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An Investigation of antifungal stewardship programmes in England

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Abstract

Objectives: To explore the current status of antifungal stewardship (AFS) initiatives across National Health Service (NHS) Trusts within England, the challenges and barriers as well as ways to improve current AFS programmes.

Methods: An electronic survey was sent to all 155 acute NHS acute Trusts in England.

Results: Forty seven Trusts, corresponding to 30% of English acute Trusts, returned a survey; 46 trusts (98%) had an antimicrobial stewardship (AMS) programme but only 5 (11%) had a dedicated AFS programme. Twenty (43%) Trusts said they included AFS as part of their AMS programmes. From those conducting AFS programmes, 7 (28%) have an AFS/management team, 16 (64%) monitor and report on antifungal usage, 5 (20%) have dedicated AFS ward rounds and 12 (48%) are directly involved in the management of invasive fungal infections.

Thirteen acute Trusts (52%) started their AFS programme to manage costs, whilst 12 (48%) commenced the programme due to clinical need; 27 (73%) declared that they would increase their AFS initiatives if they could. Of those without an AFS programme, 14 (67%) responded that this was due to lack of resources / staff time. Twelve Trusts (57%) responded that the availability of rapid diagnostics and clinical support would enable them to conduct AFS activities.

Conclusions: Although a minority of Trusts conduct AFS programmes, nearly half include AFS as part of routine AMS activities. Cost issues are the main driver for AFS, followed by clinical need. The availability of rapid diagnostics and clinical support could help increase AFS initiatives.

Introduction

Antimicrobial stewardship (AMS) initiatives have until recently largely focussed on antibacterial agents. However, a number of recent studies have highlighted the importance of antifungal stewardship (AFS), outlining significant patient benefits, as well as cost-savings. (Standiford et al 2012, Lopez-Medrano 2013, Mondain et al 2013, Valerio et al 2014, Micallef et al 2015) Issues addressed in AFS include selection of the most appropriate agent in terms of intrinsic antifungal activity (Parkins et al), whether additional diagnostic or biomarker tests are required, dose (especially with major organ dysfunction, drug interactions (Bartholomew et al) (which are a major issue with the azole antifungals), underlying therapy plan (increased or reduced immunosuppression, renal support etc.), addressing current or future adverse events and advising on therapeutic drug monitoring (TDM; Ashbee et al), potential for antifungal resistance and oral switch possibilities. I Resistance to antifungal agents has emerged as an area of major concern, both acquisition of intrinsically resistant fungi (*Candida krusei*, *Candida auris* (Schelenz et al), Mucorales and *Fusarium* spp. being good examples) and isolates with acquired resistance, notably *Candida glabrata* and *Aspergillus fumigatus*. Dual fungal infection is an increasing problem (Salehi et al). Better antifungal choices improve outcomes and reduce cost (Parkins et al; Micallef et al). Better availability and usage of non-culture based fungal disease diagnostics should also reduce unnecessary anti-bacterial use (Denning et al).We sought to explore the current status of AFS initiatives across National Health Service (NHS) acute Trusts within England.

Methods

A web-based survey containing 50 closed questions was developed and deployed by Public Health England's select survey programme as previously described (Ashiru-Oredope et al 2015), in order to explore the status of AFS in England. There was also the opportunity to provide comments (i.e. free text). The final draft was piloted for face validity (Supplementary Information Figure S1) and disseminated to all 155 NHS acute hospital trusts across England via the following networks: Lead Public Health Microbiologists (Public Health England) network, British Infection Association (BIA), UK Clinical Pharmacy Association (UKCPA) and the East of England antimicrobial pharmacist group. The survey was open for 6 weeks and reminders were issued at three weeks and again at five weeks. All NHS hospitals in England were included. NHS hospitals in Wales, Northern Ireland and Scotland and all UK private hospitals were excluded. The responses were first de-duplicated to remove multiple responses from individuals but multiple responses from the same trusts were retained if they were from different healthcare professionals (i.e. pharmacists, microbiologists etc.). Responses from non-English Trusts were also excluded from the analysis. Results were analysed using Microsoft Excel.

Results

In total, 47 hospital Trusts in England responded to the questionnaire, representing 30% of all acute Trusts. The majority (53%; 25) were district general hospitals (small, medium and large acute Trusts), followed by teaching (36%; 17) and specialist Trusts (11%; 5)(table 1). Most respondents were microbiologists (37; 69%), followed by antimicrobial pharmacists and infectious disease physicians. A wide range of specialities was covered by participating hospitals.

Only one English NHS acute Trust reported that it had no AMS programme in place (a specialist hospital). This contrasts with only five Trusts (11%) reporting having a dedicated AFS programme. Four of these were in teaching Trusts and one was in a specialist Trust. However, most Trusts had some form of informal AFS programme or monitoring ability, with 76% of Trusts having guidelines for the treatment and / or prophylaxis of invasive fungal infections.

Perceived potential benefits of AFS included improvements in safety (23), outcome (19), costs (24), reduced side-effects (20) and obtaining surveillance data (18).

Most hospital Trusts had access to a number of available laboratory tests (e.g. galactomannan, cryptococcal antigen, β-D-glucan; table 1). Interestingly, availability of laboratory testing was not related to the type of hospital (e.g. DGH, teaching hospital; data not shown). Of concern is the slow turnaround time reported in the questionnaire; most results were unavailable for at least 48 hours.

Most AFS activities were performed by a microbiologist, followed by an antimicrobial pharmacist, infectious disease physician or other pharmacist. A variety of models were suggested. Seven Trusts reported having an AFS / management team, while five reported performing dedicated AFS ward rounds. Twelve Trusts said they offered advice on patients with invasive fungal infections. Several Trusts said they saw fungaemic patients on their general daily ward rounds. A number of respondents identified that they perform ward rounds on haematology wards and intensive care units within their hospitals. Some Trusts with no dedicated AFS programme nevertheless included patients on antifungal agents as part of their AMS work. One

respondent suggested they reviewed patients on a list of 'restricted drugs' as part of their AMS round, which included high-cost antifungal agents. Most suggested they performed their AFS programme weekly, but some respondents did it more frequently. Other Trusts did it as required on an ad-hoc basis.

One respondent suggested they approached AFS using an analogy from infection prevention: *"there is a role for the infection prevention team but daily infection prevention activities are in everybody's job description. Our AFS team does not do specific AFS ward rounds – we have empowered the specialists in various clinical teams (champions) to look after this when they do their normal ward rounds. We support them and help them with audits but optimal antifungal prescribing is their responsibility."*

There were a variety of different reasons for commencing an AFS programme including: financial concerns (13; 52%), clinical need (12; 48%), attempts to improve patient management (40%) and interested individuals. Interestingly, only two respondents suggested concerns about antifungal resistance as a reason for starting their programme. A variety of resources were used for commencing AFS. The most frequent resource cited was discussions (with colleagues or experts), teaching events / meetings, and literature searches. One hospital Trust recruited two medical mycologists specifically to set up an AFS programme, whilst another AFS programme resulted from an audit of antifungal prescribing.

Patients were identified by a variety of different mechanisms. Pharmacy records were used to detect patients receiving antifungal agents (18), via microbiology

results (13) and queries from clinicians (15). Six respondents performed specialty-specific ward rounds.

Many centres have an antimicrobial pharmacist (19; across all hospital types), a microbiologist or Infectious Disease physician, a database and access to TDM. A small majority of trusts performed TDM (57%).

Most respondents reported that as part of their AFS programme, they assessed clinical response (19), highlighted drug-drug interactions (15), addressed side-effects (14) and ensured appropriate use of TDM / fungal biomarkers (17 each). Other comments included checking compliance to guidelines / evidence-based use. Measures used to assess effectiveness included monitoring the likelihood of obtaining adequate therapeutic drug levels (17), costs of antifungal agents (13), resistance profile (10) and mortality data (5). Other Trusts obtained surveillance data as part of their AFS programme. Most respondents thought their advice was 'usually' followed, though some suggested it was 'sometimes' followed.

The majority (79%) of respondents would ideally perform more AFS duties. One respondent reported they'd needed to suspend their AMS service (and hence AFS service) due to staffing issues.

A number of reasons were suggested by the 21 respondents who did not perform AFS. These included lack of time, competing priorities, perceived lack of importance and lack of expertise. Three respondents suggested that funding by NHS England for high cost antifungal drugs was a reason for not performing AFS (so any financial

savings didn't benefit the Trust). Other reasons for not performing AFS included 'lower numbers' / 'antifungal use is relatively less' and lack of interest / engagement from other specialties (e.g. haematology).

Availability of rapid diagnostics, clinical support (57% each) and more resources (52%) could help persuade some clinicians to start an AFS service, but CPD events (43%) and E-learning programmes (29%) were not considered to be beneficial.

Discussion

The clinical and financial benefits of AFS are well described (Standiford et al 2012, Lopez-Medrano 2013, Mondain et al 2013, Valerio et al 2014, Micallef et al 2015). Most studies up until now have suggested financial benefits as the principal reason for performing it. However, even small studies targeting the management of patients with candidaemia have shown improvements in mortality (Gouliouris et al 2016). There are important differences between AMS and AFS (table 2). Clinicians are less familiar with fungal infections, in terms of diagnostics and therapy and some drugs can be toxic and the azole antifungal agents have multiple interactions. Some antifungals are expensive. Patients with fungal infections (or suspected fungal infection) also typically have multiple co-morbidities and / or are extremely unwell.

We provide data on an important and emerging area from a national survey. Most respondents recognised the potential benefits of an AFS program. Not surprisingly, most NHS acute Trusts in England responded to say they had an AMS programme in place. We found that microbiologists and antimicrobial pharmacists are the

clinicians most involved in AFS. However, only 76% of acute Trusts had guidelines for the treatment and or prophylaxis of fungal infections and only 57% of Trusts performed TDM on some azoles, despite national guidelines suggesting its importance (Ashbee et al 2015).

A variety of methods for performing AFS are described, from dedicated ward rounds (at least weekly) to ad-hoc arrangements as and when required. This varied according to institution. Some hospitals perform it as part of their AMS programme (currently suspended due to lack of resources in at least one hospital) whilst one hospital had appointed two mycologists to help with AFS. Patients were typically identified by either laboratory results or pharmacy records in most cases.

Most Trusts had access to a range of fungal biomarkers, although not necessarily in their own hospital. However, the turnaround times were typically prolonged (>48 hours), which limits their clinical impact and utility for clinicians. This was highlighted in comments from several respondents. Fungal diagnostics is an area of difficulty for many clinicians and hugely important if antifungal agents are to be used appropriately and there is some evidence from this survey that some clinicians are unfamiliar and not confident with their interpretation. One laboratory expressed dissatisfaction in the funding of diagnostic tests (funded for certain patients but not others).

Most respondents thought their advice was ‘usually’ followed. However, the comments section suggests some areas (e.g. haematology / respiratory medicine) are less engaged or reluctant to follow advice from an AFS team of microbiologist

and antimicrobial pharmacist. One way, suggested by Manchester, circumvented the issue by giving ownership back to the clinical team, who ultimately are responsible for the patient.

Most respondents who perform AFS would do more if they had the available resources. One hospital had reduced its AFS programme as a clinician had left and no-one had replaced them. Standiford reported the situation where costs fell when an AFS programme was instituted and then rose when it was withdrawn (Standiford et al).

The funding mechanism in England is different from other countries in the United Kingdom. Most systemic antifungals, excluding fluconazole, itraconazole, ketoconazole and flucytosine are classified as high cost drugs, and are funded separately outside of the payment by results (PBR) or tariff system (https://www.england.nhs.uk/resources/pay-syst/drugs-and-devices/high-cost-drugs/) . Hospitals are required to provide patient level information to receive direct payment for the antifungals they use. A national Quality, Innovation, Productivity and Prevention (QIPP) incentive scheme has slightly reduced consumption on high-cost antifungals as defined daily doses (DDD), but the use of antifungals with expired or soon to expire patents (i.e. voriconazole and caspofungin) where cheaper costs will be seen has actually fallen. Most of the savings seen from the use of generic voriconazole has funded more expensive antifungals with years to run on their patents (data from www.RX-info.com). Future NHS England incentive schemes are focusing on paying the lowest cost for “off-patent” antifungals (https://www.england.nhs.uk/wp-content/uploads/2016/11/ge3-hospital-medicines-

optimisation.pdf)), but unless all high cost antifungals are removed from the tariff exclusion list, there will only be limited improvements in antifungal stewardship.

Our study, in common with a number of questionnaire studies, has a number of limitations. The return rate was only 30% which compares to other similar studies (Burns 2009). Nevertheless, we present data from a range of hospital Trusts of different types and involving different types of patients. Bias is inherent in any questionnaire; clinicians with an interest in AFS may have been more likely to respond than others.

AFS has been shown to have significant benefits to patients. We suggest that AFS is being performed in most hospitals in a variety of different ways in England which in part reflects different patient populations. Most hospitals would do more if they had the resources to do it, suggesting improvements can still be made.

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Transparency declarations

CM has received travel grants to attend scientific conferences from Astellas, Gilead, Pfizer and Novartis, educational grants from Pfizer and Novartis, attended a Pfizer Advisory Board Meeting and consulted for Astellas.

DWD holds Founder shares in F2G Ltd, a University of Manchester spin-out antifungal discovery company, in Novacyt which markets the Myconostica real-time molecular assays. He acts or has recently acted as a consultant to Astellas, Sigma Tau, Basilea, Scynexis, Cidara, Biosergen, Quintiles, Pulmatrix and Pulmocide. In the last 3 years, he has been paid for talks on behalf of Astellas, Dynamiker, Gilead, Merck and Pfizer. He is a longstanding member of the Infectious Disease Society of America Aspergillosis Guidelines group, the European Society for Clinical

Microbiology and Infectious Diseases Aspergillosis Guidelines group and the British Society for Medical Mycology Standards of Care committee.

SA has had educational grants and paid lectures from Astellas, Gilead, Merck and Pfizer and is a member of the ECIL group (European Conference for Infections in Leukaemia).

RJM has been paid for talks by Merck in the past year.

SS received educational grants from Astellas and has acted as advisor for Basilea, Pfizer, Astellas and Gilead.

DAE has received funding to attend conferences from MSD, Gilead and Astellas and consulted for Astellas.

All other authors: nothing to declare.

Disclaimer

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, the Department of Health or Public Health England.

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357 **Table 1: Results of Antifungal stewardship questionnaire**

1. Background data		
Total number of responses (de-duplicated, excluding non-English Trusts)	54	
Total number of acute Trusts with identified names	47 (30% of English Trusts)	
Number of Trusts with multiple replies (2 or 3)	6	
Number of Trusts outside England that responded (not included in analysis)	3	
Type of Hospital Trust	**Total Responding Trusts (n = 47)**	**%**
District General	25	53
Teaching	17	36
Specialist	5	11
Job Title of Respondents	**Total Respondents (n = 54)**	**%**
Microbiologists	37	69
Antimicrobial Pharmacist	8	15
Director of Infection Prevention & Control	2	4
Infectious Diseases Physician	3	6
Mycologist	1	2
Others (Clinical Pharmacy Technician, Microbiology Manager & Microbiology Registrar)	3	6
Specialties provided at the hospital	**Total Responding Trusts (n = 47)**	**%**
Burns	10	21
Haematology-Oncology	40	85
Infectious Diseases and Immunity	16	34
Intensive Care Unit (ICU)	45	96
Paediatric ICU / Neonatal PICU/NICU	36	77

Respiratory Diseases	45	96
Cardiology	44	94
Solid Organ Transplant (State)	13	28
Stem Cell Transplant: Allograft	12	26
Stem Cell Transplant: Autograft	17	36
Care of the Elderly	43	91
Others: • kidney, liver, pancreas, small bowel; renal and pancreas transplant • Neurosurgery • Maxillo-facial surgery • Ear, Nose & Throat (ENT) surgery • Cardiothoracic surgery • Cystic fibrosis • Bone tumour and bone / joint infection • Spinal cord injury rehabilitation • Intestinal failure		
Does the Trust have an AMS Programme?	**Total Responding Trusts (n = 47)**	**%**
Yes	46	98
No	1	2
Does the Trust have a dedicated AFS Programme?	**Total Responding Trusts (n = 47)**	**%**
Yes - we have a dedicated antifungal stewardship programme	5	11
Sort of - we include antifungal stewardship as part of our antimicrobial stewardship programme	20	43
Not really, but we do monitor antifungal usage	12	26
No	9	19
Benefits of AFS	**Total Responding Trusts (n =47)**	**%**

Improved safety		23	
Improved outcome		19	
Save money		24	
Reduced side-effects		20	
Obtain surveillance data to devise antifungal treatment guidelines		18	
Do you have the following fungal guidelines?		**Trusts Responding to Section (n = 36)**	**%**
Trusts who had fungal guidelines (either prophylaxis, treatment or both)		25	76
Do you perform triazole therapeutic drug monitoring?		**Trusts Responding to Section (n = 46)**	**%**
Yes		26	57
No		17	37
Don't know		3	6
Available Fungal biomarker tests		**Trusts Responding to section (n = 47)**	**%**
Galactomannan		44	94
Beta-D-glucan		36	77
PCR: PCP		41	87
PCR: Candida		22	47
PCR: Aspergillus		26	55
PCR: Pan-fungal		31	66
Mannan Ag/Ab		14	30
Cryptococcal Ag		43	91
Fungal biomarker tests turnaround times	**<48 hours**	**48 - 96 hours**	**>96 hours**
Galactomannan	5	17	14
β-D-glucan	4	15	11
PCR: PCP	8	16	8

PCR: Candida	1	8	8
PCR: Aspergillus	3	8	10
PCR: Pan-fungal	0	9	16
Mannan Ag/Ab	0	5	3
Cryptococcal Ag	19	11	7
2. In hospitals with an AFS programme in place, the majority of AFS ward rounds were performed by:		**Trusts Responding to Section (n = 25)**	**%**
Microbiologist		21	84
Antimicrobial pharmacist		13	52
Infectious disease physician		5	25
ICU pharmacist		2	8
Haematology pharmacist		1	4
ICU physician		1	4
Which of these form part of your AFS programme?		**Trusts Responding to Section (n = 25)**	**%**
Have an AFS / management team		7	28
Monitor and report on antifungal use		16	64
Dedicated AFS ward rounds		5	20
AFS team have direct involvement in management of invasive fungal infections (e.g. candidaemia and aspergillosis)		12	48
How often are AFS ward rounds performed in a typical week?		**Trusts Responding to Section (n = 25)**	**%**
Daily		3	
2 - 3 times per week		1	
Weekly		10	
Fortnightly		0	
Monthly		0	
Why was your AFS programme started?		**Trusts Responding**	**%**

	to Section (n = 25)	
Clinical need	12	48
Improve antifungal management	10	40
Manage antifungal costs	13	52
Manage antifungal resistance	2	8
Concerns over worsening outcomes of patients with fungal infections	3	12
Request from clinicians	0	0

Other, please specify

- Special interest in clinical mycology
- We don't have a separate AFS, but it is part of our AMS
- As part of Antibiotic stewardship Programme
- Part of antimicrobial stewardship rounds
- Current antimicrobial stewardship started Aug 2014-no dedicated AFS programme; but as (relatively small) part of general antimicrobial stewardship
- Started as an audit and re-audit

What resources did you use to develop your AFS programme?	**Trusts Responding to Section (n = 25)**	**%**
CPD event	6	24
Discussions with colleagues	14	56
Discussions with experts	6	24
Literature search	11	44
Peer meetings where AFS has been tried and tested	7	28
Not known	3	12

Other, please specify:

- Recruitment of 2 medical mycologists to set up AFS
- In house audit of AF prescribing
- Involvement with the ESCMID antifungal guideline writing groups

How do you target patients?	**Trusts Responding to Section (n = 25)**	**%**

Drug prescriptions (pharmacy records)	18	72
Laboratory results / organisms	13	52
Queries from clinicians	15	60
Specialty	6	24
What resources do you have available?	**Trusts Responding to Section (n 25)**	**%**
IT database for collecting data	9	36
Therapeutic drug monitoring	17	68
Antimicrobial pharmacist	20	80
Dedicated microbiologist	11	44
Infectious disease physician	5	20
Other: • Electronic prescribing - we can see who is on antifungals • Unsure about adults. Paediatrics have a motivated oncologist • The Microbiologist is often involved in starting antifungals		
How do you monitor therapy?	**Trusts Responding to Section (n = 25)**	**%**
Efficacy (i.e. clinical response)	19	76
Highlighting drug-drug interactions	15	60
Highlighting/preventing side-effects	14	56
Appropriate use of therapeutic drug monitoring	17	68
Appropriate use of fungal biomarkers	17	68
Other • Compliance to guidelines/evidence-based use • Compliance with antimicrobial prescribing guidelines • Confirming diagnosis		
How do you monitor effectiveness?	**Trusts Responding to Section (n = 25)**	**%**
Efficacy (i.e. clinical response)	21	84
Clinical parameters (e.g. respiratory function, normalisation of inflammatory markers, imaging etc.)	18	72

Highlighting / preventing side effects	15	60
Obtaining adequate therapeutic drug levels	17	68
Highlighting and reducing drug-drug interactions	18	72
Cost of antifungal drug budget	13	52
Resistance profile	10	40
Mortality data	5	25
Other • Surveillance of candidaemia and other serious fungal diseases		
Do you provide advice?	**Trusts Responding to Section (n = 25)**	**%**
Yes: Verbal advice	21	84
Yes: Written advice	16	64
No	0	0
Do clinicians follow your advice?	**Trusts Responding to Section (n = 25)**	**%**
Always	2	8
Usually	16	64
Sometimes	4	16
Rarely	0	0
Never	0	0
Don't know	0	0
Would you do more AFS if you could?	**Trusts Responding to Section (n = 34)**	**%**
Yes	27	79
No	4	12
Don’t know	3	9
3. Please specify the reasons for not performing AFS	**Trusts Responding to Section (n = 21)**	**%**
Competing priorities	10	48

Funding by NHS England for high cost antifungal drugs	3	14
Lack of interest	2	10
Lack of resources: staff time	14	67
Lack of resources: expertise	3	14
Perceived lack of importance	5	24
Other, please specify • Antifungal use is relatively less • Lower numbers • Lack of interest from haematology side		
If these barriers were addressed, would you do AFS?	**Trusts Responding to Section (n = 18)**	**%**
Yes	16	89
No	2	11
What would convince you to do AFS?	**Trusts Responding to Section (n = 21)**	**%**
Availability of rapid diagnostics (i.e. within 48h)	12	57
Clinical support	12	57
CPD Events	9	43
E-learning programmes	6	29
More resources	11	52
Comments		
"Huge impact on appropriate prescribing by implementing a systemic antifungal guideline" *"Rapid in house testing for candida isolates so we can de-escalate to azoles quickly"* *"Rapid availability of HRCT"*		
"We used to do weekly antifungal WR's which were excellent. We haven't resumed these since a colleague left and none of the other microbiologists have the expertise." *"We also struggle to fit everything in, so lack of time is a major factor. Also the fact that other things have become more 'important'...e.g. CQUIN for antibiotic reduction so time and effort are currently being directed elsewhere".* *"Antifungals are also hugely complicated so training would be greatly received....."*		

"Anti-fungal stewardship is challenging in transplant and respiratory patients: the transplant team is usually set in their ways as to how they manage their patients and also fear of clinical failure if antifungals are stopped". *"The respiratory team (bronchiectasis and CF) usually rely on radiology findings rather than on biomarkers."* *"Although GM is available the TAT is not satisfactory for stewardship"* *"We have problems with funding of this test"*
"The Trust does not invest enough in pharmacy/microbiology"
"The number of prescriptions for antifungals in the trust is very small" *"There is little or no microbiological oversight of antifungal use in haematology-oncology or respiratory, otherwise most antifungals are used on the basis of advice from a consultant microbiologist"*
"The Wythenshawe antifungal stewardship (AFS) team consists of two members of the Infectious Diseases (ID) team (a Consultant Medical Mycologist & a Consultant in ID) and an antimicrobial Pharmacist in addition to a group of Champions and it is led by ID." *"The key targets of the programme are to improve patient outcomes by updating and clarifying antifungal guidelines, involving and educating champions, implementing better diagnostics (β-D-glucan, therapeutic drug monitoring, resistance monitoring) and by stopping unnecessary courses of antifungals."* *"Mortality to fungal infections, antifungal resistance and cost of IV antifungals were chosen as outcome measures. The UHSM AFS programme has been successful in decreasing mortality to candidaemia, in stopping the increase of azole resistance in Aspergillus fumigatus and in decreasing the cost of echinocandins antifungal drugs used."* *"By integrating AFS into the team members' job plans this has achieved minimal additional staff costs. Savings in antifungal consumption has covered the increase in diagnostic costs."*
"Staff engagement has been one of the areas where we believe we have had the most success, and is showing the programme to be sustainable."

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360 **Table 2: Comparison between antimicrobial stewardship (AMS) versus antifungal**
361 **stewardship (AFS)**

	Antimicrobial stewardship	**Antifungal stewardship**
Source of infection	Patient to patient transmission	Patient to patient transmission is rare but can occur by endogenous infection with some fungi. Infection is often acquired from the environment e.g. via inhalation, inhalation, patient's own flora or devices such as catheters
Clinical data	A lot of supporting clinical data	Relative lack of clinical data
Toxicity and drug-drug interactions	Less common	More common
Diagnostic and monitoring tests	More tools available for interpretation	Fewer tools available that can also be difficult to interpret
Therapeutic drug monitoring	Therapeutic drug monitoring regularly used	Therapeutic drug monitoring developing
Staff familiarity	Greater familiarity	Less confidence and familiarity

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