NVQ course in Pathology
- Host to two University of Bradford one-year work experience students
- Host to trainees from around the UK
- Host to two oversees visitors for training and collaboration:
  - Dr Subhosmito Chakrabarty (Kolkata)
  - Dr Rita Oladele (Lagos)
4) Challenges:
- Ongoing maternity leaves, leave entitlements of staff, and part-time returns to work
- Dramatic increase in work-load in the absence of an adequate workforce.
- Laboratory space, increase necessary to accommodate 12 staff

4 Clinical service developments and personnel
The NAC has completed its seventh year of operations. The major shifts and improvements in practice and capacity are as follows:

1) Clinical and administrative personnel
The following staff were appointed or redeployed to contribute to the NAC:
- Professor David Denning, Professor of Infectious Diseases in Global Health (5 PAs)
- Dr Pippa Newton, Consultant in Infectious Diseases (6 PAs)
- Dr Eavan Muldoon (5 PAs)
- Dr Chris Kosmidis (5 PAs)
- Dr Ibrahim Hassan, Consultant in Microbiology (1 PA)
- Dr Riina Richardson, Consultant in Oral Microbiology & Infectious Diseases (4 PAs)
- Luke Cannon, CT2 in Infectious Diseases (50%)
- Dr Shomik Sibartie, Educational Fellow (50%)
- Ms Deborah Kennedy, Specialist Nurse (40%)
- Mrs Georgina Powell, Specialist Nurse (80%)
- Ms Stephanie Poliensa, Specialist Nurse (50%)
- Mr Philip Langridge, Senior Specialist Physiotherapist (50%)
- Miss Reyenna Sheehan, Specialist Physiotherapist (20%)
- Dr Maria Gamaletsou, Clinical Fellow (100%)
- Dr Gemma Hayes, Clinical Fellow (100%)
- Mrs Christine Harris, NAC manager (100%)
- Dr Graham Atherton, Senior Clinical Information Architect (Patient engagement) 40%
- Mrs Maxine Redshaw (50%)
- Ms Marian Webster (50%)
- Ms Debbie Kirby, Medical Secretary (50%)
- Mrs Megan Hildrop Clerical Assistant (25%)

2) National Aspergillosis multidisciplinary team meetings (MDT’s)
The National Aspergillosis Centre hold a variety of MDT’s to improve the management and care of our patients.

NCG/ID MDT – NAC team every Thursday to discuss problems that arise with patients and their management. These range from medication, in-patient stays, referrals, care in the community, GP and hospital physician enquires etc. The team will discuss and decide what action should be taken.

Surgical MDT – arranged when sufficient cases are listed for discussion (approximately quarterly). To discuss cases that may be suitable for surgical resection. Scans and results are reviewed with several of the cardiothoracic surgeons and our team. If patients are
suitable they are referred to the cardiothoracic surgeons for further discussion and the patient is informed.

**DFS (discharge from service)** – Patients are discharged from service when appropriate and can also be referred back to service if deterioration of disease occurs.

**Radiology MDT** – Every Thursday with consultant radiologists to discuss difficult CTs, embolisation etc.

4) **Home delivery of antifungal agents**
Healthcare at Home continue to deliver high cost antifungal medicine to patients at home, reducing some clinic visits, improving service to patients. The delivery service has been extended to PCT funded patients with other forms of aspergillosis. This service has been extended to include isavuconazole in the last 12 months.

5) **Postal bloods and sputum**
The postal blood and sputum service works well for following up antifungal drug levels between clinics, and getting much higher quality and volume samples. As *Aspergillus* PCR on sputum is not available elsewhere in the country, some of these samples are also transported in the post. PCR is much more sensitive than culture and can be used as a proxy for detecting resistance and clinical failure. An increasing number of high volume cultures to improve the culture yield for susceptibility testing come in through postal packs.

6) **Use of validated scores to assess severity of disease and outcomes (QOL)**
The St. George's Respiratory Questionnaire (SGRQ) is routinely and frequently used as a proxy measure of patients’ well-being or quality of life. Together with the MRC dyspnoea score the 2014/15 data is presented in Appendix 4. This was further augmented by an assessment of fatigue which has a major impact on quality of life.

7) **n-of-1 trials of posaconazole for third or fourth line antifungal therapy**
We have now fully evaluated the new guidelines to use posaconazole on an individual trial basis, ‘n-of-1’ trials. Patients are required to successfully meet the criteria set out by NCG of 3Kg weight gain and decrease in SGRQ score of 12 points by six months The outcome for 78 patients is shown in the figure.
This trial has been presented as a poster twice and the paper is nearly ready for submission.

5 Audits
1. Time to appointment and shared care
Most patients were booked for an appointment within 6 weeks. However, some appointments were longer mostly due to patients rescheduling appointments or not attending.

Ten patients died within the year after being seen for the first time and overall 67 patients died on service, up from the prior year. This probably reflects a combination of late diagnosis and referral, highly complex patients with azole resistance and drug intolerance, and severe underlying disease.

There continues to be considerable shared care arrangements, especially for patients requiring IV courses of therapy near their home. If the patients is under our care, and the local consultant is willing to administer AmBisome of micafungin, we sanction and pay for this. This is one of the reasons why our admission days are relatively low for the increasing volume of work. Our own OPAT service has only helped a small number of CPA patients, because of the issues of distance.

2. Clinical audits
Several clinical audits have been undertaken in 2015/16. Most of these have been completed:
- Chronic fibrosing pulmonary aspergillosis case series finalised and submitted
- CPA/ atypical mycobacterial coinfection. (Database complete, need to analyse case series)
- Posaconazole n of 1 trials (see section 4.8)
• *Aspergillus* PCR (write up complete)
• Azole resistance rates in *A. fumigatus* and antifungal stewardship (in writing phase)
• CF genotype in ABPA (data entry complete, manuscript in preparation)
• Impact of fatigue in CPA on quality of life (paper published)
• Induced sputum yield of Aspergillus PCR and culture (published)
• Aspergillus nodules and masses (published)
• Single and multiple dose Ambisome efficacy and side effects for CPA (published online)
• Survival in CPA patients (Resubmitted after 2 revisions)
• Gamma interferon production deficiency (Completed, presented, being written up by Addenbrookes)
• Gamma interferon therapy (40 patients, in progress).

6 Patient and public engagement

1. Community booklet.
A community booklet is produced and distributed to all patients who do not have access to a computer, informally at clinic. The group of patients & carers that attend the monthly support meeting at NAC play an integral role in developing and publishing the NAC community booklet each quarter. This allows readers to know what is happening in the service and with other patients and carers. It includes news items, recipes, puzzles, tips for breathing, physio and travel. It also provides contact numbers for social groups.

2. Aspergillus Website @ www.aspergillus.org.uk
The Aspergillus Website is the most comprehensive source of information about Aspergillus and the diseases it causes available on the internet. There are extensive sections for clinicians, scientists and laypeople (patients) including comprehensive collection of treatment protocols covering 43 distinct therapeutic areas and all approved antifungal drug SPC’s & PIL/VIPIL’s. We also provide information on evidence supporting other unapproved non-herbal treatments. We provide simple access to over 9,800 scientific articles (including a unique collection of 815 historical articles) and well over 14,400 conference abstracts from 1974 onwards.

The Aspergillus Website is listed at number 1, 1, 1 and 2 in Google.co.uk, number 4, 3, 4 and 4 in Google.com, number 2, 2, 7, 2 in Bing and Yahoo! for ‘aspergillus’, ‘ABPA’ ‘aspergillosis’ and ‘aspergilloma’respectively. If ‘aspergillus’ is searched in Google, there are over 6 million results. The Aspergillus Website had 65,682 unique visitors in a typical month and the Website for Patients 11,109. About 43% of visits are using smaller devices. China has overtaken the USA as the country from which we get most visits, and numbers of visits have surged to over 200,000 per month.
Our weekly blog (www.aspergillusblog.blogspot.com) has 5-7000 page requests per month this year and has recently passed 250,000 page accesses since it began in 2007.
Monthly newsletters from the Aspergillus Website are sent out to over 24,000 (free) subscribers. This figure is driven by newly registered members seeking to access our secure ‘articles’. There are ~45,000 people registered on The Aspergillus Website (40% medics, 29% scientists, 8% vets and 23% laypeople).

3. Patients & carers support meeting

This monthly meeting aims to give support to all who attend the NAC clinics. This allows people who do not have computer access to find informal support from NAC staff and encourages face to face social support between patients & carers. The meeting is attended by 8 – 15 people each month and we regularly (most months) see new attendees taking the opportunity to meet with us. The meetings are lead and organised by Dr Graham Atherton and Chris Harris.

The subjects covered and their on-line links are listed below. More recent meeting recordings have had to be moved from their former host (Slideshare) to our patients website. As of July 2015 they had been accessed over 42,000 times on Slideshare and a further 36,000 (early 2016) in their new location.

<table>
<thead>
<tr>
<th>Month</th>
<th>Speaker(s)</th>
<th>Topic</th>
<th>Duration</th>
<th>Slideshare Access</th>
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<tbody>
<tr>
<td>April 2015</td>
<td>Malcolm Richardson</td>
<td>Tour of diagnostics labs</td>
<td>0’ 00’ 00secs</td>
<td>0’ 26’ 45secs</td>
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<tr>
<td>May 2015</td>
<td>Chris Kosmidis</td>
<td>Q &amp; A session</td>
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<tr>
<td>June 2015</td>
<td>Graham Atherton &amp; Chris Harris</td>
<td>Biomes, Diagnostics &amp; Travel Tips</td>
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<td>0’ 31’ 40secs</td>
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<td>July 2015</td>
<td>Gemma Hayes</td>
<td>Aspergilosis, Asthma &amp; ABPA: Where we are and where we are going.</td>
<td>0’ 00’ 00secs</td>
<td>0’ 24’ 20secs</td>
</tr>
<tr>
<td></td>
<td>Chris Harris</td>
<td>Skype consults &amp; creative writing</td>
<td>0’ 00’ 00secs</td>
<td>0’ 31’ 40secs</td>
</tr>
<tr>
<td>August 2015</td>
<td>Alan Savage</td>
<td>Home Care, health and use of social resources in the local community</td>
<td>0’ 00’ 00secs</td>
<td>0’ 31’ 40secs</td>
</tr>
<tr>
<td></td>
<td>Chris Harris</td>
<td>Poetry</td>
<td>0’ 00’ 00secs</td>
<td>0’ 31’ 40secs</td>
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<tr>
<td></td>
<td>Graham Atherton</td>
<td>Planning Autumn Booklet</td>
<td>0’ 00’ 00secs</td>
<td>0’ 31’ 40secs</td>
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<tr>
<td>September 2015</td>
<td>Phil Langridge</td>
<td>The variety and use of positive expiratory pressure devices to aid mucus clearance</td>
<td>0’ 00’ 00secs</td>
<td>0’ 31’ 40secs</td>
</tr>
<tr>
<td></td>
<td>Graham Atherton</td>
<td>fungi@MANCHESTER</td>
<td>0’ 00’ 00secs</td>
<td>0’ 31’ 40secs</td>
</tr>
<tr>
<td>October 2015</td>
<td>Maria Gamaletsov</td>
<td>Introduction to the background of our new medic</td>
<td>0’ 00’ 00secs</td>
<td>0’ 31’ 40secs</td>
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<tr>
<td></td>
<td>Graham Atherton</td>
<td>ERS 2015 &amp; Take the Active Option</td>
<td>0’ 00’ 00secs</td>
<td>0’ 31’ 40secs</td>
</tr>
</tbody>
</table>
4. Community structure
Our online communities have been very popular since 2000 but our patient surveys indicated that up to half of our patients did not have access to a computer which denied them access to our expensive resources online. Our support community is thus a combination of online and offline meetings & resources.

The community is supported in several ways:

Online
  ● Our (Facebook & Yahoo!) worldwide communities are very active with 2000 participants
  ● The NHS Choices online community for Aspergillosis has 700 participants
  ● NACPatients.org.uk website (averaging 4000 visitors per month)
  ● Local online Facebook groups (14 groups, 8 in the UK serving 50 - 70 people)
  ● Facebook group specifically for carers
The Professional LinkedIn members (Aspergillus and Aspergillosis Group) has over 400 members and 120 are in the related ‘Damp Buildings and Human Health’ LinkedIn group.

Monthly meeting viewed live & by recordings (250-450 viewings per month in 2016)

Offline

- Monthly meeting at National Aspergillosis Centre (NAC) attended by 10-20 per month. This meeting offers social support and also a series of talks on a wide variety of subjects aimed at helping patients self manage, reducing anxiety, explaining some of the tests we do at NAC and outlining encouraging research progress.
- 120 community booklets, written quarterly are given out per month. This publication contains seasonal advice, informative articles and artwork & recipes contributed by the patient's community. Regular meetings are held to get patient & carers opinions on how we should update the booklets.
- Monthly newsletter issued to every patient attending clinic (250 per month).
- A series of 13 information leaflets are available and handed out in clinic by clinical staff as required for new and existing patients
- ‘Buddy’ phone support manned by patients (15 - 20 participants)

5. Phone buddies
Graham Atherton and Chris Harris completed a training course on Befriending and Mentoring so that they could introduce a new “buddy service” and support and guide anyone who wished to offer that service. We provide a phoneline since December 2014 for patients & carers to use for instances when they have no computer access or prefer to use a phone and speak to someone who can help. This phoneline is manned by patient/carer volunteers who report steady interest.

6. Public awareness
Promoting awareness of aspergillosis and the National Aspergillosis Centre is particularly important as we suspect that many thousands of people remain undiagnosed. This results in people not being appropriately treated and the national statistics for serious fungal disease remain low in the UK and abroad. Consequently government health & research funding is low. Improving awareness helps make far more people in the UK aware of aspergillosis and the National Aspergillosis Centre, improving the chances that more cases of aspergillosis will be looked for and found.

However awareness could be counterproductive if it is not linked to good information and advice. Our patients & carers’ community can help to spread awareness in the UK (and abroad) and provide links back to our resources, maximising the benefit.

Personal stories from patients & carers always have a high impact when told by the media. Combined with support from NAC they regularly make an important contribution to national TV and print/website news outlets, most recently during the 7th Advances Against Aspergillosis meeting in Manchester where we reached 8 million viewers via
BBC Breakfast Time, BBC NW Tonight, BBC News, BBC local radio throughout the north west of England and ex-pat communities in Spain. Stories were also run in the Guardian, The Sun, The Mirror and Good Housekeeping magazine. The NAC has engaged 2 public relations companies to assist getting key health and educational messages out.

On a more individual scale our informed patients & carers do a great job spreading awareness every day via our online communities and through local groups and fundraising events as well as to their doctors and other medical staff.

7 Research outputs, other published research summary

1. Papers and book chapters
   Amongst the 57 papers and book chapters published in calendar year 2015, there were several areas of direct relevance to patients with CPA and pulmonary aspergillosis. These were:
   - UK guidelines on the investigation and diagnostic testing of patients with fungal diseases were published in Lancet Infectious Diseases [1].
   - In January 2016, clinical guidelines for the diagnosis and management of CPA were published jointly by the European Society for Clinical Microbiology and Infectious Diseases and the European Respiratory Society [2]. This is the first ever set of management guidelines for CPA.
   - Extremely high levels of the neutrophil chom attractant PPBP are found in monocytes in CPA patients [3]. This is indicative of major ongoing inflammation in patients with CPA.
   - A review of aspergillosis was published in Thorax [4] and many of our referring physicians commented that they found this most helpful.
   - A consensus group discussed and offered an opinion of the management of patients withazole resistant aspergillosis [5], a common problem in those treated with oral azoles long term.
   - Progression from ABPA to CPA was documented in detail in 20 patients cared for at the NAC, including the time frames [6].
   - Poor antibody response to S. pneumoniae and a muted response to immunisation with Pneumovax was documented [7]. This prompted a shift to using 2 doses of Prevanar 13 vaccine to protect our patients from recurrent infection.
   - UpToDate is a key resource for doctors across the world. Both chapters on CPA in this online searchable encyclopaedia of medical practice are updated 6 monthly [8,9]
   - Estimated country burdens of serious fungal diseases including chronic and allergic aspergillosis were published for 20 countries [Appendix 5]. A call for all populations to have access to fungal disease diagnostics and antifungal treatments was issued by the Global Action Fund for Fungal Infections in May 2015 [10], an

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1 7th Advances Against Aspergillosis, Manchester, UK 3-5th March 2016. Aspergillus Website http://www.aspergillus.org.uk/content/7th-advances-against-aspergillosis-manchester accessed 26th May 2016.
NGO closely linked to the National Aspergillosis Centre. This call included a focus on CPA complicating pulmonary tuberculosis across the world.

Key papers related to CPA:

2. Advances Against Aspergillosis
The 7th Advances Against Aspergillosis meeting was held at Manchester Central, March 3rd to 5th, 2016. There were 352 attendees, from over 30 countries who discussed Aspergillus and aspergillosis over 3 days. www.advancesagainstaspergillosis.org/2016/
In addition to the main plenary sessions, breakfast meetings were held which included a ‘challenging cases’ slot on CPA, delivered by the NAC consultants. There were 128 abstracts submitted and displayed, including the first ever disclosure of a new antifungal destined for inhalation – PC945. This and other new antifungals from F2G Ltd and Cidara were the focus of a press release. Several papers from this meeting will be published in Medical Mycology as a permanent record of the meetings. Prior meetings have resulted in 229 published papers in 7 supplements.

8 Statutory reports

MRSA
No cases of MRSA were reported.

C. difficile infection
No cases of C. difficile infection were reported.
No cases of CPE (carbapenamase producer)

No SUI’s were reported.

Complaints
None

HIRS alerts
One was related to incorrect drug labelling.

9 Future developments

The developments planned for 2015/16 were (and commented on):

- Decision about utility of offering routine sputum galactomannan assay – a superficial audit suggests the test over-reads, and may not reflect Aspergillus load in the airways. No straightforward cutoff, but very high levels suggestive of active infection. Poor quality samples (mucoid, salivary) are falsely negative.
- Introduction of isavuconazole, as a second or third-line therapy for CPA, using the same evaluation methodology now used for posaconazole. Introduced using ‘n-of-1’ trials as for posaconazole.
- Implementation of a routine azole resistance service using pyrosequencing in the MRCM, and then clinical validation (2 year process). Development and validation in progress, not yet operational.
- Introduction of Skype or Facetime nurse appointments, preceded by postal sputum and blood testing, to reduce travelling costs and increase appointment intervals. Successfully introduced and found to be useful. The relevant nurse has just left (after 7 years), so will be a delay until new appointees sufficiently trained to do this.

2 http://www.manchester.ac.uk/discover/news/manchester-fungal-disease-conference/
Planning for the recruitment of an additional consultant to contribute to the growth of the service. New consultant appointed and starting in October 2016. Expertise in fungal infections and transplant ID.

Support of a nascent infectious diseases service at the Brompton Hospital with occasional joint clinics for complex aspergillosis cases. One joint clinic. Many cases, handled internally.

Developments planned for 2016/17 include:

- As multiple new experimental antifungals are in phase 1 or phase 2 development, recruitment of a clinical trials manager to orchestrate the multiple approvals required.
- Four antifungal developments being investigated are for CPA patients: primary therapy with isavuconazole, injection of a novel highly active azole antifungal into aspergillomas, weekly IV therapy as salvage therapy and possibly another oral salvage therapy.
- Manchester-wide Single Hospital Service discussions ongoing about the merger of Central Manchester FT and UHSM FT, as well as integrating all the infection services.
- Increased clinic, nursing and medical capacity is planned.
- Doubling of undergraduate teaching by UHSM ID team, to both year 3 and year 4.
- Recruitment of another academic with an interest in aspergillosis to further develop the research with what is now a globally unique cohort of patients and service.
- Plan to hold UK-wide video meetings via Skype, enabling patients & carers to participate with patient meetings using a standard telephone line rather than a computer.
Appendix 1

Categorisation of complexity (Banding)

Stage 1

- Ambulant and independent
- No evidence of antifungal resistance
- No treatment or treatment with itraconazole capsules

Stage 2

- Significant impairment of respiratory function, sufficient to impair activities of daily living, but ambulant and/or
- Concurrent anti-mycobacerial treatment and/or
- Failed or developed toxicity to itraconazole capsules and
- No evidence of azole antifungal resistance

Stage 3

- Antifungal azole resistance documented and/or
- Long term nebulised or IV antibiotic treatment required (bronchiectasis, Pseudomonas colonisation) and/or
- Wheelchair bound and/or
- HIV infected and/or
- Severe hepatic or renal disease
Appendix 2
Referral to appointment time audit - April 2015 – March 2016

Patient level data
Appendix 3
Quality of life (SGRQ) and MRC dyspnoea scores for new referrals 2015/16

Patient level data
Appendix 4  
NAC Patient Survey 2016 – Summary

All patients attending every clinic in for the four weeks during February 2016 were asked to complete this survey. 166 responded to the survey which this year we have presented as a single survey combining all three weekly clinics.

Q1. First Visit

98% patients completing the survey had attended clinic before

Q2. Waiting time

95% were satisfied or better with all waiting times (broken down into Reception, Doctor, Nurses, Blood tests, Pharmacy, X-ray and Lung Function). Slight weaknesses are identified in waiting times for Doctors and Pharmacy (1.5% and 2% unsatisfied or worse respectively).

Q3. Courtesy

Courtesy from all receptionists, medical and nurse team members are exemplary.

Q4. Quality of care

Quality of care from all medical team members was highly rated with only one person unsatisfied.
Q5. Contact from a member of the NAC team

There has been a notable rise in the number of patients being contacted by a member of the NAC team with 49% now having been contacted versus 32% in 2015. 24 comments on the quality of support show that 22 (96%) had an overwhelmingly positive experience, two had been contacted to correct problems with blood sampling and one considered advice given “has been inconsistent and unhelpful”. In 2015 98% had been satisfied or better.

Q6. Specialist physiotherapists

The proportion of patients attending our physiotherapy service is unchanged with 100% satisfied and all comments reinforcing universal approval of both staff members.

Q7 and 8. Written information about your condition?

More people (62%) have received written information compared with 2015 (55%) though there seems to be room for improvement in

- the consistency of type of information received (some only recollect seeing the community booklets, some newsletters, while others are seeing none)
- the quality of information (“still don’t fully understand all aspects of the condition”)
- the frequency of receiving information (“Some years ago”)
- the range of information (“If I ever need surgery”)
- accessibility or availability (“Have requested to do previously, but not received any” and “I get information from other hospitals after clinic visit. Never from here.”)

NOTE that only 16 out of 168 people left comments in this section and only 8 (5%) of these highlighted the issues listed above. Satisfaction levels on information received were >95%.

Q9. Potential symptoms regarding your illness or medication

More patients (61%) remembered having been told about symptoms to watch out for at home regarding adverse effects compared with 2015 (48%), most comments from patients showing good awareness of this issue.
Q10. Answers from questions to doctors

The clarity of answers from our doctors received 93% approval (98% of those who responded to the question) with one negative comment: “Doctors on ward spoke above me and did not listen to me – I felt they spoke at me and not to me” and one that may provide food for thought for further improvement: “sometimes I forget to ask anything till I am on my way home”.

Q11 & 12. Wythenshawe Hospital (UHSM)

40% of patients asked had been inpatients at Wythenshawe Hospital and of these 97% were very happy or better with how they were treated while on a ward. The only negative comment concerned the difficulties getting discharged at weekends. 90% (97% of those who responded to the question) would recommend UHSM to family and friends. Large numbers (69) of comments in this section with only 2 negative “Purse taken twice – records filled in incorrectly not listened to” and “6 months between appointments when a UHSM Doctor said 4 months”.

Many (67) others ranged from “Excellent treatment” and “For the NAC services as best in country. Prof Denning and team are worth the round trip” to importantly “In every situation I knew what was happening” and “Care and friendliness.”

Q13. Postal service for drug levels and sputum samples

Comment (40) on the postal service for drug levels and sputum samples were very positive with one writing about how important this service was to them. Several comments were suggestions for improvement:

- Better envelopes
- Containers are not a good fit in order box
- It is easy from your end, but I found it difficult to get blood taken on my end
- Make the little plastic sample pouch much larger than the samples sent
- Blood packs could be sent more quickly
- Clearer paper work and guidance for 3rd parties taking blood samples
- When I asked for pills to be sent out for me as I was running out (and did), I was told this was not possible by a nurse
- There could be more communication with the GP surgery as they always tell me this is outside of their standard practice
• When I have been sent items, the envelope has arrived damaged on at least two occasions
• Didn’t know of this service

Q14. Anti-fungal drugs delivery

There is universal approval for antifungal drug delivery service, no criticisms of the current service.

Q15. Aspergillus website

The proportion of patients visiting the Aspergillus Website is up slightly compared to 2015 to 45% and approval is 100%. Comments of those who do not visit the website are mainly divided between those who have no computer access (50%) and those who do not want to know more about their illness (30%). 1 comment considered that the website was too complex for them to understand revealing a need to make the patients section of the website more prominent.

Q16. Patient information leaflets

Suggestions for new information leaflets requested more information on diet, breathing apparatus, the range and value of exercise, the benefits of each drug.

Q17-20. Patients meetings.

7% of those responding to the question had attended one of the monthly patients meetings compared with 9% in 2015 which suggests a reduction in active interest though attendance numbers at each meeting is stable at 10-14 per month.

Comments(9) of those who do attend are very positive “I always go to meetings - they are the most informative”, “They are very good. I have learnt more from meetings than anywhere else” and “The patient meetings are very helpful; it’s a great chance to speak to others with this condition”. One or two negative comments reflect difficulties with travel distance.

50% of those who did not attend the meeting did not do so because of inconvenience (and thus presumably would be interested in attending) – over 90% of these due to the distance required to travel to the meeting. The remaining 50% who did not attend had no current interest in attending (“not needed”, “not useful”, “happy as I am”).
In 2015 the same reasons for not attending predominated but more (59%) did not attend due to inconvenient time or distance. This increase in convenience may be due to us switching the meeting to Fridays (when the main clinic takes place) and additional efforts made to arrange patient’s clinic time to the same day as the meetings.

Our meeting are streamed live in the internet and have been viewed by 7% of patients. Recordings of our meetings have been viewed by 17% (13% in 2015) of patients who responded.

**In conclusion 7% go to the meeting, 7% watch live and 17% watch a recording, so a total of 31% of patients view the meeting in some form.**

57% were aware of our regional support groups (up from 44% in 2015) but only 5% had made contact with a group. The main reasons given for not contacting were:

- Distance – 19 (29%)
- Time – 10 (15%)
- Not needed – 22 (33%)

**Q21. Hospital transport**

4% of patients used hospital transport, all were satisfied or better.

**Q22. Clinical Research**

70% were happy to participate in clinical research, all of these were satisfied or better with procedures and consent process.

**General comments (25 in all) about NAC service**

Mostly positive, *some constructive*

1 - I have had great care with every aspect of the hospital. 2 – I hope I attend a meeting this Year. 3 – If I have an appointment with one doctor, I do not want to see another. 4 – Great care from staff, always excellent service. 5 – Very satisfied with care and help. 6 – Since I first visited the NAC, I have been impressed by the standard and quality of the care from all staff here. I appreciate the efforts that have been made to improve my condition. 7 – You are doing a great job – thank you! 8 – Nursing staff are wonderful and always treat you with kindness and respect. The doctor never rushes you. 9 – Been on no meds for months now. 10 – The care, attention, professionalism at clinic and between clinics is excellent. 11 – There was some confusion over my latest clinic date. 12 - I had a letter informing me of an appointment that did not match the records / schedule. 13- I try not to think of the problems as much as possible, so I don’t read up on it. 14 – I have only been to the clinic once and saw Dr N. Who I thought was
excellent. 15- Care given was very good from the centre. Would be good if clinic appointment reports could be sent out to patients if requested. 16 – Very satisfied with everything. 17 – Very satisfied with treatment. 18 – All the staff are lovely. 19 – I have been very happy with my care at Wythenshawe hospital. 20 – The last time we were here, we had a telephone request to attend the clinic. No one here new about it and we ended up waiting for 3 hours. 21 – Find there is always a delay receiving clinic letters following meeting the consultants. 22 – Apart from one unsatisfactory consultation (first one). 23 – Very happy with the aspergillosis centre. 24 – NAC provides an excellent service – the staffs are first class. 25 – Thank goodness NAC is here. Best doctors and nurses and thanks to graham for keeping us all informed online! Saved my life getting the proper treatment for my aspergillosis.
Appendix 5

Publications from the Fungi@Manchester Group (2015)

1. Smith NL, Bromley MJ, Denning DW, Simpson A, Bowyer P. Elevated levels of the neutrophil chemoattractant pro–platelet basic protein in macrophages from individuals with chronic and allergic aspergillosis. J Infect Dis 2015;211:651-60.


