This publication was withdrawn on 13 May 2025

This guidance has been withdrawn because it’s out of date.

For information on the investigation, diagnosis and reporting of Clostridioides difficile infection, see the Royal College of Pathologists’ UK Standards for Microbiology Investigations - B10 Investigation of faecal specimens for Clostridioides difficile.

For current information on surveillance, see the Mandatory Enhanced Surveillance Protocol, linked under the ‘Support’ tab of ‘Help and support’ on the HCAI Data Capture System page.

UPDATED GUIDANCE ON THE DIAGNOSIS AND REPORTING OF *CLOSTRIDIUM DIFFICILE*

DH INFORMATION READER BOX

Policy	**Clinical**	Estates
HR / Workforce	Commissioner Development	IM & T
Management	Provider Development	Finance
Planning / Performance	Improvement and Efficiency	Social Care / Partnership Working

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Author	DH/HCAI/ infectious disease
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Description	This guidance provides healthcare providers with a new testing and diagnosing protocol for C. difficile. Specifically, the guidance identifies which two types of tests, when used in combination, will deliver the most accurate results for C. difficile infection.
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Contents


DH
Department
of Health
NHS

Executive summary

- **This revised guidance to healthcare providers identifies which two types of tests, which when used in combination, will deliver the most accurate results for *C. difficile* infection testing.**

- The new guidance reflects the results of scientific research, which assessed the accuracy and applicability of various types of testing kits for *C. difficile* currently in use in the NHS. The purpose of the revised guidance is to strengthen the *C. difficile* testing, diagnosing and reporting arrangements.

- The guidance includes a testing algorithm that provides a step-by-step means of optimising performance, with the ability to clinically categorise patients with much greater accuracy. It sets out:

  (a) who should be tested and the type of samples that should be taken;

  (b) the types of tests that should be used for detecting infections; and

  (c) what healthcare providers should do, depending on the outcome of the tests.

Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI)

UPDATED GUIDANCE ON THE DIAGNOSIS AND REPORTING OF *CLOSTRIDIUM DIFFICILE*

March 2012

UPDATED DH/ARHAI GUIDANCE ON THE DIAGNOSIS AND REPORTING OF *CLOSTRIDIUM DIFFICILE*

In 2009, a report by the NHS Centre for Evidence Based Purchasing[1] raised concerns regarding the accuracy and effectiveness of the *C. difficile* testing kits that are available to healthcare providers for the diagnosing of infections. The Department responded by issuing guidance advocating the use a two-test protocol. It also commissioned a study to review the effectiveness of the many available types of test kits, with a view to identifying the combination of tests that produce the most reliable results.

Assays were chosen to represent the three main *C. difficile* detection options in use in the NHS: toxin enzyme immunoassays (EIAs), toxin gene (NAAT or PCR) and glutamate dehydrogenase (GDH) EIA.

The selected commercial assays for the laboratory detection of *C. difficile* and diagnosis of CDI were included in an observational diagnostic study, involving four NHS laboratories, to determine the accuracy of testing algorithms using routinely submitted diarrhoeal faecal samples.

The study concluded that:

- *C. difficile* toxin EIAs are **not** suitable as stand alone tests for the diagnosis of CDI or detection of *C. difficile;* and

- that a combination of two tests, the first of which should be a NAAT or GDH EIA followed by a sensitive toxin EIA test.

The outputs from this study have been considered by ARHAI and used to update the guidance to healthcare providers. The new guidance aims to promote more effective and consistent diagnosis, testing and treatment of *C. difficile* infection (CDI). It includes an algorithm that combines optimised performance with the ability to clinically categorise patients into one of three groups (i.e CDI likely to be present; potential *C. difficile* excretor; and CDI unlikely to be present).

The full study report including other aspects of laboratory diagnosis will be reported elsewhere. A summary of the main research findings is attached at **Annex A.** The updated guidance is attached at **Annex B.**

[1] NHS centre for Evidence Based Purchasing, Evaluation report *Clostridium difficile* toxin detection assays CEP08054, February 2009

Annex A

Summary of research findings: Defining a testing algorithm to improve mandatory reporting of laboratory detection of *C. difficile*

Purpose of study

The HPA co-ordinated the research to carry out an observational diagnostic study in four NHS laboratories using routinely submitted diarrhoeal faecal samples (n = 12 441) which were examined for evidence of *C. difficile*. The large sample size enabled high precision determination of the accuracy of testing algorithms, using selected commercial assays for the laboratory detection of *C. difficile* and diagnosis of CDI.

Tests used in the study

Assays were chosen to represent the three main *C. difficile* detection options in use by the NHS: toxin enzyme immunoassays (EIAs), toxin gene (NAAT or PCR) and glutamate dehydrogenase (GDH) EIA, and compared with two reference tests (cytotoxin and cytotoxigenic culture).

In order to understand and optimise the use of algorithms, the researchers identified the relative clinical values of the two reference tests for *C. difficile* (cytotoxin and cytotoxigenic culture) by determining their relationships with patient outcomes (30-day mortality and morbidity-associated laboratory measurements).

Findings

It was confirmed that *C. difficile* toxin EIAs are not suitable as stand alone tests for the diagnosis of CDI or detection of *C. difficile***.** The two commonly used toxin EIAs included in this study were not equivalent. For further information please see the summary of the research at:
http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/ClostridiumDifficile/Guidelines

Importantly, the presence of toxin, determined by a reference method cytotoxin assay, was significantly associated with a poor clinical outcome. Conversely, culture of toxigenic *C. difficile* in the absence of toxin (i.e. cytotoxigenic culture positive, cytotoxin negative) was not associated with any significant clinical outcome worse than that of *C. difficile* negative samples. However, such samples with *C. difficile,* but no demonstrable toxin, can indicate potential *C. difficile* excretors, and this may aid infection prevention and control measures.

Conclusion

The study findings resulted in an algorithm which combines optimised performance with the ability to clinically categorise patients. It contains a two test screening protocol comprising a GDH EIA (or NAAT/PCR) followed by a sensitive

toxin EIA. If the first test (GDH or NAAT) is negative, the second test (sensitive toxin EIA) does NOT need to be performed. A third test (e.g. NAAT or PCR) may be optionally added to the algorithm to further identify samples from potential *C. difficile* excretors.

Interpretation of the test results

- If GDH EIA (or NAAT) positive, and toxin EIA positive (PPV = 91.4%), then C. *difficile* is most likely to be present and a case associated with poor outcome. Result must be *included in mandatory reporting;*
- If GDH EIA (or NAAT) positive, and toxin EIA negative, then *C. difficile* could be present i.e. potential *C. difficile* excretors – *do not include in mandatory reporting*;
- If GDH EIA negative, and toxin EIA negative (NPV = 98.9%) then *C.difficile* or CDI is very unlikely to be present – *do not include in mandatory reporting*.

PPV = Positive Predictive Value

NPV = Negative Predictive value

No test or combination of tests is infallible and the clinical condition of the patient should always be taken into consideration when making management choices. A full study report including other aspects of laboratory diagnosis, including analyses of individual tests and outcome data, will be reported elsewhere.

Annex B

UPDATED DH /ARHAI GUIDANCE ON THE DIAGNOSIS AND REPORTING OF *CLOSTRIDIUM DIFFICILE*

The 2009 DH guidance on the diagnosis and reporting of *Clostridium difficile* has been updated to reflect:

1. **The latest evidence on the combination of currently available *C. difficile* test kits likely to provide the most accurate result and;**

2. **Advice from the Department's Advisory Committee on Antimicrobial Resistance and Healthcare Associated infections (ARHAI). It supersedes all previous guidance on the laboratory diagnosis of *C. difficile* infection (CDI) and reporting of *C. difficile* to healthcare providers.[2]**

This updated guidance seeks to provide a clearer steer on the aspects which should feature in local diagnostic algorithms and reporting to the mandatory surveillance scheme. It is intended to help with reporting rather than patient management and **does not** cover relapses or re-infections.

Wider guidance on developing policies for the care and treatment of individual cases of CDI, managing outbreaks, and helping to promote antimicrobial stewardship and development of effective antibiotic prescribing policies are contained in '*Clostridium difficile infection*: How to deal with the problem'.

The Department of Health recommends that all healthcare providers move to a diagnostic algorithm consistent with the advice set out in this guidance <u>from April 2012</u>.

[2] "Bug-alert" to the NHS (27 March 2009) by the (then) Department of Health Inspector of Microbiology and Infection Control, Professor Brian Duerden;
- DH advice on the accuracy of *Clostridium difficile* toxin detection kits (March 2009); weblink:www.hpa.org.uk/hpr/archives/2009/news1209.htm)
- HPA *C. difficile* Diagnosis Working Group: *Questions and answers about the laboratory diagnosis of C. difficile infection* (March 2009); weblink: http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1238055363795),- Professor Brian Duerden, An Inspector Calls, British Infection Society/Association of Medical Microbiologists newsletter (March 2010);weblink:www.britishinfection.org/drupal/content/bisamm-newsletter)'
- CNO letter *Diagnostic testing for Clostridium difficile infection* (27 March 2011); weblink www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/dearcolleagueletters/DH_125110.

UPDATED DH /ARHAI GUIDANCE ON THE DIAGNOSIS AND REPORTING OF *CLOSTRIDIUM DIFFICILE*

This guidance relates to research findings for assays which represent the main three *C. difficile* detection options in use by the NHS: toxin enzyme immunoassays (EIAs), toxin gene (NAAT or PCR) and glutamate dehydrogenase (GDH) EIA.

STEP 1: Who to Test and Taking Samples

If a patient has diarrhoea (Bristol Stool Chart types 5-7) that is not clearly attributable to an underlying condition (e.g. inflammatory colitis, overflow) or therapy (e.g. laxatives, enteral feeding) then it is necessary to determine if this is due to CDI. Stools from all such symptomatic patients should be collected as early as possible, given that the results of testing may be used to minimise *C. difficile* transmission risk; waiting to initiate sampling/testing until, for example, at least 3 episodes of diarrhoea have occurred is NOT recommended, as this delay may increase the risk of *C. difficile* transmission.

Diarrhoeal samples should be tested for *C. difficile* from hospital patients aged ≥2 years, all community patients aged ≥65 years, and from community patients aged <65 years, wherever clinically indicated[§]. The stool sample must take on the shape of the container and ideally be at least ¼ filled (to indicate the patient has diarrhoea) before it is sent to the laboratory for testing. If in doubt, please seek advice for example from your microbiologist, Director of Infection Prevention and Control or your Infection Prevention and Control Team**.**

In suspected cases of 'silent CDI' such as ileus, toxic megacolon or pseudomembranous colitis without diarrhoea, other diagnostic procedures, such as colonoscopy, white cell count (WCC), serum creatinine and abdominal computerised tomography (CT) scanning, may be required, potentially with referral to a gastroenterologist or gastrointestinal surgeon.

STEP 2: Testing

C. difficile toxin EIAs are **not suitable as stand alone tests** for the diagnosis of CDI or detection of *C. difficile*.

The Department and ARHAI advise that organisations adhere to a two stage testing approach which consists of a GDH EIA (or a NAAT or PCR) test to screen samples, followed by a sensitive toxin EIA test (or a cytotoxin assay[1]). If the first test (GDH or NAAT) is negative, the second test (sensitive toxin EIA) does NOT need to be performed[2].

[1]Note: a cytotoxin assay (the reference method) yields slower results and this needs to be taken into account when making management and infection control decisions.
[2]Note: To further clarify samples from potential C. difficile excretors, colleagues may wish to add an optional third test (e.g. NAAT or PCR).

§ "Community patients" includes mental health patients where relevant.

STEP 3: Interpreting Testing Results

The following actions should be taken depending on the test result:

Result of 2 Test Algorithm[1]	**Interpretation**	**Include in Mandatory Reporting to HPA[2]**
GDH EIA (or NAAT) positive, toxin EIA positive	CDI is likely to be present	Yes
GDH EIA (or NAAT) positive, toxin EIA negative	*C. difficile* could be present, so may have transmission potential. Patient could be potential *C. difficile* excretor.	No, but may be suitable for local reporting.
GDH EIA (or NAAT) negative, toxin EIA negative	*C. difficile* or CDI is very unlikely to be present, so may have transmission potential. Patient could have other potential pathogens.	No

Note [1]: A cytotoxin assay may be considered as an alternative to a sensitive toxin EIA, but it yields slower results and this will need to be taken into account in making decisions about infection control.

Note [2]: unless a repeat sample within 28 days. Please refer to the Mandatory Surveillance Protocol for full case definition and further information.

It must be remembered that no test or combination of tests is infallible and the clinical condition of the patient should always be taken into consideration when making management and treatment choices.

The recommended steps to achieve effective diagnosis, testing, reporting and treatment of *C difficile* Infection are summarised in the attached flowchart.

Algorithm for Management of a Patient with Unexplained Diarrhoea
Suspected Clostridium difficile infection (CDI)

If a patient has diarrhoea (Bristol Stool Chart types 5-7) that is not clearly attributable to an underlying condition (e.g. inflammatory colitis, overflow) or therapy (e.g. laxatives, enteral feeding) then it is necessary to determine if this is due to CDI. If in doubt please seek advice.

This pathway relates to the diagnosis of CDI. Patients should be considered for treatment of CDI *before* test results are available, particularly if symptoms / signs indicate severe infection. Patients with suspected infectious diarrhoea should be isolated to prevent the transmission of *C. difficile*, norovirus or other transmissible pathogens.

Ideally isolate patient in a single room - if unable to do this within 2 hours escalate the problem.

Collect stool specimen & send to Microbiology
In order for the specimen to be processed for *C. difficile* the sample must take on the shape of the container and ideally be at least ¼ filled (to indicate the patient has diarrhoea).

Diarrhoeal samples should be tested for *C. difficile* from:
* hospital patients aged ≥2 years, and,
* community patients, aged ≥65 years, and
* community patients aged <65 years wherever clinically indicated.

GDH EIA (or NAAT) positive, toxin EIA or cytotoxin positive:
CDI is likely to be present,
- for mandatory reporting to HPA;*

OR

GDH EIA (or NAAT) positive, toxin EIA negative:
C. difficile could be present i.e. potential *C. difficile* excretor,
- not for mandatory reporting *(but may have transmission potential and be suitable for local reporting)*;

OR

GDH EIA (or NAAT) negative, toxin EIA negative: C. difficile or CDI is very unlikely to be present,
- not for mandatory reporting *but may have transmission potential (other pathogens)*

*** Please note other indications for mandatory reporting of CDI at:**
http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1179746015058
NB: A cytotoxin assay may be considered as an alternative to a sensitive toxin EIA, but it yields slower results and this will need to be taken into account when making management decisions on infection control.

Refer to the following local policies:
- Remember the **SIGHT** list (see bottom of page)
- *Clostridium difficile* Infection Policy
- *Clostridium difficile* Treatment Guideline
- Source Isolation Policy
- Source Isolation Cleaning Policy
- Inform patient, relative/carer of test result

Consider other causes of diarrhoea.
Consider continuation of single room isolation and other measures to reduce risk of CDI.

Consider other causes of diarrhoea; if not infective may consider ending single room isolation.

S	Suspect that a case may be infective when there is no clear alternative cause for diarrhoea
I	Isolate the patient within 2 hours
G	Gloves and aprons must be used for all contacts with the patient and their environment
H	Hand washing with soap and water should be carried out before and after each contact with the patient and the patient's environment
T	Test the stool for *C. difficile* by sending a specimen immediately

Glossary of Key Terms

CDI
Clostridium difficile infection.

Cytotoxin
Reference test for the presence of *C. difficile* toxins.

EIA
Enzyme immunoassay that detcts the presence of toxins.

GDH
A glutamate dehydrogenase (GDH) test detects an antigen that is produced in high amounts by *C. difficile*, both toxin and non-toxin producing.

NAAT
Nucleic Acid Amplification Test that detects the presence of toxin gene(s).

PCR
Polymerase Chain Reaction test (a type of NAAT).

Toxin test
A toxin test is used to detect the presence of *C. difficile* toxin(s) that are specific for C. difficile colitis / pseudomembranous colitis.

Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI)

UPDATED GUIDANCE ON THE DIAGNOSIS & REPORTING OF *CLOSTRIDIUM DIFFICILE*

FAQS FOR USERS OF THE GUIDANCE

March 2012

1. My Trust has a good CDI record. Why do we need to switch to a new test protocol?

- New research has shown that using *C. difficile* toxin enzyme immunoassays (EIAs) are not wholly reliable as stand-alone tests for the diagnosis of *C. difficile* infection or the detection of *C. difficile*. The most effective testing regime is to use a two test system which improves the specificity and accuracy of testing.

2. My Trust has already invested in other test protocols. What should we do?

- The Chief Nursing Officer's letter of March 2011, highlighted that research was being undertaken to assess the accuracy of the existing testing kits. Organisations were encouraged to wait for the outcome of the research before taking a decision on which of the tests to use.

- The latest scientific evidence shows that the most effective protocol was a combination of two tests, one of which should be a glutamate dehydrogenase (GDH) EIA or toxin gene test (NAAT), followed by a sensitive toxin EIA test. The new guidance draws on this scientific evidence. We expect organisations to review their approach in the light of the new guidance, and alter their practices accordingly.

3. What do you mean by "a sensitive toxin EIA test"?

- The research on which the revised guidance is based explains that *C. difficile* toxin EIAs are not suitable as stand alone tests for the diagnosis of CDI or detection of C. difficile. The two commonly used toxin EIAs included in this study were not equivalent. For further information please see the summary of the research at:

http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/ClostridiumDifficile/Guidelines/

4. Will there be an impact of the new testing protocol on numbers of reported cases of *C. difficile*?

- Based on the research undertaken for the guidance, and additional analysis by DH, the estimated general *true prevalence* (i.e. the percentage of all the samples tested that are *truly* positive) for the 12 months ending September 2011 is likely to be somewhere between 2 % and 3 %.

- For this period, a true prevalence of 2.5 % would mean that the expected number of positives recorded under the new test, if it had been *applied to the same samples taken in the above period*, would have been 16,461 positive cases.

- This would correspond to a reduction of 3,339 cases on the 19,800 positive cases actually recorded for the period. This is a 17% reduction. It is a one-off reduction applicable to this year's data, if all trusts had been using the new test for the full 12 months, instead of their existing tests. In other words, it

gives some idea of the likely reduction that will result purely from the change in testing, once *all* trusts have actually changed to the new test.

5. Will this new protocol affect my organisation's *C.difficile* Objective for 2011/12?

- No. The new testing protocol will have no impact on the figures for 2011/12. The protocol will only come into effect in April 2012, i.e. after the reporting period.

6. What will happen if my Trust fails its *C. difficile* infection objective because we were forced to change over to the new tests?

- Where there has been a breach in an organisation's *C. difficile* objective, and where the whole amount of that breach can be shown to be as a direct result of introducing the new testing regime, and not due to poor clinical practice, an organisation should not be penalised. We have provided Commissioners with a "Ready Reckoner" to help them in assessing the breaches. The "Ready Reckoner" was also shared with SHAs in September 2011.

7. Will we need to take the new guidance into account when reporting *C. difficile* infection figures from April 2012?

- Yes. The new guidance comes into effect from April 2012. Therefore, the CDI figures for the new reporting period from April will reflect the new testing system.

8. What are the implications for organisations that are using GDH followed by PCR testing for *C.difficile*?

- PCR (Polymerase chain reaction) kits are included in the guidance (NAAT is another term for PCR), i.e. GDH (or NAAT) followed by toxin test. But a testing algorithm comprising GDH followed by PCR is not supported by the latest research.

9. Is it acceptable to use a cytotoxin test instead of a sensitive toxin EIA?

- Yes, it is acceptable to use a neutralised cell cytotoxin test instead of a sensitive toxin EIA as part of the recommended two-stage algorithm. In DH/HPA evaluations, the cytotoxin test was more sensitive than the toxin EIAs. Clearly, the cytotoxin assay yields slower results than the toxin EIA, and this needs to be accounted for when making management and infection prevention decisions regarding suspected CDI cases.

10. The guide recommends a two-stage testing mechanism. But is a one-stage mechanism OK for negative samples, as long as the highly sensitive GDH test is used?

- If the first test is negative, the second test does NOT need to be performed; this is implicit in any laboratory testing algorithm, which is based on a screening

test, i.e. if the screening test is negative then the sample is negative (at the 'first hurdle'). Given that the great majority of samples will be negative by the first test, it is unnecessary to perform a second test.

11. How much will this new testing protocol cost my Trust?

- We cannot comment on specific healthcare providers. However, overall, across all the NHS, we estimate the change to be broadly cost neutral.

12. In the algorithm, what do you mean by "escalate the problem" if unable to isolate a potential patient within two hours? Does it mean the problem is likely to escalate due to transmission risk, or that an isolation room must after this time immediately be ready?

- The intention of the guidance is to raise awareness of certain aspects relating to the management of a patient with unexplained diarrhoea. Specific judgements about the likelihood of infectivity and risk of transmission of a particular patient are a matter for clinicians at local level. The new testing regimen does allow the identification of those who could be a source of *C. difficile* and therefore be a potential risk to other patients.

13. If a community sample tests positive, who reports this?

- If a GP suspects a patient has *C. difficile* he/she would send a sample to a laboratory, which will be based in an NHS trust/accredited laboratory. The lab will report the result to the GP who would inform the patient.

- It is mandatory that all acute NHS Trusts in England report all cases of *C. difficile* in patients aged 2 years and over. This applies whether the *C. difficile* is considered to have been acquired in that Trust, in another hospital, or in the community (e.g. in healthcare facilities, a nursing home, residential care facilities, or from patients at home).

14. The current primary care HPA advice on definition of diarrhoea is: 3 or more episodes a day, <14 days apart (NB this should not be confused with the definition of an episode of CDI for the purposes of mandatory reporting to the HPA which is 28 days) and the sample takes the shape of the container
(http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/ClostridiumDifficile/Guidelines
Can you have a 'diarrhoeal illness' after just one episode?

- The frequency of diarrhoea varies in definitions of CDI. Usually, definitions cite the need for at least 3 episodes of diarrhoea, for at least 2 consecutive days. Such a stringent definition is appropriate for clinical trials, but less so in a setting where transmission of infection is a concern. In primary care (excluding institutions such as nursing homes), it is reasonable to use the more stringent definition of CDI; in practice, patients would very rarely consult their GP for diarrhoea comprising 1-2 episodes per day, unless perhaps this continued for several days. Conversely, in the healthcare setting, using a single episode of unexplained diarrhoea as the threshold to instigate testing

and pre-emptive patient isolation is reasonable. Whichever the scenario, some flexibility is required to ensure that unexplained diarrhoea is appropriately investigated and managed, especially in high risk individuals.

15. How long is "an episode"?

- An episode of CDI is 28 days, with day 1 being the date of specimen collection.

16. Should all patients with diarrhoea in the community setting be tested?

- The current HPA guidance covers when to investigate patients in the community with unexplained diarrhoea (http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1203582652789). Whenever a diarrhoeal sample is submitted, relevant clinical details should be supplied, e.g. antibiotic, travel, diarrhoea contact histories. Without such information, it cannot be assumed that laboratories will test a faecal sample from a person in the community for evidence of CDI.

17. What stools should be tested for *CDI*?

- If a patient has diarrhoea (Bristol Stool Chart types 5-7) that is not clearly attributable to an underlying condition (e.g. inflammatory colitis, overflow) or therapy (e.g. laxatives, enteral feeding) then it is necessary to determine if this is due to *C. difficile*. The stool sample must take on the shape of the container and ideally be at least ¼ filled (to indicate the patient has diarrhoea) before it is sent to the laboratory for testing. If in doubt, please seek advice for example from your microbiologist, Director of Infection Prevention and Control or your Infection Prevention and Control Team.

- All diarrhoeal samples from hospital patients aged ≥2 years and, as a minimum, all diarrhoeal samples from those aged ≥65 years in the community where clinically indicated should be tested. In suspected cases of 'silent CDI' such as ileus, toxic megacolon or pseudomembranous colitis without diarrhoea, other diagnostic procedures, such as colonoscopy, white cell count (WCC), serum creatinine and abdominal computerised tomography (CT) scanning, may be required, potentially with referral to a gastroenterologist or gastrointestinal surgeon.

18. Should positive specimens from the same patient and the same episode be reported?

- No, only report a second positive from the same patient if it is defined as a new episode, as described elsewhere in these FAQs.

19. Do I need to report cases in patients aged under 2 years?

- Cases in patients aged under 2 years need not be reported as part of the mandatory surveillance. However, Trusts may use the system to record these cases if they so wish. These will be excluded from data for publication.

20. Do I need to report positive specimens from deceased patients?

- Yes, positive specimens from deceased patients should be reported as part of the mandatory surveillance.

21. Does the combined 'quikchek test' (GDH & Toxin) count as a 1 or 2 stage test i.e. is the sensitivity of the toxin component of the combined test as good as the sensitivity of the stand alone EIA Toxin test?

- This test was not evaluated and it cannot therefore be assured that it is equivalent to the GDH and/or toxin EIAs that were examined.

22. If the quikchek combined is acceptable as a 2-stage test, can we assume that GDH positive and Toxin positive results from the combined test should be reported to mandatory surveillance?'

- This test was not evaluated and it cannot therefore be assured that it is equivalent to the GDH and/or toxin EIAs that were examined.

23. Do all *C. difficile* toxin positive results need to be reported on the MESS system (MRSA Enhanced Surveillance System) irrespective of the GDH result?

- The revised guidance covers a two stage test. Only if it is positive on both tests does it need to be recorded. (Please see the algorithm in the guidance).

24. The guidance says "...not for mandatory reporting (but may have transmission potential and be suitable for local reporting)". What is meant by local reporting and what would anyone outside the Trust do with these results?

- Local reporting includes the potential to report to clinicians/wards/directorates. Local commissioners may find such information of value in determining the appropriateness of local care pathways.

25. Do I need to report positive specimens that come from patients not located within a hospital at the time of testing, or taken on admission?

- Yes, all cases of CDI that conform to the case definition must be reported, regardless of where or when the specimen was collected.

26. Do I need to report positive specimens from Welsh patients diagnosed in English laboratories?

- Yes, all cases of CDI that conform to the case definition must be reported even if they are from Welsh patients tested/diagnosed in an English laboratory.

27. Do I need to report positive specimens sent from the Independent Sector (private hospital)?

- Yes, all cases of CDI that conform to the case definition must be reported, regardless of where the specimen originated from.

28. Where can I find out more about mandatory surveillance?

- More information is available at:
http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1179746015058

29. Is the revised guidance mandatory?

- The revised guidance is based on the latest research on *C. difficile* testing. Organisations are therefore strongly advised to follow the guidance. The Care Quality Commission (CQC) recognises that healthcare-associated infections, including *C. difficile*, are a patient safety issue.

- The Code of Practice for the prevention and control of infection and related guidance sets out the 10 criteria against which a registered provider will be judged, and on how it complies with the registration requirement for cleanliness and infection control. Providers of healthcare should have policy in place for diagnostic criteria for CDI. If a provider does not follow the new guidance, they will need to provide the CQC with a valid assessment showing how their methodology improves patient safety and care, over and above the guidance.

30. Will a comparison of all commercially available kits be available?

- The researchers did not assess *all* commercially available kits in the present study. However, a larger number of kits were assessed previously and published as a CEP evaluation and in a peer-reviewed journal (Planche et al., Lancet Infect Dis. 2008;8: 777-84). At that time, this was the largest study of its kind. The present study recruited more than 20 times more patients (in order to be able to accurately distinguish between tests and combinations), and so had to reduce the number of tests examined. The results will be published in a peer-reviewed journal.

31. Where is the evidence base to move away from the established definition of diarrhoea?

- The definitions referred to have been in wide practice in the NHS at least since the publication of DH/HPA CDI guidance ("*Clostridium difficile* infection: How to deal with the Problem", January 2009). As explained in these FAQs, the definition is intended to minimise the chance of missing infection and transmission of pathogens to other patients.

32. Where can I find out more about *C.difficile* testing and diagnosis?

- The Health Protection Agency website contains more guidance, with questions and answers about the laboratory diagnosis of *Clostridium difficile* infection. Visit the website:

http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/ClostridiumDifficile/Guidelines

33. Where can I find out more about the research on which the new guidance is based?

- The research study was commissioned in 2009 to review the effectiveness of the many available types of test kits, with a view to identifying the combination of tests that produce the most reliable results. The research and the guidance has been assessed by the Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infections. The research will be published in a peer-reviewed journal. A summary of the research is available at:

http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/ClostridiumDifficile/Guidelines

34. Was a cost-benefit analysis undertaken?

Yes. The analysis by the HPA shows that overall, estimated costs associated with CDI testing by either of two single toxin EIAs or by the new algorithm were similar. More details on the analysis are attached to these FAQs.

35. Who should I contact in DH if I have any queries about the guidance?

- Please email: Mike.DeSilva@dh.gsi.gov.uk

Estimated basic costs and effects of changes to *C. difficile* laboratory testing

- If we assume that an average laboratory is currently using one test (toxin EIA 1 or 2) for the laboratory diagnosis of CDI cases. The new recommended algorithm includes an additional test (e.g. GDH EIA).
- Cost of additional GDH EIA = £3 (+ automation) + labour = £5-10 (depending on local non-consumable costs).
- Average number of tests per laboratory in England = 4200.[1] Approximately 70 trust associated CDI cases per annum.
- Therefore, estimated increased laboratory costs range from £21 000 - £42 000 (i.e. 4200 x 5 - 4200 x 10).
- **If cost per CDI = £6986 (adjusted cost GBP 2010),[1,2] then additional lab costs require a crude estimate of 3-6 CDI case to be 'saved'/prevented per annum.**

- **However, because of other potential savings, for example releasing isolation beds and transmission prevention, then <3-6 CDI cases may need to be prevented to offset increased laboratory costs.**

- False-negatives may cost in terms of additional length of stay and mortality, as well as knock on costs associated with transmission. False-positives may cost in terms of unnecessary treatment and isolation.
- We do not have precise values for these parameters and so cannot fully determine the cost implications.

- Under crude cost assumptions (see below) and using estimates of the proportion of patients with each test outcome[3], derived from the observational diagnostic study, the cost per positive patient and cost per negative patient under each testing strategy can be estimated. We find:
  <u>Cost per negative patient</u>
  - Current test 1 (EIA1) offers a reduction in the cost per negative patient compared to current test 2 (EIA 2), due to the greater sensitivity.
  - The new algorithm offers a reduction in the cost per negative patient compared to current test 1 (EIA 1) and a further reduction compared to current test 2 (EIA 2), due to the new algorithm offering the highest sensitivity.

  <u>Cost per positive patient</u>
  - As false negatives actually create a cost saving, in terms of lack of treatment and isolation costs, the greater the sensitivity the greater the cost per positive patient.
  - Therefore current test 2 (EIA 2) gives the highest cost per positive patient and current test 1 (EIA 1) the lowest, with the new algorithm between them.

- Putting these costs together, overall costs associated with each test can be estimated. We find:
  - Current test 1 (EIA 1) and the new algorithm have very similar overall costs.
  - Overall costs using current test 2 (EIA 2) are slightly higher.

- **Overall, estimated costs associated with CDI testing by either of two single toxin EIAs or by the new algorithm were similar.**

However, note that these calculations do not account for savings through, for example, decreased length of stay, mortality or prevention of onward transmission.

Assumptions:

- Estimate of the cost of a CDI case of £6,986 rounded up to £7,000.
- Assume ~7% (~£500) of the cost of a case is due to costs other than additional length of stay. Therefore, ~7% of the cost of a case is made up of *non-bed day costs* (and therefore accrued by false-positives):
    - Cost of an isolation bed day (over a non-isolated bed day) ~ £50, and a false positive case stays in isolation for 4 days ~ £200
    - Cost of treatment (vancomycin) ~ £47
    - Increased number of laboratory investigations for cases (due to additional length of stay) ~£210.
- Therefore, we are assuming that ~93% (~£6500) of the cost of a case is due to *bed day costs* (and therefore will be accrued by false-negatives).
- Positivity rate = 5%.

Caveats:

- These findings are **indicative** and rely on crude estimations and many assumptions.
- We are not accounting for the differences in effect due to mortality.
- We are ignoring reduction in transmission brought about by enhanced clinical management of positive patients and therefore ignoring the benefits this would bring.
- The value of an isolation day is likely to vary by isolation availability – the value of 'freeing' isolation days has not been explored fully here.
- Note that all costs ignore the non-hospital, societal costs of CDI, as well as in-hospital savings that may occur on improved management of patients with diarrhea.

References

1. Goldenberg SD, French GL. Diagnostic testing for Clostridium difficile: a comprehensive survey of laboratories in England*. J Hosp Infect 2011*;79:4-7.
2. Wilcox MH, Cunniffe JG, Trundle C, Redpath C. Financial burden of hospital-acquired Clostridium difficile infection. *J Hosp Infect* 1996;34:23-30.
3. Planche T, Wilcox MH, Shetty N, Crook D, Davies K, Coen P. Defining a testing algorithm to improve the laboratory diagnosis of CDI. Evaluation report to Department of Health 2011.

J Robotham, M Wilcox. February 2012