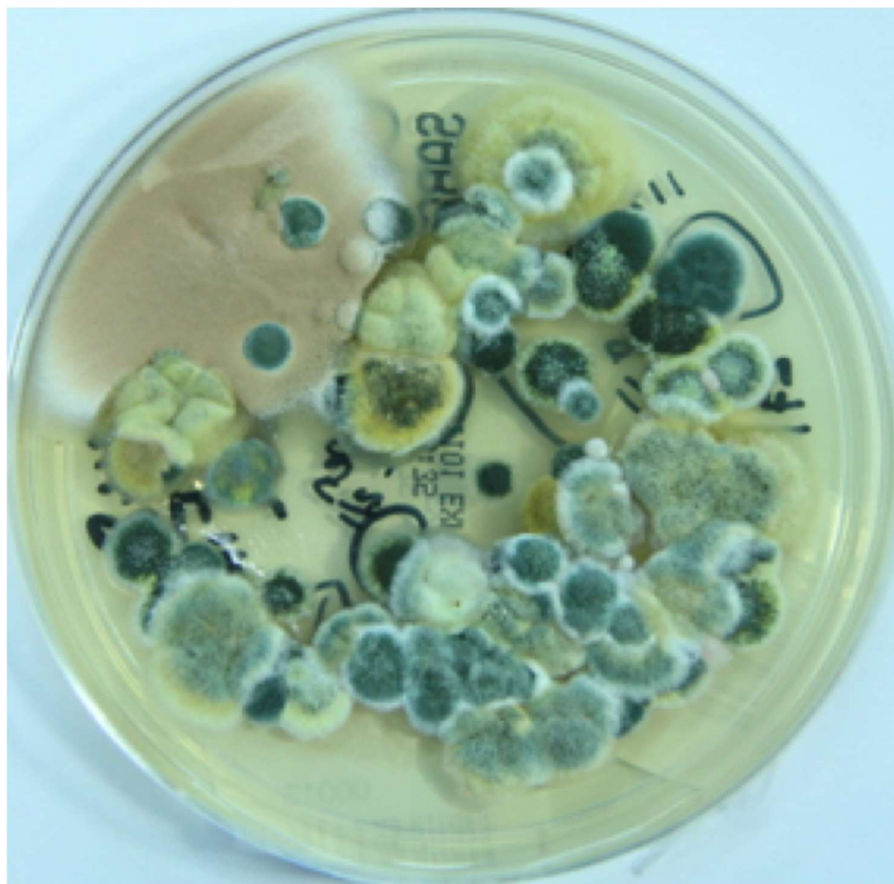


**NHS National Commissioning Group - Highly Specialised Services**

**Chronic Pulmonary Aspergillosis National Service**

**The National Aspergillosis Centre**

**Annual Report 2019-2020**



High volume culture of sputum from a CPA patient showing the diversity of environmental moulds in the respiratory tract

**A European Centre of Excellence in Medical Mycology**

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## 1 Annual Service Overview and Highlights

This report covers the eleventh full year of the National Aspergillosis Centre (NAC), commissioned as a Highly Specialised Service within the NHS.

A total of 104 new patients from England and Scotland (and a further 5 patients from Northern Ireland, Wales and The Isle of Man) were assessed at the NAC and diagnosed with Chronic Pulmonary Aspergillosis (CPA) between 1<sup>st</sup> April 2019 and 31<sup>st</sup> March 2020. This was out of a total of 297 referrals for all forms of Aspergillosis. Referral numbers have seen a significant drop due to the emergence of the COVID-19 pandemic early in 2020. We have observed a steady number of patient deaths within the service as a whole and for new patients within the first year of referral. There has been a significant increase in discharges from service due to robust MDT discussions of patients with stable disease, not on current antifungal therapy. Many of these patients are discharged from the commissioned service but remain under our care in the tertiary MFT Aspergillosis service. At the end of March 2020, we had 494 patients from England and Scotland on service and a further 24 patients from Northern Ireland, Wales, The Isle of Man and overseas (separate funding).

Waiting times for new patient appointments have significantly improved (average 4.5 weeks) due to a re-structuring of clinics and increased provision of remote advice and guidance. We have seen a steady reduction in hospital admissions (474 occupied bed days), a reduction in embolisations (6) and a steady number of surgical resections (6). Overall drug expenditure was similar to last year. A reduction may have been expected with reduced patient numbers but due to a pharmaceutical supply problems with generic Voriconazole, expenditure increased at the start of the financial year. There has been a continued reduction in prescription of intravenous antifungals over the last 4 years. This has consequently led to a reduction in OPAT homecare (164 bed days saved). This reduction in iv antifungal prescribing may, in part this year, be due to the COVID-19 pandemic but over the last 4 years mirrors the introduction of isavuconazole.

Posaconazole and isavuconazole were given as treatment trials in those intolerant to or clinically failing itraconazole and voriconazole. Posaconazole was successful in 15 of 31 (48%) and isavuconazole in 4 of 12 (33%) patients, with outcomes pending on a further 15 patients.

There have been no serious untoward incidents and no formal complaints. Feedback from the annual patient survey remains extremely good.

The NHS Mycology Reference Centre Manchester (MRCM) provides the high level diagnostic mycology service for the NAC and is UKAS accredited. The laboratory is the largest mycology laboratory in Europe with a strong performance in turnaround time, critical results reporting in 1-hour, clinical audits, publications and international representation. The MRCM has been at the forefront of diagnostic developments for Aspergillosis in the last decade, with pyrosequencing to determine azole resistance, high volume fungal sputum culture and Aspergillus IgG determination by lateral flow assay being the latest developments.

The NAC has continued its reputation in international research with 67 publications and 4 book chapters. The team delivers educational lectures and seminars nationally

and internationally. Patient support and education has continued to grow. The Aspergillus Website and Patients' website have 37,000 and 7,000 users per month respectively. This equates to 1 million page views per month with readership of the patients website up 3-fold in 2020. The NAC provides a huge resource of online and offline educational material. Patient support comes from social media, online forums and patient meetings. Raising public awareness remains at the forefront of our educational outreach activities as many remain undiagnosed.

## **2. Clinical Service**

### **2.1 Clinical Service Overview**

The NAC provides primarily outpatient care for patients with Chronic Pulmonary Aspergillosis (CPA) – this includes initial assessment and diagnosis, evaluation of disease status (banding), prescription of antifungals, and on-going long term clinical management. Referrals are from specialist hospital consultants, predominantly in respiratory medicine and infectious diseases. We aim to see patients within 6 weeks of referral.

Initial clinical assessment includes a full clinical and medication history, Aspergillus blood and sputum tests, lung function, radiological imaging, and an assessment of immune status. Baseline quality of life assessments, weight and MRC scores are documented. Patients have a consultation with our dedicated specialist nurses and are provided with written information and contacts details of the team. Patients are also seen by a dedicated specialist physiotherapist when necessary for chest clearance and breathing control and at patient request for further tailored information such as exercise programmes. We follow a clear diagnostic algorithm to ensure consistent quality of care for all patients.

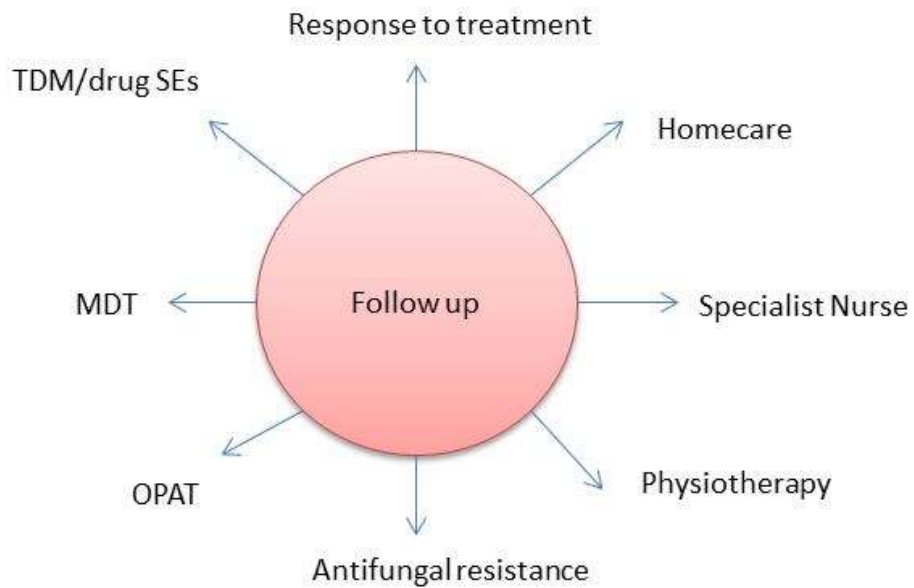
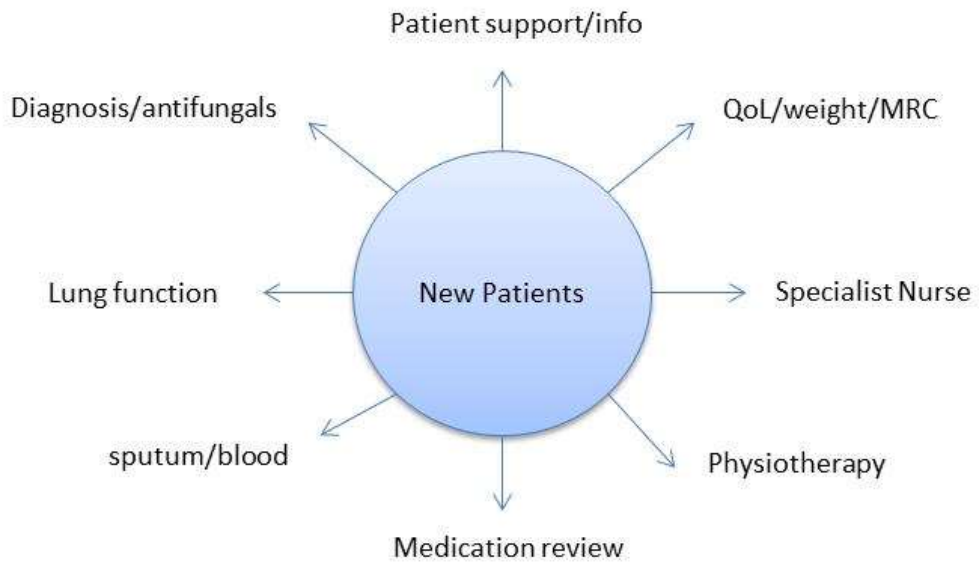
Ongoing long term management includes evaluation of symptoms and response to medication, drug side effects, TDM monitoring of drug levels, withdrawing medication when there is no effectiveness as per our agreed clinical pathways, establishing homecare medication delivery direct to the patient every 2 months, liaison with the referring local team and GP to treat co-morbidities and organise necessary tests and delivery of treatment close to home whenever possible.

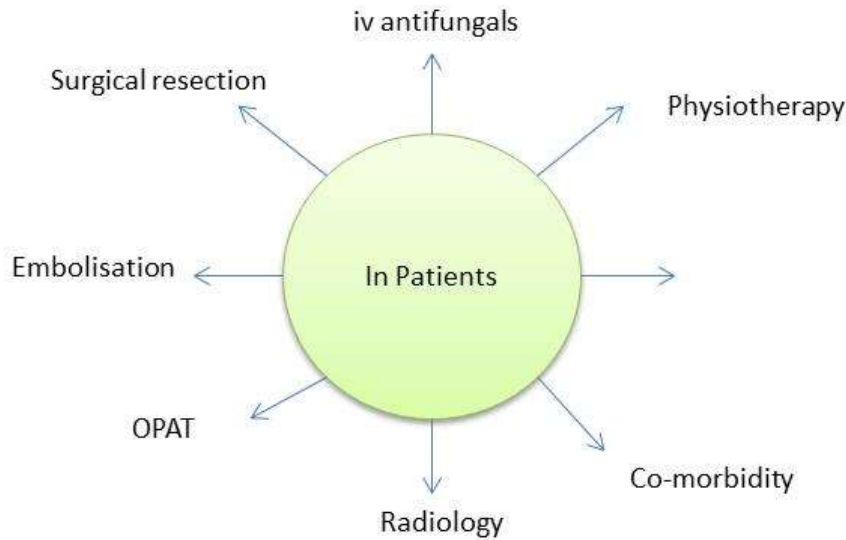
In addition to our out-patient clinics we also delivery short-term inpatient care – this includes evaluation of disease, intravenous therapy, bronchial artery embolisation, surgical resection, training in intravenous line management and delivery of iv antifungals in the community (OPAT).

Long-term inpatient supportive or palliative care is beyond the scope of this service. We provide appropriate outpatient information and support regarding symptom palliation/control and end of life care but must maintain close relations with the local parent team to ensure a seamless transfer of care back to the referring hospital when patients no longer benefit from treatment.

It is essential that patient interventions and outcomes are measured continuously, and we undertake a clinically focused programme of audit as agreed with NHS England. This report details the outcomes over the time period 1<sup>st</sup> April 2019 to 31<sup>st</sup> March 2020.

Schematic diagram of NAC services





## 2.2 Workforce infrastructure and sustainability

### Clinical and administrative personnel

The following clinical and administrative personnel have been vital members of the NAC staffing team during 2019-2020:

Professor David Denning, Professor of Infectious Diseases in Global Health (3 PAs)  
 Dr Caroline Baxter, Consultant in Respiratory Medicine (5 PAs)  
 Dr Chris Kosmidis, Consultant in Infectious Diseases (4 PAs)  
 Dr Christina Bjorling, Consultant in Infectious Diseases (2 PAs)  
 Dr Rohit Bazaz, Consultant in Infectious Diseases (5 PAs)  
 Dr Giorgio Calisti, Consultant in Infectious Diseases (5 PAs)  
 Dr Manuela Barrera, Consultant in Infectious Diseases (4 PAs)  
 Dr Riina Richardson, Consultant in Oral Microbiology & Infectious Diseases (2 PAs)  
 Mrs Christine Harris, NAC manager (100%)  
 Ms Deborah Kennedy, Specialist Nurse (30%)  
 Mrs Jenny White, Specialist Nurse (90%)  
 Ms Rochelle Baron, Specialist Nurse (60%)  
 Ms Smitha James, Specialist Nurse (60%)  
 Ms Francesca Woolnough, Specialist Nurse (50%)  
 Ms Judith Ford, Specialist Nurse (50%)  
 Mrs Carol Toner, Band 3 HCA (100%)  
 Mr Philip Langridge, Senior Specialist Physiotherapist (70%)  
 Ms Mairead Hughes, Specialist Physiotherapist (40%)  
 Dr Nicholas Power, Clinical Fellow (50%)  
 Dr Firas Maghrabi, Clinical Research Fellow (50%)  
 Dr Suha Akili, Clinical Fellow (50%)  
 Dr Emily Rooney, Educational Clinical Fellow (50%)  
 Dr Frkhinda Jbueen, Clinical Research Fellow (50%)  
 Ms Fiona Lynch, Specialist Senior Pharmacist (40%)

Dr Graham Atherton, Senior Information Technology Architect and Patient engagement (100%)  
Dr Helen Findon, Website design and administrator for Patients (40%)  
Dr Elizabeth Bradshaw, Medical Writer and Web Manager (100%)  
Mr Marcin Walczak, EPR and Clinical Database Manager (100%)  
Ms Carmel Marshall, B4 Administration Team Leader (70%)  
Ms Ruvimbo Nkomazana, B3 Administration and secretarial support (70%)  
Ms Linda Shaughnessy – B2 Administration and secretarial support (70%)  
Mrs Megan Hildrop - B2 Administration and secretarial support (70%)  
1 x vacant B2 Administration and secretarial support (70%)

We have had no sustained issues with clinical staff recruitment and have adequate resilience within the team. There has been a higher turn-over of administrative staff including a vacant post.



## 2.3 Clinical Activity - Referrals, Caseload and In-patient Hospital Activity

The total referrals, patient caseload, in-patient stays and procedures for 2019/2020 are shown below:

| Activity Measure                 | M01 | M02 | M03 | M04 | M05 | M06  | M07 | M08 | M09 | M10 | M11 | M12 | YTD  |
|----------------------------------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|------|
|                                  | Apr | May | Jun | Jul | Aug | Sept | Oct | Nov | Dec | Jan | Feb | Mar |      |
| Referrals                        | 13  | 35  | 28  | 37  | 28  | 28   | 15  | 25  | 19  | 33  | 21  | 15  | 297  |
| New Patients Testing             | 8   | 9   | 8   | 13  | 11  | 8    | 5   | 9   | 6   | 11  | 9   | 7   | 104  |
| Outpatient Follow up attendances | 98  | 142 | 99  | 108 | 139 | 121  | 110 | 138 | 89  | 125 | 100 | 78  | 1347 |
| Caseload - Band 1                | 159 | 158 | 140 | 141 | 144 | 143  | 144 | 143 | 140 | 138 | 133 | 125 | 125  |
| Caseload - Band 2                | 330 | 332 | 343 | 344 | 348 | 350  | 352 | 346 | 344 | 338 | 342 | 347 | 347  |
| Caseload - Band 3                | 26  | 27  | 26  | 26  | 26  | 25   | 26  | 26  | 25  | 24  | 23  | 23  | 23   |
| Occupied Bed Days                | 94  | 69  | 24  | 16  | 25  | 89   | 33  | 3   | 62  | 31  | 28  | 0   | 474  |
| Inpatient Discharges             | 4   | 3   | 3   | 3   | 3   | 5    | 2   | 1   | 1   | 2   | 1   | 0   | 28   |
| iv Homecare                      | 15  | 7   | 14  | 41  | 17  | 32   | 13  | 0   | 0   | 0   | 0   | 25  | 164  |
| Surgical Resection               | 1   | 3   | 0   | 0   | 0   | 1    | 0   | 0   | 0   | 0   | 1   | 0   | 6    |
| Embolisations                    | 1   | 0   | 1   | 0   | 1   | 0    | 0   | 1   | 0   | 1   | 0   | 1   | 6    |
| Patient Death                    | 7   | 4   | 8   | 3   | 6   | 7    | 4   | 7   | 7   | 6   | 6   | 4   | 69   |
| Discharge from service           | 0   | 2   | 9   | 3   | 1   | 3    | 1   | 5   | 8   | 8   | 8   | 8   | 56   |

\* The NCG funds patients from England and Scotland only

\*\* Appendix 1 shows the clinical definition of case bands

### Referrals

There were a total of 297 Aspergillosis referrals from England and Scotland during the year 2019 to 2020. From within these, 104 (35%) received a confirmed diagnosis of CPA. The proportion of referrals with a diagnosis of CPA remained stable compared to the previous year (35.7%). However, there has been a reduction in overall referrals, the major impact being during the first 3 months of 2020 due to the emergence of the global pandemic of Coronavirus (COVID-19, SARS-CoV-2). Additional to this, there have been improvements in our referral triage processes and an increase in provision of remote advice alone. All new patients are now discussed at our weekly MDT to ensure a unified agreed diagnosis.

### Out-patient waiting times

The mean time from referral to clinic consultation was 4.5 weeks (Appendix 2). 5 patients had long wait times due patient driven factors such as personal choice to reschedule appointments, being too unwell to attend or having difficulty with transport. There were 9 transitions from another form of aspergillosis into CPA, 1 transfer from the TB service and 1 disease relapse. 6 patients had delays to establish diagnosis and commence treatment due to undergoing further investigations, such as repeat CT thorax, before confirming a definitive diagnosis of CPA.

### Geographical location

Appendix 2 shows the area of residence that referrals originated. This data also highlights referrals from outside the commissioned areas that are not included in reported numbers: 3 from Wales, 1 from the Isle of Man and 1 from Italy. Appendix 3 displays maps of the geographical locations (postcode areas) of the new patient referrals and all patients on service.



### Caseload

At the end of March 2020, 494 patients from England and Scotland were on service with an additional 18 patients from Wales, 1 from Northern Ireland, 3 from The Isle of Man and 2 from overseas. Patients with CPA are banded according to disease severity, impact on functional ability and presence of antifungal resistance (Appendix 1). During 2019-2020 there has been a fall in Band 1 patient numbers from 159 to 125 patients, a rise in Band 2 patient numbers from 330 to 347, and a small fall in Band 3 from 26 to 23 patients. Band 1 has fallen due to a combination of discharges from service for stable patients off therapy, a shift of patients into Band 2 and a reduction in Band 1 referrals. The principal reasons for patients shifting from Band 1 to 2 patients are: a high prevalence of intolerable side effects to itraconazole, increased usage of voriconazole first line for patients with aspergillomas or extensive disease due to concerns regarding the short-lived clinical response to itraconazole and continued concern about a high rate of resistance with itraconazole. There has been a reduction in percentage of Band 1 referrals as a proportion of the total referrals: 2017/2018 Band 1 53%, Band 2 46%; 2018/2019 Band 1 53%, Band 2 45%; 2019/2020 Band 1 45%, Band 2 53%. The small reduction in Band 3 has been due to patient discharges from service when no further therapy is currently available or disease has been stable off therapy.

Within the total caseload there have been 69 deaths which is a stable proportion compared to previous years (65 deaths in 2018-19 and 58 in 2017-18). There has been a significant increase in patient discharges from service this year (56 discharges compared to 33 the previous year) due to robust MDT discussions about the need for on-going care of patients not on therapy. Appendix 4 details those discharged from service

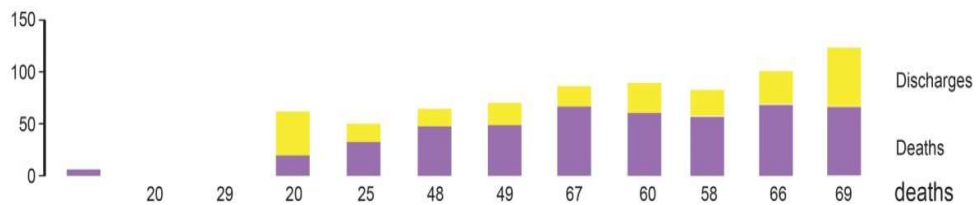
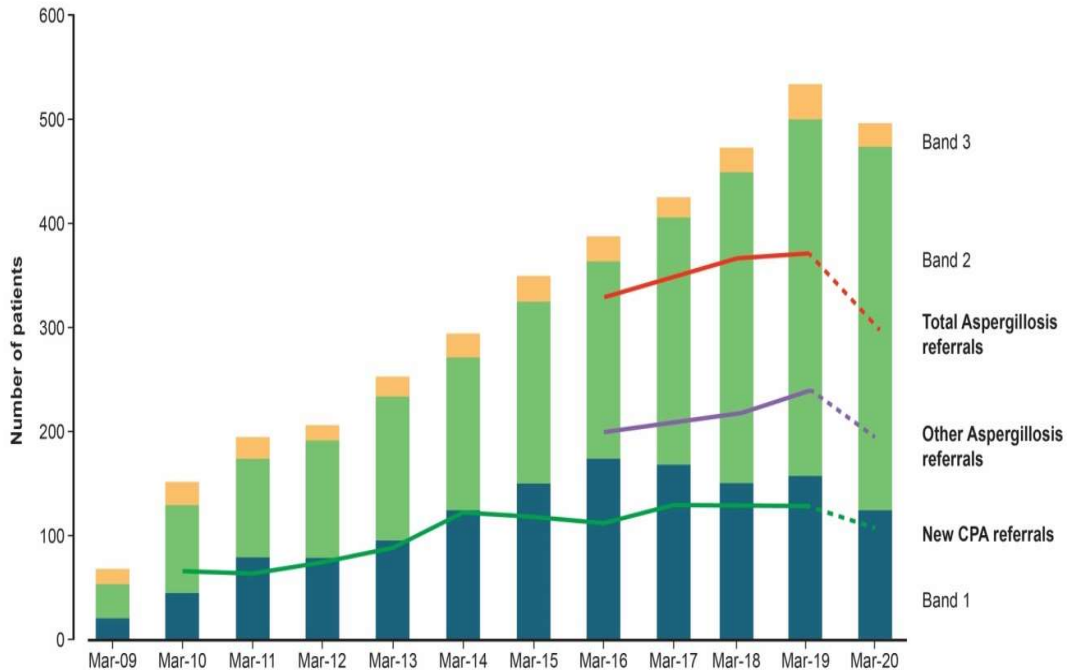
### In-patient Hospital Activity

There were 28 admissions with 474 bed days, lower than the prior year of 694. There has been a continual reduction in hospital admissions and bed days since 2016. Hospital admissions are reducing due to more patients being clinically stable on oral antifungals. The reduced use of iv antifungals which has been evident since the introduction of Isavuconazole. In-patient bed days are additionally kept low with the use of the OPAT service and some patients receiving courses at their local hospital (3 this year). Full details of hospital admission data can be found in Appendix 5.

Six patients underwent surgical resection and 6 underwent bronchial artery embolization (13 last year), some because of poorly controlled disease attributable to azole resistance.

|                    | 2010-11 | 2011-12 | 2012-13 | 2013-14 | 2014-15 | 2015-16 | 2016-17 | 2017-18 | 2018-19 | 2019-20 | Total |
|--------------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|-------|
| Embolisation       | 16      | 15      | 13      | 9       | 13      | 6       | 20      | 12      | 13      | 6       | 123   |
| Surgical resection | 4       | 3       | 2       | 3       | 4       | 4       | 3       | 6       | 4       | 6       | 39    |

NAC Referrals and Caseload 2009 to 2020



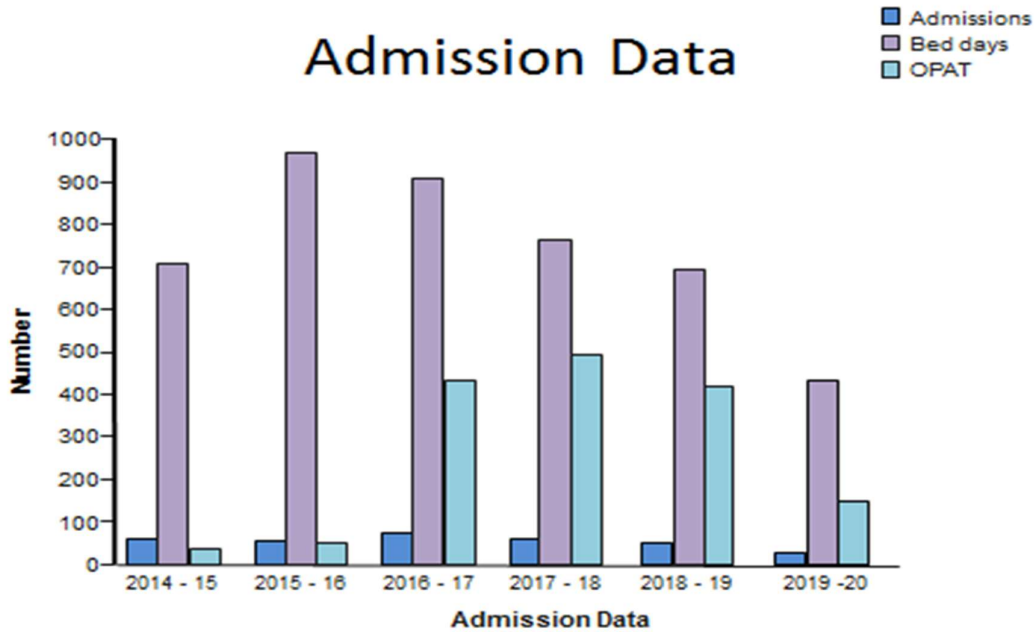
### OPAT Activity

The outpatient parenteral antimicrobial therapy (OPAT) team provides intravenous therapy and clinical monitoring for patients deemed suitable to receive their therapy in the community. During the financial year 2019-20 the OPAT team successfully treated the following number of patients referred from the National Aspergillosis Centre:

- 14 courses of iv therapy in total were delivered to 10 patients: 11 intravenous micafungin, 1 iv Ambisome, 1 iv antibiotics
- Bed days saved: 164

### Intravenous Antifungals

There was a total of 20 courses of iv antifungals administered in 2019-2020 (Appendix 5). 7 of these were iv Ambisome and 13 were iv Micafungin.



## 2.4 Treatment Outcomes

### New referrals

Clinical data for all new patients is presented in Appendix 6. Clinical markers that are monitored include the MRC (medical research council) dyspnoea scale, SGRQ (St George’s Respiratory Questionnaire, weight and serum Aspergillus IgG antibody levels.

There were 12 deaths and 5 patients who were discharged within the first year. There was one direct referral of an in-patient.

Of the remaining patients that attended on-going clinic follow up, clinical parameters indicated:

- improvement in 65%
- stability in 26%
- deterioration in 9%

Those with deterioration had antifungal therapy changed or referral for surgery when alternative antifungal therapy was unsuitable.

## 2.5 Antifungal Trial Data

We continue to use n-of-1 trials for posaconazole and isavuconazole. 42 patients were trialled on posaconazole and 16 on isavuconazole in the year April 2019 to March 2020. A successful outcome is primarily determined by demonstrating a 3kg increase in weight or a 12-point improvement in SGRQ after 6 months. If patients do not meet these criteria their case will be discussed at MDT to review all clinical markers

including aspergillus serology and CT scan to determine if appropriate to continue. The outcomes are shown in the table below alongside data from the previous 2 years. Full details of antifungal trial data can be found in Appendix 7. Overall success for posaconazole remains stable but isavuconazole patients experienced more adverse side effects this year necessitating a stop in therapy. This was despite therapeutic drug level monitoring.

#### **Trials of posaconazole and isavuconazole 2019-2020**

| <b>Outcomes</b> | <b>Posaconazole</b> |      | <b>Isavuconazole</b> |      |
|-----------------|---------------------|------|----------------------|------|
|                 |                     | %    |                      | %    |
| Success         | 15                  | 48.3 | 4                    | 33.3 |
| Failure         | 13                  | 41.9 | 8                    | 66.7 |
| Death           | 3                   | 9.9  | 0                    | 0    |
| <b>Total</b>    | <b>31</b>           |      | <b>12</b>            |      |
| <b>Pending</b>  | <b>11</b>           |      | <b>4</b>             |      |

#### **Trials of posaconazole and isavuconazole 2018-2019 National Aspergillosis Centre**

| <b>Outcomes</b> | <b>Posaconazole</b> |      | <b>Isavuconazole</b> |      |
|-----------------|---------------------|------|----------------------|------|
|                 |                     | %    |                      | %    |
| Success         | 15                  | 41.7 | 7                    | 46.7 |
| Failure         | 19                  | 52.8 | 8                    | 53.3 |
| Death           | 2                   | 5.6  | 0                    | 0.0  |
| <b>Total</b>    | <b>36</b>           |      | <b>15</b>            |      |

#### **Trials of posaconazole and isavuconazole 2017-2018 National Aspergillosis Centre**

| <b>Outcomes</b> | <b>Posaconazole</b> |      | <b>Isavuconazole</b> |      |
|-----------------|---------------------|------|----------------------|------|
|                 |                     | %    |                      | %    |
| Success         | 24                  | 49.0 | 6                    | 28.6 |
| Failure         | 20                  | 40.8 | 11                   | 52.4 |
| Death           | 5                   | 10.2 | 4                    | 19.0 |
| <b>Total</b>    | <b>49</b>           |      | <b>21</b>            |      |

## 2.6 Intravenous antifungal therapy

Intravenous antifungal therapy is most often used when azole therapy has failed or resistance has developed.

There was a total of 20 courses of intravenous antifungals given in 2019-2020.

Of the 13 courses of Micafungin

- 6 had documented improvement
- 6 remained stable without significant improvement
- 1 worsened despite treatment and died.

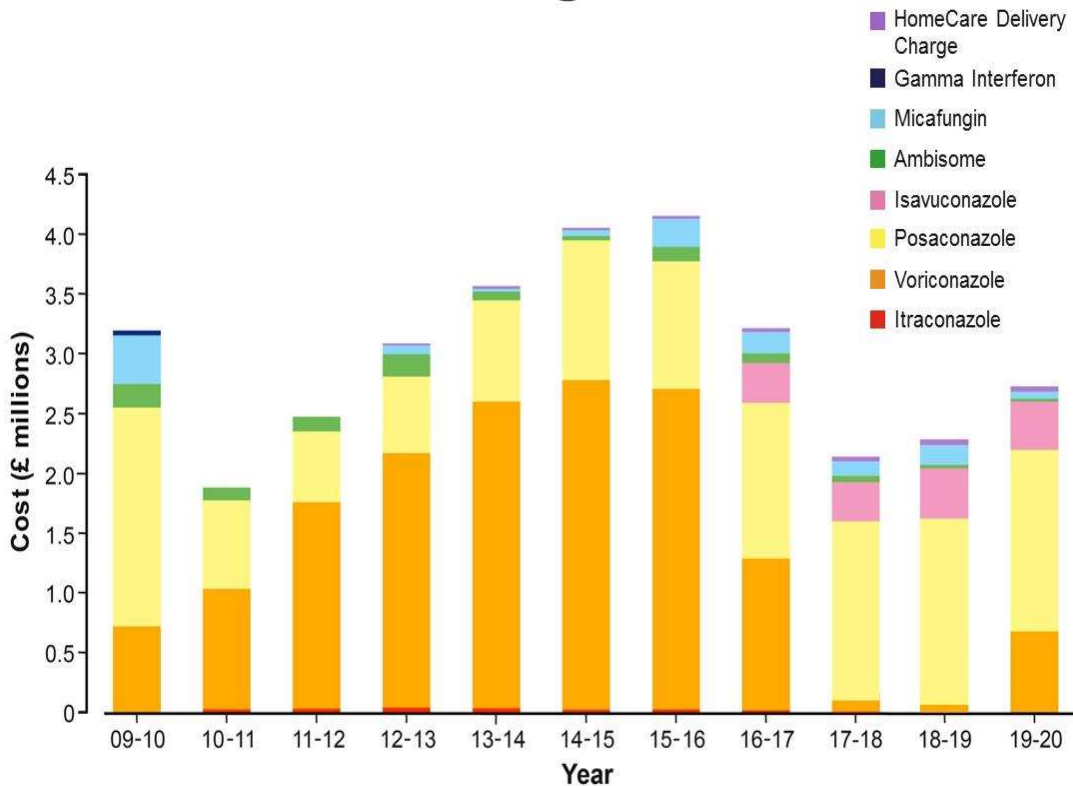
Of the 7 courses of Ambisome

- 3 courses had to be discontinued due to adverse renal side effects
- 2 had documented improvement
- 2 were stable without improvement after treatment

## 2.7 Antifungal prescribing and expenditure

Antifungal prescribing has remained stable. The cost of voriconazole increased due to national pharmaceutical supply problems of the generic brand raising costs through prescription of brand name. This issue was present for approximately 3 months.

# NCG drug costs



## 3. Specialist Nurse Service

The NAC has a highly specialised nursing service. This year the service has continued to:

- Answer patient enquiries and provide support via a patient phone line available 5 days a week.
- Provide high quality care to patients attending clinics and for those admitted to hospital.
- Provide remote antifungal therapeutic drug monitoring through reviewing results daily, adjusting patient doses and communicating these changes to the patient, GP and homecare delivery service.
- Deliver a paid postal service to provide remote blood and sputum testing

During 2019-2020 the NAC nursing service has developed the following:

- Identified from feedback that new patients require an increased level of support and guidance during their first clinic visit. This has led to the implementation of a named specialist nurse or senior healthcare support worker, to accompany the patient through their first clinic visit pathway. The aim of this is to improve communication with the patient, improve compliance with treatment, improve their clinic appointment experience and help to reduce the time. This has also helped to build rapport with the patients and the nursing team.
- Two senior specialist nurses are now independent prescribers, improving patient access to treatments and enhanced knowledge of medicine management

The NAC nursing service challenges in 2019-2020:

- Temporary staff shortages - 2 nurses left in 2019-2020
- Nursing team role changed early in the COVID-19 pandemic, providing Trust PPE training and working on virtual COVID-19 ward, while continuing to provide a NAC nurse service and support telephone clinics

The service continues to have positive feedback from patients and this is reflected in the annual patient survey.

#### **4. Physiotherapy Service**

The physiotherapy service provides patient assessments for airway clearance, nebulised drug challenges, spirometry and provision of appropriate exercise programmes along with referral to pulmonary rehabilitation.

After successful recruitment to a new 0.5 whole time equivalent post (Mairead Hughes), several key achievements marked this year.

Audit/ Service evaluation:

- A service evaluation was conducted Feb-May 2019 of 500 patients (36% ABPA, 54% CPA, 6.4% SAFS, 6% Aspergillus Bronchitis)
  - 42% had a diagnosis of COPD (of whom 18% had sputum issues), 32% had a diagnosis of Asthma (of which 39% had sputum issues), 6.5% ILD, 32% Bronchiectasis (41% sputum issues)
    - Of those with ABPA 6.25% previously antibiotic nebs, 15% had tried nebulised Fungizone, 15% had a drug history which included nebulised SABA, 12% had prev TB/NTM, 11% had used hypertonic saline for induction or in the community, 28% had issues with sputum
  - Of those with CPA,
    - 16.5% had Pseudomonas/Staph/Strep colonisation, 12% had had a hospital discharge within the last one month (an extra 9% within 3 months), 6% had gamma interferon/ mannose binding protein deficiency, 26% had a MRC of 3-5 or mention of an increase in MRC, 7% LTOT with 3% CPAP/NIV use
  - Of those with SAFS
    - 22% had anxiety, depression or ongoing mental health issues, 35% had musculoskeletal issues (osteoporosis, arthritis related chronic pain), 17% with SinoNasal issues, 8% GORD, 22% recent treatment for LRTI (antibiotic or steroid)
  - Other observations
    - Only 5% of CPA patients had mention of referral to pulmonary rehabilitation despite 26% having history of increased SOB or a MRC 3-5 (you get a 36.4% reduction in COPD exacerbations when pulmonary rehab is completed)
    - Several patients have no local respiratory/ID consultant but have chronic pseudomonas/ NTM
  - Take home points- many of our patients are complex, have daily battles with sputum, anxiety, depression, musculoskeletal problems and breathlessness. We need to acknowledge the potential for those with COPD to benefit from pulmonary rehabilitation and prompt local referral to such services.

#### Publication

An evaluation of nebulised amphotericin B deoxycholate (Fungizone®) for treatment of pulmonary aspergillosis in the UK National Aspergillosis Centre Akaninyene A. Otu, Philip Langridge, David W. Denning Mycoses First published: 03 September 2019 <https://doi.org/10.1111/myc.12996>

#### **Abstract**

Antifungal treatment options for allergic bronchopulmonary aspergillosis (ABPA) and severe asthma with fungal sensitisation (SAFS) are largely limited to itraconazole based on the outcome of randomised controlled trials. It is unclear if nebulised amphotericin B deoxycholate (Fungizone®) is a viable therapeutic option. We

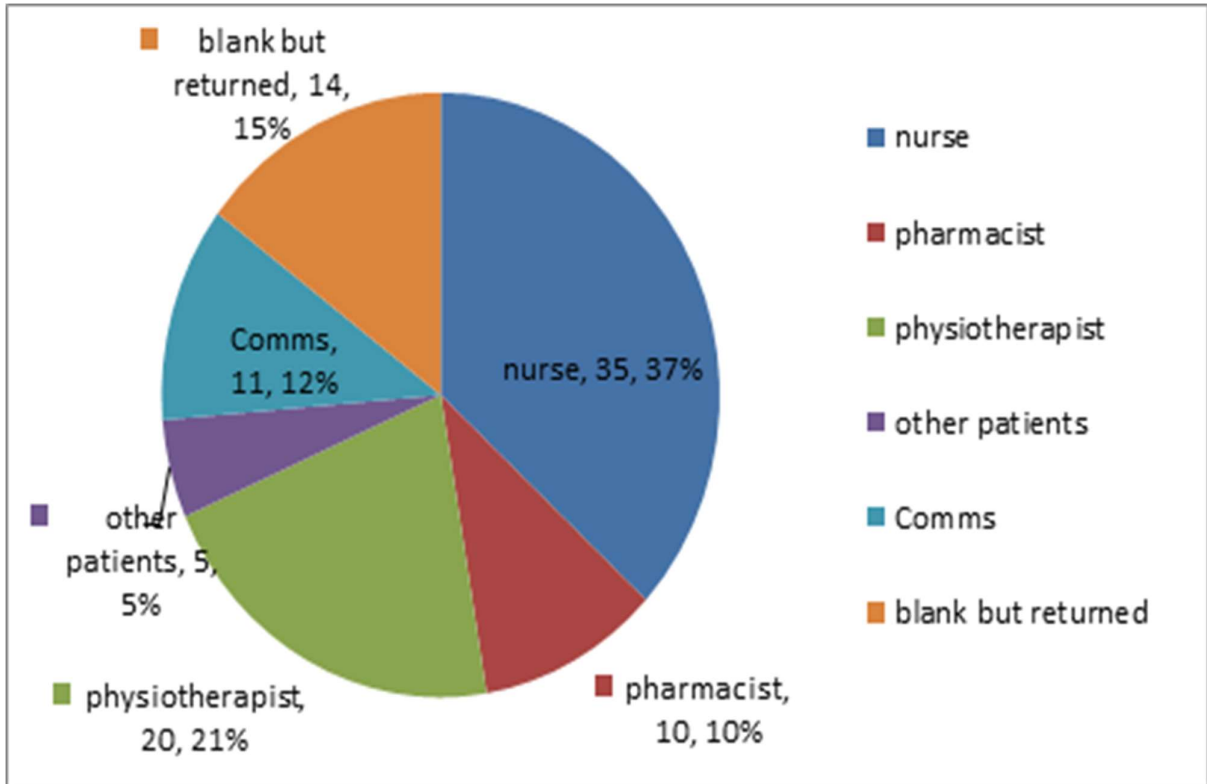


evaluated the safety and efficacy of nebulised Fungizone® in the long-term treatment of various forms of pulmonary aspergillosis. We assessed the records of 177 patients with various forms of pulmonary aspergillosis attending the National Aspergillosis Centre in Manchester who had received Fungizone®. Patients first received a challenge test with nebulised Fungizone® in hospital with spirometry pre/post-Fungizone® and nebulised salbutamol given pre-Fungizone®. Tolerability and changes in Aspergillus IgE, Aspergillus IgG and total IgE were evaluated. Sixty-six per cent (117/177) were able to tolerate the test dose of Fungizone® and in all cases the reason for discontinuation of the first test dose was worsening breathlessness. Twenty-six (21%) stopped therapy within 4-6 weeks, and the commonest reason cited for discontinuation of therapy was increased breathlessness, hoarseness and cough. Eighteen (10.2%) patients continued the Fungizone® for >3 months of which 5 (27.8%) recorded an improvement in total IgE, Aspergillus-specific IgE and Aspergillus IgG. Eleven had ABPA, four had SAFS, two had Aspergillus bronchitis and one had Aspergillus sensitisation with cavitating nodules. Among these 18 patients, sputum fungal culture results went from positive to negative in five patients, became positive in one patient, remained positive in three patients, and remained negative in seven patients. Nebulised Fungizone® appears to be a poorly tolerated treatment for pulmonary Aspergillosis with high dropout rates. There appears to be both clinical and serological benefits following sustained treatment with nebulised Fungizone® in some patients.

A poster describing this research was presented at 9th Trends in Medical Mycology Held on 11–14 October 2019, Nice, France, Organized under the Auspices of EORTC-IDG and ECMM

#### Patient support

- We explored the feasibility of weekly drop-in patient education sessions offered at multiple times during the Friday all day clinic covering a variety of topics including exercise, relaxation, dealing with shortness of breath, bothersome cough. Attendance was very poor (n=2) so the pilot was discontinued.
- We surveyed patients over 4 weeks asking who other than the doctor would they like a discussion with. There were 68 respondents and the relative proportions were the same across the CPA/ non-CPA clinics;



A few patients wrote some comments, which were as follows:

|  |  |                           |
|--|--|---------------------------|
| "happy with seeing doctor today thanks"  | "always available if I need them"  | "happy to see the doctor" |
| "in general, I would find it helpful to talk to the physio & maybe the pharmacist though not today especially"   | "I find out all I need to know off the doctor thank you"   |                           |
| "I only have mild symptoms so don't actually need to see anyone else at present (but may in future). I think it is great that you have provided the aspergillois newsletter and a sheet to ask questions. Thanks so much for all you do. :)" | "I only have mild symptoms so don't actually need to see anyone else at present (but may in future). I think it is great that you have provided the aspergillois newsletter and a sheet to ask questions. Thanks so much for all you do. :)" |                           |

A patient agreed to share how physiotherapeutic interventions in our clinic had dramatically improved her symptoms and quality of life:

<https://youtu.be/9MwMS6oNKmA>

## 5. Manchester Regional Mycology Centre

### Background to the Mycology Reference Centre

The laboratory, in partnership with the National Aspergillosis Centre, was awarded the status of the first European Confederation of Medical Mycology Centre of Excellence in January 2017. This accreditation has been maintained for 2018 - 2019.

The Mycology Reference Centre Manchester (MRCM) has completed its ninth year of operations and has expanded in step with the evolution and continued growth of the National Aspergillosis Centre. There have been numerous developments and continued growth in its portfolio of tests and activities. In 2018 the laboratory became a member of the Manchester University NHS Foundation Trust Division of Laboratory Medicine, and became the only stand-alone mycology laboratory in the UK to be accredited by the UK Accreditation Service (UKAS). The laboratory has successfully retained its accreditation status following UKAS surveillance inspections.

The objective of the MRCM is to provide a mycology reference service embracing all aspects of medical and public health mycology. The vision, scope and research activities can be viewed on the Centre's website: [www.mrcm.org.uk](http://www.mrcm.org.uk)



### Role and Functions

The key aims and objectives of the MRCM are to provide and maintain:

- An exemplary reference mycology service for the National Aspergillosis Centre (NAC), clinics and hospitals in the UK and beyond,
- International, national and local leadership in medical mycology diagnostic services, and training,
- A service, which is comprehensive, interpretative, accredited and appropriate to user needs,
- Education and training for all staff, including participation on national and international courses, that is appropriate and relevant to the departmental goals,
- A safe, appropriate and comfortable working environment which is inspirational and motivating that empowers a team environment.

- To maintain UKAS ISO 15189 Accreditation,
- Maintain a research programme in house at the MRCM in collaboration with the NAC and support others undertaking mycology research within the Manchester Fungal Infection Network, within industry, and playing an integral part in clinical trials.,
- An excellent and close working relationship with Wythenshawe Hospital Infectious Diseases and the NAC. Good working relationships within microbiology, pathology and with other departments within the Trust, and colleagues in other hospitals and Universities.

### **Service strategy**

- The MRCM has expanded appropriately to meet the requirements of the National Aspergillosis Centre, with an emphasis on antifungal susceptibility testing and a range of molecular tools. Growth of the MRCM has provided much needed support for NHS research, including clinical trials of new antifungal agents (four during the time span of this report).
- A major innovation and income stream has been the establishment of the Mould Surveillance Service: mouldy houses, hospital environments and work-places.

### **Research and Development**

- Provision of undergraduate and post-graduate research training and supervision in many areas of medical mycology: BSc. Research projects, Masters projects, MD and PhD programmes.
- Supporting clinical trials and Infectious Diseases research and development projects
- Development and evaluation of new diagnostic kits and platforms:
  - Pyrosequencing for mutations in *Aspergillus fumigatus* that confer resistance to azole antifungal drugs, now in routine use following UKAS accreditation
  - Evaluation of a lateral flow device (LD Bio, France) for *Aspergillus fumigatus* IgG/IgM in CPA and ABPA patients

### **Key achievements - summary**

- Sustained development of a rapid-access clinical advice and support service
- Provision of new staff
- Introduction of new assays:
- Introduction of 'high volume culture' of respiratory samples to increase the yield of *Aspergillus* and other filamentous fungi from NAC and other patients
- Expansion of DNA-sequence identification of unknown mould and yeasts isolated from respiratory specimens

- Pyrosequencing for mutations in *Aspergillus fumigatus* that confer resistance in clinical samples directly in clinical samples

#### **Representation on national and international committees:**

1. EUCAST Antifungal Susceptibility Testing Committee as a Collaborating Laboratory
2. Standards for Microbiology Investigations (SMI) Steering Committee and Bacteriology Working Group
3. British Society for Medical Mycology
4. International Society for Human and Animal Mycology
5. Public Health England English surveillance programme for antimicrobial utilisation and resistance (ESPAUR)
6. Academy of the European Confederation of Medical Mycology
7. British Society for Antimicrobial Chemotherapy Grants committee
8. Testing laboratory for UK NEQAS for Microbiology – Mycology identification and susceptibility schemes
9. Test centre for all Fungal PCR Initiative (FPCRI) schemes – fungal PCR for *Aspergillus*, *Candida*, *Pneumocystis*, *Mucorales* and tissue
10. Prof Malcolm Richardson: Co-authorship of *Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium*. Lancet Infectious Diseases, 2019.
11. Dr Riina Richardson (RR) is the speciality representative for the Steering Committee and the Working Group for Microbiology Standards in Clinical Bacteriology (SMIs). These are standards for microbiological diagnostics in the UK but broadly used in Europe and beyond.
12. RR is the UK representative for the European Confederation of Medical Mycology (ECMM) Excellence Centre Assessment Committee setting the standards and accrediting centres for the diagnostics and management of mycoses globally.
13. RR is the Mycologist on the British Association for Sexual Health and HIV (BASHH) UK National Guideline on the Management of Vulvovaginal Candidiasis working group.
14. RR is actively involved with the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) working groups and have been invited to contribute to the development of European guidelines on fungal infections (*Candidaemia* guideline, *Rare yeasts* guideline).
15. RR was elected as the Educational Officer for the ESCMID Fungal infection study group.
16. RR is the Lead for the European Fungal PCR Initiative (EFPCRI) *Pneumocystis* Working Group.

#### **Research and test evaluation activities:**

Consolidation of test portfolio offered for the benefit of CPA patients:

- The use of Beta-D-glucan, PCR and other diagnostic tests in antifungal stewardship
- Ongoing experience regarding sensitivity testing on *Aspergillus* isolates to include terbinafine, micafungin, isavuconazole, and investigational compounds, for example, ibrexafungerp.
- Real-time PCR for *Aspergillus* in respiratory secretions and blood
- Molecular identification of fungi, including unusual *Aspergillus* species. This is a nation-wide service
- Monitoring of NAC/CPA patients houses, workplaces for *Aspergillus*
- Provision of mycology services to national and international pharmaceutical companies who are developing new antifungal drugs.

**Publishing activities:** contributions to National Aspergillosis Centre and the Manchester Fungal Infection Group publication output (see appendix)

#### **Training:**

- 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
- Host to one University of Manchester MD student
- Host to medical microbiology trainees
- Institute Pasteur, Paris – lectures
- Lecturing on University of Leeds Masters in Bioscience
- Lecturing on University of Keele masters in Medical Microbiology
- Host to overseas visitors for training and collaboration

#### **Presentations and global outreach:**

- Society for Indian Human and Animal Mycologists meeting (SIHAM)
- British Society for Medical Mycology meeting
- INFORM: ISHAM Regional Meeting in collaboration with Gilead Sciences (Dubai) meeting
- Departments of Haematology, UK
- Departments of Clinical Microbiology, UK
- Filmed lectures: Gilead Antifungal Information Network
- Fungal Update meeting 2019 (London)
- 29<sup>th</sup> ECCMID, 2019, 11 presentations/posters (Amsterdam)
- Trends in Medical Mycology, 2019, 9 presentations/posters

**Challenges:** reconfiguration of senior management team due to the planned retirement of the Director – Professor Malcolm Richardson.

## **6. Mortality Report**

Morbidity and mortality meetings were introduced at the NAC in August 2017. An attendance registry is kept. Four patients were discussed from April 2019 to March 2020. There is a Trust requirement to discuss patients who died while inpatient, however we have also introduced discussion of patients who died outside of the Trust. A mortality review proforma is completed for every patient discussed.

Examples of actions and learning points from such meetings below:

- Case 1:
  - Patient with CPA discharged from hospital and did not receive follow up in clinic. Presented one year later with haemoptysis.
  - Root cause analysis performed: system relied on a fax being sent from the ward to the admin team. Also, this case was not labelled as CPA at the time, so it went to the general infectious diseases admin, not the NAC admin.
  - Action: We introduced a unified email address for all such queries: Re-audited this 6 months later and no patients were lost to follow up since.
- Case 2:
  - Patient with previous lung cancer and CPA. Failing all antifungal therapy. In hospital for several weeks due to recurrent chest infections under the aspergillosis team. Passed away in hospital.
  - Mortality review identified that patient struggled with anxiety and depression. No formal psychiatry follow-up was in place.
  - Action: It was agreed since to liaise with the clinical psychologist team to see if cover can be offered for CPA patients with end stage disease and mental health issues, either as inpatient or in clinic.

## 7. Statutory reports

### 7.1 MRSA

No cases of MRSA were reported.

### 7.2 *C. difficile* and CPE infections

No cases of *C. difficile* infection were reported.

No CPE (carbapenamase producer) cases were reported

### 7.3 Serious Untoward Incidents (SUIs)

No SUI's were reported.

### 7.4 Complaints

No formal complaints were made in 2019-20.



## 7.5 Hospital Incident Reporting System (HIRS) alerts

A total of 2 HIRS were submitted in 2019-2020

1. Problem identified: Documents filed in wrong patient notes. Outcome: documents re-filed. Action: reminder sent to administrative staff to ensure accurate record filing
2. Problem: Failure of laboratory to process 1 postal voriconazole blood level. Outcome: Sample not processed as per new specimen acceptance policy based on recent stability testing of un-spun samples up to 3 days. Action: Postal kit information sheets updated to ensure postal samples are not sent prior to a weekend to ensure laboratory arrival within 3 days.

|         | SUI | HIRS | Complaints |
|---------|-----|------|------------|
| 2013-14 | 1   | 0    | 3          |
| 2014-15 | 0   | 0    | 1          |
| 2015-16 | 0   | 1    | 0          |
| 2016-17 | 0   | 0    | 1          |
| 2017-18 | 0   | 3    | 0          |
| 2018-19 | 0   | 1    | 0          |
| 2019-20 | 0   | 2    | 0          |

## 8. Audit and Quality Improvement Report

The NAC has a strong programme of audit and quality improvement that runs continuously throughout the year. Our clinical fellows are actively engaged in this programme allowing opportunities for publications and conference poster presentations.

A selection of our projects that have directly influenced patient care are presented below.

### Penicillin allergy documentation and referral for NAC patients

Presented: December 2019

Background:

- Penicillins are the most common drugs used for flare ups in patients with chronic lung disease like those with CPA. Allergy is common, but often over-reported; patients are then withheld potentially useful or even lifesaving penicillin treatment. Guidelines suggest that allergy should be documented and all patients referred to an allergy specialist for clarification

Results:

- <75% of cases had documented allergy status or were referred to a specialist for clarification of the allergy nature.

Conclusions:

- Documentation of allergy status can be improved
- An electronic referral process to allergy services will be introduced
- The NAC team will be educated on importance of allergy documentation through local department teaching sessions

Risk of skin cancer in CPA patients on voriconazole

Presented: November 2019

Background:

- Voriconazole is associated with skin cancer risk; should not be used beyond 6 months if possible. This is well described in transplant patients, but not in CPA. We reviewed CPA database for diagnosis of skin cancer

Results:

- 11 patients had skin cancer since 2009 (eight on long term voriconazole). Incidence rate was 4.88 per 1000 person/year in patients who received voriconazole and 2.79 per 1000 person/year in patients who did not receive voriconazole. Did not reach statistical significance. 3 patients had relapse, one required reconstructive surgery. All patients had photosensitivity (skin reaction to voriconazole) before cancer diagnosed

Conclusions:

- risk of skin cancer on voriconazole not as high as in transplant patients
- Continue to monitor for photosensitivity
- Skin examination
- Submitted for publication, February 2020

Audit of pneumococcal vaccination in CPA clinic

Presented: January 2020

Background:

- Prevenar vaccination is recommended in the immunocompromised, but it is not known whether it is effective in patients with CPA. It is being administered

in the NAC clinic. The effectiveness of the vaccine in terms of serological response was assessed.

Results:

- Patients with ABPA responded better than CPA
- Two doses of Prevenar gave similar responses to the polysaccharide vaccine

Conclusions:

- No evidence that Prevenar is more effective than polysaccharide vaccine (Pneumovax). Pneumovax should be the recommended option in the NAC clinics.

## 9. Research and Publications

The NAC and MRCM have close research partnerships with The University of Manchester (Manchester Fungal Infection Group) and the Manchester NIHR Biomedical Research Centre. There are also close international collaborations meaning there is a diversity of research publications from basic science to frontline translational medicine. During the year 2019 there have been 65 original publications and 4 book chapters directly relevant to Aspergillosis. A full list of publications can be seen in Appendix 9. Highlighted below are 4 articles which have direct clinical implications for NAC patients.

### 1) Isavuconazole and voriconazole for the treatment of chronic pulmonary aspergillosis: A retrospective comparison of rates of adverse events.

**Mycoses 2019; 62: 217-222.**

Bongomin F, Maguire N, Moore CB, Felton T, Rautemaa-Richardson R

**Background:** Long-term oral triazole antifungal therapy is the cornerstone of management for patients with chronic pulmonary aspergillosis (CPA). Itraconazole is the first-line choice of treatment. Voriconazole, posaconazole or isavuconazole can be used as alternative treatments in case of resistance or intolerance. All of these can cause significant adverse drug reactions.

**Objectives:** To evaluate how CPA patients tolerate voriconazole and isavuconazole after prior triazole therapy.

**Methods:** We performed a retrospective observational study at the UK National Aspergillosis Centre. Medical records for all consecutive CPA patients started on isavuconazole and voriconazole during an observation period of 12 and 6 months respectively were analysed.

**Results:** During this study period, 20 patients were started on isavuconazole and 21 patients on voriconazole. Adverse events were seen in 18 of 21 (86%) the patients in the voriconazole group and 12 of 20 (60%) in the isavuconazole group ( $P = 0.02$ ). For

those who developed adverse events to these agents, the rates of discontinuation of therapy were comparable (ie 10/18 [56%], voriconazole vs 8/12 [67%], isavuconazole; P = 0.54). Five (25%) patients in the isavuconazole group who were intolerant to other triazoles tolerated the standard dose of isavuconazole.

**Conclusions:** Compared with isavuconazole, adverse events were significantly higher in CPA patients commenced on voriconazole. Isavuconazole may be an option for those patients who are intolerant to other triazoles.

### **2) Therapeutic drug monitoring and adverse events of delayed-release posaconazole tablets in patients with chronic pulmonary aspergillosis.**

**J Antimicrob Chemother 2019; 7: 1056-1061**

Kosmidis C, Rodriguez-Goncer I, Rautemaa-Richardson R, Richardson MD, Moore CB, Denning DW.

Posaconazole delayed-release tablets offer better bioavailability than the liquid suspension, but no post-marketing data are available in patients with chronic pulmonary aspergillosis (CPA). We aimed to explore the pharmacokinetics by using therapeutic drug monitoring and any adverse events of posaconazole tablets in patients with CPA. A lower-than-recommended posaconazole tablet dose achieved therapeutic levels in most patients and was better tolerated. Males were more likely to achieve a therapeutic level. Underlying conditions affected the degree and frequency of adverse events.

### **3). Evaluation of LD Bio Aspergillus ICT lateral flow assay for IgG and IgM antibody detection in chronic pulmonary aspergillosis.**

**J Clin Microbiol 2019;57:e00538-19**

Stucky Hunter ES, Richardson MD, Denning MD

Detecting *Aspergillus*-specific IgG is critical to diagnosing chronic pulmonary aspergillosis (CPA). Existing assays are often cost- and resource-intensive and not compatible with resource-constrained laboratory settings. Using a newly developed lateral flow module for antibodies to *Aspergillus* the test was found to have excellent sensitivity for the serological diagnosis of CPA. Given the short run time (15 minutes), simplicity, and limited resources needed it was shown to be a suitable diagnostic tool for CPA as an initial screening test or for use in resource-constrained settings.

## **10. Patient and public engagement**

The NAC communications team was re-named the NAC CARES team in February 2020.

**CARES** (Community, Awareness, Research, Education, Support) encompasses the broad range of activities undertaken to support and involve patients and carers.

Nurses, physiotherapists, doctors, pharmacists, communications, patients, their families and carers are all one **Community** striving to recognise each other's needs and to provide for them as best we can.

Patients and carers cannot make best use of the services offered by NAC unless they are fully **Aware** of everything we do. NAC staff will not be able to offer the best service they can unless they are **Aware** of the expectations of the patient.

NAC needs its patients to be involved in our world leading **Research**, patients need to feel involved in the Research process, and trust it. Involvement is end-to-end, progressive, two-way and a mutually beneficial experience.

**Education** encompasses learning about aspergillosis. It reaches out to the clinical and patient/carers communities nationwide and encourages all concerned to 'think fungus' when faced with difficult diagnoses and declining response to treatment. It encourages clinicians to get a more complete understanding of this disease, for example if they are caring for an aspergillosis patient or carer. It signposts all stakeholders to NAC resources and encourages them to use us.

The entire community needs **Support** which comes in many forms: information, learning, mental and physical health support, thereby making everyone's day a little easier or a little more effective as we fight aspergillosis together.

Over the last 12 months the Communications team have met groups of patients hundreds of times online and dozens of times offline.

The physiotherapy team (Phil Langridge and Mairead Hughes) and have held online sessions, some recorded that are now available online.

The Nursing team (in particular Jenny White, Deborah Kennedy and Carol Toner) have worked with the CARES team to produce booklets for each form of aspergillosis containing an appropriate series of information leaflets. These are intended to give to new patients. All of the nursing team work hard to collect annual patient survey and collect Quality of Life data on a weekly basis.

Pharmacist Fiona Lynch has made herself available to patient groups to answer any medication related queries and MFT-Wythenshawe Pharmacy have presented a talk to the patient & carer Monthly group giving us all a glimpse behind the scenes and signposting us to the 24 hour helpline.

### 10.1 Patients survey 2020

The NAC has administered a patient survey annually each year in Q1. Some questions are retained each year, while others vary according to service changes.

The complete results of the patient survey are detailed in Appendix 9. The survey was intended to run over 4 weeks from February to March 2020. All questionnaires were completed in the Friday CPA clinic.

37 questionnaires were completed, but the process was halted prematurely due to the shutdown of the clinic due to the outbreak of COVID-19. This is comparatively few considering that 86 questionnaires were completed in 2019 and 160 were completely in 2018. Given this shortcoming, comparing this questionnaire results with those of

2019 & 2018 may be problematic and conclusions risk being less representative of our patient population.

Some questions have been deleted or changed between 2018 and 2020 so some comparisons can no longer be made.

#### Summary of main points (2019-2020)

1. The level of overall service quality remains excellent, but there are areas identified for improvement along with some highlights of the success from improvements already made.
2. Although overall satisfaction is extremely high, satisfaction of staff courtesy and quality of care has fallen slightly this year, a marginal trend that has continued for 2 years now.
3. The number of patients that are being contacted between visits to clinic has increased markedly compared with 2019. This is mainly due to the specialist nursing team providing advice and guidance via telephone between appointments. There was 100% approval of the contact.
4. The number of patients having a consultation with a specialist nurse has also increased dramatically with 100% approval of knowledge and communication and several very positive comments made.
5. The number of patients that are being seen by a physiotherapist rose significantly compared to 2019 but are still a little short on 2018 figures, 100% approval of the consultation. The demand for physiotherapy will vary with patient caseload and underlying diagnosis.
6. 82% of patients had not considered end of life care and 90% did not want to discuss the subject. The NAC approach to palliative and end of life care has been discussed within the team. Although not part of the current commissioned pathway, recognition of patients within the last year of their life is vital to ensure optimal use of the gold standard framework. Our team is committed to improving knowledge in this area and plan to work with our hospital palliative care team to develop pathways.
7. The number of people who have been admitted has fallen significantly from 32% to 23%.
8. Patients continue to be very satisfied with the postal service for drug levels and sputum samples. There are occasional problems with sputum packaging and local GP services being unable to carry out phlebotomy. This is most common in areas where GP practices use central 'hubs' for phlebotomy. Our service now sends two blood tubes to take account of the different manufacturers used predominantly in the UK (S-Monovette and BD vacutainer)
9. The home delivery service for antifungal medication remains a service with excellent feedback. There was only one instance where a patient felt the customer service was below expected.
10. Patient information leaflets are well accepted and approved of, but 26% did not recall receiving one. We have had a recent change in practice for a specialist nurse to accompany patients through their first visit. This will aid deliver of vital patient information. We are additionally looking into providing the leaflet in more languages.

11. Only 16% of patients had visited the [aspergillosis.org](http://aspergillosis.org) website, so we will aim next year to build up awareness of that resource as it is universally approved of amongst readers.
12. Face-to-face patient meetings are held once per month and are attended by a only a small proportion of patients. Many find it inconvenient due to travel distance, are concerned about cross-infection or are worried about missing their call to see a doctor. Due to the COVID-19 pandemic more people are currently attending this meeting using Zoom and it is likely we will move to this platform long-term.
13. 14% of patients are members of our Facebook support groups and 30% of those who are not members wish to receive more information on how to join. Taken together, this is the most popular means of support for patients online and it also has the biggest potential to grow.
14. Information leaflets and quarterly booklets continue to have high approval and awareness from the patients.
15. Regional support groups (offline) remain small as they are strongly dependent on locality. Each is also available online and there is some activity.

### **10.2 Community booklet & Newsletter**

A community booklet is produced on a quarterly basis and 1000 per year were distributed to all patients who do not have access to a computer, informally at clinic. It is intended to provide information on access to support for all patients including those who do not have access to our online resources, for example if they do not have a computer or internet access.

This allows all readers to know what is happening in the service and with other patients and carers. It includes news items, why and how to use facemasks, coping with stress, medicine advice details and seasonal advice e.g. allergies. It also provides contact numbers or website addresses for groups that offer social support. This is supplemented with a short monthly newsletter which covers our face-to-face monthly patients support meetings, shorter-lived news and a quick reference guide to online groups.

### **10.3 The Aspergillus Website @ [www.aspergillus.org.uk](http://www.aspergillus.org.uk)**

The Aspergillus Website remains the world's most comprehensive resource for the pathogenic and allergenic fungus *Aspergillus* and the diseases that it causes. It is completely free to all users. It is supported from the UK National Health Service and unrestricted educational grants from various corporate donors, notably Mayne Pharma, Pfizer, Dynamiker, Gilead and Zambon. The Aspergillus Website provides simple, free access to >43,000 pages all indexed in Google, ready to be searched, over 14,300 scientific articles (including a unique collection of 836 historical articles) and ~17,000 conference abstracts from 1974 onwards. The comprehensive list of drugs and drug interactions with antifungals is continually up-dated. The drug interaction database is popular and well used. This database is also available as an 'App' via Android and OS smartphones to allows ease of access and use, which are now updated in real-time, meaning users are always working with the latest updated information. Over 2,300 potentially harmful interactions are listed. Over 300 of the new (Android) Apps have been downloaded. Externally there are over 80,000 active links to [www.aspergillus.org.uk](http://www.aspergillus.org.uk) and [www.aspergillosis.org](http://www.aspergillosis.org). The Aspergillus Website is listed



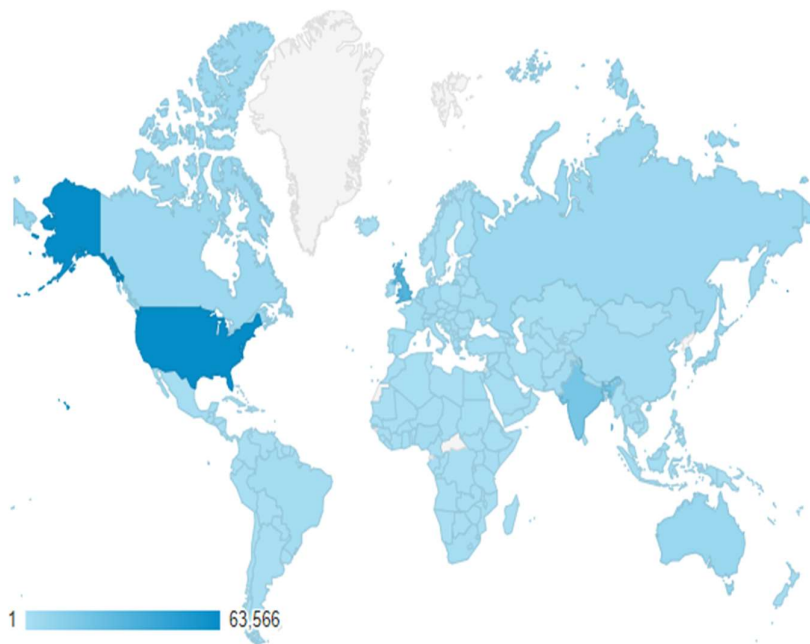
at number 1, 1, 4 and 4 in Google for 'aspergillus', 'ABPA' 'aspergillosis' and 'aspergilloma' respectfully.

Searching Twitter for 'aspergillus' ranks the National Aspergillosis Centre Twitter page at number 1 and Mycology Reference Centre Manchester as number 2. Searching Facebook for 'aspergillus' or 'aspergillosis' lists our 40 groups and pages as (by far) the major content on the platform, Our largest group, Aspergillosis Support, has >2250 members which has grown at the rate of 14 members per week throughout 2020 and activity on that group alone is in excess of 67,000 events in 2020.

The way we count monthly figures of our websites has now changed in order to get greater depth of information about our users and how they browse our websites in order that we may refine how we deliver our information, and who we deliver it to. This means that we are counting a smaller subset of our user statistics and as a result the numbers are not comparable to previous year's figures.

The Aspergillus Website and Patients' website have 37,000 and 7,000 users per month respectively. This equates to 1 million page views per month with readership of the Patients website (aspergillois.org) up 3 fold in 2020. Smaller devices (smartphones and tablets) continue to rise as a proportion of all devices used to access our websites, patients in particular preferring to use them 69.5% (2019 65%) of the time reflecting changes in how we all browse the internet.

Overall usage of the Aspergillus Website seems to have levelled out over the last twelve months and this website is based on software that will be obsolete by 2022, so we are taking this opportunity to move it to a new software platform and rethink several sections in order to streamline what we offer. This will be coupled with a more focussed approach to targeting the specialist professional groups that use this website.



Mapping of [www.aspergillus.org.uk](http://www.aspergillus.org.uk) (see figure above, darker shading = more users) shows that The Website reaches people in 215 countries. USA is the country from which we get most visits with UK and India in the next 2 places, Australia and Netherlands in 4th & 5th place respectively.

Country usage of the Aspergillus Website in early 2020

| Country ?          | Acquisition                                    |  |  |
|--------------------|--|--|--|
|                    | Users ? ↓                                      | New Users ?                                    | Sessions ?                                     |
|                    | 220,714<br>% of Total:<br>100.00%<br>(220,714) | 220,443<br>% of Total:<br>100.05%<br>(220,331) | 265,826<br>% of Total:<br>100.00%<br>(265,826) |
| 1.  United States  | 63,566 (28.40%)                                | 63,051 (28.60%)                                | 72,677 (27.34%)                                |
| 2.  United Kingdom | 33,507 (14.97%)                                | 32,700 (14.83%)                                | 42,288 (15.91%)                                |
| 3.  India          | 19,350 (8.65%)                                 | 18,965 (8.60%)                                 | 22,509 (8.47%)                                 |
| 4.  Australia      | 6,468 (2.89%)                                  | 6,379 (2.89%)                                  | 7,609 (2.86%)                                  |
| 5.  Netherlands    | 5,582 (2.49%)                                  | 5,501 (2.50%)                                  | 6,561 (2.47%)                                  |
| 6.  Russia         | 5,443 (2.43%)                                  | 5,397 (2.45%)                                  | 6,369 (2.40%)                                  |
| 7.  Canada         | 5,270 (2.35%)                                  | 5,234 (2.37%)                                  | 6,025 (2.27%)                                  |
| 8.  Japan          | 4,923 (2.20%)                                  | 4,848 (2.20%)                                  | 5,635 (2.12%)                                  |
| 9.  South Korea    | 3,800 (1.70%)                                  | 3,768 (1.71%)                                  | 4,215 (1.59%)                                  |
| 10.  China         | 2,989 (1.34%)                                  | 2,948 (1.34%)                                  | 3,621 (1.36%)                                  |
| 11.  Germany       | 2,976 (1.33%)                                  | 2,900 (1.32%)                                  | 3,675 (1.38%)                                  |
| 12.  Philippines   | 2,570 (1.15%)                                  | 2,555 (1.16%)                                  | 2,958 (1.11%)                                  |
| 13.  Belgium       | 2,455 (1.10%)                                  | 2,426 (1.10%)                                  | 2,822 (1.06%)                                  |
| 14.  Ukraine       | 2,450 (1.09%)                                  | 2,427 (1.10%)                                  | 2,971 (1.12%)                                  |
| 15.  Brazil        | 2,330 (1.04%)                                  | 2,295 (1.04%)                                  | 2,850 (1.07%)                                  |

Over 51% of users access the Aspergillus Website using phone or tablet. Twitter posts are put out three times per day and seen by 40,000 (@AspergillusWeb – 1,958 followers which is a 50% increase on 2019). Monthly newsletters from the Aspergillus Website are sent out to over 27,000 (free) subscribers and we intend to learn much more about our readers and get better focus for our mailing list in the coming year to improve activity still further, including a newsletter intended for patients alone.

#### **10.4 Website for patients and carers ([aspergillus.org](https://aspergillus.org))**

The Patient's Website was refreshed in 2019 and readership is now increasing rapidly and in July 2020 attracted over 7800 (1800 in June 2019) unique visitors who looked at over 12,000 pages. The top countries utilising the Patients' Website by origin are: 1.USA 2.UK 3.France 4.India 5.Russia. The Patients website is available in eight languages and we can see that 45% of users have a language other than English as their preferred choice (this figure for the Aspergillus Website is 27%). Most common languages used are French 12%, Russian 10%, Arabic 6% and Spanish 7%. This is an important observation as we need to be able to reach non-English speakers in the UK as well as abroad as nearly 900,000 people (2% of the total UK population) reported having little or no English in the 2011 UK census. This same resource tells us that we need to add several more immigrant languages so that we include all of the most popular immigrant languages, which has been carried out. There are >400 active links to this website excluding [aspergillus.org.uk](https://aspergillus.org.uk).

The provision of live and recorded online events held by the National Aspergillus Centre, happening on a monthly basis are now hosted within the Facebook communities and generally get >500 viewers each month.

#### **10.5 Patient & carers support meetings**

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. The meetings are led and organised by Dr Graham Atherton with assistance from Chris Harris and Helen Findon.

The subjects covered are available at <https://aspergillus.org/monthly-patientcarer-support-meeting-recordings/> and include:

- Dr Jenny Shelton (Imperial College) Citizen Science Meets Mycology – a project designed to map environmental antifungal resistance
- Georgia Taylor (MFT) on Air Pollution and Sustainability
- Dr Caroline Baxter (NAC) Neurological Side Effects of Azole Antifungals
- Dr Jorge Amich (MFIG) Unravelling the *A. fumigatus* – *P. aeruginosa* Interaction in the Context of Co-infection
- Prof Kyle Pattinson (Oxford University) Breathing with your Brain

However, since March 2020 this meeting has had to be hosted online using Zoom software as Wythenshawe Hospital has been closed to patients during the COVID-19 pandemic. This has progressed smoothly with the exception of being able to put these recordings online as Zoom software records the faces of participating patients and it is not appropriate to publish those online. Nevertheless, we have increased attendance to over 30 per month.

#### **10.6 Community structure**

Our online communities have been very popular since the year 2000 but our patient surveys indicated that up to half of our patients do not have access to a computer which denies them access to our extensive resources online. Our support community is thus a combination of online and offline meetings & resources.

The community is supported in several ways:

### Online

Many patients and carers use online support discussion groups and NAC & the Fungal Infection Trust (FIT) supports these people in several ways:

- Our (Facebook) communities worldwide are very active with >3,000 participants engaging up to 940 times per day and 12,000 per month (July 2020)

<https://www.facebook.com/groups/aspergillussupport/>

- The NHS Choices (Now NHS online) online community is no longer hosted on NHS website but has over 3000 members

- Local online Facebook groups (30 groups, 13 in the UK serving 793 people)

- Facebook group specifically for carers & family (195 members)

<https://www.facebook.com/groups/aspergillosis.carers/>

- The Professional LinkedIn members Aspergillus and Aspergillosis Group has over 540 members

- The provision of live and recorded online events held by the National Aspergillosis Centre, happening on a monthly basis are now hosted within the Facebook communities and generally get >500 viewers each month.

- Weekly meeting via Zoom conferencing software - attended by 4 to 10 people.

### Offline

- Monthly meetings at the National Aspergillosis Centre (NAC) are 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. The COVID pandemic has forced this meeting online.

- 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).

- Three information booklets have been produced which are each a collection of leaflets intended for use by CPA, ABPA or Aspergillus bronchitis patients.

- A series of 13 information leaflets are available and handed out in clinic by clinical staff as required for new and existing patients

## **11 Raising public awareness and educational outreach**

### **11.1 Public awareness**

Promoting awareness of aspergillosis and the National Aspergillosis Centre is particularly important as we suspect that many thousands of people remain undiagnosed. The result is that 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. There does appear to be more public visibility of fungal diseases in the press, with major press articles on *Candida auris*, azole resistance in *Aspergillus* and numerous other stories published.

Additionally, our informed patients and carers are important advocates and ambassadors for the diseases and NAC.

Last year we took our lead on where our efforts are most needed from the comments and discussions made by people in our patients groups.

- Patients are incorrectly diagnosed or not diagnosed at all for an average of 5 years. We are attempting to get support to produce e-learning for non-specialist clinicians to address this need.
- We have updated and re-written the information that the British Lung Foundation publish on aspergillosis, intended for patients and carers with a wide variety of lung diseases, some of which may be masking a form of aspergillosis. <https://www.blf.org.uk/support-for-you/aspergillosis>

## 11.2 Educational resources and outreach

The NAC leads several important educational initiatives for health professionals including: the Aspergillus Website ([www.aspergillus.org.uk](http://www.aspergillus.org.uk)), Leading International Fungal Education (LIFE) ([www.LIFE-Worldwide.org](http://www.LIFE-Worldwide.org)) (launched in 2012 in English and Spanish), the global advocacy foundation - Global Action Fund for Fungal Infections (GAFFI) ([www.GAFFI.org](http://www.GAFFI.org)) and a database and app for antifungal drug interactions ([www.antifungalinteractions.org](http://www.antifungalinteractions.org)).

Working with the charity the Fungal Infection Trust the world's first online Microscopy and Histology course ([www.microfungi.net](http://www.microfungi.net)), in 4 Modules has now been translated into French, Spanish, Portuguese and Chinese. The course is approved by the Royal College of pathologists for Continuing Professional Development (CPD). In July 2020, there were 1624 registered users in 126 countries on Microfungi.net (756 in 2018). Users can refer to the course materials indefinitely, even if they have completed all the modules and received their certificates. 243 learners are registered to use the translated Modules. Certificates are not awarded for the introductory Module 1 but 230 have been awarded for Module 2, 208 for Module 3 and 51 for Module 4 as of July 2020, a total of 489.

Collectively these online resources provide a substantial proportion of the world's high quality educational and advocacy materials for the world in fungal diseases.

9<sup>th</sup> Advances against Aspergillosis and Mucormycosis 2020 was held in Lugano, Switzerland on 27<sup>th</sup>-29<sup>th</sup> February but was severely impacted by the first outbreak of COVID-19 in Northern Italy that began the same week. All staff from the University of Manchester and many from MFT did not travel and that included the NAC CARES team. Despite this, the team ensured a pack of promotional and awareness material was sent and distributed at the meeting.

The NAC consultant team delivers frequent international lectures at Respiratory and Infectious Diseases Conferences raising clinical awareness of this disease. Additionally, the whole team delivers regular internal and regional training for trainees.

The CARES team held a successful online event (WAD2020 Coffee morning) on the 27<sup>th</sup> February 2020 for patients and carers, attended by 35 people. This event coincided with World Aspergillosis Day 2020 which was marked by many medical mycology partners around the world, via several social media campaigns, urging

doctors to ‘think fungus’ when they have treated a patient with antibiotics several times without success, and urging more investment in better diagnostics. The campaign has a new dedicated WAD 2020 website <https://www.aspergillosisday.org/world-aspergillosis-day-feb-27th/> which attracted over 1100 users and reached 52 countries.

Some of the patients in our Facebook community run a small fundraising group (originally set up with the help of the CARES team in 2018) working on behalf of the Fungal Infection Trust and helped advocate and promote WAD 2020 this year. The Aspergillosis Trust opted to work alone without CARES support late in 2019.

## **12. Financial Position**



Overall, there has been no significant increase or reduction in our financial position. There was a reduction in direct patient income due to reduced caseload and referrals. There was a significant cost incurred by the unavailability of generic Voriconazole. The next financial year should see a reduction in drug costs for Posaconazole as generic brands are introduced and become available to the Trust. The table below outlines our income streams. The total homecare costs in 2019-2020 were £45430 which has been included this year within the drugs income.

### 13. Future Service Developments

The following developments are planned for 2020/2021

- **Service re-specification with NHSE**  
We plan to continue our work with NHSE to re-develop the NAC service specification to ensure the service delivers the best possible patient care and experience.
- **Implementation of an annual patient review process**  
We plan to introduce an annual clinic review for all patients. Patients will be assessed by individual members of the MDT team including a doctor, specialist nurse, physiotherapist and pharmacist. Cases will be subsequently discussed with the wider MDT to ensure optimal clinical care, antifungal stewardship and communication with patient GPs and secondary care consultants.
- **Establishing virtual patient consultations**  
To reduce patient travel and widen patient care choices, we plan to implement a secure virtual patient consultation platform.
- **Remote advice and guidance service**  
There is an ever increasing demand for clinical advice and guidance without direct patient consultation. We plan to develop standardised documentation for this advice and formalise a process for recording and reporting the activity of this service.
- **Mortality review process**  
We are establishing an enhanced mortality review process to include a review of CPA care for all patients that die while under our service. As patients are often not local we do not always know cause of death but we want to ensure there is a team review of the care that our service has provided to all patients.
- **Intravenous antifungal outcome measures**  
We aim to improve and standardise reporting of outcomes for patients receiving iv antifungals
- **Antifungal resistance reporting to be added to our reporting metrics**
- **Patient Feedback**  
We aim to improve patient feedback. We want to be able to reach a wider and more representative cohort of patients and allow feedback to be done continually, in real-time, rather than retrospectively.
- **Palliative Care**  
We wish to form partnerships with our local palliative care teams to enhance end of life care and delivery of the gold standards framework for patients in our service.

## Appendix 1 Categorisation (Banding) of CPA disease complexity

### 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-mycobacterial 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 New Patient Audit

### NATIONAL ASPERGILLOSIS CENTRE

#### New patient audit April 2019 – March 2020

| MONTH        | DATE REFERRED | APPOINTMENT DATE | WAITING TIME - weeks | POSTCODE | AREA           | COMMENTS                                 | Band | Antifungal at 1st visit | Antifungal at 3 months | Priority     |               |
|--------------|---------------|------------------|----------------------|----------|----------------|--|------|-------------------------|------------------------|--------------|---------------|
| <b>APRIL</b> | 04/03/2019    | 11/04/2019       | 5                    | L32      | Liverpool      |  | 1    | Itra                    | Itra                   | Routine      |               |
|              | 28/11/2018    | 18/04/2019       | 3 months             | WN1      | Wigan          | dna x 2                                  | 1    | None                    | None                   | Routine      |               |
|              | 07/03/2019    | 05/04/2019       | 4                    | BH19     | Dorset         |  | 2    | Vori                    | Vori                   | Routine      | Died 13/12/19 |
|              | 29/03/2019    | 12/04/2019       | 2                    | RG4      | Caversham      |  | 2    | Vori                    | Vori                   | not selected |               |
|              | 21/03/2019    | 12/04/2019       | 3                    | ST2      | Stoke on Trent |  | 2    | Vori                    | Vori                   | Soon         |               |
|              |               | 08/02/2019       | 0                    | M27      | Manchester     | Transition IA/AB Missed from Feb numbers | 2    | Vori                    | Vori                   |              | Died 16/04/19 |
|              |               |                  | 0                    | WV6      | Wolverhampton  | relapse April                            | 2    | Isavu                   | Posa                   |              |               |
| <b>MAY</b>   | 13/03/2019    | 02/05/2019       | 7                    | WA5      | Warrington     |  | 2    | Vori                    |                        | Routine      | Died 9/7/19   |
|              | 13/03/2019    | 02/05/2019       | 7                    | ST6      | Stoke on Trent |  | 1    | Itra                    | None                   | Soon         |               |
|              | 01/04/2019    | 03/05/2019       | 4                    | L7       | Liverpool      |  | 1    | None                    | Itra                   | Routine      |               |
|              | 16/04/2019    | 10/05/2019       | 4                    | BB2      | Blackburn      |  | 2    | Vori                    | Posa                   | Soon         |               |
|              | 02/04/2019    | 10/05/2019       | 6                    | B93      | West Midlands  |  | 2    | Vori                    | Vori                   | Routine      |               |
|              | 01/05/2019    | 10/05/2019       | 1                    | M35      | Manchester     |  | 2    | Vori                    | Mica                   | Urgent       | Died 28/12/19 |
|              | 11/04/2019    | 17/05/2019       | 5                    | WN1      | Wigan          |  | 2    | None                    | None                   | Soon         |               |
|              | 15/05/2019    | 24/05/2019       | 2                    | CW10     | Middlewich     |  | 2    | None                    | Itra                   | Routine      |               |
|              | 07/05/2019    | 31/05/2019       | 3                    | DE72     | Derby          |  | 1    | Itra                    | Itra                   | Routine      |               |

|             |            |            |              |      |                     |   |   |       |                 |         |                |
|-------------|------------|------------|--------------|------|---------------------|---|---|-------|-----------------|---------|----------------|
| <b>JUNE</b> | 11/04/2019 | 21/06/2019 | 10           | SK7  | Stockport           |   | 1 | Itra  | Itra            | Routine |                |
|             | 11/04/2019 | 14/06/2019 | 9            | OL5  | Oldham              |   | 1 | None  | None            | Routine |                |
|             | 06/06/2019 | 14/06/2019 | 1            | DN14 | North<br>Humberside |   | 2 | Isavu | Isavu           | Urgent  |                |
|             | 28/05/2019 | 14/06/2019 | 2            | M32  | Manchester          |   | 1 | Itra  | Itra            | Soon    |                |
|             | 01/05/2019 | 21/06/2019 | 7            | WF2  | Wakefield           |   | 1 | Itra  | Itra            | Routine |                |
|             | 23/05/2019 | 28/06/2019 | 5            | LS26 | Leeds               |   | 1 | None  | None            | Routine |                |
|             | 16/05/2019 | 28/06/2019 | 6            | LL48 | Wales               |   | 2 | Vori  | Posa            | Routine |                |
|             |            | 30/05/2019 | 0            | PL9  | Plymouth            | Transition IA                                     | 2 | Posa  | Posa            |         |                |
|             |            | 26/04/2018 | 0            | WN7  | Leigh               | Delayed<br>diagnosis,<br>initial CT<br>monitoring | 2 | None  | None            |         |                |
| <b>JULY</b> | 16/08/2018 | 11/07/2019 | 11<br>months | WA9  | Merseyside          | transport<br>issues                               | 2 | Vori  | None            | Soon    |                |
|             | 19/06/2019 | 05/07/2019 | 2            | OL11 | Rochdale            |   | 2 | Vori  | Vori            | Soon    |                |
|             | 30/05/2019 | 05/07/2019 | 2            | OL16 | Rochdale            |   | 2 | Vori  | Posa            | Soon    |                |
|             | 11/06/2019 | 05/07/2019 | 3            | WN3  | Wigan               |   | 1 | None  | Vori            | Routine |                |
|             | 28/05/2019 | 12/07/2019 | 6            | B24  | Birmingham          |   | 1 | Itra  | DFS (2x<br>DNA) | Routine |                |
|             | 31/05/2019 | 12/07/2019 | 6            | M5   | Manchester          |   | 1 | Itra  |                 | Routine | Died<br>5/8/19 |
|             | 01/04/2019 | 11/07/2019 | 14           |      | Italy               |   | 2 | Isavu | DFS             | Routine |                |
|             | 16/05/2019 | 19/07/2019 | 9            | IM8  | Isle of Man         | Re-scheduled<br>23/6                              | 1 | Itra  | None            | Routine |                |
|             | 17/07/2019 | 19/07/2019 | 1            | BL8  | Bury                |   | 3 | Vori  | Vori            | Urgent  |                |
|             | 03/07/2019 | 19/07/2019 | 2            | WF12 | Huddersfield        |   | 2 | Vori  | Vori            | Routine |                |
|             | 01/07/2019 | 26/07/2019 | 3            | WA14 | Cheshire            |   | 1 | Itra  | Itra            | Routine |                |
|             | 03/07/2019 | 26/07/2019 | 3            | BN25 | West Sussex         |   | 1 | Itra  | Itra            | Routine |                |
|             | 28/02/2019 | 05/07/2019 | 5 months     | OX13 | Oxfordshire         | difficulty with<br>journey                        | 2 | Vori  | Vori            | Routine |                |

|                  |            |            |   |      |               |  |   |      |             |              |                  |
|------------------|------------|------------|---|------|---------------|--|---|------|-------------|--------------|------------------|
|                  | 24/04/2019 | 30/05/2019 | 5 | FY1  | Blackpool     |  | 2 | Vori | Vori        | Routine      |                  |
|                  | 07/06/2019 | 25/07/2019 | 0 | SE28 | London        | TB service   | 2 | Vori | Vori        |              |                  |
| <b>AUGUST</b>    | 23/07/2019 | 22/08/2019 | 4 | WA7  | Cheshire      |  | 2 | Vori | Vori        | Routine      | Died<br>25/12/19 |
|                  | 08/07/2019 | 14/08/2019 | 5 | B71  | West Midlands |  | 1 | Itra | Itra        | Routine      |                  |
|                  | 24/07/2019 | 30/08/2019 | 5 | DE21 | Derby         |  | 1 | None |             | Routine      | Died<br>11/12/19 |
|                  | 08/07/2019 | 02/08/2019 | 4 | B44  | Birmingham    |  | 1 | None | Vori        | Soon         |                  |
|                  | 26/06/2019 | 16/08/2019 | 7 | PR2  | Preston       | CNC 19/7/19  | 1 | Itra | None        | Routine      |                  |
|                  | 08/07/2019 | 16/08/2019 | 5 | HU8  | Hull          |  | 1 | None | DFS         | Routine      |                  |
|                  | 02/08/2019 | 23/08/2019 | 2 | E10  | London        |  | 1 | None | Vori        | Soon         |                  |
|                  | 25/07/2019 | 30/08/2019 | 5 | CV32 | Warwickshire  |  | 2 | Vori | None        | Soon         |                  |
|                  |            | 03/01/2019 | 0 | LS26 | Leeds         | Transition IA  | 2 | Vori | Vori        |              |                  |
|                  |            |            |   |      |               | Delayed<br>diagnosis,<br>awaited<br>repeat<br>CT/MDT |   |      |             |              |                  |
|                  | 01/04/2019 | 03/05/2019 | 4 | WA8  | Widnes        |  | 1 | None | Posa        |              |                  |
|                  |            | 11/01/2019 | 0 | M23  | Manchester    | Transition AB  | 2 | Vori | Vori        |              | Died<br>9/11/19  |
| <b>SEPTEMBER</b> | 08/08/2019 | 06/09/2019 | 4 | M21  | Manchester    |  | 2 | Vori | None        | Soon         |                  |
|                  | 11/09/2019 | 27/09/2019 | 2 | SK7  | Stockport     |  | 2 | None | None        | not selected |                  |
|                  | 31/07/2019 | 27/09/2019 | 8 | FY2  | Blackpool     |  | 2 | Vori | Vori        | Routine      |                  |
|                  | 23/08/2019 | 13/09/2019 | 3 | WA2  | Warrington    |  | 2 | Vori | Vori        | Soon         |                  |
|                  | 06/08/2019 | 20/09/2019 | 6 | TF2  | Shropshire    |  | 1 | None | None        | Routine      |                  |
|                  | 28/08/2019 | 20/09/2019 | 4 | B91  | Birmingham    |  | 2 | None | f/u July 20 | Soon         |                  |
|                  | 26/07/2019 | 30/08/2019 | 5 | WN3  | Wigan         |  | 2 | Vori | Vori        | Routine      | Died<br>07/01/20 |
|                  |            | 26/10/2018 | 0 | M43  | Manchester    | Transition IA  | 1 | Itra | Itra        | Routine      |                  |
|                  |            |            |   |      |               |  |   |      |             |              |                  |

|                 |            |            |   |      |               |                                  |   |      |             |              |               |
|-----------------|------------|------------|---|------|---------------|----------------------------------|---|------|-------------|--------------|---------------|
| <b>OCTOBER</b>  | 28/08/2019 | 03/10/2019 | 6 | SK9  | Stockport     |                                  | 1 | None | None        | Routine      |               |
|                 | 11/09/2019 | 17/10/2019 | 5 | LL53 | Wales         |                                  | 1 | None | None        | Routine      |               |
|                 | 11/09/2019 | 11/10/2019 | 4 | LA2  | Lancaster     |                                  | 1 | None | Posa        | Routine      |               |
|                 | 24/09/2019 | 11/10/2019 | 2 | M22  | Manchester    |                                  | 1 | None | DFS         | not selected |               |
|                 | 14/09/2019 | 11/10/2019 | 4 | OL10 | Oldham        |                                  | 2 | Vori | Vori        | Routine      |               |
|                 | 17/09/2019 | 18/10/2019 | 4 | M4   | Manchester    |                                  | 1 | None | None        | Routine      |               |
| <b>NOVEMBER</b> | 28/10/2019 | 28/11/2019 | 4 | SK3  | Stockport     |                                  | 2 | Vori | Vori        | Urgent       |               |
|                 | 28/10/2019 | 20/11/2019 | 4 | WF2  | Wakefield     |                                  | 1 | None | Itra        | Routine      |               |
|                 | 15/10/2019 | 15/11/2019 | 4 | WN8  | Wigan         |                                  | 1 | None | None        | Routine      |               |
|                 | 15/11/2019 | 29/11/2019 | 2 | BL3  | Bolton        |                                  | 1 | Itra | Itra        | not selected |               |
|                 | 09/10/2019 | 29/11/2019 | 7 | M30  | Manchester    |                                  | 1 | None | None        | Routine      |               |
|                 | 28/10/2019 | 29/11/2019 | 4 | CH4  | Chester       |                                  | 2 | Vori | Vori        | Routine      |               |
|                 | 30/09/2019 | 08/11/2019 | 5 | L17  | Liverpool     |                                  | 2 | Vori | Vori        | Routine      |               |
|                 | 15/11/2019 | 22/11/2019 | 1 | PR4  | Preston       |                                  | 2 | Vori | Vori        | Routine      |               |
|                 | 20/05/2019 | 31/05/2019 | 2 | HX7  | Halifax       | Delayed diagnosis, CT monitoring | 2 | Vori | None        | Urgent       |               |
| <b>DECEMBER</b> | 29/10/2019 | 12/12/2019 | 7 | WS1  | Walsall       |                                  | 1 | None | Vori        | Routine      |               |
|                 | 28/10/2019 | 06/12/2019 | 6 | PR4  | Preston       |                                  | 2 | Vori | Vori        | Soon         |               |
|                 | 31/10/2010 | 13/12/2019 | 6 | LA3  | Morecambe     |                                  | 1 | Itra | Posa        | Routine      |               |
|                 | 12/08/2019 | 13/09/2019 | 4 | M24  | Middleton     | Delayed diagnosis, CT monitoring | 1 | Vori | Vori        | Routine      |               |
|                 | 09/04/2019 | 13/06/2019 | 9 | M40  | Manchester    | Delayed diagnosis, CT monitoring | 1 | Vori | None        | Routine      |               |
|                 | 28/10/2019 | 20/11/2019 | 3 | S65  | Rotherham     |                                  | 1 | None | Vori        | Routine      | Died 20/03/20 |
| <b>JANUARY</b>  | 28/11/2019 | 17/01/2020 | 6 | NE29 | North Shields |                                  | 2 | Vori | f/u July 20 | Routine      |               |
|                 | 20/11/2019 | 03/01/2020 | 6 | BL7  | Bolton        |                                  | 1 | None | f/u May 20  | Routine      |               |

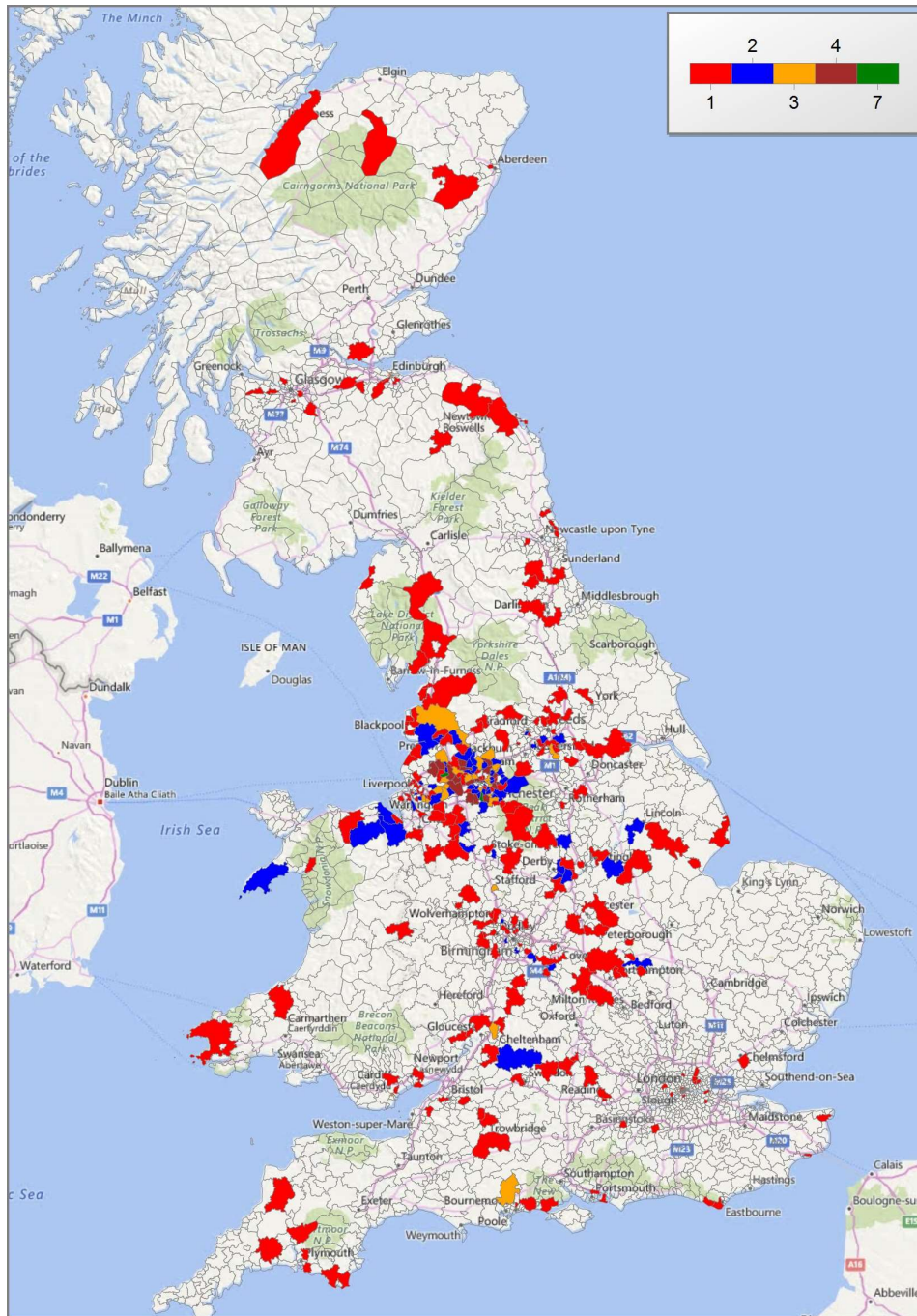
|                 |            |            |    |      |                 |                                       |   |      |              |         |               |
|-----------------|------------|------------|----|------|-----------------|---------------------------------------|---|------|--------------|---------|---------------|
|                 | 18/11/2019 | 03/01/2020 | 6  | M23  | Manchester      |                                       | 1 | None | DFS          | Routine |               |
|                 | 21/11/2019 | 03/01/2020 | 6  | BH21 | Dorset          |                                       | 1 | Itra | f/u April 20 | Routine |               |
|                 | 09/12/2019 | 10/01/2020 | 4  | GL51 | Gloucestershire |                                       | 2 | Posa | f/u July 20  | Routine |               |
|                 | 13/12/2019 | 17/01/2020 | 5  | M22  | Manchester      |                                       | 2 | Vori | f/u April 20 | Routine |               |
|                 | 04/12/2019 | 17/01/2020 | 6  | RH16 | York            |                                       | 2 | Mica | f/u April 20 | Routine |               |
|                 | 07/11/2019 | 24/01/2020 | 11 | M40  | Manchester      |                                       | 2 | Vori | Vori         | Routine |               |
|                 |            | 19/07/2019 | 0  | LL16 | Wales           | Transition - IA                       |   | None | Posa         |         |               |
|                 |            | 25/08/2017 | 0  | M41  | Manchester      | Transition – simple aspergilloma      | 1 | None |              |         | Died 3/2/20   |
|                 | 20/06/2019 | 05/07/2019 | 2  | BB2  | Blackburn       | Missed from numbers in July           | 1 | Itra | Itra         | Routine |               |
|                 | 25/09/2019 | 27/09/2019 | 1  | WA15 | Cheshire        | Transition IA                         | 2 | Vori | Vori         | Urgent  |               |
|                 |            |            |    |      |                 |                                       |   |      |              |         |               |
| <b>FEBRUARY</b> | 13/01/2020 | 14/02/2020 | 4  | CV8  | Coventry        |                                       | 1 | None | f/u May 20   | Routine |               |
|                 | 23/01/2020 | 21/02/2020 | 4  | M26  | Manchester      |                                       | 2 | Vori | f/u April 20 | Soon    |               |
|                 | 09/01/2020 | 07/02/2020 | 4  | OL2  | Oldham          |                                       | 1 | None | f/u June 20  | Routine |               |
|                 | 07/01/2020 | 07/02/2020 | 4  | FY6  | Blackpool       |                                       | 1 | Itra | f/u May 20   | Routine |               |
|                 | 13/01/2020 | 14/02/2020 | 4  | LN4  | Lincoln         |                                       | 2 | Itra | f/u April 20 | Routine |               |
|                 | 09/01/2020 | 13/02/2020 | 5  | M11  | Manchester      |                                       | 1 | None | f/u May 20   | Routine |               |
|                 | 03/01/2020 | 13/02/2020 | 6  | GL7  | Cirencester     |                                       | 2 | Vori | f/u Aug 20   | Routine |               |
|                 |            | 18/09/2017 | 0  | OL12 | Rochdale        | Delayed diagnosis after MAI treatment | 1 | None | f/u April 20 |         |               |
|                 | 06/11/2019 | 13/12/2019 | 5  | M4   | Manchester      |                                       | 2 | Vori |              | Routine | Died 17/03/20 |
|                 |            |            |    |      |                 |                                       |   |      |              |         |               |
| <b>MARCH</b>    | 30/01/2020 | 06/03/2020 | 5  | ST7  | Stoke on Trent  |                                       | 2 | Vori | f/u April 20 | Routine |               |
|                 | 06/02/2020 | 06/03/2020 | 4  | WF17 | West Yorkshire  |                                       | 1 | Itra | f/u June 20  | Routine |               |
|                 | 20/02/2020 | 13/03/2020 | 3  | OL7  | Ashton-u-Lyne   |                                       | 2 | Vori | f/u April 20 | Soon    |               |



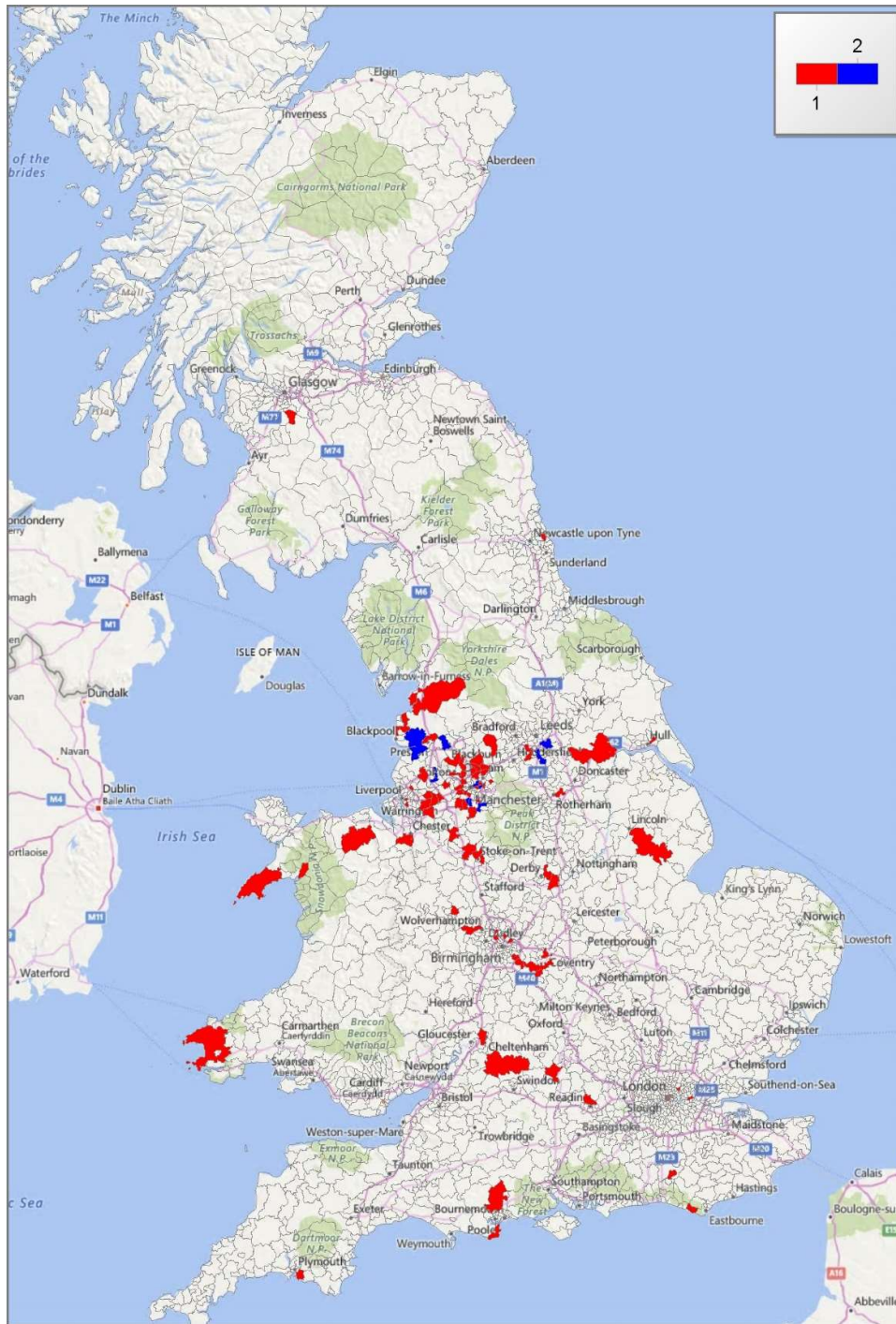
|  |            |            |   |      |               |                                    |   |      |             |         |
|--|------------|------------|---|------|---------------|------------------------------------|---|------|-------------|---------|
|  | 03/02/2020 | 13/03/2020 | 4 | SA62 | Pembrokeshire |                                    | 1 | None | f/u June 20 | Routine |
|  | 25/02/2020 | 20/03/2020 | 4 | CV2  | Coventry      |                                    | 2 | Vori | f/u June 20 | Routine |
|  |            | 25/01/2019 | 0 | M43  | Manchester    | <b>Transition IA</b>               | 2 | Posa | f/u June 20 |         |
|  | 05/08/2019 | 06/09/2019 | 5 | G75  | Scotland      | <b>Missed in numbers from Sept</b> | 2 | None | None        | Routine |

## Appendix 3 Geographical location of patients attending NAC

Graph 1 All patients on NAC service 2020



Graph 2 New patient referrals 2019-2020



## Appendix 4 Discharges from service

| Date of discharge | Antifungal at discharge | CPA Band | Geographical area | Reason                             |
|-------------------|-------------------------|----------|-------------------|------------------------------------|
| 10/05/2019        | Itraconazole            | 1        | Merseyside        | In care home                       |
| 17/05/2019        | None                    | 2        | Lancaster         | does not wish to attend            |
| 17/06/2019        | Voriconazole            | 2        | Scotland          | No longer attends clinic           |
| 17/06/2019        | Itraconazole            | 1        | Middlesex         | Stable                             |
| 12/06/2019        | none                    | 1        | Manchester        | Stable                             |
| 01/06/2019        | Itraconazole            | 1        | Liverpool         | Stable                             |
| 18/04/2019        | None                    | 3        | Wigan             | dna x 2                            |
| 18/05/2019        | Itraconazole            | 2        | Lancashire        | stable                             |
| 12/03/2019        | None                    | 2        | Manchester        | unable to attend                   |
| 27/06/2019        | Itraconazole            | 1        | Skelmersdale      | Stable                             |
| 01/06/2019        | None                    | 1        | Oldham            | Stable                             |
| 12/07/2019        | None                    | 2        | Halifax           | Does not wish to travel            |
| 05/07/2019        | Itraconazole            | 1        | Derbyshire        | Stable                             |
| 25/07/2019        | None                    | 1        | Cheshire          | does not wish to travel            |
| 08/07/2019        | None                    | 1        | Salford           | Stable                             |
| 01/08/2019        | None                    | 2        | London            | dna x 3                            |
| 19/08/2019        | None                    | 1        | Manchester        | dna x3                             |
| 01/08/2019        | None                    | 2        | Liverpool         | dna x 5                            |
| 16/10/2019        | None                    | 2        | St Helens         | transport issues                   |
| 14/11/2019        | None                    | 2        | Trafford          | Stable                             |
| 21/11/2019        | Itraconazole            | 1        | Wigan             | Stable                             |
| 25/11/2019        | None                    | 2        | Ormskirk          | Stable                             |
| 01/11/2019        | Posa trial              | 2        | Bournemouth       | difficulty with travel             |
| 01/11/2019        | None                    | 2        | Manchester        | Stable                             |
| 12/12/2019        | None                    | 2        | Scotland          | post-surgery/stable -MDT decision  |
| 18/12/2019        | None                    | 2        | Preston           | Stable -MDT decision               |
| 12/12/2019        | None                    | 2        | Gloucester        | Stable -MDT decision               |
| 19/12/2019        | None                    | 3        | Blackburn         | Stable                             |
| 01/12/2019        | None                    | 2        | Scotland          | Stable                             |
| 17/12/2019        | None                    | 1        | St Helens         | Stable- MDT decision               |
| 19/12/2019        | Itraconazole            | 1        | Scotland          | Stable -MDT decision               |
| 12/12/2019        | None                    | 2        | Liverpool         | Stable- MDT decision               |
| 10/01/2020        | None                    | 3        | Wigan             | Stable                             |
| 02/01/2020        | None                    | 1        | Telford           | Stable - MDT decision              |
| 03/01/2020        | None                    | 2        | Plymouth          | Stable review locally              |
| 16/01/2020        | None                    | 2        | Manchester        | Stable - MDT decision              |
| 16/01/2020        | None                    | 2        | Glossop           | Stable - MDT decision              |
| 10/01/2020        | None                    | 3        | St Helens         | Stable                             |
| 10/01/2020        | None                    | 2        | Liverpool         | Stable                             |
| 10/01/2020        | Itraconazole            | 1        | Chester           | Stable                             |
| 30/01/2020        | None                    | 1        | Wigan             | Stable - MDT decision              |
| 06/02/2020        | None                    | 1        | Manchester        | Stable - MDT decision              |
| 17/02/2020        | None                    | 1        | Hull              | Patient requested discharge        |
| 06/02/2020        | Itraconazole            | 1        | Birmingham        | Stable - MDT decision              |
| 14/02/2020        | None                    | 2        | Dorset            | Stable - MDT decision              |
| 14/02/2020        | None                    | 2        | Leigh             | Stable - MDT decision              |
| 14/02/2020        | None                    | 2        | Plymouth          | Stable - MDT decision              |
| 03/02/2020        | None                    | 1        | Stockport         | dna x 2, patient request discharge |
| 17/03/2020        | None                    | 1        | Wigan             | dna x 3                            |
| 16/03/2020        | Itraconazole            | 2        | Manchester        | dna x 3                            |
| 24/03/2020        | None                    | 2        | Norfolk           | Stable                             |
| 20/03/2020        | None                    | 1        | Manchester        | Stable                             |
| 20/03/2020        | None                    | 2        | Littleborough     | Stable                             |
| 18/03/2020        | None                    | 1        | Manchester        | dna x 2                            |
| 27/03/2020        | None                    | 1        | Manchester        | dna x 4                            |
| 06/03/2020        | None                    | 1        | Preston           | Stable - MDT decision              |

## Appendix 5 Admissions and OPAT activity

| ADMISSIONS AND OPAT 2019-20 |            |            |          |                |                 |              |
|-----------------------------|------------|------------|----------|----------------|-----------------|--------------|
| MONTH                       | ADMITTED   | DISCHARGED | BED DAYS | TREATMENT      | PROCEDURE       | Antifungal   |
| <b>APRIL (1)</b>            | 04/04/2019 | 23/04/2019 | 19       | Micafungin     |                 |              |
|                             | 16/04/2019 | 19/04/2019 | 3        |                | RULobectomy     |              |
|                             | 29/03/2019 | 20/04/2019 | 22       | AmBisome       |                 |              |
|                             | 14/02/2019 | 01/04/2019 | 46       | Micafungin     |                 |              |
|                             | 10/04/2019 | 17/04/2019 | 7        |                | Embolisation    | Voriconazole |
|                             | 03/04/2019 | 18/04/2019 | 15       | AmBisome       | OPAT            |              |
| <b>APRIL (2)</b>            |            |            |          |                |                 |              |
| <b>May (1)</b>              | 12/04/2019 | 03/05/2019 | 21       | AmBisome       |                 |              |
|                             | 03/05/2019 | 10/05/2019 | 7        | AmBisome       |                 |              |
|                             | 14/05/2019 | 30/05/2019 | 16       |                | LULobectomy     | Voriconazole |
|                             | 01/05/2010 | 03/05/2019 | 2        |                | vascular repair | Voriconazole |
|                             | 08/05/2019 | 11/05/2019 | 3        |                | RULobectomy     |              |
|                             | 07/05/2019 | 22/05/2019 | 15       |                | LULobectomy     | Posaconazole |
|                             | 15/05/2019 | 20/05/2019 | 5        | IV antibiotics |                 | Posaconazole |
|                             | 21/05/2019 | 28/05/2019 | 7        | IV antibiotics | OPAT            | Posaconazole |
| <b>May (2)</b>              | 25/04/2019 | 25/05/2019 | 30       | NTM treatment  |                 | None         |
| <b>June (1)</b>             | 25/05/2019 | 10/06/2019 | 16       | Mica           |                 |              |
|                             | 11/06/2019 | 13/06/2019 | 2        | Mica           | OPAT            |              |
|                             | 24/06/2019 | 25/06/2019 | 1        |                | Embolisation    | Itraconazole |
|                             | 07/06/2019 | 15/06/2019 | 8        | Picc line/mica |                 |              |
|                             | 15/06/2019 | 27/06/2019 | 12       | Mica           | OPAT            |              |
| <b>June (2)</b>             |            |            |          |                |                 |              |
| <b>July (1)</b>             | 09/07/2019 | 12/07/2019 | 3        | Picc line/Mica |                 |              |
|                             | 13/07/2019 | 30/07/2019 | 17       | Mica           | OPAT            |              |
|                             | 28/06/2019 | 04/07/2019 | 6        | Picc line/Mica |                 |              |
|                             | 05/07/2019 | 20/07/2019 | 15       | Mica           | OPAT            |              |
|                             | 26/06/2019 | 03/07/2019 | 7        | Picc line/Mica |                 |              |
|                             | 03/07/2019 | 12/07/2019 | 9        | IV antibiotics | OPAT            |              |
| <b>July (2)</b>             |            |            |          |                |                 |              |
| <b>Aug (1)</b>              | 29/07/2019 | 01/08/2019 | 3        | Picc line/Mica |                 |              |
|                             | 01/08/2019 | 18/08/2019 | 17       | Mica           | OPAT            |              |
|                             | 09/08/2019 | 22/08/2019 | 12       | IV antibiotics |                 |              |
|                             | 19/08/2019 | 29/08/2019 | 10       | Picc line/Mica |                 |              |
|                             | 20/08/2019 | 21/08/2019 | 1        |                | Embolisation    | Posaconazole |
| <b>Aug (2)</b>              | 08/08/2019 | 22/08/2019 | 14       | IV antibiotics | OPAT            |              |

|                  |            |            |    |                             |              |              |
|------------------|------------|------------|----|-----------------------------|--------------|--------------|
|                  |            |            |    |                             |              |              |
| <b>Sept (1)</b>  | 16/08/2019 | 08/09/2019 | 23 | Micafungin                  |              | Voriconazole |
|                  | 23/08/2019 | 07/09/2019 | 15 | Micafungin                  |              |              |
|                  | 07/09/2019 | 13/09/2019 | 6  | Micafungin                  | OPAT         |              |
|                  | 09/08/2019 | 12/09/2019 | 34 | AmBisome                    |              | Voriconazole |
|                  | 22/08/2019 | 01/09/2019 | 10 | Picc line/Mica              |              |              |
|                  | 02/09/2019 | 19/09/2019 | 10 | Micafungin                  | OPAT         |              |
|                  | 05/09/2019 | 12/09/2019 | 7  | AmBisome                    |              |              |
|                  | 30/08/2019 | 15/09/2019 | 16 | Micafungin                  | OPAT         |              |
|                  | 16/09/2019 | 24/09/2019 | 8  | Surgery                     | Bi-lobectomy |              |
|                  |            |            |    |                             |              |              |
| <b>Sept (2)</b>  | 09/09/2019 | 20/09/2019 | 11 | IV antibiotics              |              |              |
|                  |            |            |    |                             |              |              |
| <b>Oct (1)</b>   | 27/09/2019 | 25/10/2019 | 28 | AmBisome                    |              |              |
|                  | 25/10/2019 | 30/10/2019 | 5  | Assessment for embolisation |              |              |
|                  | 02/10/2019 | 15/10/2019 | 13 | IV antibiotics              | OPAT         | Voriconazole |
|                  |            |            |    |                             |              |              |
| <b>Oct (2)</b>   |            |            |    |                             |              |              |
|                  |            |            |    |                             |              |              |
| <b>Nov (1)</b>   | 22/11/2019 | 25/11/2019 | 3  |                             | Embolisation | Voriconazole |
|                  |            |            |    |                             |              |              |
| <b>Nov (2)</b>   |            |            |    |                             |              |              |
|                  |            |            |    |                             |              |              |
| <b>Dec (1)</b>   | 16/10/2019 | 17/12/2019 | 62 | complex post-surgery        |              | Mica/vori    |
|                  |            |            |    |                             |              |              |
| <b>Dec (2)</b>   |            |            |    |                             |              |              |
|                  |            |            |    |                             |              |              |
| <b>Jan (1)</b>   | 18/12/2019 | 05/01/2020 | 18 | complex post-surgery        |              | Micafungin   |
|                  | 02/01/2020 | 15/01/2020 | 13 |                             | Embolisation | Micafungin   |
|                  |            |            |    |                             |              |              |
| <b>Jan (2)</b>   |            |            |    |                             |              |              |
|                  |            |            |    |                             |              |              |
| <b>Feb (1)</b>   | 31/01/2020 | 12/02/2020 | 12 |                             | RL lobectomy | Posaconazole |
|                  | 16/01/2020 | 13/02/2020 | 28 | Picc line/Mica              |              | Micafungin   |
|                  |            |            |    |                             |              |              |
| <b>Feb (2)</b>   |            |            |    |                             |              |              |
|                  |            |            |    |                             |              |              |
| <b>March (1)</b> | 05/03/2020 | 06/03/2020 | 1  |                             | Embolisation | Voriconazole |
|                  | 14/02/2020 | 10/03/2020 | 25 | Micafungin                  | OPAT         |              |
|                  |            |            |    |                             |              |              |
| <b>March (2)</b> |            |            |    |                             |              |              |



## Appendix 6 Clinical data for new patients 2019-2020

| NCG report for SGRQ/MRC/IgG |     |            |       |        |               |     |            |       |        |                     |     |            |       |        | 2019-20                                   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|-----------------------------|-----|------------|-------|--------|---------------|-----|------------|-------|--------|---------------------|-----|------------|-------|--------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| 1st Appoint                 | MRC | IgG test 1 | SGRQ  | Weight | 2nd Appoint   | MRC | IgG test 2 | SGRQ  | Weight | 3rd Appoint         | MRC | IgG test 3 | SGRQ  | Weight | Outcomes                                  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 11/04/2019                  | 4   | 71         |       | 46.3   | 28/06/2019    | 4   | 54         |       | 46.9   | 30/08/2019          | NR  | 52         |       | 45.9   | Improved IgG                              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 18/04/2019                  | NR  | 70         |       | 71.9   | 22/11/2019    | 1   | 60         | 23.17 | 72.5   | Discharged          |     |            |       |        | Improving                                 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 05/04/2019                  | 4   | 821        | 85.59 | 72.1   | 05/07/2019    | 2   | 181        |       | 68.7   | Died 13/12/19       |     |            |       |        | died                                      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 12/04/2019                  | 4   | 188        | 86.06 | 53     | 26/07/2019    | 4   | 136        |       | 51.1   | 11/10/2019          | 4   | 134        |       | 52.4   | Improved IgG                              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 12/04/2019                  | 4   | 1550       | 66.02 | 62     | 23/08/2019    | 5   | 1035       | 76.53 | 59.7   | 29/11/2019          | 5   | 887        | 63.47 | 59.6   | Improved IgG & QOL                        |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 08/02/2019                  | 5   | 167        |       | 51     | Died 16/04/19 |     |            |       |        |                     |     |            |       |        | died                                      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 12/04/2019                  | 3/4 | 470        | 60.57 | 52.7   | 31/05/2019    | 2-3 | 288        |       | 51.6   | 19/07/2019          | 4   | 198        | 66.1  | 47.8   | Improved IgG, stable                      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 02/05/2019                  | 5   | 552        | 82.94 | 51.6   | 14/06/2019    | 5   | 568        |       | 50.3   | Died 03/07/19       |     |            |       |        | died                                      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 02/05/2019                  | 5   | 335        |       | 57.1   | 19/07/2019    | 4   | 192        |       | 56.5   | 24/01/2020          | 4   | 48         | 76.8  | 58.1   | Improved                                  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 03/05/2019                  | 2   | 94         |       | 73.4   | 02/08/2019    | 4   | 76         | 84.07 | 73.5   | 27/12/2019          | 2   | 70         |       | 74.1   | Improved                                  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 10/05/2019                  | 4   | 193        | 72.61 | 113    | 20/09/2019    | 4   | 107        |       | 101.8  | 25/10/2019          | 4   | 120        | 84.08 | 99.8   | Improved IgG, weight and QoI deteriorated |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 10/05/2019                  | 4   | 53         | 72.23 | 66     | 30/08/2019    | NR  | 48         |       | 58.1   | 28/02/2020          | 3/4 | 38         |       | 57.3   | Improved IgG, weight deteriorated         |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 10/05/2019                  | 5   | 425        | 75.3  | 67.1   | 21/06/2019    | 5   | 399        | 80.16 | 67.1   | 23/08/2019          | 4/5 | ND         |       | 58.8   | died                                      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 17/05/2019                  | 4   | 85         | 92.09 | 63     | 29/11/2019    | 3   | 29         | 74.22 | 71.2   | 10/01/2020          | 4   | 27         |       | 70.6   | Improving                                 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 24/05/2019                  | 4   | 245        |       | 92     | 12/07/2019    | 4   | 182        |       | 87.9   | 04/10/2019          | 4   | 148        |       | 91.2   | Improving IgG, stable                     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 31/05/2019                  | 2   | 648        | 39.79 | 59     | 16/08/2019    | 2   | 541        |       | 59.6   | 22/11/2019          | 2   | 479        |       | 59.2   | Improving IgG, stable                     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 21/06/2019                  | 1   | 155        |       | 66.1   | 23/08/2019    | 1   | 154        |       | 61.5   | 22/11/2019          | 1   | 144        |       | 60.7   | Improving IgG, weight deteriorating       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 14/06/2019                  | 2   | 157        | 11.44 | 76     | 23/08/2019    | 2   | 113        |       | 75.3   | 20/12/2019          | 2   | 87         | 45.03 | 78.7   | Improving IgG                             |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 14/06/2019                  | 5   | 128        | 67.41 | 71     | 11/10/2019    | 4   | 153        | 48.21 | 69.6   | 17/01/2020          | 2   | 163        |       | 73     | IgG deteriorating, QOL & weight improving |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 14/06/2019                  | 3   | 81         | 75.31 | 34.4   | 09/08/2019    | 2   | 53         |       | 34     | 21/02/2020          | 3   | 35         |       | 38     | Improved                                  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 21/06/2019                  | 1   | 82         | 10.49 | 52.5   | 30/08/2019    | NR  | 59         |       | 51.6   | 06/12/2019          | 1   | 59         | 5.92  | 51.6   | Stable                                    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 28/06/2019                  | 1   | 71         | 14.46 | 87     | 04/10/2019    | 2   | ND         | 3.4   | 85.9   | rescheduled to June |     |            |       |        | Stable                                    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 28/06/2019                  | 4   | 178        | 83.08 | 45.5   | 18/10/2019    | 4   | 188        | 88.95 | 47     | 13/12/2019          | 4/5 | 198        |       | 46.7   | slight rise IgG, clinically stable        |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 16/08/2019                  | 4   | 84         | 90.73 | 56.8   | 15/11/2019    | 4   | 78         |       | 58.5   | f/u Nov 20          |     |            |       |        | Stable                                    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 26/04/2019                  | 2   | 175        |       | 52     | 31/05/2019    | 2   | 142        |       | 50.6   | 24/01/2020          | 2   | 93         |       | 47.9   | Improving Ig                              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 11/07/2019                  | 2   | 160        | 93.94 | 48.8   | dna x 2       |     |            |       |        | Discharged          |     |            |       |        | insufficient data                         |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 05/07/2019                  | 3   | 148        |       | 40.7   | 29/11/2019    | 3   | ND         | 48.71 | 41.4   | 27/03/2020          | 3   | ND         | 48.71 | 41.4   | Stable                                    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 05/07/2019                  | 4   | 157        |       | 48.6   | 30/08/2019    | NR  | 139        | 95.13 | 53.6   | 25/10/2019          | 3   | 101        |       | 59.5   | Improved                                  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 05/07/2019                  | 2   | 19         |       | 43.9   | 23/08/2019    | 2   | ND         |       | 43.3   | 29/11/2019          | 2   | 18         |       | 45.4   | Improved                                  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 12/07/2019                  | 2   | 612        | 8.28  | 47.6   | dna x 3       |     |            |       |        | Discharged          |     |            |       |        | insufficient data                         |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 12/07/2019                  | 4/5 | 454        | 98.25 | 45     | Died 05/08/19 |     |            |       |        |                     |     |            |       |        | died                                      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 11/07/2019                  | 4   | 153        | 94.58 | 54     | Discharged    |     |            |       |        |                     |     |            |       |        | insufficient data                         |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

|            |     |      |       |      |                                     |     |      |       |      |                     |    |      |       |      |                                       |
|------------|-----|------|-------|------|-------------------------------------|-----|------|-------|------|---------------------|----|------|-------|------|---------------------------------------|
| 19/07/2019 | 5   | 395  | 80.81 | 59.4 | 25/10/2019                          | 5   | 171  |       | 56.1 | cancelled 24/1/20   |    |      |       |      | Improved IgG                          |
| 19/07/2019 | 5   | 607  | 71.77 | 51   | 25/10/2019                          | 2   | 180  |       | 58.3 | 31/01/2020          | 3  | 133  | 66.32 | 54.5 | Improved IgG, stable                  |
| 19/07/2019 | 4   | 169  | 75.95 | 70.7 | 18/10/2019                          | 3   | 98   |       | 76.3 | 14/02/2020          | 4  | 69   | 65.87 | 77.3 | Improved                              |
| 26/07/2019 | 3   | 95   |       | 52.7 | 27/09/2019                          | 3   | ND   |       | 50.1 | 13/12/2019          | NR | 31   |       | 49.3 | Improved IgG, weight deteriorated     |
| 26/07/2019 | NR  | 638  |       | 59   | 04/10/2019                          | 3   | 466  |       | 60   | 17/01/2020          | 3  | 696  | 72.42 | 61   | Deteriorated - having surgery         |
| 05/07/2019 | 4   | 780  |       | 47.1 | 04/10/2019                          | 4   | 841  |       | 47.5 | 07/02/2020          | 5  | 138  |       | 47.6 | Improved                              |
| 30/05/2019 | 4   | 126  | 75.9  | 71.8 | 09/08/2019                          | 5   | 90   | 75.37 | 75.3 | 18/10/2019          | 3  | 89   |       | 76.1 | Improved                              |
| 25/07/2019 | Tel | Tel  |       | Tel  | discharged - did not wish to travel |     |      |       |      |                     |    |      |       |      | Stable                                |
| 22/08/2019 | 4   | 155  |       | 49.7 | 27/09/2019                          | 2   | 175  |       | 50.3 | 29/11/2019          | 4  | >200 |       | 49.2 | died                                  |
| 14/08/2019 | 3   | 23   | 81.64 | 43.3 | 11/10/2019                          | 5   | 25   |       | 44.4 | 7/2/20 rescheduled  |    |      |       |      | Stable                                |
| 30/08/2019 | 4   | 167  | 94.88 | 37   | Died 11/12/19                       |     |      |       |      |                     |    |      |       |      | died                                  |
| 02/08/2019 | 1   | 184  |       | 55.2 | 25/10/2019                          | 2   | 140  |       | 57   | 03/01/2020          | 2  | 137  | 48.22 | 59.5 | Improved                              |
| 16/08/2019 | 1   | 1049 | 30.6  | 62.3 | 27/09/2019                          | NR  | 454  |       | 63.3 | 29/11/2019          | 2  | 526  |       | 59   | Deterioration - CT showed cancer      |
| 16/08/2019 | 1-2 | 38   | 10.69 | 48.2 | 27/9/19 rescheduled                 |     |      |       |      | cancelled 8/11/19   |    |      |       |      | insufficient data                     |
| 23/08/2019 | 1   | 49   | 60.28 | 52.6 | 29/11/2019                          | 1   | ND   |       | 53.8 | 10/01/2020          | 2  | 69   |       | 52   | slight deterioration, therapy changed |
| 30/08/2019 | 1   | 188  | 70.31 | 45.6 | 08/11/2019                          | 2   | 197  |       | 44.5 | 06/12/2019          | 1  | 146  |       | 43.8 | Improved IgG, weight deteriorated     |
| 30/08/2019 | 4   | 135  |       | 41   | dna 29/11/19                        |     |      |       |      | 03/01/2020          | 4  | 87   |       | 38.8 | Improved IgG, weight deteriorated     |
| 03/05/2019 | 2   | 42   |       | 68   | 20/09/2019                          | 5   | 36   | 70.23 | 66.8 | 01/11/2019          | 5  | ND   | 73.25 | 65.1 | Improved IgG, weight deteriorated     |
| 04/08/2019 | NR  | 52   |       |      | 27/09/2019                          | 5   | 57   |       | 55   | Died 29/11/19       |    |      |       |      | died                                  |
| 06/09/2019 | 3   | 109  | 93.66 | 54.8 | 18/10/2019                          | 2   | 115  | 93.96 | 52.1 | 29/11/2019          | 5  | ND   |       | 54.5 | Stable                                |
| 27/09/2019 | 4   | 428  |       | 37   | 15/11/19 rescheduled                |     |      |       |      | 21/02/2020          | 4  | 676  |       | 41.5 | IgG deteriorated, referred surgery    |
| 27/09/2019 | 2   | 445  | 43.44 | 69.5 | 29/11/2019                          | NR  | 1264 |       | 66.4 | 28/02/2020          | 2  | 159  | 28.44 | 66.3 | Stable                                |
| 13/09/2019 | 4   | 78   | 62.17 | 67.6 | 13/12/2019                          | 3   | 50   |       | 71.5 | f/u April 20        |    |      |       |      | Improved                              |
| 20/09/2019 | 1   | 157  | 35.36 | 51   | 22/11/2019                          | 2   | ND   |       | 52.1 | 20/12/2019          | 2  | 130  |       | 51.6 | Stable                                |
| 20/09/2019 | 2   | 113  | 53.03 | 64.2 | 18/10/2019                          | 2   | ND   |       | 65.2 | 20/3/20 rescheduled |    |      |       |      | Stable                                |
| 30/08/2019 | 2   | 63   | 41.81 | 59.6 | 27/09/2019                          | 2   | ND   |       | 59.4 | Died 7/1/20         |    |      |       |      | died                                  |
| 26/07/2019 | NR  | 96   |       | 74.5 | 22/11/2019                          | 3   | 94   | 58.56 | 82.3 | f/u May 20          |    |      |       |      | Improved                              |
| 03/10/2019 | 2   | 170  |       | 94.9 | 06/12/2019                          | 1   | 145  |       | 94.5 | f/u May 20          |    |      |       |      | Improved IgG, stable                  |
| 17/10/2019 | 4   | 177  |       | 77.9 | f/u April 20                        |     |      |       |      |                     |    |      |       |      | insufficient data                     |
| 11/10/2019 | 1   | 23   | 44.59 | 65.4 | 22/11/2019                          | 1   | ND   | 44.05 | 43.3 | 03/01/2020          | 1  | 18   | 45.63 | 64.8 | Stable                                |
| 11/10/2019 | 5   | 97   |       | 39.2 | 13/12/19 cancelled                  |     |      |       |      |                     |    |      |       |      | insufficient data                     |
| 11/10/2019 | 1   | 176  | 7.95  | 72.8 | 06/12/2019                          | 1   | 183  |       | 69.3 | f/u April 20        |    |      |       |      | Stable                                |
| 18/10/2019 | 4   | 74   | 38.25 | 54.6 | 17/01/2020                          | 1   | 61   |       | 56.9 | f/u April 20        |    |      |       |      | Improving                             |
| 28/11/2019 | NR  | 160  |       | 78.6 | 28/02/2020                          | 3   | 121  |       | 78.8 | f/u May 20          |    |      |       |      | Improved IgG, stable                  |
| 20/11/2019 | 4   | 77   |       | 65.4 | 10/01/2020                          | 5   | ND   | 81.25 | 61.6 | 07/02/2020          | 2  | 104  |       | 64.3 | Rising IgG, changed therapy           |
| 15/11/2019 | 4   | 102  |       | 76.9 | 10/01/2020                          | 4/5 | ND   |       | 80.7 | 21/2/20 rescheduled |    |      |       |      | Improving                             |
| 29/11/2019 | 2   | 112  | 68.1  | 49.7 | 24/01/2020                          | 4   | ND   |       | 49   | f/u April 20        |    |      |       |      | Stable                                |
| 29/11/2019 | 4   | 708  | 71.9  | 50.8 | 03/01/2020                          | 4   | ND   |       | 49.8 | f/u May 20          |    |      |       |      | insufficient data                     |
| 29/11/2019 | 4   | 152  |       | 37   | 03/01/2020                          | 5   | 107  |       | 36.3 | 14/02/2020          | 3  | 71   |       | 33.9 | Improving, other cause weight loss    |
| 08/11/2019 | 3   | 668  | 78.31 | 51.2 | 06/12/2019                          | 3   | 679  |       | 53.4 | 13/03/2020          | NR | ND   |       | NR   | Improving                             |
| 22/11/2019 | 5   | 150  |       | 58.2 | 17/01/2020                          | NR  | 134  |       | NR   | 20/03/2020          | NR | ND   |       | NR   | Improved IgG                          |
| 01/11/2019 | 1   | 1070 |       | 70.7 | 31/01/2020                          | 1   | 628  |       | 71.8 | 27/03/20 cancelled  |    |      |       |      | Improved IgG, stable                  |
| 12/12/2019 | 4   | 102  |       | 51.7 | 17/01/2020                          | 4   | 139  |       | 50.5 | f/u April 20        |    |      |       |      | insufficient data                     |
| 06/12/2019 | 4   | 184  | 48.2  | 54.9 | 10/01/2020                          | 3/4 | ND   |       | 54.5 | 27/03/2020          | NR | ND   |       | NR   | insufficient data                     |
| 13/12/2019 | 1   | 110  | 35.34 | 52.1 | 07/02/2020                          | 2   | 169  |       | 49.1 | f/u April 20        |    |      |       |      | Deterioration - therapy changed       |



|            |     |      |       |       |               |    |      |       |      |               |   |     |  |      |  |
|------------|-----|------|-------|-------|---------------|----|------|-------|------|---------------|---|-----|--|------|--|
| 13/09/2019 | 1   | ND   | 9.26  | 50.2  | 20/12/2019    | 1  | 176  |       | 53.6 | f/u April 20  |   |     |  |      | improvement in weight                    |
| 08/11/2019 | 4   | 77   | 58.64 | 51.8  | 20/12/2019    | 4  | ND   |       | 52   | f/u July 20   |   |     |  |      | Stable                                   |
| 20/11/2019 | NR  | 199  |       | NR    | 03/01/2020    | 5  | 989  |       | 76.1 | Died 20/03/20 |   |     |  |      | died                                     |
| 17/01/2020 | 3/4 | 134  |       | 60.2  | f/u July 20   |    |      |       |      |               |   |     |  |      | insufficient data                        |
| 03/01/2020 | 3   | 598  | 51.51 | 64.4  | 14/02/2020    | 4  | 532  |       | 62.8 | 13/03/2020    | 4 | 396 |  | 65.2 | Improved IgG and weight                  |
| 03/01/2020 | 1   | 123  | 73.11 | 35    | 14/02/2020    | 2  | 87   | 82.91 | 31.5 | 20/03/2020    | 2 | 65  |  | 31.4 | Improved IgG, SGRQ & weight deteriorated |
| 03/01/2020 | 2   | 1756 | 55.49 | 44.5  | 31/01/2020    | NR | 1716 |       | 44.9 | f/u April 20  |   |     |  |      | Improved IgG, stable                     |
| 10/01/2020 | 2   | 61   | 38.42 | 60.4  | 07/02/2020    | 3  | ND   |       | 61.7 | f/u July 20   |   |     |  |      | Stable                                   |
| 17/01/2020 | 4   | ND   |       | 49.1  | 14/02/2020    | 4  | 80   |       | 59.3 | 20/03/2020    | 5 | ND  |  | 49.8 | Stable                                   |
| 17/01/2020 | 2   | 76   | 78.89 | 66.5  | f/u April 20  |    |      |       |      |               |   |     |  |      | insufficient data                        |
| 24/01/2020 | 2   | 80   |       | 66.5  | 6/3/20 dna    |    |      |       |      | f/u April 20  |   |     |  |      | insufficient data                        |
| 25/10/2019 | 2   | 35   |       | 83.6  | f/u April 20  |    |      |       |      |               |   |     |  |      | insufficient data                        |
| 25/10/2019 | 3   | 98   | 39.55 | 88.4  | Died 06/02/20 |    |      |       |      |               |   |     |  |      | died                                     |
| 05/07/2019 | 2   | 98   |       | 43    | 03/01/2020    | 1  | 84   | 20.51 | 45   | f/u June 20   |   |     |  |      | Improving                                |
| 27/09/2019 | 4   | 170  |       | 55    | 24/01/2020    | 4  | 111  |       | 56   | f/u April 20  |   |     |  |      | Improved IgG, stable                     |
| 14/02/2020 | 3   | 103  |       | 50.4  | 27/03/2020    | NR | ND   |       | NR   | f/u July 20   |   |     |  |      | Insufficient data                        |
| 21/02/2020 | 5   | 31   | 83.4  | 51.9  | f/u April 20  |    |      |       |      |               |   |     |  |      | Insufficient data                        |
| 07/02/2020 | 2   | 79   | 53.04 | 41.6  | f/u June 20   |    |      |       |      |               |   |     |  |      | Insufficient data                        |
| 07/02/2020 | 5   | 174  |       | 81.7  | f/u May 20    |    |      |       |      |               |   |     |  |      | Insufficient data                        |
| 14/02/2020 | 3   | 62   | 85.1  | 43.1  | f/u April 20  |    |      |       |      |               |   |     |  |      | Insufficient data                        |
| 13/02/2020 | NR  | 17   |       | 65.5  | f/u May 20    |    |      |       |      |               |   |     |  |      | Insufficient data                        |
| 13/02/2020 | NR  | 124  |       | 75    | f/u Aug 20    |    |      |       |      |               |   |     |  |      | Insufficient data                        |
| 17/01/2020 | 1   | 82   | 27.19 | 57    | f/u April 20  |    |      |       |      |               |   |     |  |      | Insufficient data                        |
| 13/12/2019 | 3   | 99   |       | 62.15 | 14/02/2020    | 3  | 117  |       | 57.5 | Died 17/03/20 |   |     |  |      | died                                     |
| 06/03/2020 | 4   | 510  | 86.37 | 60.7  | f/u April 20  |    |      |       |      |               |   |     |  |      | Insufficient data                        |
| 06/03/2020 | 2   | 140  |       | 61.3  | f/u May 20    |    |      |       |      |               |   |     |  |      | Insufficient data                        |
| 13/03/2020 | NR  | 112  |       | 64.6  | f/u April 20  |    |      |       |      |               |   |     |  |      | Insufficient data                        |
| 13/03/2020 | 2   | 135  |       | 61.2  | f/u June 20   |    |      |       |      |               |   |     |  |      | Insufficient data                        |
| 20/03/2020 | 5   | 134  |       | 60.6  | f/u June 20   |    |      |       |      |               |   |     |  |      | Insufficient data                        |
| 15/03/2020 | 1   | ND   |       | 82.7  | f/u Aug 20    |    |      |       |      |               |   |     |  |      | Insufficient data                        |
| 06/03/2020 | 1   | 120  |       | 91.3  | f/u June 20   |    |      |       |      |               |   |     |  |      | Insufficient data                        |

## Appendix 7 Antifungal Trial Data

| POSACONAZOLE TRIALS 2019-2020 |                |                |               |          |  |
|-------------------------------|----------------|----------------|---------------|----------|--|
| Trial start date              | 4 month review | 6 month review | Trial Outcome | Continue | Comments   |
| 22/10/2019                    | Feb-20         | Apr-20         |               |          | Achieved targets at 4/12   |
| 01/11/2019                    | Mar-20         | May-20         |               |          | Achieved targets at 4/12   |
| 09/08/2019                    | Dec-19         | Feb-20         | Continue      | Yes      |  |
| 01/11/2019                    | Mar-20         | May-20         | Failed        | No       | Stopped after 7 days due to GI side effects/dizziness                      |
| 20/09/2019                    | Jan-20         | Mar-20         | Failed        | No       | Stopped due to rash Dec 2019   |
| 07/02/2020                    | Jun-20         | Aug-20         |               |          |  |
| 21/02/2020                    | Jun-20         | Aug-20         | Failed        | No       | Stopped due to GI side effects 9/3/20                                      |
| 09/03/2020                    | Jul-20         | Sep-20         |               |          |  |
| 27/05/2019                    | Sep-19         | Nov-19         | Continue      | Yes      |  |
| 29/11/2019                    | Mar-20         | May-20         |               |          | Achieved targets at 4/12   |
| 10/05/2019                    | Sep-19         | Nov-19         | Continue      | Yes      |  |
| 20/03/2020                    | Jul-20         | Sep-20         | Failed        | No       | stopped after 3 days due to GI side effects                                |
| 01/07/2019                    | Nov-19         | Jan-20         | Continue      | Yes      |  |
| 16/08/2019                    | Dec-19         | Feb-20         | Failed        | No       | stopped due to dizziness/shaking 12/9/19                                   |
| 25/10/2019                    | Feb-20         | Apr-20         |               |          | Achieved targets at 4/12   |
| 16/08/2019                    | Dec-19         | Feb-20         | Died 23/09/19 |          | Patient died 23/09/19  |
| 13/09/2019                    | Jan-20         | Mar-20         | Failed        | No       | Achieved targets at 4/12, CT progression at 6 months                       |
| 20/09/2019                    | Jan-20         | Mar-20         | Continue      | Yes      |  |
| 13/09/2019                    | Jan-20         | Mar-20         | Failed        | No       | stopped 25/10/19 due to clinical deterioration                             |
| 07/02/2020                    | Jun-20         | Aug-20         |               |          | Achieved targets at 4/12   |
| 02/12/2019                    | Apr-20         | Jun-20         |               |          |  |
| 07/02/2020                    | Jun-20         | Aug-20         | Failed        | No       | stopped 8/4/20 due to nausea, weight loss                                  |
| 03/05/2019                    | Sep-19         | Nov-19         | Continue      | Yes      |  |
| 01/05/2019                    | Sep-19         | Nov-19         | Failed        | No       | stopped August 19 - did not achieve therapeutic levels due to GI condition |
| 02/08/2019                    | Dec-19         | Feb-20         | Continue      | Yes      |  |
| 03/01/2020                    | May-20         | Jul-20         |               |          |  |
| 24/01/2020                    | May-20         | Jul-20         |               |          |  |
| 31/05/2019                    | Sep-19         | Nov-19         | Continue      | Yes      |  |
| 06/09/2019                    | Jan-20         | Mar-20         | Died 22/09/19 |          | Patient died 22/09/19  |

|                               |        |        |               |     |  |
|-------------------------------|--------|--------|---------------|-----|--|
| 18/10/2019                    | Feb-20 | Apr-20 | Failed        | No  | stopped after 1 week due to nausea/anorexia                                      |
| 15/11/2019                    | Mar-20 | May-20 | Failed        | No  | stopped 03/01/20 due to new changes on radiology and worsening symptoms          |
| 10/05/2019                    | Sep-19 | Nov-19 | Died 23/05/19 |     | Patient died 23/05/19  |
| 08/11/2019                    | Mar-20 | May-20 |               |     |  |
| 10/04/2019                    | Aug-19 | Oct-19 | Failed        | No  | Symptoms no better after 6 months, stopped Oct 19 to treat MAI infection         |
| 04/05/2019                    | Sep-19 | Nov-19 | Continue      | Yes |  |
|                               |        |        |               |     |  |
|                               |        |        |               |     |  |
| <b>Pending from 2018/2019</b> |        |        |               |     |  |
|                               |        |        |               |     |  |
| 15/02/2019                    | Jun-19 | Aug-19 | Continue      | Yes |  |
| 03/01/2019                    | May-19 | Jul-19 | Failed        | No  | Achieved targets at 4/12, stopped June 2019 due to rash. Posa resistant July 19. |
| 06/02/2019                    | Jun-19 | Aug-19 | Continue      | Yes |  |
| 08/02/2019                    | Jun-19 | Aug-19 | Continue      | Yes |  |
| 22/03/2019                    | Jul-19 | Sep-19 | Continue      | Yes |  |
| 18/01/2019                    | May-19 | Jul-19 | Continue      | Yes |  |
| 01/03/2019                    | Jul-19 | Sep-19 | Continue      | Yes |  |
|                               |        |        |               |     |  |

|                    |
|--------------------|
| Success            |
| Fail               |
| Pend to 20/21 data |
| Died               |

| ISAVUCONAZOLE TRIALS 2019-2020 |                |                |               |          |  |
|--------------------------------|----------------|----------------|---------------|----------|--|
| Trial start date               | 4 month review | 6 month review | Trial outcome | Continue | Comments   |
| 01/05/2019                     | Sep-19         | Nov-19         | Failed        | No       | stopped due to deterioration in symptoms               |
| 10/04/2020                     | Aug-20         | Oct-20         | Failed        | No       | Stopped due to peripheral neuropathy                   |
| 24/01/2020                     | May-20         | Jul-20         | Failed        | No       | Stopped 6/3/20 due to skin blistering                  |
| 24/05/2019                     | Sep-19         | Nov-19         | Failed        | No       | Failed to keep appointments - discontinued             |
| 01/04/2019                     | Aug-19         | Oct-19         | Failed        | No       | stopped after 3/52 due to headaches/GI disturbance     |
| 08/11/2019                     | Mar-20         | May-20         |               |          | Achieved targets at 4/12                               |
| 01/03/2020                     | Jul-20         | Sep-20         |               |          | Achieved targets at 4/12                               |
| 01/07/2019                     | Nov-19         | Jan-20         | Success       | Yes      |  |
| 01/09/2019                     | Jan-20         | Mar-20         | Failed        | No       | stopped Oct 19 - did not achieve therapeutic levels    |
| 14/06/2019                     | Oct-19         | Dec-19         | Success       | Yes      |  |
| 03/01/2020                     | May-20         | Jul-20         |               |          |  |
| 15/11/2019                     | Mar-20         | May-20         |               |          |  |
| <b>Pending from 2018/2019</b>  |                |                |               |          |  |
| 28/12/2018                     | Apr-19         | Jun-19         | Failed        | No       | Achieved targets at 4 months but not 6 months, stopped |
| 14/09/2018                     | Jan-19         | Mar-19         | Failed        | No       | Panzole resistance, stopped Jan 2019                   |
| 04/01/2019                     | May-19         | Jul-19         | Success       | Yes      |  |
| 01/03/2019                     | Jul-19         | Sep-19         | Success       | Yes      |  |

Success

Fail

Pend to 20/21  
data

Died

### Clinical data for patients deemed successful at drug trial

| Drug Trial    | Date trial started | Weight   |          | MRC      |          | SQRQ     |          | CT       | Asp IgG  | Notes  |
|---------------|--------------------|----------|----------|----------|----------|----------|----------|----------|----------|--|
|               |                    | Baseline | 6 months | Baseline | 6 months | Baseline | 6 months |          |          |  |
| Posaconazole  | Jan-19             | 81.7     | 85.6     | 2        | 2        | 66.18    | 60.03    | Improved | Improved |  |
| Posaconazole  | Feb-19             | 48.2     | 49       | 4        | 2        | 59.45    | 75.33    | Improved | Stable   |  |
| Posaconazole  | Feb-19             | 73.1     | 70       | 5        | 4        | 82.73    | 81.55    | Improved | Improved |  |
| Posaconazole  | Feb-19             | 54.3     | 51.4     | 4        | 0        | 76.62    | 51.5     | Improved | Improved |  |
| Posaconazole  | Mar-19             | 85.2     | 81.6     | 4        | 4        | 81.82    | 62.65    | Stable   | Improved |  |
| Posaconazole  | Mar-19             | 54.4     | 53.9     | 2        | 2        | 54.41    | 36.81    | Stable   | Improved |  |
| Posaconazole  | May-19             | 87.9     | 89       | 2        | 2        | 74.99    | 67.98    | Stable   | Improved |  |
| Posaconazole  | May-19             | 51.7     | 46.1     | 3        | 2        | 60.57    | NR       | Improved | Improved |  |
| Posaconazole  | May-19             | 48.7     | 49.5     | 3        | 2        | 52.43    | 54.87    | Stable   | Improved |  |
| Posaconazole  | May-19             | 35.1     | 32.75    | 3        | 3        | 57.86    | 74.37    | Stable   | Improved | Weight and SGRQ due to separate condition        |
| Posaconazole  | May-19             | 52.3     | DNA      | 5        | DNA      | 87.74    | DNA      | NR       | Improved | Parent team prescribed, Discharged               |
| Posaconazole  | Jul-19             | 54       | 55       | 4        | 4        | 84.88    | 86.47    | Stable   | Improved |  |
| Posaconazole  | Aug-19             | 49.4     | 63.5     | 4        | 3        | 95.13    | 71.3     | Improved | Improved |  |
| Posaconazole  | Aug-19             | 72       | 79.6     | 3        | 3        | 70.24    | 42.97    | Stable   | Stable   |  |
| Posaconazole  | Sep-19             | 63.8     | 63.5     | 3        | 3        | 58.14    | 29.65    | Improved | NR       |  |
| Isavuconazole | Jan-19             | 65.8     | 66       | 4        | 3        | 94.54    | 96.4     | Stable   | Stable   |  |
| Isavuconazole | Mar-19             | 55.3     | DNA      | 4        | DNA      | 72.72    | DNA      | Stable   | Improved | DNA as in-patient locally, improved at 10 months |
| Isavuconazole | Jun-19             | 71       | 73       | 5        | 2        | 67.41    | NR       | improved | Improved |  |
| Isavuconazole | Jul-19             | 87.2     | 71       | 2        | 2        | 75.58    | Unable   | Stable   | Stable   | Developed advanced cancer                        |

## Appendix 8 Publications and Book Chapters

### Journal publications calendar year 2019

1. Abastabar, M., Hosseini, T., Valadan, R., Lagzian, M., Haghani, I., Aslani, N., Badali, H., Nouripour-Sisakht, S., Nazeri, M., Gholami, S., Vakili, M., Bowyer, P., Shokohi, T. & Hedayati, M. T Novel point mutations in *cyp51A* and *cyp51B* genes associated with itraconazole and posaconazole resistance in *Aspergillus clavatus* Isolates. *Microbial Drug Resistance* (Larchmont, N.Y.) 2019, 25; 652-662.
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5. Barac A, Kosmidis C, Alastruey-Izquierdo A, Salzer HJF; CPAnet. Chronic pulmonary aspergillosis update: A year in review. *Med Mycol* 2019; 57(Supplement\_2): S104-S109.
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Key Book chapters related to CPA

Denning DW. Clinical manifestations and diagnosis of chronic pulmonary aspergillosis. UpToDate: <http://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-chronic-pulmonary-aspergillosis> (2011-).

Denning DW. Treatment of chronic pulmonary aspergillosis. UpToDate: <http://www.uptodate.com/contents/treatment-of-chronic-pulmonary-aspergillosis> (2011- )

Vandenborgh L-V, Enaud R, Coron N, Denning DW, Delhaes L. From culturomics to metagenomics: clinical relevance of mycobiome in chronic respiratory diseases. *ERS Monograph – The lung mycobiome*. Eds. Cox MJ, Ege M, von Mutius, 2019. Ch 6, pp. 88-118.

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## Appendix 9 Patient Survey Results

### Patients survey 2020

#### Detailed analysis (2020 figure boxed in grey)

##### **Q1. Is this your first visit to the National Aspergillosis Centre?**

8% Yes – up 3% on 2019.

##### **Q2 How satisfied are you with the courtesy shown to you by:**

2020: Receptionist 95%, Clinic Nurses 97%, Aspergillus specialist nurse 96%, Doctor 97%, Comms team 100% and Physio 100%.

NB All figures are for satisfied or better.

2019: Receptionist 98%, Clinic Nurses 98%, Aspergillus specialist nurse 99%, Doctor 98% and Physio 97%.

##### **Q3. How satisfied are you with the quality of care you received from:**

2020: Receptionist 94%, Clinic Nurses 97%, Aspergillus specialist nurse 96%, Doctor 96%, Comms team 100% and Physio 100%.

2019: Receptionist 98%, Clinic Nurses 98%, Aspergillus specialist nurse 99%, Doctor 98% and Physio 97%.

##### **Q4. Have you been contacted by a member of the NAC team, after or in between clinic visits?**

2020: 52% Yes. 79% of these contacts were from a nurse, 14% from a doctor and 7% admin.

100% satisfied or better.

*Very positive comments: Co-operative, today helped me as much as poss, Good, Very approachable*

2019: 31% Yes. 75% of these contacts were from a nurse, 12.5% from a doctor and 12.5% admin.

100% satisfied or better

##### **Q5. Have you had a consultation with a specialist nurse (aspergillosis nurse) today?**

2020: 24% had consulted with a nurse, all were 100% satisfied or better with their knowledge and communication.

*All positive comments.*

2019: 6% had consulted with a nurse, all were 100% satisfied or better with their knowledge and communication.

##### **Q6. Have you received care from the specialist physiotherapists (Phil or Mairead)?**

2020: 24% had received care from Physio, all were 100% satisfied or better.

*There were 3 comments, two were positive and one 'Not sure who they are'*

2019: 15% had received care from Physio, all were 100% satisfied or better.

##### **Q7. Have you received any written information about your condition?**

2020: 62% (18) had received information. There were 2 comments which were neutral or positive

2019: 67% (48) had received information. There were 6 comments which were neutral or positive, one praised a letter by Prof Denning in particular. One was a concern "I never have any feedback after appointments like my other clinic visits at different hospitals "

**Q7a. How satisfied are you with this information you received about your condition?**

2020: 100% were satisfied or better.

2019: 95% were satisfied or better.

**Q8. Did someone tell you about potential symptoms regarding your illness or medication to watch out for at home?**

2020: 80% Yes.

2019: 74% Yes.

**Q9. When you had important questions to ask a doctor did you get answers that you could understand?**

2020: 100% yes.

2019: 100% yes, though one comment stated "The lack of continuity is an issue. One feels that one is starting from the beginning again with each new face that one sees. It would be helpful if patients, where possible, could be scheduled in with the same clinic doctor on each appointment"

**Q10. We would like to offer best supportive care/end of life care to our patients. We understand that this can be a sensitive subject.**

**Is this something you have thought about?**

2020: 82% (23) have not thought about this.

One comment made: 'I didn't think that this is applicable yet'

2019: 78% have not thought about this

**Q11. Would you like the opportunity to discuss end of life care with the NAC team?**

2020: Around 90% did not want to discuss, with slight difference in preference about who the conversation should be with (doctor rather than nurse).

2019: 90%

**Q12. Have you ever had an in-patient stay here at Wythenshawe hospital?**

2020: 23% yes, of which 100% felt that they had been treated with respect and dignity.

Comment: Very well looked after

2019: 32% yes, of which 96% felt that they had been treated with respect and dignity. One individual answered no.

NOTE this figure was 35% in 2018, 32% in 2019 – continuing fall

**Q13. Would you recommend Wythenshawe Hospital to friends and family?**

2020: 100% yes

Comments: Had resection of lung (aspergilloma removed), All staff here are very good, Good, For specialist (lung) care, otherwise distance is too far from home, A great team who are sensitive to my illness, Better than Blackpool Vic, Everyone is friendly and gives lots of support, Good care, Good care

2019: 99% yes

**Q14. We provide a postal service for drug levels and sputum samples. If you have used this service, have you any comments or ideas how this can be improved?**

No complaints. Very good, Very good, Very good service, Smaller pots to fit in postal boxes, Packaging doesn't fit well (container cover doesn't close properly once jar is inside), Ensure return label enclosed, Local surgery seems to struggle with the concept.

**Q15. We have commissioned a company to deliver antifungal drugs to patients' homes. If you have had this service, do you have any comments?**

2020: Comments: Reliable service, Excellent, Been fine, Very good, Its very useful, Our last order was short and I had to call the company several times to chase up our order. I was disappointed at the lack of communication, Great service, Very good service, Very good services.

**Q16. Do you travel to clinic by hospital transport?**

2020: 7% Yes.

No-one commented about the quality of the service.

**Could you please provide us with the first part of your postcode? Eg. M23**

2020: M28 (Worsley, 14miles), DA15 (Sidcup, 248miles)

2019: 10%

**Q17. Are you generally happy to participate in clinical research?**

2020: 77% Yes, of these 100% happy with procedures and consent process.

2019: 78%

**Q18. We have developed several patient information leaflets. How useful did you find them?**

2020: 74% thought our leaflets were useful. Of the remaining people (26%) none had received a leaflet.

**Is there any other information that you feel would be useful?**

2020: No comments made

**Q19. Have you visited the new Aspergillosis patient website?**

(<http://www.aspergillosis.org/>)

2020: 16%



Of those that had visited, 100% were satisfied or better.

2019: 19%

**If you have not visited, is there a reason why?**

There were 2 comments, one indicated that they had no access to a computer, the other that they has lost the website address.

**Q20. We have regular monthly patient meetings here in Manchester  
Have you attended a patient meeting?**

2020: 3% Yes

2019 0%

Further questions revealed that nearly 50% did not attend because it was inconvenient or too far to travel. The remainder were not interested in attending the meeting as they were 'happy as they are'.

Given that we make attending the meeting as physically convenient as possible by holding it close to the Friday clinic there isn't much more we can do to allow people to physically attend.

In addition, we have asked at meetings about why some people don't attend and a common answer other than distance is the fear of infection from other patients during the meeting, or they are concerned that they will miss their appointment in clinic if they attend the patients meeting.

We have run these meeting using Zoom during the COVID-19 lockdown and that has been quite successful. Many more people have now learned or acquired the equipment to use Zoom including all of our 'regulars' at this Friday meeting and when asked no-one objected to us moving this meeting to purely happen online.

**Q21. Over the last year, the presentations from the patient meetings have been recorded and put on the aspergillosis patient website. Have you viewed any of the presentations?**

2020: 7% of patients have viewed presentations. **These are loaded onto our website at [aspergillosis.org](http://aspergillosis.org) and get lots of interest online, not necessarily from NAC patients.**

2019: 4%

**Q22. It has been possible for patients and carers, if they were not able to attend a meeting, to view the meetings live over the internet using Facebook. Have you ever watched a meeting live over the internet?**

2020: 4% replied yes. **We make these live presentation available in our Facebook groups in an attempt to boost viewing numbers and usually get 10 – 20 people watching, some not NAC patients.**

2019: 4%

**Q23. We have a very active Aspergillosis Support group (>2000 members) on Facebook (<http://www.facebook.com/groups/aspergillosissupport/>). Are you a member?**

2020: 14% are currently members.

**If no would you like more information?**

2020: 30% want more information.



**Q24. There is a weekly online social chat for patients & carers on Thursday at 10am, currently using Zoom software. You can attend using your phone or any computer. Details are in the Quarterly Booklet. Have you ever heard of it?**

2020: 11% yes

2019: 3%

**Q24a. Have you ever attended it? Would you like to know more?**

2020: 12% yes

**25) We publish a quarterly booklet for the Aspergillosis community that you can pick up in the clinic waiting room. Have you ever read it?**

2020: 64% yes.

**26) There have been several patient led support groups set up around the UK.**

**a) are you aware of these groups?**

2020: 26% Yes.

2019: 30%

**b) If yes, have you made contact with a group?**

2020: Of those who replied 1 (3%) had made contact (4% in 2019)

2019: 4%

**c) If no, why have you not made contact?**

2020:

7 replies (55%) not interested/inconvenient.

6 replies (45%) did not know and some presumably might like to join but it heavily depends on the group being in their area.

**d) Would you like information about setting one up in your area? (if yes, please let a member of staff know)**

2020: No replies to this question. Presumably no-one wants to run a group.

NOTE these groups are hosted by patient volunteers. They are asked to encourage local awareness of aspergillosis and NAC and some have members that regularly meet up in face-to-face meetings or via the phone for social contact but there are few who now do this. The same people host online Facebook group pages and these are more popular with 252 members across 12 regional groups. It is clearly more difficult to generate interest offline than it is online.

### **General comments**

Doctors and nurses are very cooperative Thanks

This time of year everyone gets a bit poorly