

DIAGNOSTICS

DiagnosticsUpdate.com

Issue No: 19

Third Quarter 2018



IMPACT OF A **DIAGNOSTICS - DRIVEN** **ANTIFUNGAL** STEWARDSHIP PROGRAMME

**CERVICAL CANCER
SCREENING**

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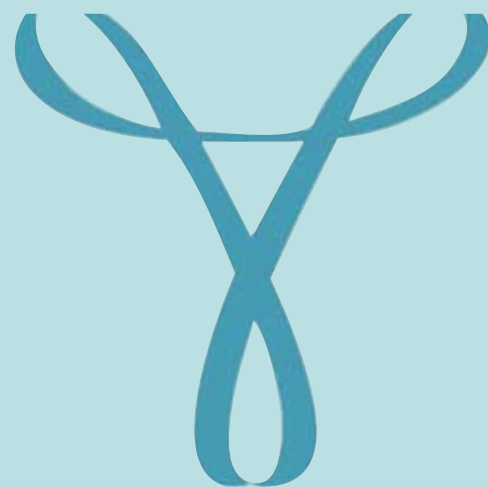
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CERVICAL CANCER SCREENING

A New design with your patient and practice in Mind



Cervical cancer is the most prevalent cancer in Africa resulting in morbidity.

More than 15.3 million women in South Africa are potentially at risk of developing cervical cancer. As such, there is a need to develop an optimal screening strategy to prevent cervical cancer.

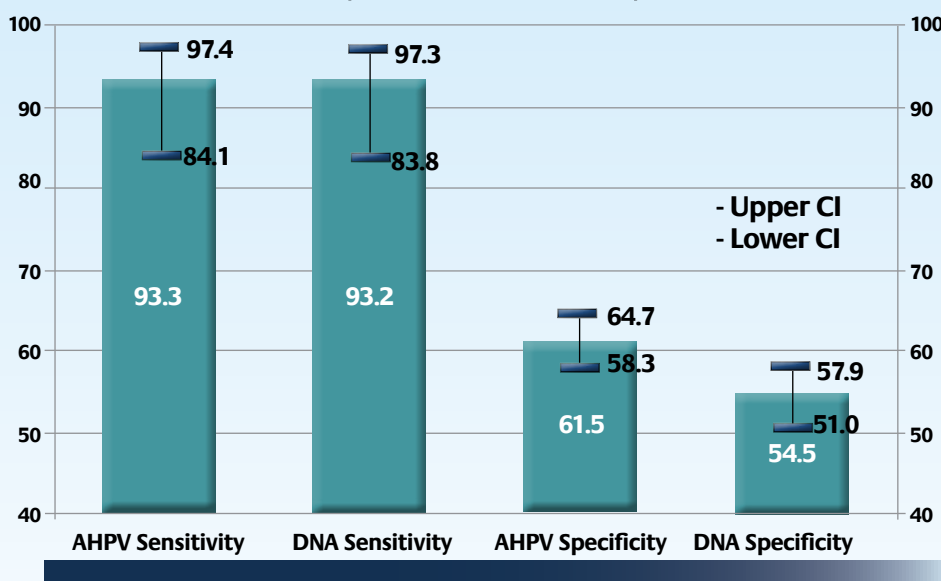
The optimal screening strategy should identify those cervical cancer precursors likely to progress to invasive cancers (maximising the benefit of screening) and avoid the detection and unnecessary treatment of transient HPV infection and its associated benign lesions that are not destined to become cancerous (minimising the potential harm of screening).

Am J Clin Pathol 2012; 137:516-542

The Aptima HPV Assay targeting E6/E7 mRNA is the next generation in cervical cancer screening. Aptima HPV targets 14 high risk serovars of HPV.

Numerous studies have shown that mRNA E6/E7 identifies the presence and activity of high-risk HPV infection destined to lead to disease (Tinelli A et al. *Curr Pharm Biotechnol* 2009 10 (8):767-771 & Cuschieri k et al *J Med Virol* 2004 73 (1): 65-70).

The CLEAR Trial: ASC-US ≥ 21 Years Population Detection of ≥CIN2 (directed biopsies)



Maximising the Benefits

With the intervals between recommended screenings for cervical cancer extended, identifying those patients at risk becomes increasingly important. Excellent sensitivity means minimising false-negative test results.

The Aptima HPV assay targeting mRNA has been shown to have equivalent sensitivity to DNA assays. (Dockter 2009, Szarewski 2008, Szarewski 2012, Reuschenbach 2010, Clad 2011, Ratnam 2011, CLEAR 2011, Ovestad, Wu. 2010, Monsenego 2011, Cuzick 2011, Iftner 2012, CLEAR 2015).

Minimizing Potential Harm

Minimising false -positives helps clinicians target the right patient for colposcopy. In the NILM arm of the

CLEAR trial, Aptima HPV showed 24% fewer false- positive tests compared to the HPV DNA assay.

This will minimise patient anxiety and the potential of over-treatment and over burdening the health care system.

Longitudinal Data & Primary Screening

Recently (April 2016), the Aptima has obtained a primary screening claim. This is based on a longitudinal clinical trial of a large cohort of women. The conclusion of the results support the use of Aptima HPV as a safe and effective assay for primary cervical cancer screen (CLEAR Am J Clin Pathol 2015 144:473-483). It has been shown in this trial that patients that are negative for Aptima

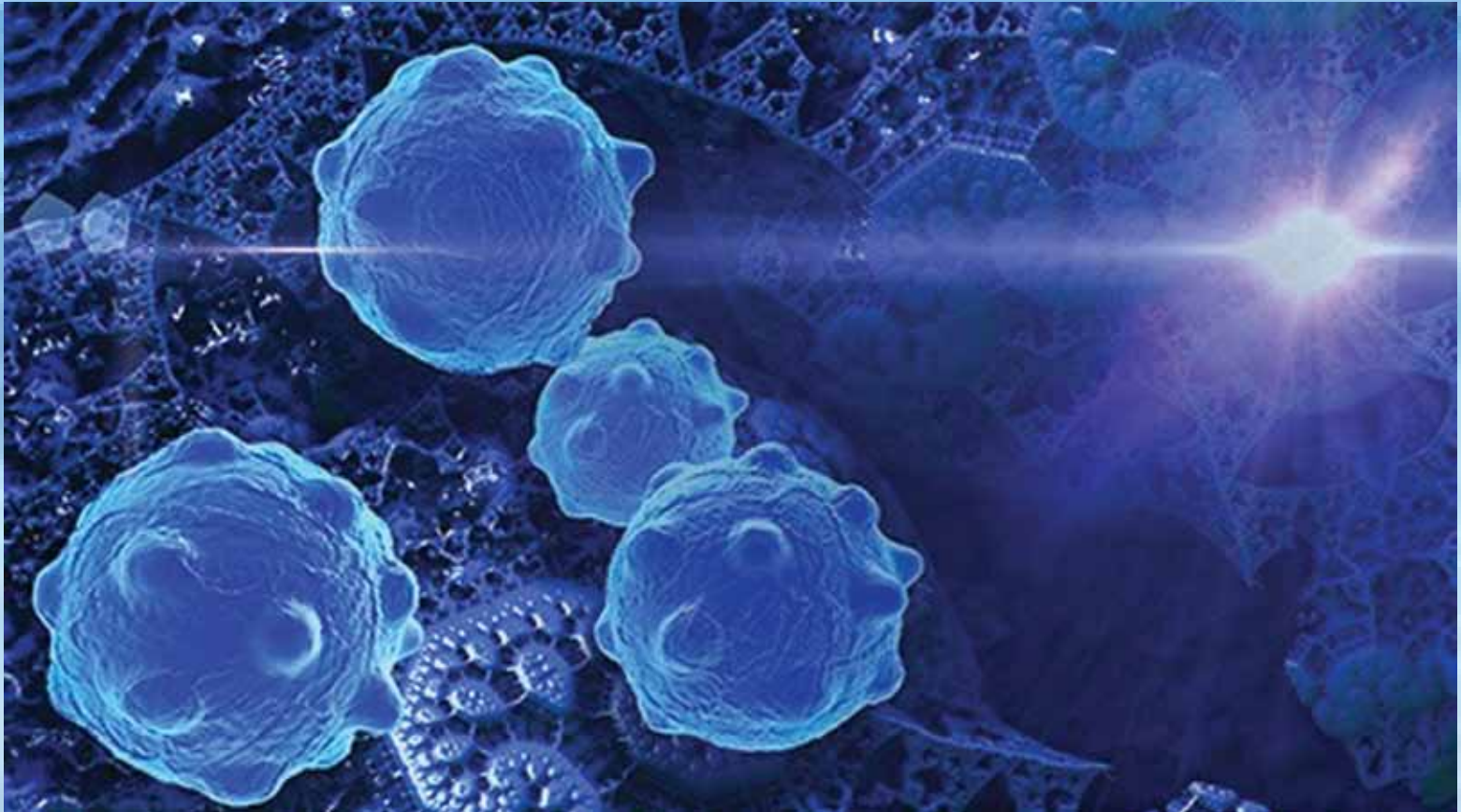
HPV assay have a 0.3% chance of developing a CIN II + lesion in the next 3 years. This allows for the increase of the screening intervals to 3 years.

The clinical performance of the Aptima HPV assay when used in a primary screening modality has been investigated in multiple studies by independent investigators. Thirteen peer-reviewed publications from ten separate clinical studies report the performance of Aptima HPV in primary screening in women enrolled in nine countries (China, Canada, France, Mexico, England, Denmark, The Netherlands, The United States, and Germany).

The data from these studies show

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Antimicrobial stewardship (AMS) aims to preserve the future effectiveness of antimicrobial agents and to reduce unintended adverse patient outcomes related to overuse.

Promoting selection of the optimal antimicrobial regimen, duration and route of administration are key in this endeavour.

There are two fundamental tools in AMS: guidelines for empirical therapy; and reliable diagnostic tests that can guide initiation and discontinuation of antimicrobial therapy. Antifungal stewardship (AFS) shares the aims and approaches of AMS but has its own specific features and challenges, which include limited availability of diagnostic testing, long laboratory turn-around times, the lack of AFS expertise outside specialist centres and a paucity of evidence identifying effective AFS interventions

outside specific patient cohorts. Due to these challenges, there is a need for different leadership and communication models if AFS is to be effectively practised.

The focus of most AFS programmes has been on the management of invasive candidosis, the most common severe nosocomial fungal infection.⁵ However, to date, most attention has been paid to reducing the use of expensive antifungal agents rather than the impact of AFS on patient outcomes or antifungal resistance.

Candida species are an increasingly prevalent cause of bloodstream infections (BSIs) in the ICU.

Although candidaemia has a high attributable mortality, there is significant variation between centres and patient groups.

Early and appropriate initiation

of antifungal therapy has been reported to improve outcomes.

Blood cultures remain the mainstay of diagnosis but their sensitivity is poor due to the low intensity of fungaemia.

This is a major challenge also for molecular methods. Biomarker tests such as serum β -1-3-D-glucan (BDG) are available but their specificity is low.

Therefore, clinicians often rely on their clinical experience and judgement.

This has led to overuse of empirical and prophylactic antifungal therapy, in particular echinocandins, in many ICUs.

The AFS programme at Wythenshawe Hospital has been developed over the past 8 years. The key targets of the programme are to improve patient outcomes by:

- (i) updating and clarifying antifungal guidelines;
- (ii) involving and educating champions;
- (iii) improving access to timely diagnostic testing; and
- (iv) reducing unnecessary use of antifungal therapy.

A local guideline for suspected or proven invasive candidosis (Figure 1) was developed based upon the ESCMID guideline for diagnosis and management of invasive candidosis in non-neutropenic adult patients.

Due to its very high negative predictive value in a low-prevalence setting such as ours, serum BDG testing was introduced as a rule-out test to guide the discontinuation of therapy in the absence of other microbiological evidence of invasive candidosis.

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The launch of the guideline in January 2014 was followed up by an online clinical educational quiz for prescribers, circulation of guideline posters, and the active presence of the Infectious Diseases (ID) team in the ICUs. An intensive-care physician was recruited by the AFS team as an AFS champion.

The aim of this project was to evaluate the compliance of the ICUs with the current local guideline. Additionally, we aimed to evaluate the impact of the AFS programme on the use of antifungal therapy, and on mortality due to invasive candidosis.

Methods

There are two separate ICUs in Wythenshawe Hospital staffed by separate intensive-care teams:

- (i) a cardiothoracic and heart-lung transplant ICU; and
- (ii) a mixed medical and surgical (including burns) ICU; these two ICUs have a total of 71 beds. The compliance of the intensive-care teams with the current local invasive candidosis guideline was audited over a 4 month audit period (April-July) in 2014 and

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ANTIFUNGAL STEWARDSHIP IN THE ICU

UHSM INVASIVE CANDIDOSIS IN CRITICAL CARE ALGORITHM

1. Persisting clinical signs of infection?

Fever or other ongoing SIRS response especially if despite broad-spectrum antibacterials (± fluconazole prophylaxis)

NO
Consider other causes & reassess

2. Host risk factors present?

Steroids/immunosuppressives, Candida in clinical samples, TPN, unresolved abdominal sepsis, central venous lines, neutropaenia, haematological malignancy, renal support, burns

NO
Consider other causes & reassess

↓ YES ≥ 2

SUSPECTED INVASIVE CANDIDOSIS?

(Sometimes referred to as "possible" or "probable" in other guidelines)

↓

1. Send samples to microbiology

- 2 sets of blood cultures (with FAN bottle if on antimicrobials)
- Serum sample for beta-D-1,3-glucan test (Fungitell)
- Line tips Sometimes when removed
- Infected tissue / pus if present

↓

2. Commence antifungal therapy

1st line: iv echinocandin (micafungin 100 mg OD (> 40kg wt) or 2 mg/kg rounded up to nearest 50mg OD (<40 kg)
2nd line and if echinocandin contraindicated (allergy, history of echinocandin therapy): iv amphotericin B (AmBisome 3mg/kg od)
• Consult the Infectious Diseases team

↓

3. Review microbiology results at 48-96 hours

NEGATIVE

POSITIVE

↓

↓

Stop antifungals

Reconsider diagnosis & reassess

If indicated repeat investigation twice weekly

Note: Negative beta-D-1,3-glucan test rules out candidaemia if sterile site cultures are also negative

Treatment of uncomplicated candidaemia is normally for **two weeks after the last positive blood culture**

Repeat blood cultures @48-72 hours to assess clearance

Switch to oral fluconazole can be considered after 10 days if the causative Candida is susceptible to it.

Change lines & ensure to deep focus of infection

Examine eyes to exclude endophthalmitis (at least one dilated retinal examination) and cardiac valves for endocarditis (cardiac echo)

Note: Positive beta-D-1,3-glucan test alone is not an indication for continued treatment.

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Eggimann P, Marchetti O. Is (1→3)-(3-D-glucan the missing link from bedside assessment to pre-emptive therapy of invasive candidiasis? Crit Care. 2011;15(6):1017

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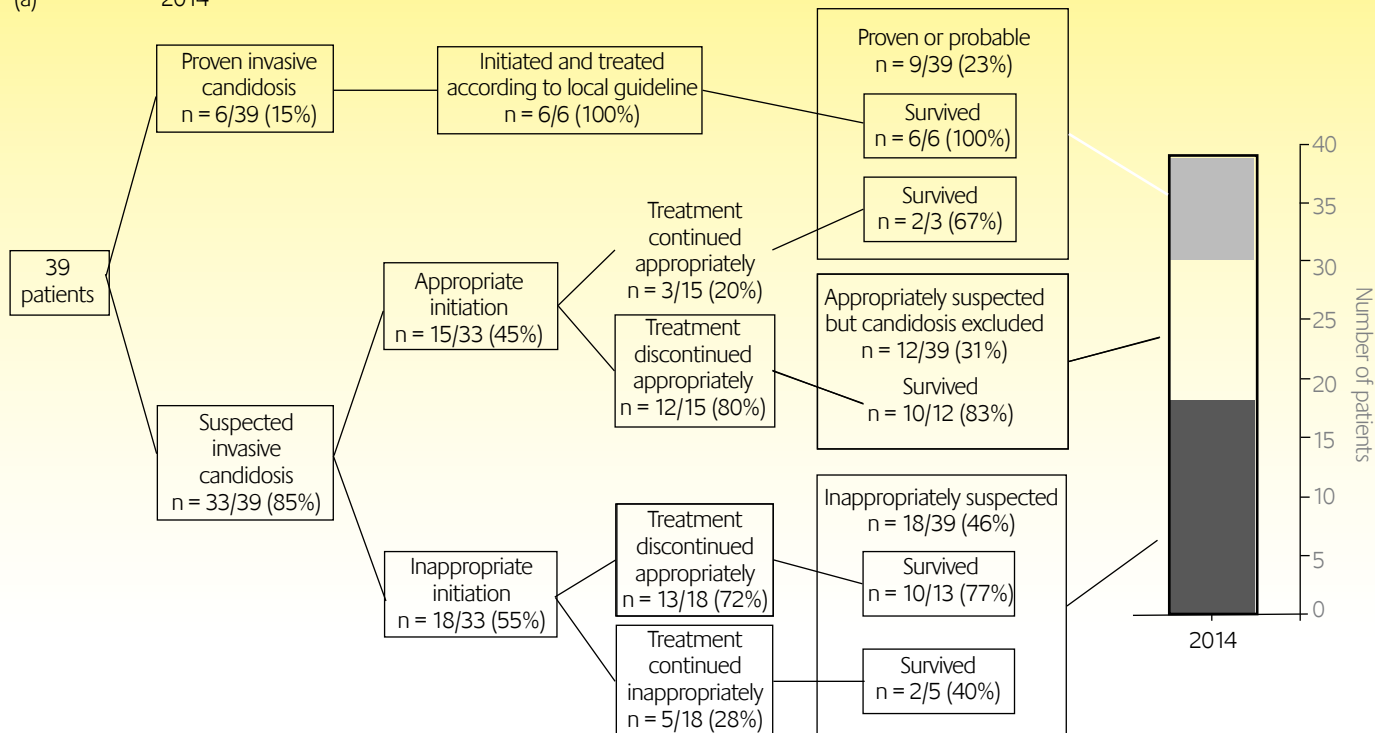
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re-audited over the same period in 2016.

All patients who were prescribed micafungin during the audit periods were identified from pharmacy databases. Patients treated for indications other than suspected or proven invasive candidosis, or those

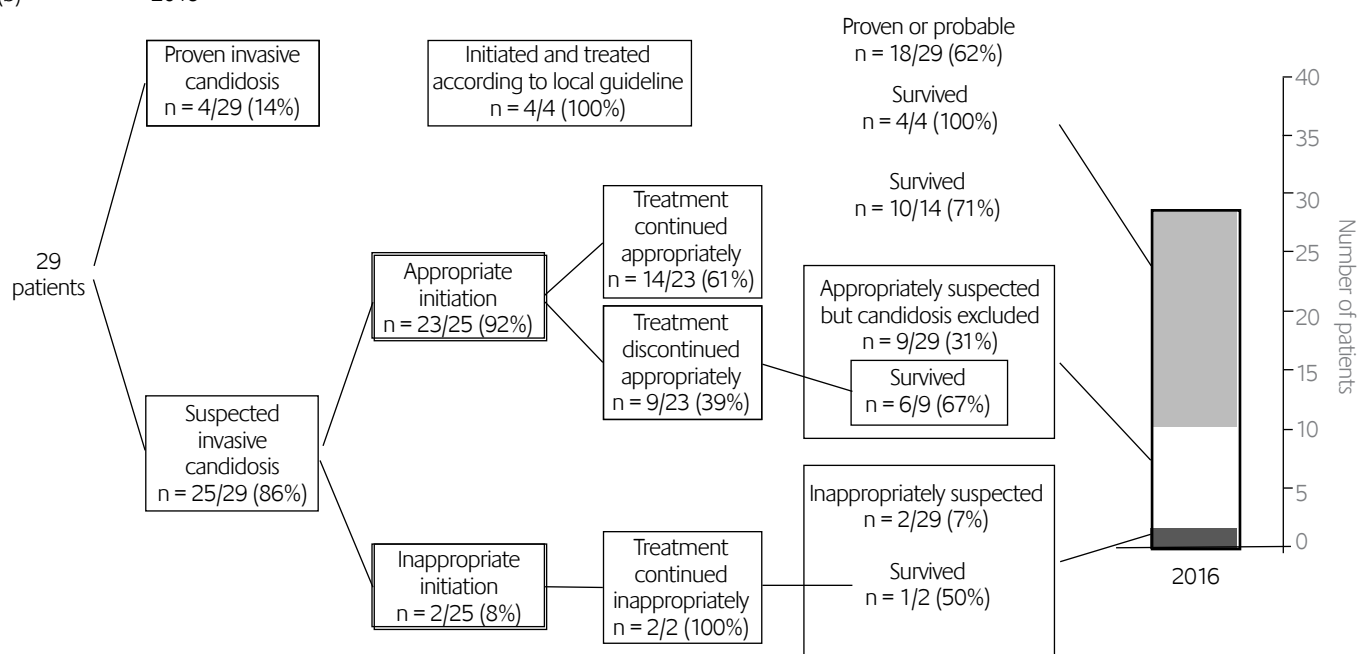
(a)

2014



(b)

2016



In 2016, there was no additional involvement beyond routine clinical practice.

As per the local guideline (Figure 1), patients with *Candida* spp. isolated from blood cultures were classified as 'proven invasive candidosis'. Patients with persistent clinical symptoms, host risk factors for candidosis and with

other diagnostic evidence of invasive candidosis (e.g. positive serum BDG or *Candida* spp. isolated from line tip cultures) were classified as 'probable invasive candidosis'. The use of antifungal therapy was defined as appropriate in all patients with proven or probable invasive candidosis. Patients with persistent clinical symptoms and host risk factors for candidosis but with negative blood cultures were classified as 'suspected invasive candidosis'.

Initiation of antifungal therapy was deemed appropriate in patients with persistent clinical symptoms and host risk factors for candidosis but no diagnostic evidence of invasive candidosis

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(e.g. negative blood culture for Candida or negative BDG). In contrast, antifungal therapy was deemed inappropriate in patients with 'suspected invasive candidosis' but with no clinical symptoms and/or host risk factors for candidosis.

Hospital micafungin consumption data were analysed for a 3 year period (April 2014–March 2017). The data were obtained from the AFS team database. Appropriateness of antifungal treatment, compliance with the guideline, all-cause mortality during the 4 month audit periods and micafungin consumption were used as outcome measures.

The incidence of invasive candidosis at Wythenshawe Hospital was audited for a 12 year period (2005–16). Cases of Candida spp. BSIs were identified from laboratory databases and the incidence calculated per 100000 bed-days.

Statistical analysis

Comparison of the proportions of patients with 'proven or probable invasive candidosis', 'appropriately suspected but candidosis excluded' or 'inappropriately suspected' in 2014 and 2016 was made using a Pearson χ^2 test and two-proportion Z-tests in SPSS version 22 (IBM Corp., Armonk, NY, USA).

Analysis of changes in the incidence of invasive candidosis was made by linear regression. Statistical significance was set at $P < 0.05$.

Ethics

This study was a retrospective service evaluation and ethical

approval was not required, as per UK Health Research Authority guidelines.

Results 2014 audit period

During the 4 month period in 2014, 39 patients admitted to ICU were treated for suspected or proven invasive candidosis (Figure 2a). Of these, 6 (15%) had Candida spp. isolated from blood cultures, with 3 patients receiving extracorporeal membrane oxygenation (ECMO). All patients with proven invasive candidosis were treated according to the local guideline. When assessed by the AFS team, the initiation of micafungin treatment was deemed appropriate in 15/33 (45%) of

the suspected invasive candidosis cases; in 3/15 (20%) patients micafungin was continued for at least 2 weeks (Figure 2a).

For the remaining 12/15 (80%) patients treatment was discontinued within 1 week following advice from the AFS team, based upon negative blood culture or BDG result. Overall for those patients where treatment was deemed appropriate, 14/15 (93%) had blood cultures taken and 6/13 (46%) had BDG tests performed. One patient was prescribed a higher dose (150mg) of micafungin in the absence of clinical suspicion of aspergillosis or oesophageal candidosis.

In 18/33 (55%) cases of suspected invasive candidosis the initiation of treatment was deemed inappropriate. In 15/18 (83%) the indication recorded for the initiation of micafungin

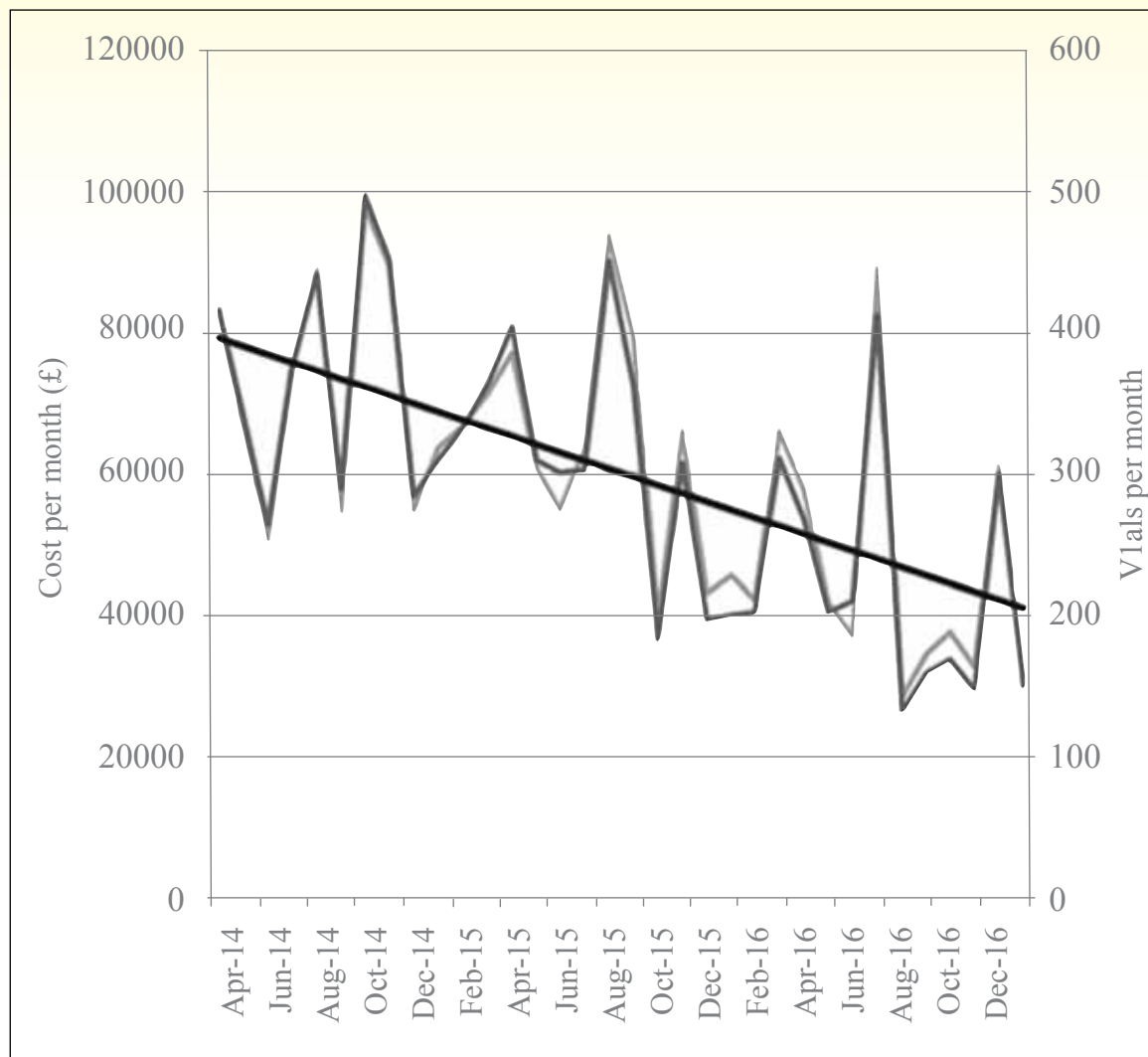
therapy was Candida spp. isolated from a single non-sterile site sample such as sputum or urine in the absence of clear risk factors for invasive candidosis.

In 3/18 cases there was no clear indication of fungal infection. Micafungin treatment was discontinued within 1 week on the advice of the AFS in 13/18 (72%) cases where it was deemed inappropriate.

Overall, only 10/33 (30%) patients with suspected invasive candidosis had serum BDG requested and only one was taken at the time of initiation of micafungin therapy. Of all samples, 9/10 (90%) were negative.

The correctly timed sample was negative but was not used to guide the stopping of therapy as the patient died soon after

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treatment was initiated.

None of the patients with proven invasive candidosis died within 30 days of micafungin initiation. Eight patients with suspected invasive candidosis died within 30 days of the initiation of treatment.

These patients suffered from: multi-organ failure whilst on ECMO (n=1), pulmonary

haemorrhage (n=1), post-surgical complications (n=2), pneumonia (n=3) and interstitial lung disease (n=1). None of these patients had BDG testing performed on initiation of micafungin therapy. One patient who was on ECMO had *Candida albicans* DNA detected by PCR in blood, and died 8 days after initiation of micafungin; however, this patient was also bacteraemic with *Klebsiella* and *Escherichia* species.

2016 audit period

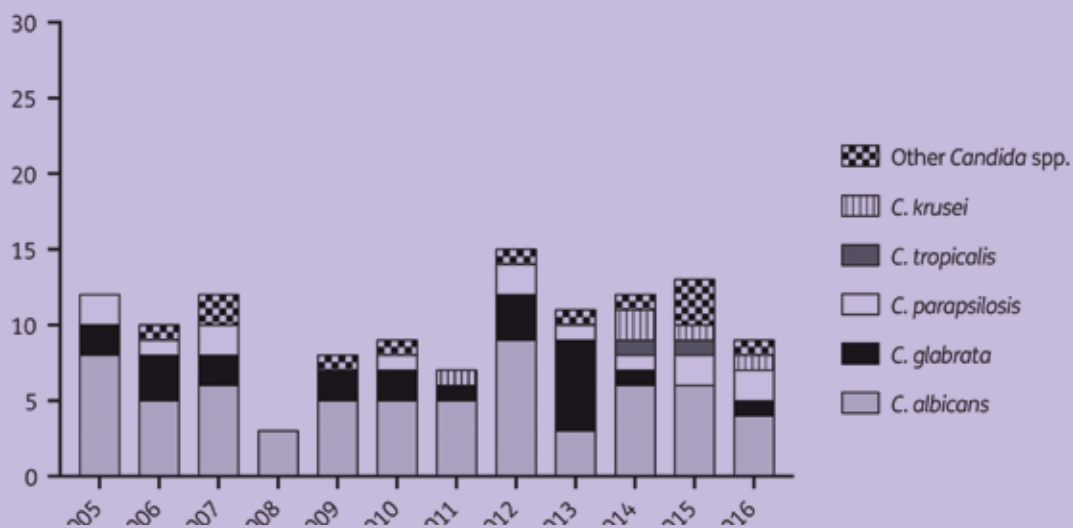
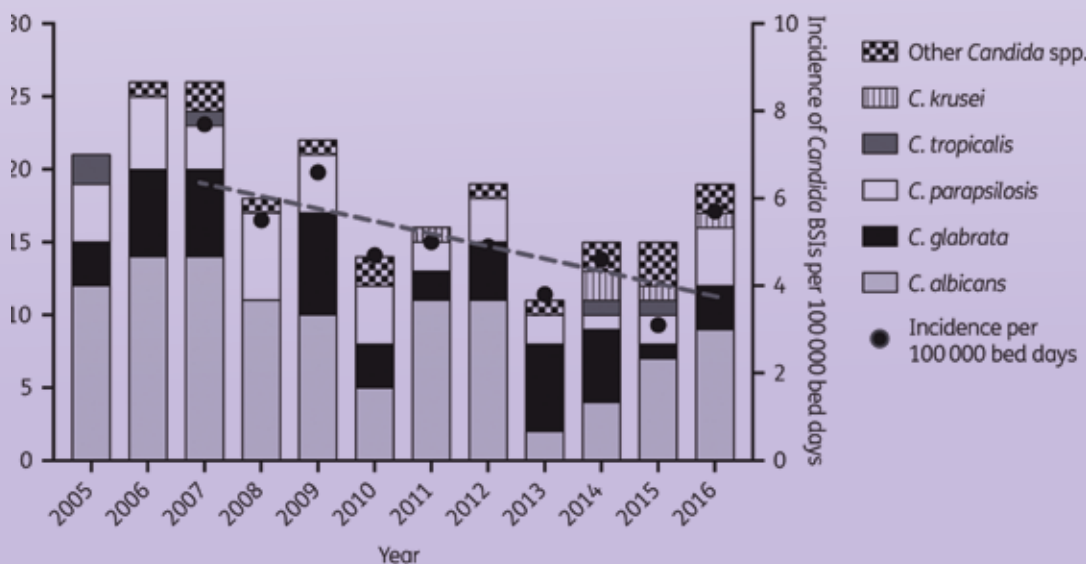
Twenty-nine patients admitted to ICU were treated for suspected or proven invasive candidosis (Figure 2b). Of these, 4/29 (14%) had *Candida* spp. isolated from blood cultures. All patients (n=4) with proven invasive candidosis were treated according to the local guideline and all had positive serum BDG test results.

When assessed by the AFS team, the initiation of micafungin treatment was deemed appropriate in 23/25 (92%) patients with suspected invasive candidosis (Figure 2b). The treatment was discontinued within a week for 9/23 (39%) patients following advice from the AFS team, based on negative blood culture and/or BDG results. For 14/23 (61%) patients the treatment was continued for 2 weeks based on positive BDG or other clinical factors. Overall, of those patients for whom the initiation of treatment was deemed appropriate, 21/23 (91%) had blood cultures done, and 21/23 (91%) had BDG done; 8/21 (38%) BDG results were negative, and in 5 cases the negative result was used to guide discontinuation of therapy. One patient was prescribed a higher dose (150mg) of micafungin in the absence of clinical suspicion of aspergillosis or oesophageal candidosis.

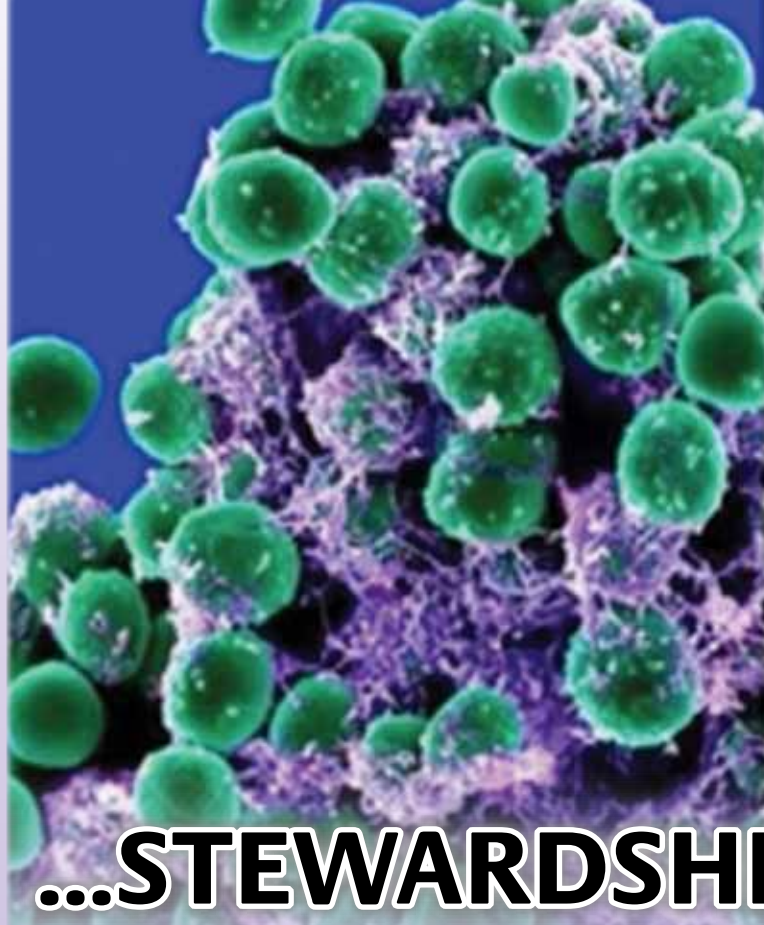
In 2/25 (8%) cases of suspected invasive candidosis the treatment was deemed inappropriate by the AFS team. In one case the indication recorded for the initiation of micafungin therapy was *Candida* spp. isolated from sputum in the absence of clear risk factors for invasive candidosis. In the other case there was no clear indication of fungal infection. Treatment was inappropriately continued for both patients. One patient had a blood culture performed but no BDG testing, and the other had neither blood culture nor BDG testing.

No patient with proven invasive candidosis died within 30 days of micafungin commencement. Eight patients with suspected invasive candidosis died within 30 days of micafungin initiation.

These patients suffered from: multi-organ failure whilst on ECMO (n=2) or left ventricular assist device (LVAD) (n=1), post-surgical complications (n=3),



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pneumonia (n=1) and bacterial sepsis (n=1).

Comparison of 2014 and 2016

Between 2014 and 2016, there were significant changes in the numbers of patients categorized as 'proven or probable invasive candidosis', 'appropriately suspected but candidosis excluded' and 'inappropriately suspected' ($P=0.01$). The number of patients with 'proven or probable invasive candidosis' significantly increased from 9/39 (23%) in 2014 to 18/29 (62%) in 2016. Over the same period the number of patients 'inappropriately suspected' significantly reduced from 18/39 (46%) to 2/29 (7%).

Micafungin and laboratory expenditure

The monthly micafungin expenditure at the Wythenshawe Hospital decreased from £81000 (e90000) per month to £40000 (e45000) (#49%) during the 24-month follow-up (Figure 3).

There was no change in the vial price of micafungin or in the consumption of other antifungal agents over the same period.

The BDG measurements were provided by the Mycology Reference Laboratory (MRCM) located at the Wythenshawe Hospital site. The mean monthly consumable costs for BDG tests (Fungitell, Associates of Cape Cod, MA, USA) in 2016 were £3739, which allows up to 21 tests done twice weekly. The cost of laboratory technician time (6h per week) to do the tests was some £390 per month. Therefore, the total cost of BDG testing at Wythenshawe Hospital was £4129 per month.

Invasive candidosis incidence

The total number of patients reported with *Candida* spp. in blood cultures and the incidence of *Candida* BSIs per 100000 bed-days at Wythenshawe Hospital between 2005 and 2016 are summarized in Figure 4. The incidence of culture-positive invasive candidosis at Wythenshawe Hospital

decreased significantly from 7.7/100000 bed-days in 2007 to 5.7/100000 bed-days in 2016 ($R^2=0.44$, $P=0.037$; Figure 4a).

The number of cases with *Candida* spp. isolated from the bloodstream in ICUs has remained stable (Figure 4b). In most years, *C. albicans* was the most common finding, followed by *Candida glabrata* and *Candida parapsilosis*.

There has been no marked change in the species distribution over the years.

Discussion

Successful AFS programmes build on implementation of guidelines for prompt administration of empirical antifungal therapy coupled with diagnostic tests that can guide safe discontinuation of therapy.

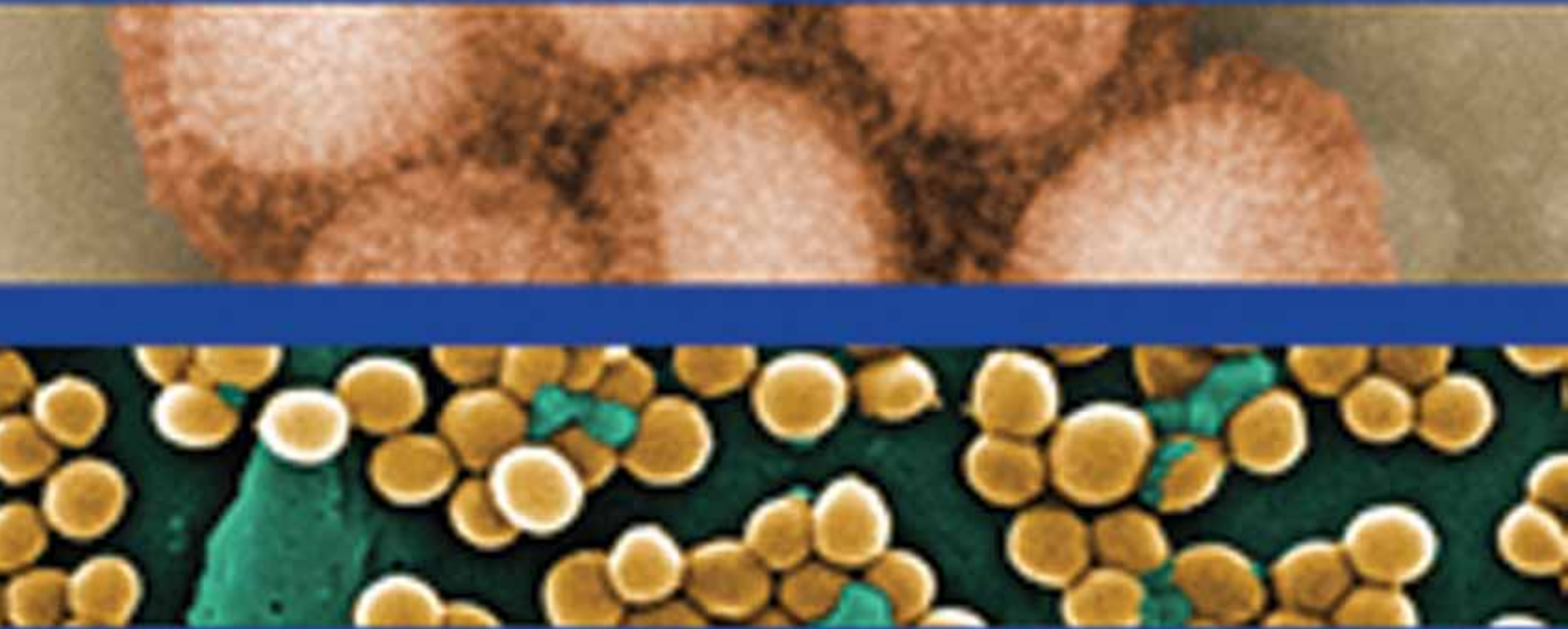
The aim of our programme was not to restrict the initiation of antifungal therapy in patients at risk of invasive *Candida* infection, as timely administration of empirical antifungal agents to

patients with invasive candidosis is associated with reduced mortality.^{18,19}

During the data collection periods in 2014 and 2016, the overall crude mortality in patients with proven or probable invasive candidosis was 19% (5/27). This compares favourably with the overall crude mortality due to invasive candidosis of 45% (a reduction of 58%), reported by our centre for the period of 2003–07, 27 and 35% by others.^{16,28}

The knowledge that early initiation of antifungal therapy improves outcomes, and the introduction of less toxic antifungal agents, such as the echinocandins, puts pressure on clinical teams to treat patients with early empirical therapy. Full diagnostic work-up including investigations for alternative causative organisms and use of fungal biomarkers such as serum BDG to guide discontinuation of antifungal therapy is fundamental for

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avoiding overuse of antifungal drugs. Our AFS strategy led to a 90% reduction in inappropriately initiated courses between 2014 and 2016.

Reassuringly, the number of patients in whom invasive candidosis was appropriately suspected but excluded did not increase between 2014 and 2016. This demonstrates that the guideline recommending early initiation of antifungal therapy was not driving an increase in unnecessary empirical antifungal use. In contrast, the overall antifungal consumption approximately halved during the 2 year study period (Figure 3). This is in keeping with the reduction in the number of inappropriately initiated empirical antifungal courses during the same time period. A marked temporal variability is demonstrated in the use of antifungal agents.

The number of patients with

proven or probable invasive candidosis doubled from 9 in 2014 to 18 in 2016. This increase is largely due to an increase in the number of patients with probable invasive candidosis as a result of increased use of the BDG test. However, the number of patients with *Candida* species isolated from blood culture in all of 2016 increased compared with 2015 and 2014 (Figure 4a). Figure 4 also demonstrates the marked natural fluctuation in the number of cases each year, which is likely to contribute to the spike in 2016. This does not, however, detract from the general trend towards a reduction in cases with *Candida* reported from blood culture.

Intravenous antifungal agents are commonly prescribed empirically for patients at risk of invasive fungal infections. These high-risk patients are typically cared for by clinical specialties familiar with invasive fungal infections such as intensive-care medicine, haematology and transplantation. However, there

is a growing body of evidence that the involvement of infection specialists will improve outcomes in patients within these cohorts diagnosed with complex infection.²⁹ Implementing an AFS programme is challenging and requires credibility and good interpersonal skills to influence clinical practice. Our approach of recruiting an intensive-care champion facilitated an excellent working relationship between the ID and intensive-care teams, to which we attribute our success in influencing practice.

The close working relationship between the AFS champion and ID team, fostered confidence in the clinical assessment of patients with suspected invasive candidosis, and increased the use of diagnostic tests, thus improving compliance with the local guideline. This ultimately led to a reduction in the input required from the AFS team and the resources needed for stewardship rounds.

Antifungal agents remain

expensive, and decreasing inappropriate use will affect the healthcare costs of ICU patients.

The monthly expenditure on BDG testing is equivalent to 20 doses of micafungin. Any additional doses that were not administered contributed to the increased savings. In this, minimizing laboratory turnaround times is key to success. By involving AFS champions, this can be achieved with minimal additional clinical staff costs. Due to the design of the BDG test kit the cost per test is lower the more tests are done at a time, which highlights the benefits of laboratory centralization. It is important to acknowledge that the incidence of candidaemia affects the negative predictive value of the BDG test, which is high only in low incidence settings.

There are some limitations to this study. Firstly, the sample size is limited due to the low incidence

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of invasive candidosis.

As the focus of this study was to audit the adaptation of the new ICU candidaemia guideline, only patients in ICUs were included.

However, the majority of candidaemias occur in the ICU, and during the audit periods there were no patients with invasive candidosis on non-ICU wards. Secondly, this was a retrospective study and the data collection depended on documentation in patient

records. However, the key variables analysed were available for all patients. During the audit periods there were no significant changes in the provision of clinical services at the University Hospital of South Manchester or overall mortality on ICUs.

Thus it is likely that the reduction in mortality due to invasive candidosis was due to the implementation of the AFS programme.

The impact of seasonal variation in candidaemia was minimized by including the same months in

both audit periods.

To further analyse the effectiveness of AFS, a prospective multicentre study using a stepped-wedge, cluster-randomized trial design would be ideal.

In conclusion, our real-world experience demonstrates that a clear and concise clinical guideline utilizing an informative biomarker and implemented with the help an AFS champion can be safe and effective at reducing inappropriate initiation of antifungal agents as well as improving patient outcomes.

The cost of instituting the AFS programme was more than covered by the savings associated with reduced antifungal consumption.

Funding

The project was funded by and data were generated and analysed as part of the routine operations of the University Hospital of South Manchester NHS Foundation Trust, the Manchester University NHS Foundation Trust and the University of Manchester. No external funding was received.

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BLOOD DONATION: THE MOST VALUED SERVICE TO MANKIND

Blood donation is harmless and safe in the body. Rather, it is a social responsibility. The donor is donating for it as it will be used in saving lives of his fellow beings. He himself may use the same during his own need. MILLIONS OF people owe their lives to people whom they will never know or meet in their lifetime. They are none other

than those people, who have donated their blood freely and without any reward – voluntary blood donors. Voluntary unpaid donors are the foundation of a safe blood supply which saves millions of human beings from the jaws of untimely death. We need to extend a hearty appreciation to these unsung heroes who give the precious gift of life to mankind.

Nothing is comparable to the preciousness of human blood. In spite of the rapid and remarkable conquests of medical science today, there is no laboratory that manufactures blood. It is only in human beings that human blood is made and circulated. For those who require blood for saving their lives, sharing from other fellows is the only means. Hence, donation rather voluntary donation is the only way of accumulating blood at safe storage to meet emergency requirements for saving lives.

Blood is required for treatment of accidental injuries, burns,

diseases like Haemorrhagic, Anaemia, Leukaemias, Thalassemias and Haemolytic ailments. In times of accidental injuries that shed huge amounts of blood and also in various types of surgical operations for medical treatments, we require blood for transfusion. Unavailability of blood may cost lives. Hence, importance of blood donation is tremendous. This is the greatest gift one can give to the fellow humans. Voluntary blood donors are saviors of mankind. If someone really loves oneself and other fellow beings, the only way to express it is to donate blood voluntarily.

Safe blood transfusion comes under legal protection as it is life-saving and also fatal.

The role of blood in a living creature is unique. The different components of blood have different activities to perform. Red Blood Cells (RBC) transport oxygen throughout the body, White Blood Cells (WBC) constitute body's defense mechanism, Platelets helps in stopping bleeding and plasma transports proteins including anti-bodies. Blood also evacuates wastes products from all organs of the body. There are four main blood groups ie, O, A, B and AB.

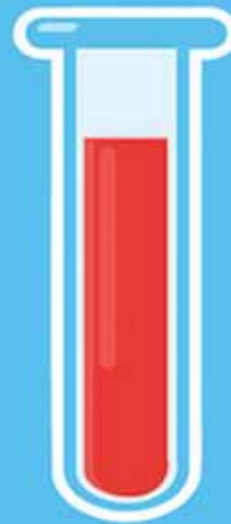
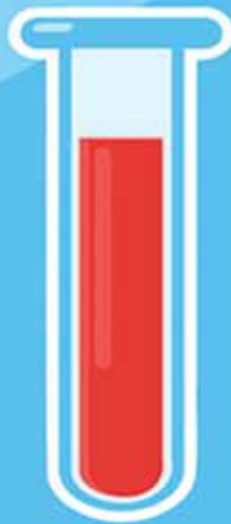
Group O is the most common and therefore, the most in demand.

Fear of needles, fear of pain, fear of sight of blood, fear of future weakness, fear of possible ill effects, objection from elders, ignorance and illiteracy etc are all reasons for many people who are hesitant in donating blood. All these myths and misconceptions are to be removed in order that adequate amount of blood is made available at blood banks for saving the patients. Blood collected from voluntary donors are stored at blood banks and it will be readily made available to needed patients on replacement basis. All units of blood collected are tested for malaria, hepatitis B & C, VDRL and HIV. Voluntarily donated blood are screened for potentially life-threatening infections such as HIV and hepatitis viruses. Hence, blood recipients have nothing to worry and regular donors can maintain their safe status.

Age: between 18 to 60 years.
Body weight: 45 kg and above.
Pulse rate: 60 to 100 per minute and regular
Blood pressure: Systolic 100 to 140, Diastolic 70 to 100.

TO PAGE 13





Hemoglobin: minimum 12.5gm/100ml of blood.
Oral temperature: not exceeding 37.50C.

There are also persons who should not donate blood. They are those:

- who are feeling unwell;
- who are anaemic;
- who are either pregnant or breast-feeding;
- who have heart disease, high or low blood pressure, epilepsy, diabetes;
- who are taking anti-biotics;
- who are immunised with live vaccines;

who are being treated for malaria during last three months;
who received blood during the preceding three months;
who had major operations during last six months.

The average amount of blood present in an adult is four to five liters or about eight per cent of the body weight. Life cycles of the different components are short. The RBC lives about 120 days while white cells last about three to nine days. New blood cells are constantly generated in the body. A person can donate blood 168 times during his 18 to 60 years. The quantity of

blood present in one kg of body weight is 76ml for males and 66 ml for females. Out of this eight ml per kg body weight is donatable. Males can donate for every three months while females for every four months. All donated blood is recuperated within 21 days. At one time only 350 ml will be taken from a donor in not more than 20 minutes time including time for rest and refreshment.

Blood donation is harmless and safe in the body. Rather, it is a social responsibility. The donor is donating for it as it will be used in saving lives of his fellow beings. He himself

may use the same during his own need. So, today's donor may be tomorrow's recipient. Without their humane gifts of noble donors, that also from the heart, many lives might have lost for want of blood. Therefore, the most generous and biggest ever contribution to mankind is blood donation.

"The gift of blood is the gift of life. There is no substitute for human blood. Blood cannot be manufactured – it can only come from generous donors."

Source: <http://www.merineews.com>

THE BENEFITS OF DONATING BLOOD

There's no end to the benefits of donating blood for those who need it. According to the American Red Cross, one donation can save as many as three lives, and someone in the United States needs blood every two seconds.

It turns out that donating blood doesn't just benefit recipients. There are health benefits for donors, too, on top of the benefits that come from helping others. Read on to learn the health benefits of donating blood and

the reasons behind them.

Benefits

Donating blood has benefits for your emotional and physical health. According to a report by the Mental Health Foundation, helping others can:

- reduce stress
- improve your emotional well-being
- benefit your physical health
- help get rid of negative feelings
- provide a sense of belonging and reduce isolation

Research has found further evidence of the health benefits that come specifically from donating blood.

Lower risk of heart disease

Blood donation may lower the risk of heart disease and heart attack. This is because it reduces the blood's viscosity.

A 2013 study found that regular blood donation significantly lowered the mean total cholesterol and low-density lipoprotein cholesterol, protecting

against cardiovascular disease. Researchers note this is consistent with findings in other studies which found that blood donors had a lower risk of heart disease and heart attack.

Donating blood regularly may also lower iron stores. This may reduce the risk of heart attack.

High body iron stores are believed to increase the risk of heart attack. Lower risk of cancer.
Source: <https://www.healthline.com>

CERVICAL CANCER SCREENING

FROM PAGE 03

that Aptima HPV has similar clinical performance compared to other clinically validated HPV tests when used for primary screening for cervical pre-cancer and cancer.

Reliability in results

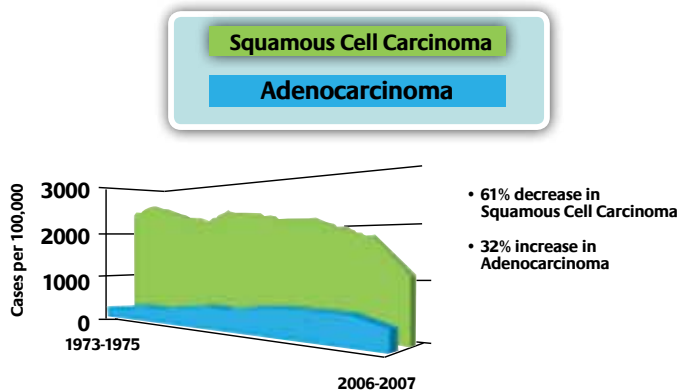
The Aptima HPV assay has an in-built internal control which

is added at the beginning of the specimen processing which controls all the activities of the assay to ensure confidence in the result.

Genotyping of the HPV

It has been found that squamous cell carcinomas are on the decrease and adeno carcinomas are on the increase.

Adenocarcinoma A Rising Trend

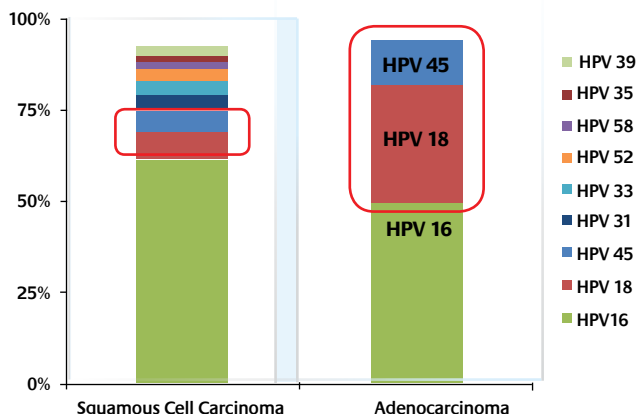


Adegoke et. al j. of women's health October 2012, 21 (10): 1031-1037

Three genotypes are responsible for adenocarcinomas 16/18/45. Aptima HPV mRNA E6/E7 is able to differentiate the HPV genotypes into four main groups

Genotype 16, Genotype 18, Genotype 45 and other groups comprising of (31, 33, 35, 39, 51, 52, 56, 58, 59, 66, 68)

HPV Types & Cervical Carcinomas*



* Any genotype that did not contribute more than 2% was not included in this chart

Figure 1 (adapted from de Banjose at al.)
Table 2: Cumulative relative contribution of the 3 most common HPV types in squamous cell carcinomas (SCC) and adenocarcinoma (ADC)

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