

TABLE 1. PROFLOW GDH VERSUS EXPECTED RESULT.

|   | Positive                    | Negative |
|---|-----------------------------|----------|
| Positive  | (TP) 49                     | (FP) 2   |
| Negative  | (FN) 1                      | (TN) 41  |
| Sensitivity: $49/49+1 = 0.98$ (98%)   | NPV: $41/41+1 = 0.98$ (98%) |          |
| Specificity: $41/41+2 = 0.95$ (95%)   | PPV: $49/49+2 = 0.96$ (96%) |          |
| TN: true negative; TP: true positive; FN: false negative; FP: false positive. |                             |          |

TABLE 2. SENSITIVITY, SPECIFITY, NPV AND PPV FR PROFLOW GDH TO OTHER LATERAL-FLOW GDH TESTS.

|                 | ProFlow GDH | Techlab QuikChek | Premier Immunocard | Techlab QuikChek Complete |
|-----------------|-------------|------------------|--------------------|---------------------------|
| Sensitivity (%) | 98          | 93               | 83.2               | 91                        |
| Specificity (%) | 95          | 93               | 91.9               | 93                        |
| PPV (%)         | 96          | 79               | 66.2               | 76                        |
| NPV (%)         | 98          | 98               | 92                 | 98                        |

'Clostridium difficile is a Gram-positive, anaerobic, spore-forming bacillus that causes severe diarrhoea and other intestinal disease'

recommendations with regard to testing algorithms, and a document has been released recently in relation to this, as an infection control advisory notice. This document recommended glutamate dehydrogenase (GDH) as a screening tool for the diagnosis of *C. difficile*.

### Lateral-flow evaluation

This study evaluated the sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) of a new lateral-flow GDH test (ProFlow GDH, Pro-Lab Diagnostics) for its ability to detect CDI in the faeces of patients with diarrhoea, and to evaluate its use as a primary screening method for the diagnosis of CDI.

ProFlow *C. difficile* GDH is a qualitative lateral-flow immunoassay for the detection of GDH antigen in stool. The assay uses antibodies specific to GDH coated on the membrane in the test line. During testing, the GDH present in the stool specimen reacts with the anti-GDH antibody (conjugated with gold particles) and migrates up the membrane by capillary action. This in turn reacts with the anti-GDH coated on the test line. The presence of a coloured 'test' line (T) indicates a positive result, while absence of colour indicates a negative result (Fig 1). To serve as a procedural control, a colour will always appear on the control line (C).

### Sample collection


This study was conducted for Pro-Lab Diagnostics. Samples were obtained from leading microbiology laboratories, with each sample tested according to the standard laboratory algorithm, consisting of a GDH screen and molecular test to confirm (data available on request).

### Results comparison

A total of 93 samples of known result were tested (43 negatives, 50 positives) and the ProFlow GDH produced two false positives and one false negative (Table 1). A UK National External Quality Assessment Scheme (NEQAS) sample was also tested and this produced the expected positive result. Table 2 shows the results of a comparison of sensitivity, specificity, NPV and PPV between ProFlow GDH and other lateral-flow GDH tests available on the market.

### Simple and accurate screening

The results show ProFlow GDH from Pro-Lab Diagnostics has the qualities to be a useful screening tool to aid in the diagnosis of *C. difficile*. ProFlow GDH is a simple and accurate test that can be used in conjunction with other products from Pro-Lab Diagnostics (eg ProFlow C.diff Tox A-B, Prolisa C.diff GDH EIA) to satisfy the recommendations of the DH/ARHAI Guidance on the Diagnosis and Reporting of *Clostridium difficile*.

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# Evaluation of a lateral-flow GDH test to screen for *Clostridium difficile* infection

*Clostridium difficile* has gained notoriety as a hospital 'superbug', which has led to strict monitoring and controls on infection rates for hospital trusts. Accurate diagnosis, effective infection control and the use of good screening tools is a major contributor to success, as Charlotte Duncan explains.

*Clostridium difficile* is a Gram-positive, anaerobic, spore-forming bacillus that causes severe diarrhoea and other intestinal disease and is a major nosocomial pathogen resulting in high rates of morbidity and mortality.<sup>1-13</sup> It is the most serious cause of antibiotic-associated diarrhoea (AAD) and has been associated with a range of symptoms.<sup>2</sup> Major risk factors include: antimicrobial therapy, age ( $\geq 65$  years), immunosuppression, nasogastric intubation and antinuclear medication.<sup>2</sup> Asymptomatic carriage, mild watery diarrhoea, pseudomembranous colitis (PMC), toxic megacolon and ultimately death are all possible outcomes of

exposure to the organism.<sup>3</sup>

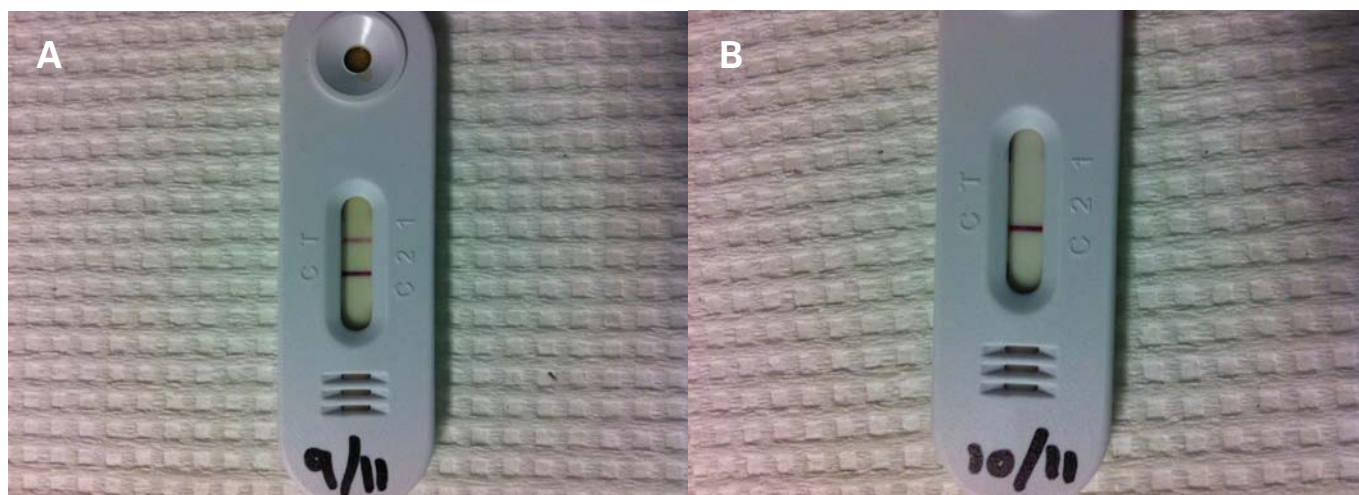
Symptoms may appear immediately following antimicrobial therapy or several weeks after therapy is completed.<sup>2</sup> The main feature of *C. difficile* infection (CDI) is diarrhoea, defined as loose stools two or three times in 24 hours,<sup>6</sup> with stools having a typical malodorous smell.<sup>3</sup> In those who develop CDI, clinical features can vary considerably, from mild diarrhoea to life-threatening PMC.<sup>5</sup>

The clinical manifestations and pathological changes associated with CDI are attributed to the production of two exotoxins (toxins A and B) that have enterotoxic and cytotoxic properties,

respectively.<sup>4</sup> These toxins can be found in the faeces of 15–25% of patients with antibiotic-associated diarrhoea and in more than 95% of patients with PMC.<sup>2</sup>

Mild cases of *C. difficile* infection can often be cured by discontinuing the antibiotics responsible.<sup>13</sup> In more serious cases, oral administration of metronidazole and, if that fails, then vancomycin are currently the treatments of choice. Relapses of *C. difficile* AAD have been reported in up to 20% of cases.<sup>13</sup>

Accurate diagnosis of CDI is critical to patient management and control of the spread of infection. It is also necessary for monitoring the disease trends and tracking infection patterns, as well as monitoring the efficacy of intervention methods. Laboratory diagnosis of *C. difficile* has depended on the demonstration of TcdA or TcdB,<sup>8</sup> and various tests are available. However, with raised public awareness and the prospect of financial penalties, laboratories are balancing accuracy, sensitivity, specificity with cost to produce the most effective testing algorithm. The Department of Health will soon to be releasing guidelines and



Results obtained with the ProFlow GDH lateral-flow test: a) positive; b) negative.