

Fungitell for antifungal treatment stratification

Medtech innovation briefing

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Summary

- The **technology** described in this briefing is Fungitell, which measures serum levels of (1–3)-beta-D-Glucan (BDG), a marker of fungal infection.
- The **innovative aspects** are that the Fungitell test is designed to determine the presence of several different fungal pathogens within 1 hour, which is much faster than current culture-based methods.
- The intended **place in therapy** would be in secondary care, as an addition to standard care, where suspected fungal infections are treated empirically (that is, based on signs and symptoms). Fungitell may guide antifungal treatment to be stopped sooner in patients who test negative.
- The **main points from the evidence** summarised in this briefing are from 5 non-UK studies (1 prospective cohort study, 2 retrospective cohort studies, 1 randomised parallel pilot study and 1 systematic review with a meta-analysis) including a total of 4,708 patients. They show that Fungitell has the potential to safely rule out invasive fungal disease, avoid unnecessary prescriptions and to stop antifungal treatment.

- **Key uncertainties** around the evidence are that none of the studies reported useful comparisons against a standard-care approach to antifungal treatment decisions. None were based in the UK and so results may not be generalisable to current NHS practice.
- The **cost** of Fungitell is £737.05 per test kit (excluding VAT), which can run up to 42 patient samples in duplicate, plus the cost of additional lab-based consumables and equipment. The cost per patient therefore depends on the number of samples in each run. The overall **resource impact** may be similar to, or less than, standard care. This would only happen if the additional test costs were offset by a reduction in the costs of unnecessary antifungal treatments and associated adverse effects. One UK-based single-centre study abstract has confirmed the potential for cost savings in an adult intensive care unit.

The technology

The Fungitell assay (Associates of Cape Cod) is an in vitro diagnostic test for the qualitative detection of (1–3)-beta-D-Glucan (BDG) in serum. BDG is a major cell-wall component of most pathogenic fungi and tiny quantities are released into circulation during infection. Detection of elevated levels of BDG is designed to help the presumptive diagnosis of invasive fungal diseases and could help guide antifungal treatment in at-risk patients, such as people with stem cell transplants or intra-abdominal candidiasis, and people having steroids or other immune-suppressing treatment.

Fungitell is a kinetic colourimetric assay that works with computer software. If BDG is present in a serum sample, the Fungitell reagent reacts with the BDG and turns yellow. The rate of this colour change is measured against a standard curve of BDG concentrations to produce estimates of concentration in the sample. The results range from non-detectable (less than 31 pg/ml) to over 500 pg/ml and are displayed as a value on the computer screen. The sample must be diluted and retested for any values over 500 pg/ml. Fungitell can detect the presence of many pathogenic fungal infections including candidiasis, aspergillosis and fusariosis, but cannot differentiate these by type. Fungitell cannot identify fungal infections caused by certain fungal species such as *Cryptococcus*, the yeast phase of *Blastomyces dermatitidis* or Mucorales such as *Absidia*, *Mucor* and *Rhizopus*.

One Fungitell kit comprises 2 flat-bottom microtiter plates and all necessary reagents. Each microtiter plate is set up with 5 standards, 1 negative control and up to 21 patient

samples, all in duplicate (following the recommended protocol), meaning that 1 kit can provide test results for up to 42 patients. Additional equipment needed for the test would be readily available in most pathology laboratories. If needed, other consumables are available from the manufacturer on request.

To use Fungitell, 0.5 ml of serum is needed per patient which is then centrifuged. The serum samples, negative control and standards are pipetted into a microtiter plate. Fungitell reagents are added and the plates are agitated in an incubating plate reader at 37°C. The mean rate of change is calculated using measurements of optical density recorded over 40 minutes. Samples that are cloudy, off-colour, or turbid can be diluted in reagent grade water, retested and the dilution factor accounted for when reporting of the results.

Fungitell test values of 80 pg/ml or more in at-risk patients are interpreted as positive for BDG. However, a positive result cannot fully determine the presence of fungal disease and Fungitell should be used with other diagnostic procedures. A Fungitell test value of less than 60 pg/ml should be interpreted as negative; values from 60 pg/ml to 79 pg/ml suggest a possible fungal infection. Although Fungitell gives results using clinically validated thresholds, the test is described as qualitative rather than quantitative. This is because many clinical factors, including total fungal burden, site of infection and type of fungus, can cause the reactivity of BDG to vary. The thresholds given are therefore not definitive.

Invasive fungal diseases fall into 3 categories: possible, probable and proven, based on a combination of host factors, clinical criteria and mycological criteria ([EORTC/MSG diagnostic criteria](#)). Repeat testing is recommended before diagnosis and during surveillance when stopping antifungal treatment is the aim.

Full information of the Fungitell test procedure, quality control and accuracy and precision data can be found in the [instructions for use](#).

Innovations

The Fungitell assay takes 1 hour compared with culture-based fungal diagnostic methods, which often take weeks to produce a result.

Using the test could inform clinical decisions on prescribing or stopping treatment with antifungal drugs. Tests that improve clinical decision-making in antifungal prescribing have

the potential to support antimicrobial stewardship.

Current NHS pathway

Diagnosing fungal infections in secondary care is currently done using radiological assessment, mycological cultures, histological examination and microbiological investigation including polymerase chain reaction (PCR) and BDG and galatomannan biomarker tests. Blood cultures are currently the standard method for diagnosing fungal infections. The use of histology, radiology or PCR depends on patient health, type of fungal infection and the centre in which treatment is done. Tests for rapidly identifying bloodstream bacteria and fungi have been previously addressed in the NICE diagnostic guidance on [LightCycler SeptiFast Test MGRADE, SepsiTtest and IRIDICA BAC BSI assay](#). However, insufficient evidence was found to recommend routine adoption of these similar molecular diagnostic tests in the NHS.

The decision to prescribe antifungal therapy for suspected invasive fungal disease in secondary care is made by a clinician, and is generally based on medical history, clinical examination and assessment of risk plus the results of diagnostic tests. Antifungal treatment strategies include prophylactic, fever-driven (empiric), diagnosis-driven (pre-emptive) and targeted therapy ([Ruping et al. 2008](#)).

The most common invasive fungal diseases treated in secondary care in the NHS are invasive candidiasis, invasive aspergillosis, and *Pneumocystis pneumonia*.

These diseases are associated with high morbidity and mortality rates and many patients die before diagnosis. Current diagnosis with blood cultures take up to 4 weeks from the time they arrive in the laboratory to provide a result which would delay starting appropriate treatment. Empirical antifungal therapy is therefore usually started in high-risk patients. Non-culture-based test methods which can help rule out fungal infection could help to stop unnecessary antifungal therapy earlier and reduce the considerable toxicity and costs of the treatment, and potentially contribute to a reduction in the development of resistance.

Fungal diagnosis using BDG was included in the revised [EORTC/MSG diagnostic criteria](#) for probable invasive fungal infections.

Guidelines from the [European Society for Clinical Microbiology and Infectious Diseases on the diagnosis and management of Candida diseases \(2012\)](#) recommend considering the

Fungitell test for candidaemia detection in adults as well as for ruling out infection. These guidelines recommend starting antifungal therapy based on strong clinical suspicion and the use of an echinocandin as first-line therapy. Diagnostic tests should be used to rule out infection and to stop unnecessary therapy.

NICE is aware of the following CE-marked devices that appear to fulfil a similar function as Fungitell:

- [Fungus \(1-3\)-beta-D-Glucan Assay](#) (Dynamiker Biotechnology)
- [Goldstream Fungus \(1-3\)-beta-D-Glucan Tests](#) (Era Biology Group).

Population, setting and intended user

Fungitell would be used for people who are suspected of, or at high risk of, invasive fungal disease. High-risk people in secondary care are typically those with haematological malignancies, HIV or bone marrow or organ transplants. Fungitell would most likely be used in conjunction with current diagnostic procedures as a rule-out test for invasive fungal diseases and to guide antifungal therapy. In pre-emptive treatment strategies, it could be used to prevent unnecessary antifungal prescription. In empiric treatment strategies it could help inform a decision to stop antifungal treatment earlier.

The test would be carried out in secondary or tertiary care clinical laboratories and run by qualified laboratory staff after training on the test and system.

Costs

Technology costs

One Fungitell kit includes all necessary reagents for duplicate tests on 42 individual patient serum samples (21 duplicate samples on 2 sequential plates). In this scenario, the cost of the test per patient would be £17.55 (excluding VAT). In practice, the cost of the test per patient will vary depending on the number of patient samples run per plate, using 1 kit. If fewer than 42 duplicate tests are run, a whole plate must still be used and so the cost per patient would increase. Additional costs include readily available laboratory consumables such as pipette tips, glass dilution and storage tubes, an incubating plate reader, and proprietary consumables purchased from the company if needed. Other costs

associated with the test include staff costs, maintenance contracts and additional quality assurance requirements.

Table 1 Current UK costs of the Fungitell test and optional components

Description	Cost (excluding VAT)	Additional information
Fungitell test kit	£737.05	Includes 2 microtiter plates and all reagents to run up to 42 tests.
Additional equipment supplied by the company if needed		
Certified beta-glucan-free pipette tips	£85.50 £96.35	1,000 microlitre tips (768 tips). 250 microlitre tips (960 tips). Purchased separately.
Certified beta-glucan-free glass dilution tubes	£11.75	50 tubes per pack. Purchased separately.
Biotek ELx808iu plate reader instrument	Price provided on an individual basis.	Usually based on a rental and kit purchase agreement with the company.
Annual service and calibration agreement for the Biotek ELx808iu plate reader	£1,200.00	Per year.

The company also provides onsite training including equipment installation, analyst training and data interpretation at no extra cost.

Costs of standard care

A range of diagnostic test methods may be used alongside medical history, clinical examination and assessment of risk to prescribe antifungal treatment for invasive fungal disease. The unit costs of microbiological tests at a reference laboratory range from £55 to £59 per patient sample. The cost per hour of a band 5 healthcare or biomedical scientist, who would carry out the test, is £33 to £35 ([Personal Social Services Research](#)

Unit, 2016).

Resource consequences

Five NHS centres and 2 public health laboratories currently use Fungitell in England and Wales and these numbers are understood to be increasing.

Fungitell would be used as an adjunct to current diagnostic procedures and represents additional acquisition and staff time costs. These costs could be offset if it led to a reduction in unnecessary use of antifungal therapy or antifungal-associated adverse events, such as allergic and gastrointestinal reactions. Adverse effects vary depending on treatment type: some drugs have predictable side effects or drug-to-drug interactions and need additional monitoring; others have few adverse effects. One specialist commentator stated that in their large UK tertiary referral teaching hospital (1,000 beds), they see antifungal-associated adverse events on a weekly basis. This is despite the fact that they conduct therapeutic drug monitoring on site and have a very experienced team advising on the use of antifungals. Severe adverse drug reactions are rare. Fungitell could also contribute to good antimicrobial stewardship. Antimicrobial stewardship is an important issue in healthcare and a number of guidelines have been published in relation to this (for example, NICE's guideline on [systems and processes for effective antimicrobial medicine use](#) and Public Health England's [start smart – then focus](#)).

Frequently prescribed antifungals include:

- anidulafungin (£299.99 per 100-mg vial)
- caspofungin (£416.78 per 70-mg vial; £327.67 per 50-mg vial)
- micafungin (£341.00 per 100-mg vial; £196.08 per 50-mg vial)
- fluconazole (£29.28 per 200-mg vial; price varies according to dosage and medicinal form)
- voriconazole (£460.32 for 28×200-mg tablets)
- liposomal amphotericin B (£821.87 for 10×50-mg vials).

The patent for caspofungin expired in April 2017 and generic versions may be available in the future, which would reduce any calculated cost saving. However it would not limit other benefits of reducing the unnecessary use of antifungal agents.

One economic study was identified from the literature search which evaluated the cost effectiveness of active BDG surveillance with pre-emptive antifungal therapy in patients admitted to adult intensive care units ([Pang et al. 2017](#)). The test used in this study was usually Fungitell. A Markov model was designed to simulate the outcomes of active BDG surveillance with pre-emptive therapy (surveillance group) and no surveillance (standard care group). Costs were higher in the BDG surveillance group compared to the standard-care group. The surveillance group had a lower candidiasis-associated mortality rate and lost fewer quality-adjusted life years than the standard-care group. The study concluded that BDG surveillance with pre-emptive therapy was cost effective. The study was based on the perspective of Hong Kong healthcare providers' results and therefore may not be generalisable to UK practice.

One conference abstract reported a resource impact study using Fungitell to stop antifungal treatment in a UK tertiary referral teaching hospital ([Richardson et al. 2015](#)). Following a 4-month study period, they reported that the monthly expenditure on antifungal therapy in the adult intensive care unit setting was reduced by €3,800, or £2,714 (using a historical conversion rate of £1=€1.40 from 30 June 2015).

Regulatory information

Fungitell was CE marked as an in vitro diagnostic device in June 2008.

A search of the Medicines and Healthcare products Regulatory Agency website revealed that no manufacturer field safety notices or medical device alerts have been issued for this technology.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

No equality considerations were identified.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the [interim process and methods statement](#). This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Four studies were identified that reported the use of Fungitell for antifungal treatment stratification. This included 1 prospective cohort study ([Nucci et al. 2016](#)), 2 retrospective cohort studies ([Posteraro et al. 2016](#), [Prattes et al. 2014](#)) and a randomised parallel pilot study ([Hanson et al. 2012](#)) in a total of 4,708 patients. One systematic review and meta-analysis was selected for inclusion on the basis of providing pooled diagnostic accuracy outcomes solely on the Fungitell test from the most recent and largest number of studies ([He et al. 2015](#)). None of the studies in the meta-analysis overlaps with the 4 primary studies selected for review in this briefing.

Overall assessment of the evidence

Overall, the evidence on utility and resource outcomes from the use of the Fungitell test for antifungal treatment stratification is of limited quality. Only 1 study ([Hanson et al. 2012](#)) included a comparator group, and no outcomes were compared between the antifungal strategies. Two studies ([Posteraro et al. 2016](#), [Prattes et al. 2014](#)) provided data from a real-world setting, but these were limited by their retrospective study design.

The primary studies applied strict inclusion criteria and had fairly small sample sizes. The studies were non-UK-based, primarily limited to adults at risk of candidaemia and single-centre studies. The study populations therefore may not be representative of the eligible population and results may not be generalisable to current NHS practice or other patient populations.

The systematic review and meta-analysis by [He et al. \(2015\)](#) reported the pooled diagnostic specificity (0.76; 95% confidence interval 0.74 to 0.78), which is a limitation of

the Fungitell test. False-positive results could contribute to the unnecessary prescription of antifungal treatment, or its unnecessary continuation.

The current evidence base suggests that Fungitell has the potential to improve current care pathways for patients with invasive fungal diseases. However, there is a need for randomised controlled trials to answer the question of whether BDG-based antifungal strategies could benefit patients in terms of efficacy, exposure to antifungal therapy and costs compared with other untargeted treatments.

Table 2 summarises the clinical evidence as well as its strengths and limitations

Table 2 Summary of the selected studies

<u>Nucci et al. (2016)</u>	
Study size, design and location	n=85 ICU patients at risk of developing candidaemia (57 BDG positive, 7 candidaemia, 21 negative). All patients were tested using blood cultures and BDG tests. Multicentre prospective cohort study in 4 tertiary care hospitals, Brazil.
Intervention and comparator(s)	BDG (Fungitell)-based stopping of empirical antifungal treatment. Three consecutive negative BDG results were considered negative for candidaemia, and antifungal therapy was stopped. BDG positive and candidaemia patients (confirmed by at least 1 positive blood culture) continued antifungal treatment. Single arm, no comparator.
Key outcomes	All 21 patients with baseline negative BDG stopped antifungal therapy on day 4, none of whom developed recurrent candidaemia during the follow up period of 30 days. However, 3 patients received another antifungal treatment after day 4 of the study. No patients developed recurrent candidaemia. The median durations of antifungal therapy for the BDG-negative group, BDG positive group and candidaemia group were 3, 10 and 14 days respectively (p<0.001).

<p>Strengths and limitations</p>	<p>The multicentre methodology provides a more generalisable population. Consecutive enrolment reduces the potential for selection bias. The outcomes were also prospectively defined.</p> <p>The modified prediction rule resulted in more selective criteria and only 4% of patients in the ICUs were eligible.</p>
<p><u>Posteraro et al. (2016)</u></p>	
<p>Study size, design and location</p>	<p>n=279 ICU patients at high risk of invasive candidiasis.</p> <p>198 met the eligibility criteria and were included in study – 63 were BDG positive (47 candidaemia, 16 probable candidaemia) and 135 were BDG-negative.</p> <p>Retrospective observational study in a tertiary care centre, Italy.</p>
<p>Intervention and comparator(s)</p>	<p>BDG (Fungitell) based diagnostic and therapeutic algorithm for antifungal treatment of invasive candida infection.</p> <p>Candidaemia was confirmed by blood cultures (proven candidaemia) or positive biomarkers such as BDG or mannan/antimannan plus high-risk factors (probable candidaemia).</p> <p>Single arm, no comparator.</p>
<p>Key outcomes</p>	<p>The median days of antifungal therapy in BDG positive patients was 10 compared to 5 in BDG-negative patients (p=0.04).</p> <p>In the non-candidaemia group, 135/151 patients were BDG-negative, however qualified for empiric antifungal treatment. Of these, only 25 received antifungal therapy, which would have reduced antifungal use from an estimated 89.4% to 16.5% (difference = 72.9%). Of these 25 patients, 14 patients had delayed BDG results and received antifungal therapy until negative BDG results became available.</p> <p>The therapeutic approach had little impact in the ICU mortality (112 out of 198 patients died with 21 deaths attributable to candida septicaemia).</p>
<p>Strengths and limitations</p>	<p>Large study population and retrospective analysis of prospectively collected data. This provides resource outcomes in a real-world setting for using Fungitell results to rule out invasive fungal disease.</p> <p>Definitions for patients requiring or not requiring antifungal therapy were unclear. It is unclear whether study outcomes were defined prospectively or retrospectively.</p>

<u>Prattes et al. (2014)</u>	
Study size, design and location	n=66 adult patients with suspected invasive fungal infections. Retrospective cohort study in a Medical University Hospital, Austria.
Intervention and comparator(s)	Measurement of BDG (Fungitell) in addition to routine diagnostic measures. Single-arm study, no comparator.
Key outcomes	Antifungal therapy was started in 40 patients. BDG results led to stopping systemic antifungal therapy in 13 patients, none of whom developed IFIs. In 26 patients, no antifungal therapy was started. BDG results led to starting antifungal therapy in 7 of these patients. Overall, BDG results confirmed the initial clinical decision in 46 patients (27 receiving antifungal therapy, 19 without). The test predicted 77% (10/13) of suspected, probable and proven IFI cases.
Strengths and limitations	The study provides some, although limited, clinical outcomes in a real-world setting for early stopping of antifungal therapy according to the BDG (Fungitell) results. A higher cut-off was used to define a positive BDG result in comparison to the manufacturer's protocol (120 pg/ml vs 80 pg/ml). The study is limited in terms of the retrospective nature and low sample size, particularly in candidaemia cases. No repeat testing was performed, except on indeterminate results.
<u>Hanson et al. (2012)</u>	
Study size, design and location	n=64 ICU patients at risk of invasive candidiasis (1 proven and 5 probable cases of invasive candidiasis). Single centre, randomised, non-blinded parallel group pilot study in a medical ICU, US.

Intervention and comparator(s)	<p>Pre-emptive antifungal therapy based on BDG (Fungitell) results (active surveillance group, n=47), compared with a standard care, empiric antifungal therapy group with physicians blinded to the BDG results (standard-care group, n=17).</p> <p>Two subjects in the active surveillance group were excluded because of icteric sera.</p>
Key outcomes	<p>Fungitell performed best when 2 sequential specimens used the ≥ 80 pg/ml cut-off value for a positive result. It had overall sensitivity, specificity, positive and negative predictive values of 100%, 75%, 30% and 100% respectively.</p> <p>Treatment with pre-emptive antifungal therapy had a significant effect on median glucan concentrations ($p < 0.001$) with a quicker decline compared to no antifungal therapy (slope: 2.7 vs -0.2, $p = 0.06$)</p> <p>Twenty-one subjects received pre-emptive therapy for a median duration of 13 days. In all, 10 (48%) subjects experienced 15 adverse events that were possibly related to the drug. No serious drug-related adverse events were observed.</p>
Strengths and limitations	<p>Effort was made to randomise patients in a 3:1 ratio to the active surveillance and standard-care groups.</p> <p>The sample size was not statistically based as no power calculations were performed. There were a small number of subjects with proven/probably invasive candidiasis primarily because of poor accrual. No comparisons were made between the active surveillance and standard-care groups. It was also evident that the pre-emptive protocol was not fully adhered to (86.7% of cases).</p>
<u>He et al. (2015)</u>	
Study size, design and location	<p>n=4,214 subjects from 28 studies (n=2,821 from 18 studies were specific to Fungitell in 7 case-control and 11 cohort studies).</p> <p>Systematic review and meta-analysis.</p>
Intervention and comparator(s)	<p>BDG tests, including Fungitell, Fungitec G-assay and Wako assay.</p> <p>Reference standards included EORTC/MSG criteria, histopathologic examination and microbiological culture.</p>

Key outcomes	<p>The pooled sensitivity, specificity and diagnostic odds ratio for the Fungitell test were 0.75 (95% CI 0.71 to 0.79), 0.76 (95% CI 0.74 to 0.78) and 11.50 (95% CI 6.56 to 20.15) respectively. The pooled AUC-SROC was 0.8855. When stratified analysis was done based on assay type, the AUC-SROC was 0.8514.</p> <p>The χ^2 and I^2 tests for heterogeneity of the 18 studies were 67 ($p < 0.00001$) and 75% respectively.</p> <p>They reported that the cut-off value of 60 pg/ml had better diagnostic accuracy than the 80 pg/ml cut-off value (AUC-SROC 0.8973 vs 0.8726) for the Fungitell test.</p>
Strengths and limitations	<p>Methods were clearly described, reproducible and appropriate to the clinical question.</p> <p>Studies included in the meta-analysis covered a range of different IFD diagnoses; therefore diagnostic accuracy results may not be generalisable to different types of infections. Pooled negative and positive predictive value results were not included. Only full-text and English-language studies were included, which may have led to an omission of relevant studies.</p>
<p>Abbreviations: AUC-SROC, area under the summary receiver operating curve; BDG, beta-D-glucan; CI, confidence interval; EORTC/MSG, European Organisation for Research and Treatment of Cancer/Mycoses Study Group, ICU, intensive care unit; IFD, invasive fungal disease; IFI, invasive fungal infection.</p>	

Recent and ongoing studies

- [Prospective Clinical Evaluation of Beta-D-Glucan Assay in Blood and BAL](#). ClinicalTrials.gov identifier: NCT01576653. Status: currently recruiting patients. Indication: invasive fungal infection. Devices: Fungitell assay.
- [Interest of Beta 1-3 D Glucan Assays in Screening for the Onset of Invasive Aspergillosis in Neutropenic Patients with Acute Leukaemia. \(BETA GLUCAN\)](#). ClinicalTrials.gov identifier: NCT02851680. Status: study has been completed. Indication: invasive fungal infections. Devices: Fungitell assay.

- A retrospective audit of the use of the Fungitell test in 3 intensive care units in 1 tertiary referral hospital in the UK ([Richardson et al. 2015](#)) was mentioned by 1 of the specialist commentators. The study reports both clinical and cost outcomes in 72 patients. This was presented as a conference abstract at Trends in Medical Mycology (TIMM) in 2015, and is intended for submission to a peer-reviewed publication.

Specialist commentator comments

Comments on this technology were invited from clinical experts working in the field. The comments received are individual opinions and do not represent NICE's view.

Two of the 4 specialist commentators said that they are currently using Fungitell routinely and 1 other was familiar with it.

Level of innovation

One specialist commentator considered the Fungitell test to be highly innovative and to have revolutionised antifungal stewardship in their intensive care units. Two other commentators considered the Fungitell test to have some innovative features, but commented that the concept of lab testing for invasive fungal disease is not novel.

One commentator considered that increasing use of PCR tests is beginning to supersede the Fungitell technology. However, most clinicians perceive that the current approach of having a low threshold for treating with antifungal drugs is safer than relying on laboratory tests that are not 100% accurate and not uniformly available across the NHS, or which may not offer acceptable turnaround times for results.

Potential patient impact

Commentators considered that patients who would particularly benefit from the technology would be patients in intensive care and immunocompromised patients.

One commentator advised that in a low-incidence setting, the test would allow antifungal treatment to be stopped safely. Two added that this would result in less exposure to toxic drugs, and could potentially lead to fewer blood tests, reduced side effects and reduced length of stay in hospital. They also considered that on occasion, the test could identify fungal infection earlier which would result in a better outcome and reduced mortality.

However, they indicated that the likely primary use of the test would be to limit the number of patients who are empirically prescribed antifungal treatment.

Potential system impact

Three commentators considered that the main potential system benefit of the Fungitell test is the safe reduction in antifungal treatment. One added that it makes the early start of empiric antifungal treatment based on clinical suspicion more affordable and another added that the potential for reduced antifungal drug use would reduce the opportunity for the development of antifungal drug resistance.

Two of the commentators thought that use of the test would lead to cost savings from the reduced use of antifungal drugs; with another stating that their centre has already generated significant cost savings from using the test. One added that use of the test could make savings by reducing hospital stays. However, 1 commentator highlighted that the test kit is expensive and not cost effective for individual hospitals because of the small number of test samples that would be run on each plate. Instead they thought it would be better suited to use in a reference laboratory, when the throughput of samples would be high enough to allow each plate to be run with the maximum number of samples.

Two commentators highlighted that the test would need additional staff and training costs and 1 commentator considered the test to be more expensive than ELISA tests currently used. Three of the commentators considered the test to be an addition to the current standard of care, however one considered the test would replace empiric antifungal treatment.

One specialist commentator highlighted that the test would have to be run in a glucan-free environment (for example, a molecular laboratory). Another advised that consideration needs to be given to providing space to accommodate the analyser, the turnaround times and how often the test will be done.

One specialist commentator highlighted that in their experience it is better to run the samples in triplicate, to avoid the need to re-run tests when the duplicate results are discordant. In this case one Fungitell kit (2 plates) can provide test results for a maximum of 28 patients, if testing in triplicate. Additional costs could also be incurred in the case of a batch failure because of whole plate contamination, which is not uncommon.

General comments

One specialist commentator considered that the greatest benefit from the Fungitell test would be if it were available on demand, with samples processed individually or in small batches. One commentator highlighted that BDG level is not routinely tested, but considered it would be beneficial if it was offered. Another commentator highlighted that additional evidence would be useful to address uncertainties in special patient groups such as neonates in intensive care, and people having extracorporeal membrane oxygenation or solid organ transplant, but that a lack of clinical expertise and confidence in evaluating test results could prevent Fungitell from being routinely adopted.

Specialist commentators

The following clinicians contributed to this briefing:

- Dr Riina Richardson, consultant in medical mycology and senior lecturer in infectious diseases and medical education, University Hospital of South Manchester and NHS Mycology Reference Centre Manchester; and Division of Infection, Immunity and Respiratory Medicine, Faculty of Biology, Medicine and Health, University of Manchester, UK. No conflicts of interest declared.
- Dr James Gray, consultant microbiologist, Birmingham Women's and Children's NHS Foundation Trust. No conflicts of interest declared.
- Dr Elizabeth Johnson, director of Public Health England Mycology Reference Laboratory. Dr Johnson received a one-off payment from BioRad for chairing a meeting on the utility of the *Aspergillus* galactomannan test at the TIMM conference 2015 in Lisbon.
- Ms Isha Rizal, advanced biomedical scientist and section leader, Newcastle-Upon-Tyne Hospitals. No conflicts of interest declared.

Development of this briefing

This briefing was developed for NICE by Newcastle and York External Assessment Centre. The [interim process and methods statement](#) sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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