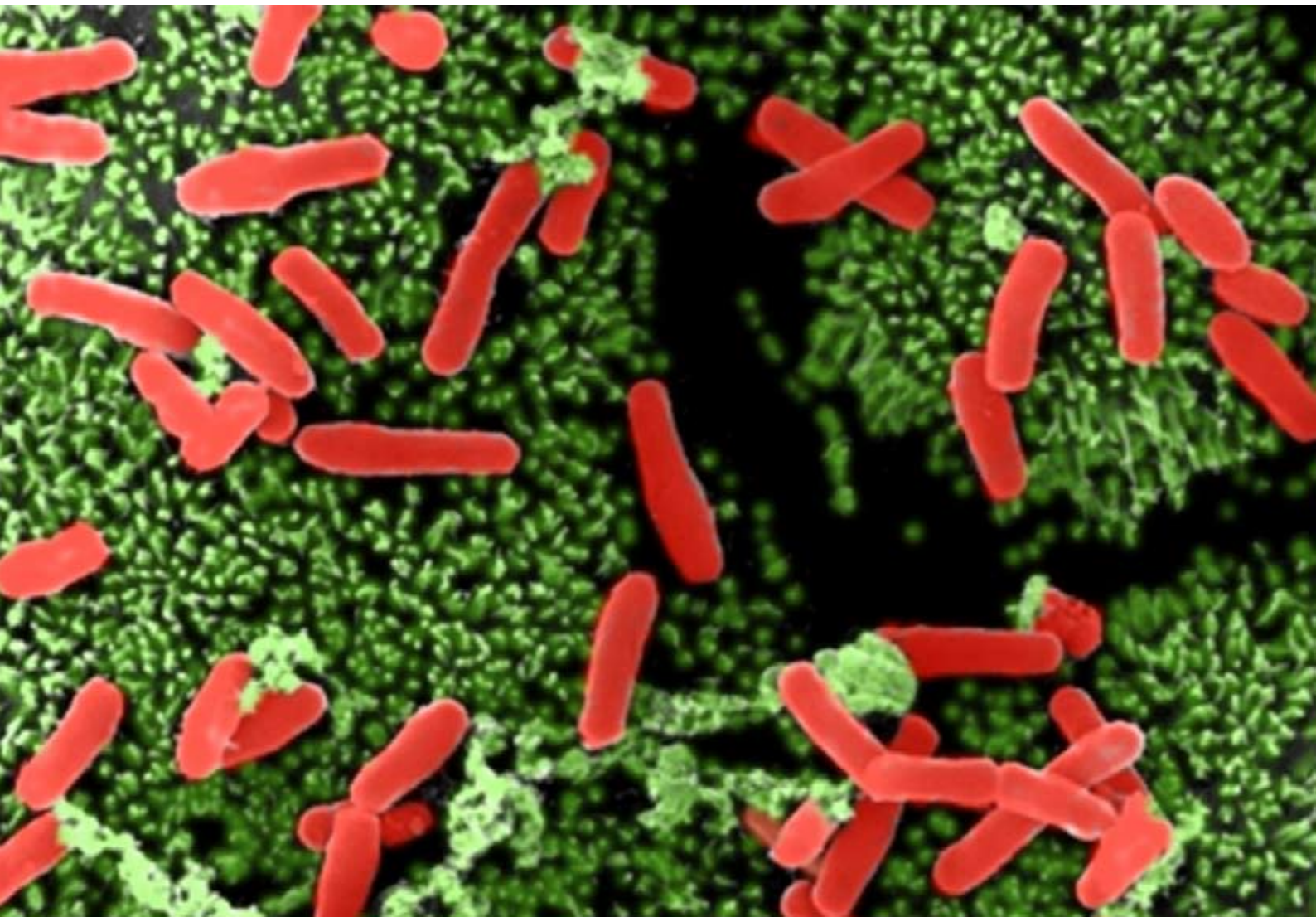
Health Protection Agency

DH Department of Health

Clostridium difficile infection:

How to deal with the problem



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Front cover image: *Clostridium difficile* attached to intestinal cells.
Reproduced courtesy of Dr Jan Hobot, Cardiff University School of Medicine.

Clostridium difficile infection:

How to deal with the problem

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Foreword

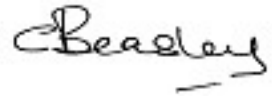
The NHS is working hard to tackle healthcare-associated infections (HCAIs) and we are seeing reductions. But HCAIs still present us with a great challenge. This has led to requests to the Department of Health and the Health Protection Agency (HPA) for advice on the most effective methods of prevention and control of this infection and the management of outbreaks. The existing national guidance (Clostridium difficile *Infection*: *Prevention and Management*) was issued by the Department of Health and the then Public Health Laboratory Service in 1994. Although the basic premises of the prevention and control strategy for *C. difficile* infection set out in the 1994 document remain appropriate in general terms, it was clear that the guidance should be reviewed in the light of experience and evidence over the last decade and re-cast in a style that reflects the modern NHS.

This guidance has been produced by a working group established by the HPA's Steering Group on Healthcare Associated Infection at the request of the Department of Health. It outlines newer evidence and approaches to delivering good infection control and environmental hygiene, highlights the principles set out in various advisory and guidance documents produced by the Department over recent years, and updates the 1994 guidance. It takes into account a national framework for clinical governance which did not previously exist, a framework that gives significant weight to infection control as a matter of patient safety and highlights that all clinicians have a personal responsibility for infection prevention and control.

We hope that clinical practitioners and NHS managers will find this guidance useful in developing policies for the care and treatment of individual cases of *C. difficile* infection, managing any outbreaks that might occur, and helping to promote antimicrobial stewardship and the development of effective antibiotic prescribing policies.

We thank the members of the working group who contributed so much of their knowledge, expertise and time to produce this guidance.

Sir Liam Donaldson
Chief Medical Officer
Department of Health



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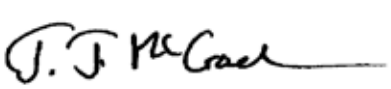

Justin McCracken
Chief Executive
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Scope and purpose

This guidance updates and replaces Clostridium difficile *Infection: Prevention and Management* published by the Department of Health in 1994. It is aimed at a wide range of healthcare professionals from board to ward, involved in the prevention and control of *Clostridium difficile* infection (CDI) and in managing outbreaks, in particular clinicians and NHS managers. It is designed to help them deliver the *NHS Operating Framework* target to reduce CDI across the NHS.

Effective application of this evidence-based framework, supported by other good practice advice, such as *Saving Lives* (Department of Health, 2007d), will enable organisations to develop systems to prevent and control CDI. The guidance adds detail to the principles identified in *Saving Lives* and also aligns with the principles identified within *The Operating Framework for the NHS in England 2008/09* (Department of Health, 2007a).

There are a number of detailed recommendations throughout this document, with 10 key recommendations for healthcare providers and commissioners highlighted as having the greatest impact in helping management address the problem of CDI.

All recommendations have been aligned with relevant sections of the *The Health Act 2006: Code of practice for the prevention and control of healthcare associated infections* (Department of Health, 2008a) (henceforth referred to as the Code[1]) and provide guidance on what action NHS bodies might take in order to fulfil the Code's requirements for addressing CDI.

The guidance therefore brings together, amplifies and complements other advisory and guidance documents in relation to CDI including:

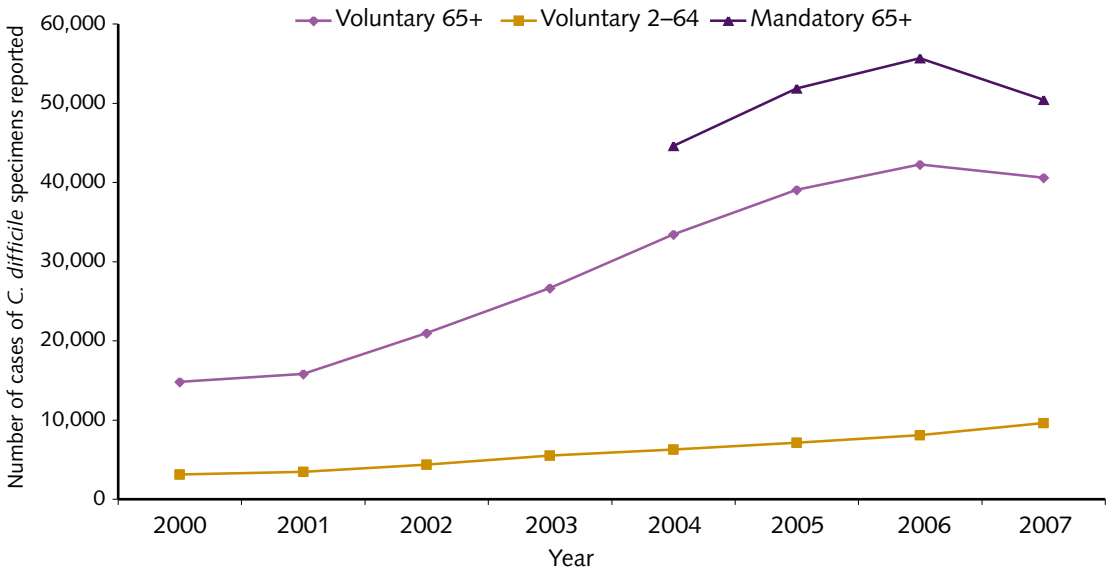
- *Infection caused by* Clostridium difficile (Chief Medical Officer/Chief Nursing Officer, 2005);
- *Saving Lives: Reducing infection, delivering clean and safe care. High Impact Intervention No. 7 – Care bundle to reduce the risk from* Clostridium difficile (Department of Health, 2007b);
- *Saving Lives: Reducing infection, delivering clean and safe care – Antimicrobial prescribing* (Department of Health, 2007d);
- *Saving Lives: Isolating patients with healthcare-associated infection* (Department of Health, 2007e);
- *Changes to the mandatory healthcare associated infection surveillance system for* Clostridium difficile *infection* (Chief Medical Officer/Chief Nursing Office, 2008); and
- *Clean, Safe Care: Reducing infections and saving lives* (Department of Health, 2008b).

1 From April 2009, the new Care Quality Commission will take over the functions of the Healthcare Commission, the Commission for Social Care Inspection and the Mental Health Act Commission. As part of these changes the Code will be revised and re-issued. However, the requirements for infection prevention and control will remain essentially the same.

Introduction

The NHS is making progress in addressing *C. difficile* infection, but more needs to be done to reduce the number of cases and improve patient care. The significant activity and focus on the management and control of CDI has meant that there has been a promising decrease in the number of infections (see Figure 1[2]). Mandatory surveillance data showed that for April–June 2008, the NHS had reduced *C. difficile* infections in all age groups; the total number of cases for that period was 10,846, of which 8,663 were in patients aged 65 years and over. This represents a 35% reduction compared with the same quarter the previous year (for April–June 2007: total was 16,868, of which 13,924 were aged 65 years and over).

Figure 1: CDI cases in patients aged 2–64 years and 65+ years (Health Protection Agency, 2007)



The working group was asked to review the 1994 report on the prevention and management of CDI to take account of latest evidence, various infection control and prevention documents issued by the Department of Health in recent years and in light of the rise of reported cases of CDI among patients of all ages from the 1990s to 2006 (see Figures 2a and 2b).

2 The graph shows the cases reported to the Health Protection Agency voluntary reporting scheme for patients aged 2–64 years and 65+ years in NHS acute trusts in England for 2000 to 2007. Cases reported through the mandatory reporting scheme for patients aged 65+ years in 2004 are also shown. Mandatory reporting was extended to include patients aged 2 years and over in April 2007 (data not included).

Why did CDI increase?

The reasons for the rise in CDI from the late 1990s are complex.

Between 1990 and 2004, rates of CDI changed in different age groups in England (in selected health regions). While it is apparent that the greatest increases occurred in those in the 60–64 age group, there were also significant rises in younger people over this period. There appears to have been a gradual increase in rates in the early 1990s, followed by pronounced increases, first around 1996/97 and then 2001/02.

Over 50,000 cases of CDI were reported in England in 2007, of which 20% were in younger age groups previously not considered to be high risk. Some acute NHS trusts reported successful control and low rates of CDI but more than half of acute NHS trusts had rates greater than 2 per 1,000 admissions in patients aged 65 and older. CDI was cited as the underlying cause of death on 4,056 death certificates. There is increased awareness among doctors and they have been reminded of their duty to include CDI on death certificates when appropriate.

Figure 2a: *C. difficile* infection rates from laboratory reports submitted under the voluntary reporting scheme in people aged 45–64 in England (excludes figures from the North West, South East and London regions) (Health Protection Agency, 2006)

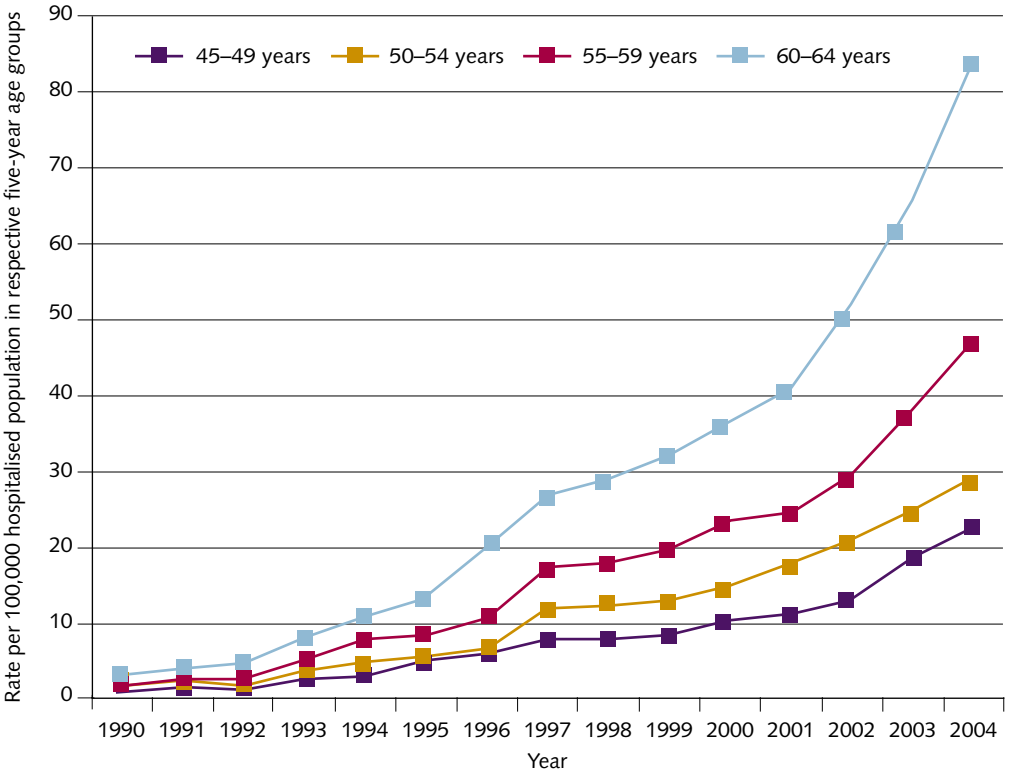
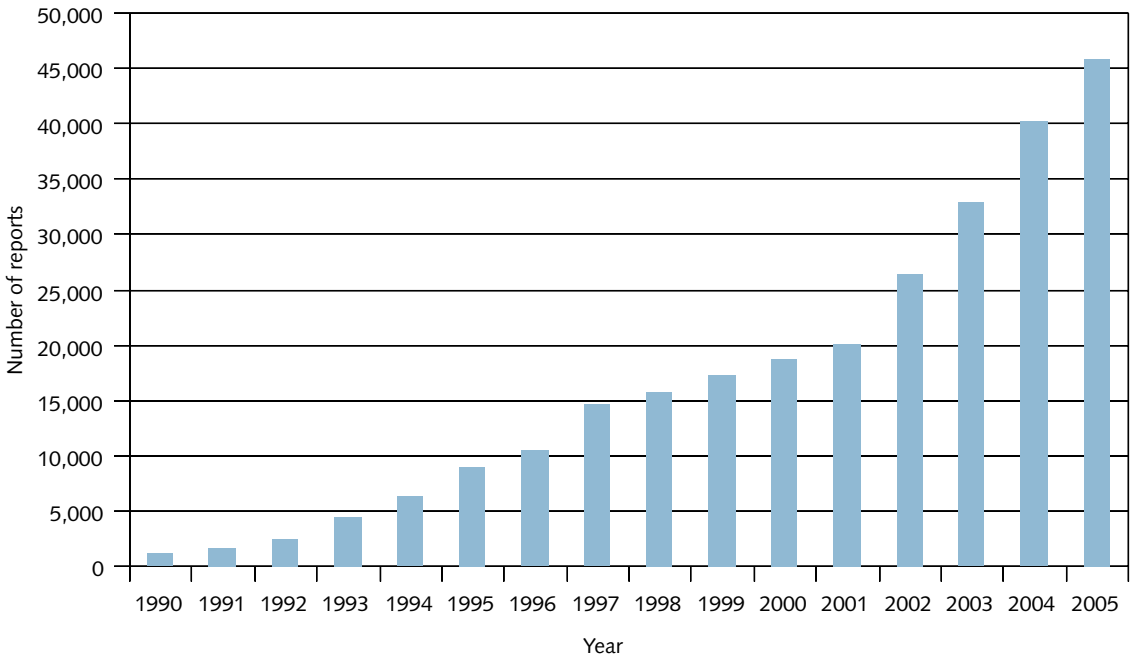


Figure 2b: Number of *C. difficile* infections (all ages) reported through the voluntary reporting scheme, 1990 to 2005 in England (Health Protection Agency, 2006)



The working group noted that the Healthcare Commission (HCC)/Health Protection Agency (HPA) review (Health Protection Agency, 2006) and the HCC's report on healthcare-associated infection (HCAI) (Healthcare Commission, 2007a) pointed to problems in awareness and implementation of the 1994 guidelines and suggested that this may have contributed to the rise.

Changes in healthcare practice, including increased testing, and patient risk profile, particularly in relation to age, may also have contributed, as have complex epidemiological changes, such as an increase in community-acquired CDI and the appearance in Northern Europe, the USA and Canada of a previously uncommon but more virulent strain, known as the pulse field type 1 (NAP1) or ribotype 027 (Warny et al., 2005; Kuijper et al., 2006). In North America, increasing rates were reported in Canada and the USA from March 2003, involving a more severe course, higher mortality, increased risk of relapse and more complications linked to the emergence of this new strain. It was subsequently recognised as causing outbreaks in England, the Netherlands, Belgium and France.

Voluntary surveillance and strain typing indicated that the more recent increases reported since 2003 were associated with this virulent strain, which may have produced more severe disease, increased therapeutic failure, and resulted in higher colectomy rates, greater relapse or reinfection and higher mortality rates (Warny et al., 2005; Kuijper et al., 2006; Ricciardi et al., 2007).

Although the ribotype 027 strain has deletions in the *tcdC* gene which result in increased toxin production, this alone may be insufficient to explain its epidemic behaviour, as strains isolated many years ago also possessed the deletions in the *tcdC* gene but did not cause outbreaks in that period (McDonald et al., 2005). Fluoroquinolone resistance and fluoroquinolone use have been implicated, but outbreaks have been seen in units with modest or little use of fluoroquinolones. Generally, those units have used other selecting antibiotics such as extended-spectrum cephalosporins.

In addition to the role of these different strains, community-associated CDI has been increasingly recognised. A study in Germany found a high CDI incidence (9.3%) among 703 patients with diarrhoea visiting their GP (Weil et al., 2007), and a British study reported an incidence of 20–30 cases per 100,000, with many cases having been neither recently admitted to hospital nor in receipt of antibiotics (Wilcox et al., 2008). The extent of, and risk factors for, community acquisition and any relationship to strain changes require further exploration.

Approach to compiling the guidance

The guidance is presented in two parts. The **Core Guidance** consists of key recommendations, followed by a summary of healthcare recommendations and provides a concise document that can be copied for dissemination to a wide audience for action. The second part is the **Extended Guidance**. This provides the detailed rationale and evidence behind each of the healthcare recommendations presented in the Core Guidance. It also contains a list of appendices, which provide further information to help, support and manage CDI. A list of research recommendations are also detailed (see Appendix 1) which are aimed at informing and stimulating the research community as a whole.

This guidance is based on a report produced by a working group established by the HPA's Steering Group on Healthcare Associated Infection (see Appendix 10). This guidance adopts the same approach as the 1994 working group report, which was derived from a review of the literature and expert opinion and updates the extensive literature reviews of CDI carried out by:

- the National *Clostridium difficile* Standards Group (2004); and
- the joint review by the HCC and HPA (Health Protection Agency, 2006) of the epidemiology of CDI, and the survey of directors of infection prevention and control (DIPCs) (Health Protection Agency, 2006).

It takes into account various infection control and prevention documents issued by the Department of Health in recent years and also considers the HCC report on HCAI (Healthcare Commission, 2007a) which provided the most recent published evidence on practice in the NHS at the time of writing the report.

A formal systematic review with grading of the level of evidence provided by each study was not done. Like the 2006 HCC/HPA epidemiology review, the working group did not consider that the evidence had changed sufficiently over the years to alter the 1994 report's main recommendations. Equally it did not warrant the extra time and resources needed for a full systematic review using the tools now available to appraise quasi-experimental (www.idrn.org/orion.php) (Stone et al., 2007a, b) and epidemiological studies (www.strobe-statement.org) (von Elm et al., 2007; Vandenbroucke et al., 2007). Therefore a simple grading system for the recommendations is provided (see Table 1).

An extensive description of the pathogenesis of CDI is not included in this guidance as it has been well covered by both the National *Clostridium difficile* Standards Group (2004) and the HCC/HPA (Health Protection Agency, 2006) reviews. However, key elements to note are:

- antibiotics disturb the normal gut flora, some more than others;
- the spores of *C. difficile* are the transmissible form and contaminate the environment, where they survive for long periods;
- the ingested spores germinate in the disturbed gut;
- the *C. difficile* bacteria produce two principal toxins – A and B – which cause diarrhoea and colitis; and
- the attack rate is variable (greater in older patients), complicating our understanding of the epidemiology of outbreaks.

The clinical presentation ranges from mild diarrhoea to severe colitis with dehydration, pseudmembranous colitis, megacolon and perforation.

What is new in this guidance?

This guidance updates and replaces the 1994 working group report on the prevention and management of *C. difficile* infection (Department of Health, 1994). It outlines newer evidence and approaches to delivering good infection control and environmental hygiene, considering, where relevant, national policy, recent practice and examples considered by the working group to represent 'good practice', before making healthcare recommendations.

It takes into account a national framework for clinical governance that did not exist in 1994. This framework gives significant weight to infection control as a matter of patient safety and highlights that all healthcare staff should take personal responsibility for good infection control practice (National Audit Office, 2000; Chief Medical Officer, 2003).

It acknowledges the Code and each recommendation is assessed in relation to the 11 specific duties. It indicates when a suggested action is required by, or will help towards compliance with, a specific duty. It also takes account of the updated National Evidence-based Guidelines for Preventing Healthcare Associated Infections in NHS Hospitals in England (Pratt et al., 2007).

It draws on the HCC reports into the CDI outbreaks at Stoke Mandeville Hospital, (Buckinghamshire Hospitals NHS Trust), the University Hospitals of Leicester NHS Trust and the Maidstone and Tunbridge Wells NHS Trust (Commission for Healthcare Audit and Inspection, 2006; Healthcare Commission, 2007b, c), and the joint HCC/HPA review (Health Protection Agency, 2006) which concluded that the 1994 guidelines "*may not have been sufficiently prescriptive in their requirements to implement verified prevention and control practices*".

This guidance therefore builds on the recommendations made in 1994, and develops these guided by the following three principles:

- "**CDI should be managed as a diagnosis in its own right**" (Healthcare Commission, 2007b).
- "**The safety of patients cannot be compromised**" but is "**at the centre of everything we do**" and cannot be compromised by other strategic or financial objectives (Commission for Healthcare Audit and Inspection, 2006; Healthcare Commission, 2007a).
- Infection control, including CDI, is "**everybody's business**" (Committee on Public Accounts, 2000; Healthcare Commission, 2007a), requiring not only a 'board to ward' approach in the hospital but active engagement of primary care trusts (PCTs), health protection units (HPUs) and strategic health authorities (SHAs), using the rubric of clinical and corporate governance. *The Operating Framework for the NHS in England 2008/09* (Department of Health, 2007a) and the Code also make it clear that the Department of Health expects the NHS to implement effective infection prevention and control policies and procedures from board to ward.

Adopting these principles makes individual doctors and nurses responsible for initiating early diagnosis and prompt isolation, and for compliance with guidelines for hand hygiene, antibiotic prescribing and wearing disposable gloves and aprons. It puts the onus on trust management and PCTs to ensure that isolation facilities match demand; that resources are made available for antimicrobial management teams (AMTs), surveillance, audit, rapid diagnosis, environmental cleaning and education; that there are collaborative links with HPUs and SHAs; and that patients and the public are kept informed proactively of policies and practice, as appropriate.

Core Guidance

C. difficile infection (CDI) causes serious illness and outbreaks among hospital in-patients. Normally it affects the elderly, the debilitated and patients who have had antibiotic treatment.

It is important that when a patient presents with diarrhoea, the possibility that it may have an infectious cause is considered. Patients with suspected potentially infectious diarrhoea should be isolated.

We draw attention to 10 key recommendations for healthcare providers and commissioners. Following these, from board to ward, will reduce cases of CDI.

Key recommendations

1. Clinicians (doctors and nurses) should apply the following mnemonic protocol (SIGHT) when managing suspected potentially infectious diarrhoea:

S	Suspect that a case may be infective where there is no clear alternative cause for diarrhoea
I	Isolate the patient and consult with the infection control team (ICT) while determining the cause of the diarrhoea
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 toxin, by sending a specimen immediately

2. **Doctors** should consider CDI as a diagnosis in its own right, grading each confirmed case for severity, treating accordingly and reviewing each patient daily, monitoring bowel function using the Bristol Stool Chart (Appendix 1). PCTs should ensure that trusts establish a multidisciplinary clinical review team consisting of a microbiologist, infectious disease or infection prevention and control doctor, a gastroenterologist or surgeon, a dietician and an infection prevention and control nurse. The team should review all CDI patients at least weekly to ensure that the infection is optimally treated and the patient is receiving all necessary supportive care.

3. **Trusts** should provide sufficient capacity to isolate or cohort all known CDI patients. For example, in cases where single-room isolation or cohorting on normal wards is not halting the spread of infection, and the advice of the ICT is to open or create a designated isolation ward, this should be done, taking external advice from the HPU if necessary. Isolation wards that are not composed of single rooms are termed cohort wards. As reinfection is a common

cause of recurrence in *C. difficile* and this is difficult to prevent in high-prevalence, open cohort wards, isolation wards or single rooms are desirable. However, it is strongly recommended that patients in whom the cause of diarrhoea has not been determined should be isolated in a single room pending diagnosis. If CDI is confirmed, they may be nursed in a cohort ward if one is available. If a large point source outbreak of diarrhoea occurs such that there are insufficient singe rooms for every affected patient, then the ward should be immediately closed to admissions.

4. All **trusts** should establish an **antimicrobial management team** (AMT) or equivalent. This should consist of an antimicrobial pharmacist, a consultant microbiologist or infectious diseases specialist and an information technology specialist. Trusts should ensure the prudent use of antibiotics and develop programmes to capture and feed back data to directorates and wards on antibiotic use and CDI rates for the hospital as a whole.

5. **Trusts** should develop restrictive antibiotic guidelines that use narrow-spectrum agents alone or in combination for empirical and definitive treatment where appropriate. These guidelines should avoid the use of clindamycin and second- and third-generation cephalosporins (especially in the elderly) and minimise the use of fluoroquinolones, carbapenems and prolonged courses of aminopenicillins. Guidelines should specifically seek to reduce the use of repeated courses of antibiotics in hospitals.

6. **Clinical directors** should ensure that good antimicrobial practice becomes embedded at the patient level through one or more of the following:
   - Designated 'link physicians' for units where there is local concern about the level of CDI, such as units for the care of the elderly.
   - Daily review of drug charts by ward pharmacists to check compliance with antibiotic guidelines and to liaise with the ward doctor.
   - AMT ward rounds that give feedback to ward doctors and consultants.

7. **Consultants** should review antibiotic prescribing on all their ward rounds, stopping unnecessary prescriptions and changing those that do not comply with guidelines, as should their juniors on their own ward rounds.

8. **Directors of nursing and human resources** should ensure that each clinical area has reliable systems in place for training, auditing and feeding back to staff on cleaning, isolation, hand hygiene and protective clothing practices. Some trusts have found that a network of infection control link practitioners is an effective approach to delivering these functions.

9. **Trusts** should ensure that all clinical areas assess cleanliness and that they have introduced the National Specifications for Cleanliness (or an equivalent process). In particular, they should ensure that an appropriate auditing process (which is designed to ensure that monitoring is at its most intense in areas of very high and high risk) is in place and fully complied with. The results of this should be discussed at regular (at least monthly) meetings of matrons, and infection prevention and control and cleaning staff.

10. **Trusts** should support the control and reduction of CDI from board level downwards, prioritising the management of risk to patients and ensuring that the safety of patients is not compromised by the pursuit of other strategic objectives. They should assess the performance of all units of management through regular audit and feedback so that activity at a ward level is appropriate and consistent with trust and national policy. Trusts should ensure that education and training of all staff on infection prevention and control actually happens in a timely manner and is informed by audit results.

Grading of recommendations

A simple grading system for the recommendations is given in Table 1. A grade A, B or C appears in brackets after each recommendation. Reference is also given to the Code, highlighting, where applicable, the specific duties.

Table 1: Graded strength of evidence underlying the recommendations

Grade	Strength of evidence
A	Strongly recommended and supported by systematic review of randomised controlled trials (RCTs) or individual RCTs
B	Strongly recommended and supported by non-RCT studies and/or by clinical governance reports and/or the Code
C	Recommended and supported by group consensus and/or strong theoretical rationale

Summary of healthcare recommendations

1. Clinical definitions and laboratory diagnosis

(Recommendations 1.20 to 1.29 of the Extended Guidance)

1.1 The ICT should:

i. adhere to the following definitions for use in identifying and managing incidents of CDI:

- ***C. difficile* infection**: one episode of diarrhoea, defined either as stool loose enough to take the shape of a container used to sample it or as Bristol Stool Chart types 5–7 (Appendix 1), that is not attributable to any other cause, including medicines (Appendix 2), and that occurs at the same time as a positive toxin assay (with or without a positive *C. difficile* culture) and/or endoscopic evidence of pseudomembranous colitis (PMC). **(Code: Duty 10l; Annex 2)** B
- **A period of increased incidence (PII)** of CDI: two or more new cases (occurring >48 hours post admission, not relapses) in a 28-day period on a ward.
- **An outbreak of *C. difficile* infection**: two or more cases caused by the same strain related in time and place over a defined period that is based on the date of onset of the first case.
  (Code: Duty 2c; Annex 1) B

ii. draw up comprehensive local guidelines for the diagnosis and management of CDI, including PII (see recommendation 2.5) and outbreaks (see section 8).
(Code: Duties 2c, 10c, 10l; Annex 1; Annex 2) C

1.2 As speed of diagnosis is important for the efficient use of isolation facilities, clinicians should, in line with the SIGHT protocol, ensure that stool specimens are sent for toxin testing as soon as infective diarrhoea is suspected.
(Code: Duty 1b) B

1.3 Laboratories should ensure that toxin testing is available seven days a week, that intervals between requests for samples (for hospital in-patients) and their delivery to the laboratory should be minimised and that results are communicated to the ward as soon as they are available. Performance of the above should be audited. **(Code: Duty 9; Annex 1)** B

1.4 If a commercial *C. difficile* kit is used, this should have a dual toxin A and B formulation (as toxin A negative/B positive strains exist). The kit should offer the best performance criteria in terms of sensitivity, specificity and negative and positive predictive values. Values for specificity and sensitivity are listed by manufacturers, but independent evaluations (once common in the literature in the 1990s) are now rare (Barbut et al., 2003), and several new products have yet to be independently evaluated. **(Code: Duty 9)** B

1.5 Only test stools from symptomatic patients, i.e. only liquid/loose stools that take the shape of the container (Bristol Stool Chart types 5–7) should be examined. 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 CT (computerised tomography) scanning, may be required. B

1.6 Do not retest for *C. difficile* toxin (CDT) positive cases if patients are still symptomatic within a period of 28 days unless symptoms resolve and then recur and there is a need to confirm recurrent CDI. B

1.7 More than one test per patient may be required if the first test is negative but where there is a strong clinical suspicion of CDI. Retest a second sample 24 hours later. Further tests might be necessary in light of clinical evidence. B

1.8 Generally it is not advisable to test children under the age of 2 years in whom toxigenic strains of *C. difficile* and toxins A and B may be present in the absence of symptoms. B

1.9 Sudden increases in the number and/or severity of cases detected in a ward or across several units within a hospital are legitimate reasons for typing requests. However, this is best undertaken in a planned way, following discussion with the relevant regional laboratory or reference laboratory. C

2. Surveillance

(Recommendations 2.32 to 2.39 of the Extended Guidance)

2.1 All NHS trusts in England are required to participate in the Department of Health's mandatory CDI reporting system and to report all cases of CDT-positive diarrhoea in patients over 2 years of age. The Department will continue to work with the HPA and Connecting for Health (CfH) and investigate the uploading of patients' demographic data from laboratory computer systems to avoid transcription errors and improve reporting consistency.
(Code: Duties 2c, 10k, 10l; Annex 1; Annex 2; Appendix 2i) B

2.2 Trusts should be strict in adhering to the criteria for testing and reporting. Only diarrhoea samples should be tested.
(Code: Duties 9, 10k; Annex 1; Appendix 2i) B

2.3 All samples (hospital and wider community) should be tested for all patients aged 65 years and above and for those aged less than 65 years if this is clinically indicated. Diagnostic laboratories should provide information that differentiates clearly between hospital-associated and community-associated specimens. They should clearly state the location of the patient at the time of sample submission and, if known, any previous hospital in which they were in-patients in the last four weeks. **(Code: Duty 10k)** B

2.4 There should be continuous local surveillance of cases of CDI, with:

- hospitals or trusts recording and reporting each month all cases (in all age groups) to directorates, wards and units with analysis of trends and exceptional events. Review of these reports should be a standing item on the agenda for directorate meetings; and
  (Code: Duties 2c, 10l; Annex 1; Annex 2; Appendix 2i) B
- quarterly, or more frequent, reports of CDI to be provided to those accountable for HCAI in specific areas or units, and to be included in infection control committee meetings and board meetings.
  (Code: Duties 2c, 10l; Annex 1; Annex 2; Appendix 2i) B

2.5 Trusts should adhere to the standard definition of a PII and outbreak (see recommendation 1.21 in the Extended Guidance). The following actions are to be undertaken if a PII is identified on a ward (see Figure 3 in the Extended Guidance):

i. Urgently inform the clinical director, matron, ward manager and directorate manager.

ii. Conduct a weekly *C. difficile* ward audit using the Department of Health's *C. difficile* High Impact Intervention (HII) tool by the infection control doctor or nurse. The audit should continue until the weekly score is >90% in three consecutive weeks and there have been no further >48 hours cases of CDI on the ward during that period. Feed back the audit results to the matron or ward manager.

iii. Carry out a weekly antibiotic review in the ward (using local tools); this is the responsibility of the antibiotic pharmacist.

iv. Clean the whole ward with chlorine-containing agent until no further symptomatic patients are present on the ward. Emphasise that each bed space needs to be cleaned separately with separate cloths.

v. Use the HPA *Clostridium difficile* Ribotyping Network for England (CDRNE) or Centre for Infections to undertake PCR (polymerase chain reaction) ribotyping of all isolates from patients in the ward.

vi. The ICT should carry out an automatic review of ward PIIs each week.

vii. An incident meeting should be held as determined by the size and rate of growth of the PII by assessment of the situation by the DIPC and/or the duty microbiologist with the clinical director and consultants, depending on the number of cases.

2.6 Trusts should report all outbreaks as serious untoward incidents (SUIs) to the PCT and the SHA and subject them to a root cause analysis. This includes all ward closures that are due to diarrhoea shown to be associated with *C. difficile*. **(Code: Duties 10c, 10k; Annex 2)** B

2.7 Local surveillance should include the number of patients with severe infection, the number requiring surgery and the number dying where CDI caused or contributed to the death. A regular review should be conducted of deaths within 30 days of diagnosis of CDI to ensure that a common standard of assessment of causation or contribution to death is being applied. This will be facilitated by compliance with recommendation 3 to establish a multidisciplinary clinical review team. **(Code: Duty 2c; Annex 1)** B

2.8 Frozen storage of small aliquots of toxin-positive stool samples (e.g. a small Eppendorf tube full at –20°C for a rolling year) is recommended. This is so that a retrospective culture can be made should it become apparent that an outbreak of CDI or a change in incidence has taken place that might warrant culture of the organism for typing (Brazier and Duerden, 1998). Obtaining isolates is also advisable in order to monitor antimicrobial susceptibility, especially the emergence of resistance to the current first-line treatment options of metronidazole and vancomycin. C

3. Management and treatment of CDI

(Recommendations 3.28 to 3.38 in the Extended Guidance)

3.1 Clinicians (doctors and nurses) should apply the following mnemonic protocol (SIGHT) when managing suspected potentially infectious diarrhoea:

S	Suspect that a case may be infective where there is no clear alternative cause for diarrhoea **(Code: Introduction)** B
I	Isolate the patient and consult with the infection control team (ICT) while determining the cause of the diarrhoea **(Code: Duties 8, 10d)** B
G	Gloves and aprons must be used for all contacts with the patient and their environment **(Code: Duty 10; Annex 2)** B
H	Hand washing with soap and water should be carried out before and after each contact with the patient and the patient's environment **(Code: Duties 4e, 10; Annex 2)** A
T	Test the stool for toxin, by sending a specimen immediately. **(Code: Duty 1b)** B

3.2 Patients should be monitored daily for frequency and severity of diarrhoea using the Bristol Stool Chart (see Appendix 1). B

3.3 All antibiotics that are clearly not required should be stopped, as should other drugs that might cause diarrhoea (see Appendix 2). **(Code: Duty 10j; Annex 2)** B

3.4 CDI should be managed as a diagnosis in its own right, with each patient reviewed daily regarding fluid resuscitation, electrolyte replacement and nutrition review. Monitor for signs of increasing severity of disease, with early referral to ITU as patients may deteriorate very rapidly. B

3.5 PCTs should ensure that trusts establish a multidisciplinary clinical review team, consisting of a microbiologist, an infectious diseases or infection prevention and control doctor, a gastroenterologist or surgeon, a dietician and an infection prevention and control nurse.

3.6 The team should review all CDI patients at least weekly to ensure that the infection is being treated optimally and that the patient is receiving all necessary supportive care. B

3.7 Assess the severity of CDI each day as follows:

- **Mild CDI** is not associated with a raised WCC; it is typically associated with <3 stools of types 5–7 on the Bristol Stool Chart per day. B
- **Moderate CDI** is associated with a raised WCC that is $<15 \times 10^9$/L; it is typically associated with 3–5 stools per day. C

- **Severe CDI** is associated with a WCC >15 × 10^9/L, or an acute rising serum creatinine (i.e. >50% increase above baseline), or a temperature of >38.5°C, or evidence of severe colitis (abdominal or radiological signs). The number of stools may be a less reliable indicator of severity. C
- **Life-threatening CDI** includes hypotension, partial or complete ileus or toxic megacolon, or CT evidence of severe disease. B

3.8 Treat according to severity (see also the treatment algorithms, Figures 3 and 4):

- **Mild and moderate CDI** – oral metronidazole 400–500 mg tds for 10–14 days. A
- **Severe CDI** – oral vancomycin 125 mg qds for 10–14 days. A In severe CDI cases not responding to oral vancomycin 125 mg qds, high-dosage oral vancomycin (up to 500 mg qds, if necessary administered via a nasogastric tube) +/- intravenous (iv) metronidazole 500 mg tds is recommended. The addition of oral rifampicin (300 mg bd) or iv immunoglobulin (400 mg/kg) may also be considered. C
- **Life-threatening CDI** – oral vancomycin up to 500 mg qds for 10–14 days via nasogastric tube or rectal installation plus iv metronidazole 500 mg tds. Such patients should be closely monitored, with specialist surgical input, and should have their blood lactate measured. Colectomy should be considered, especially if caecal dilatation is >10 cm. Colectomy is best performed before blood lactate rises >5 mmol/L, when survival is extremely poor. B

3.9 If diarrhoea persists despite 20 days' treatment but the patient is stable and the daily number of type 5–7 motions has decreased, the WCC is normal, and there is no abdominal pain or distension, the persistent diarrhoea may be due to post-infective irritable bowel syndrome. The patient may be treated with an anti-motility agent such as loperamide 2 mg prn (instead of metronidazole or vancomycin). The patient should be closely observed for evidence of a therapeutic response and to ensure there is no evidence of colonic dilatation. C

3.10 **For first recurrence**, repeat the same antibiotic used to treat the initial episode (unless the first episode was treated with metronidazole and the recurrence is severe CDI, in which case vancomycin should be used). B

3.11 **For subsequent recurrences**, use vancomycin 125 mg qds. Consider the alternatives listed in the treatment algorithm in Figure 4. C

4. Prevention of CDI through antibiotic prescribing

(Recommendations 4.34 to 4.46 in the Extended Guidance)

4.1 All trusts should establish an AMT or equivalent. This should consist of an antimicrobial pharmacist, a consultant microbiologist or infectious diseases specialist, and an information technology specialist. Antimicrobial pharmacists have a valuable role in AMTs and PCTs, and providers should actively encourage their involvement and, where necessary, support recruitment to these posts. **(Code: Duty 2c; Annex 1)** B

4.2 Restrictive antibiotic guidelines should be developed by trusts, through the AMT, stressing the following recommendations:

- Use narrow-spectrum agents for empirical treatment where appropriate.
- Avoid use of clindamycin and second- and third-generation cephalosporins, especially in the elderly.
- Minimise use of fluoroquinolones, carbapenems and prolonged courses of aminopenicillins. **(Code: Duties 10j, 10l)** B

4.3 Restricted broad-spectrum antibiotics should be used when indicated by the patient's clinical condition, and should be reviewed on results of microbiological testing or according to the local sensitivities of causative organisms. The guidelines on indications for use should be easy to understand and follow. **(Code: Duties 10j, 10l)** B

4.4 Guidelines should:

- name specific antibiotics for specific infections;
- give guidance on therapeutic courses of antibiotic dosage, duration (in general 5–7 days), automatic stop dates (which can only be written by doctors) and dates for iv–oral switch;
- minimise polypharmacy;
- include surgical prophylaxis (mostly limited to one dose administered as near as possible to the operation);
- be regularly reviewed;
- be easily available; and
- be easy to understand and to follow.

(Code: Duty 10j) B

4.5 Guidance should be given on repeated antibiotic prescription for the same or sequential infections and should be easy to understand and follow. **(Code: Duties 10j, 10l)** B

4.6 All consultants should be responsible for reviewing antibiotic prescriptions on all their ward rounds, stopping unnecessary prescriptions and changing those that do not comply with the guidelines, as should their juniors on their own ward rounds. **(Code: Duty 10j)** C

4.7 Antibiotics should be prescribed only when there is clinical evidence of bacterial infection. Evidence of infection (i.e. the reason for administering antibiotics) should be clearly documented in the clinical record. **(Code: Duty 10j)** C

4.8 Antibiotics started inappropriately or without sufficient evidence should be stopped. Antibiotics should be stopped where microbiology results do no support the diagnosis of bacterial infection in the suspected site or elsewhere. Antibiotic prescriptions that depart from guidelines without justified clinical or microbiological indications should be changed or stopped. The traditional approach of completing a course of antibiotics once it has been started is no longer appropriate in these circumstances. **(Code: Duty 10j)** C

4.9 Trusts should, through the AMT, develop programmes to capture and feed back data on both antibiotic use (in defined daily doses per 1,000 bed days), differentiating between out-patient and in-patient prescriptions, and *C. difficile* rates (as cases per 1,000 admissions) for the hospital as a whole. Wards and directorates should be provided with antibiotic prescription data and *C. difficile* rates each month. **(Code: Duties 2c, 2e; Annex 1)** B

4.10 It is not always possible to define the place or time of acquisition of CDI and the influence of prior antibiotic use. Cases with diarrhoea on admission or within 48 hours of admission should be carefully assessed against recent admissions to interpret local epidemiological trends. Cases in the community should be assessed for past hospitalisation and antibiotic use.

4.11 **Clinical directors** should ensure that good antimicrobial practice becomes embedded at the patient level through one or more of the following:

- Designated 'link physicians' for units where there is local concern about levels of CDI, such as units for the care of the elderly. Such link physicians should be responsible to their directorate's medical infection control lead, and should be the person with whom the AMT liaises regarding antibiotic guidelines, audit, and feedback of antibiotic use and CDI rates to junior staff. B
- Daily review of drug charts by ward pharmacists to check compliance with antibiotic guidelines and to discuss deviations with the ward or prescribing doctor, with support from the AMT. B
- AMT ward rounds to review antibiotic prescriptions, changing prescriptions where necessary and giving verbal feedback to the ward doctor and written feedback in a letter to the consultant. The frequency of rounds and the wards attended will vary with local circumstances. B
- In a critical care environment, joint daily rounds between intensivist, microbiologist and pharmacist should be considered.
  (Code: Duties 2c, 2e, 10j, 11d; Annex 1; Annex 2; Annex 3; Appendix 2i) B

4.12 Trusts should, in consultation with the AMT, liaise with organisations responsible for postgraduate training to co-ordinate teaching of antibiotic prescribing to doctors, pharmacists and nurses as part of their formal in-house training programme.

4.13 There should be mandatory core training in prudent antibiotic use for doctors, pharmacists and nurses in addition to an introductory session on each induction programme. Post-registration, this training should be repeated by all such staff every three years and should specifically cover those antibiotics that provoke CDI. **(Code: Duty 11d; Annex 3)** **C**

5. Prevention through isolation

(Recommendations 5.13 to 5.23 of the Extended Guidance)

5.1 It is strongly recommended that patients with suspected potentially infectious diarrhoea (at least one episode of diarrhoea) should be moved immediately into a single room with a self-contained toilet and its own hand basin. Specimens should be sent immediately for *C. difficile* toxin testing (see SIGHT protocol). If the room does not have its own toilet facilities then a commode should be arranged. **(Code: Duties 4e, 8, 10d; Annex 2)** B

5.2 The Bristol Stool Chart (Appendix 1) should be used to monitor the patient's diarrhoea. B

5.3 All staff or visitors entering an isolation-room should use disposable gloves and aprons for all contact with the patient and the patient's environment, and wash their hands with soap and water before and after each patient contact (see SIGHT protocol). **(Code: Duty 10a; Annex 2)** A

5.4 The patient should remain isolated until there has been no diarrhoea (types 5–7 on the Bristol Stool Chart) for at least 48 hours, and a formed stool has been achieved (types 1–4). **(Code: Duties 8, 10d; Annex 2)** C

5.5 If isolation in a single room is not possible because the single room capacity is exceeded, patients with confirmed CDI should be nursed in a dedicated *C. difficile* ward. An alternative is cohort nursing in a bay with a solid partition, including a door, separating it from the rest of the ward. However, this requires rigorous supervision to maintain cleanliness in toilets/commodes and to ensure staff contact precautions in such bays are observed. A dedicated cohort ward is therefore preferable.

5.6 Where single-room isolation or cohort nursing in a bay is not halting or reducing the spread of infection and the advice of the ICT is to open or create a designated isolation ward, this should be done. If necessary, take external advice from the HPU. **(Code: Duties 8, 10d)** B

5.7 If the patient has not been previously isolated on suspicion, because the diagnosis was not suspected, once confirmed, the patient should be transferred to a single room or isolation ward as soon as possible after diagnosis and no later than the end of the day of diagnosis. An audit should be done of the numbers of patients isolated and the percentage of suspected and confirmed cases isolated during the working day. The infection control link practitioner will have a key role in this process. Minimising the movement of patients between wards will reduce the exposure of other patients to *C. difficile* when a case of CDI is recognised. **(Code: Duties 2e, 2f)** B

5.8 Transfer and movement of patients should be reduced to an operationally effective minimum. Where patients need to attend departments for essential investigations, they should be 'last on the list' unless earlier investigation is clinically indicated. In advance of the transfer, the receiving area should be notified of the patient's CDI status. Arrangements should be put in place to minimise the patient's waiting time and hence contact with other patients. Transfer to other healthcare facilities should, if possible, include notification of the individual's CDI status and be appropriate, i.e. the patient should be called for when the department is ready for them and their transfer planned so that they are not held in communal waiting areas. Staff, including ambulance personnel, should adopt appropriate infection control precautions when in contact with the patient. **(Code: Duties 2f, 6, 10a; Annex 1; Annex 2)** B

5.9 After transport of the patient with CDI, the risk of cross-infection to other patients is minimal. Good infection control practices and cleaning should suffice to prevent cross-infection. Faecal soiling should be cleaned then treated using chlorine-containing agents.
(Code: Duties 2f, 3, 5, 7, 10i; Annex 1; Annex 2) B

5.10 All clinical waste and linen from patients with CDI, including bedding and adjacent curtains, should be considered as contaminated and should be managed in accordance with local guidelines and national guidance.
(Code: Duties 4f, 4g; Annex 1; Appendix 2f) B

5.11 Infection control precautions for handling deceased patients are the same as those used when the patient is alive. Faecal soiling around the cadaver should be cleaned first with detergent and then with a chlorine-containing cleaning agent. Plastic body bags are not necessary, but may be used as part of general practice in accordance with standard precautions for all patients. There is negligible risk to mortuary staff or undertakers provided that standard infection control precautions are used. **(Code: Duty 10i; Annex 2; Appendix 2d)** B

6. Prevention through environmental cleaning and disinfection

(Recommendations 6.27 to 6.34 in the Extended Guidance)

6.1 Environmental cleaning of rooms or bed spaces of *C. difficile* patients should be carried out at least daily using chlorine-containing cleaning agents (at least 1,000 ppm available chlorine). **(Code: Duties 4, 10i; Annex 2)** B

6.2 All commodes, toilets and bathroom areas of CDI patients should be cleaned after each use with chlorine-containing cleaning agents (at least 1,000 ppm available chlorine). **(Code: Duty 10i; Annex 2)** B

6.3 All clinical areas should be regularly assessed for cleanliness and results fed back to clinical and cleaning teams. Infection prevention and control teams, matrons and cleaning staff should meet regularly (at least monthly) to discuss results across the hospital. Particular attention should be paid to toilet and bathroom scores. **(Code: Duties 2e, 4, 10i, 10l, 11d; Annex 2; Annex 3)** B

6.4 Terminal cleaning of a mattress, bed space, bay or ward area after the discharge, transfer or death of a patient with CDI should be thorough. All areas should be cleaned using chlorine-containing cleaning agents (at least 1,000 ppm available chlorine), and the curtains should be changed. Consideration should be given to the use of vaporised hydrogen peroxide to provide total disinfection of the environment/equipment in single rooms/isolation wards. Trusts should have a specific protocol for this and carry out an audit of compliance with it. **(Code: Duties 4, 10i; Annex 2)** B

6.5 The ward environment should not be cluttered. The recent Releasing Time to Care: The Productive Ward initiative by the NHS Institute promotes this. Medical equipment should ideally be for single patient use, but if that is not possible it should be thoroughly cleaned before and after each new patient use. This process should be recorded and audited together with regular checks of the integrity of surfaces including mattress covers. **(Code: Duty 4f; Annex 1)** B

6.6 Chlorine-containing cleaning agents should be made up to the correct concentration and stored in accordance with manufacturers' instructions, with particular attention being paid to compliance with health and safety regulations (HM Government, 1974; Health and Safety Executive, 2005).
(Code: Duty 10i; Annex 2) B

6.7 Routine environmental screening for *C. difficile* is not recommended, but may be useful to ascertain whether cleaning standards are suboptimal, notably in the outbreak or hyperendemic setting.

6.8 Trusts should ensure, through their directors of nursing and human resources, that each clinical area is covered by an infection control link practitioner, whose role and job description should include training, auditing and feeding back to staff on cleaning, isolation, hand hygiene and personal protective clothing practices. This could be either a member of the clinical team or one of a number of designated posts attached to the infection prevention and control team, each covering several clinical teams or a clinical directorate full time.
(Code: Duties 2e, 11d; Annex 3) B

7. Hand hygiene in the prevention of CDI

(Recommendations 7.19 to 7.23 of the Extended Guidance)

7.1 All healthcare workers should wash their hands with soap and water before and after contact with patients with suspected or proven CDI or any other infective diarrhoea, and after contact with the patient's immediate environment or body fluids, in line with the SIGHT protocol. Hands should be dried thoroughly thereafter. **(Code: Duty 10a; Annex 2)** A

7.2 All healthcare workers must use disposable gloves and aprons for any physical contact with such patients, and the patient's immediate environment and body fluids, in line with the SIGHT protocol. Gloves and aprons should be removed after use and disposed of in line with infection control directives or guidance before washing hands as above. **(Code: Duty 10a; Annex 2)** B

7.3 Alcohol handrub **must not** be used as an alternative to soap. It can be applied **after** washing to rid hands of remaining non-clostridial organisms. **(Code: Duty 10a; Annex 2)** B

7.4 Trusts should audit hand hygiene and disposable glove and apron use among staff caring for patients with suspected or proven infective diarrhoea. This audit should occur as soon as ICTs become aware of such cases. Infection control link practitioners have a key role in this. **(Code: Duties 2e, 10a, 11d; Annex 2; Annex 3)** B

7.5 Trusts should implement the *clean**your**hands* campaign at all times, making it a top priority within their clinical governance framework, and ensure widespread and frequent audit and feedback, using standardised measures. Infection control link practitioners have a key role in this. **(Code: Duties 2e, 10a, 11d; Annex 2; Annex 3)** B

8. Coping with high prevalence

(Recommendations 8.14 to 8.20 of the Extended Guidance)

8.1 Increase the activity of the ICT:

- Institute at least weekly meetings involving all aspects of bed and estates management within the trust.
- Institute daily review of new and existing cases of CDI (review the clinical condition of patients and adherence to infection control precautions).
- Ensure that there is coverage by an infection control link practitioner (see recommendation 6.34 in the Extended Guidance) in all affected areas.

(Code: Duties 4a, 10c; Annex 1; Annex 2) B

8.2 Review and maximise isolation procedures:

- Depending on availability of single rooms, consideration should be given to establishing an isolation ward(s).
- Draw up a detailed operational plan for both clinical management and estates/bed/nursing support.
- The use of cohort nursing in bays may be considered, but the difficulties in maintaining cleanliness in toilets/commodes and supervising staff contact precautions may render this action ineffective, and it is not evidence-based.

(Code: Duties 4a, 8; Annex 1) B

8.3 Institute intensive local surveillance:

- All ICTs should routinely report cases of CDI back to wards and senior trust management on a monthly basis (see recommendation 2.35 in the Extended Guidance).
- In the event of an outbreak declared by the DIPC on advice from the microbiologists (endorsed by management and formally recorded in publicly available documents), the DIPC should ensure collation of information on cases every day and keep senior management informed.

(Code: Duty 10l; Annex 2; Appendix 2i) B

8.4 Optimise ward cleaning and disinfection:

- In the absence of easy biological indicators of the persistence of *C. difficile* spores in the environment, adhere tightly to cleaning protocols and use sporicidal agents.
- Obvious soiling with faeces (particularly on touch points) and dirty linen are potent sources for cross-infection and should be removed immediately.

(Code: Duties 4, 10i; Annex 2) B

8.5 Communicate diagnostic microbiology results as rapidly as possible:

- Ribotyping of representative isolates should be undertaken using one of the specialist laboratories listed in Appendix 5, which can be accessed via the regional microbiologist.
- The AMT should ensure that the guidance on antibiotic usage is strictly followed.

(Code: Duties 10j, 10k) B

8.6 Reduce the movement of patients and staff to an operationally effective minimum:

- Movement of patients with diarrhoea both within and between wards will lead to the spread of CDI.
- Isolation wards and cohort bays should have minimal contact with uninfected ward areas.
- Great care should be given to identifying and preventing the movement of beds, commodes, trolleys and other equipment between areas.
- Compliance with guidelines should be audited.

(Code: Duty 6; Annex 1) B

8.7 Enhance communications with all parties and staff:

- Review communication of the situation to, and advice from, the HPU, regional microbiologist, HPA Centre for Infections (CfI) and SHA each day, as appropriate.
- Establish timely and relevant communication to all sections of the trust, including patients, and to PCTs.
- Ensure that patient information leaflets are given out.
- Provide feedback on progress with CDI control to affected wards.
- Consider issuing press statements and information to the media and general public.

(Code: Duties 5, 10k) B

9. CDI in the community

(Recommendations 9.24 to 9.35 in the Extended Guidance)

9.1 All cases of diarrhoea among people in the community aged 2 years and above should be investigated for CDI unless there are good clinical or epidemiological reasons not to. This should be included in laboratory protocols for the investigation of diarrhoea. Laboratories should report back positive results as a matter of urgency. Samples should indicate clearly who should be informed of the result. Mandatory reporting applies to all cases where the patient is aged 2 years or older. B

9.2 In the first instance, NHS acute trusts should identify where the patient was when the specimen was taken (e.g. in a GP surgery or ward). Cases in which specimens were taken before admission of the patient to hospital or within 48 hours of admission should be termed community-onset CDI. This categorisation will not allow a true measure of community acquisition, but it will separate those cases acquired during the current admission period from those acquired before then (either in the same trust or in another setting). B

9.3 There is a consensus across Europe and the US that healthcare-associated CDI should be defined as that occurring up to four weeks after discharge from a healthcare unit (e.g. hospital). There is a grey period of eight weeks after this time (i.e. from one to three months after hospital discharge) where it is uncertain whether a CDI case is hospital or community associated. C

9.4 If there is a significant number of cases of community-onset CDI, further investigations should be undertaken to assess whether they reflect true community-acquired infections or recent discharges from hospital. Understanding the source and causes of infection will help in targeting efforts to reduce infections. C

9.5 An outbreak is defined as "two or more cases caused by the same strain related in time and place over a defined period based on the date of onset of the first case". Institutions such as care homes should therefore maintain a log of cases by date and location, to aid recognition of an outbreak. B

9.6 If more than two cases of diarrhoea that are suspected or known to be infectious occur within a few days at a care home or other community institution, the registered manager is responsible for reporting this to the local HPU/consultant in communicable disease control. B

9.7 Outbreaks of CDI in institutional settings should be investigated in the same way as in the acute hospital setting. B

9.8 Those in the community who have contact with people with diarrhoea should wear disposable gloves and aprons for all contact with them and their environment. After contact they should dispose of the gloves and aprons and wash their own hands with liquid soap and water, whether or not their hands are visibly soiled. Alcohol handrub can be used after this. A

9.9 Staff in the community who have diarrhoea should not work unless they have been symptom-free for 48 hours or the diarrhoea has been shown to be non-infectious and not a risk to others. Staff with continuous severe diarrhoea should be investigated and followed up. B

9.10 The PCT, HPU and DIPC in a locality should jointly prepare local protocols on the investigation and management of cases according to national guidance and should define out-of-hours arrangements between relevant parties. C

9.11 Guidance on prescribing antibiotics in the community should be followed. Proton pump inhibitors (PPIs) should be used only when there is a clear clinical indication. C

9.12 There should be no restriction on institutions, such as care homes, receiving patients who have had CDI and are now clinically asymptomatic. Care should be taken to communicate the individual's infectious status clearly to staff and GPs, issuing a proforma letter such as the one in Appendix 3. C

10. Death certification

(Recommendations 10.14 to 10.18 of the Extended Guidance)

10.1 If a patient with CDI dies, the death certificate should state whether CDI was part of the sequence of events leading directly to death or whether it was the underlying cause of death. If either case applies CDI should be mentioned in Part 1 of the certificate. **(Code: Duty 5)** B

10.2 If CDI was not part of the sequence of events leading directly to death but contributed in some way to it, this should be mentioned in Part 2. **(Code: Duty 5)** B

10.3 If a doctor is in doubt about the circumstances of death when writing the certificate, they should consult with the trust's multidisciplinary clinical review team for CDI. B

10.4 Doctors have a legal duty to mention CDI on a death certificate if it was part of the sequence of events directly leading to death or contributed in some way. **(Code: Duties 11c, 11d, 11e)** B

10.5 Medical directors should ensure that training is provided on death certification and should audit certificates to check that they accurately record HCAI. **(Code: Duties 11c, 11d, 11e)** B

11. Governance, audit and performance indicators

(Recommendations 11.14 to 11.21 of the Extended Guidance)

11.1 Trusts should ensure that they comply with Duty 2b of the Code in respect of the appointment of a DIPC and his/her role. In addition, the DIPC should report at least quarterly on CDI to the chief executive and trust board. More frequent reporting on action is necessary if the incidence of infection is comparatively high or there is evidence of an outbreak. **(Code: Duties 2b, 10c)** B

11.2 The DIPC should have the qualifications and experience required for the post, as detailed in the DIPC role profile. A trust board member should take specific responsibility for regular liaison with the DIPC and also with consultant microbiologists and the infection prevention and control team, especially if the DIPC is not from an infection-related specialty. **(Code: Duties 2a, 2b)** B

11.3 Trusts and PCTs should work closely together when monitoring CDI against the targets. Web-based surveillance data will be used to monitor progress in reducing CDI. Relevant stakeholders (e.g. the Department of Health, PCTs, SHAs) should have access to the data. **(Code: Duty 10k; Appendix 2i)** B

11.4 The HPA should provide PCTs with information on reported cases to the PCT where it has responsibility for monitoring a local acute trust or health economy. B

11.5 Acute trusts should ensure that information analysts and specialists are available to give adequate local support to the DIPC and AMT in monitoring antibiotic use. This is made clear in recommendation 4.1, and the requirement for adequately resourced information technology is a duty under the Code. Ideally, automated processes should be set up in SHAs to facilitate the development of accurate databases on antibiotic use, and data should be collated nationally. **(Code: Duty 2c; Annex 1)** B

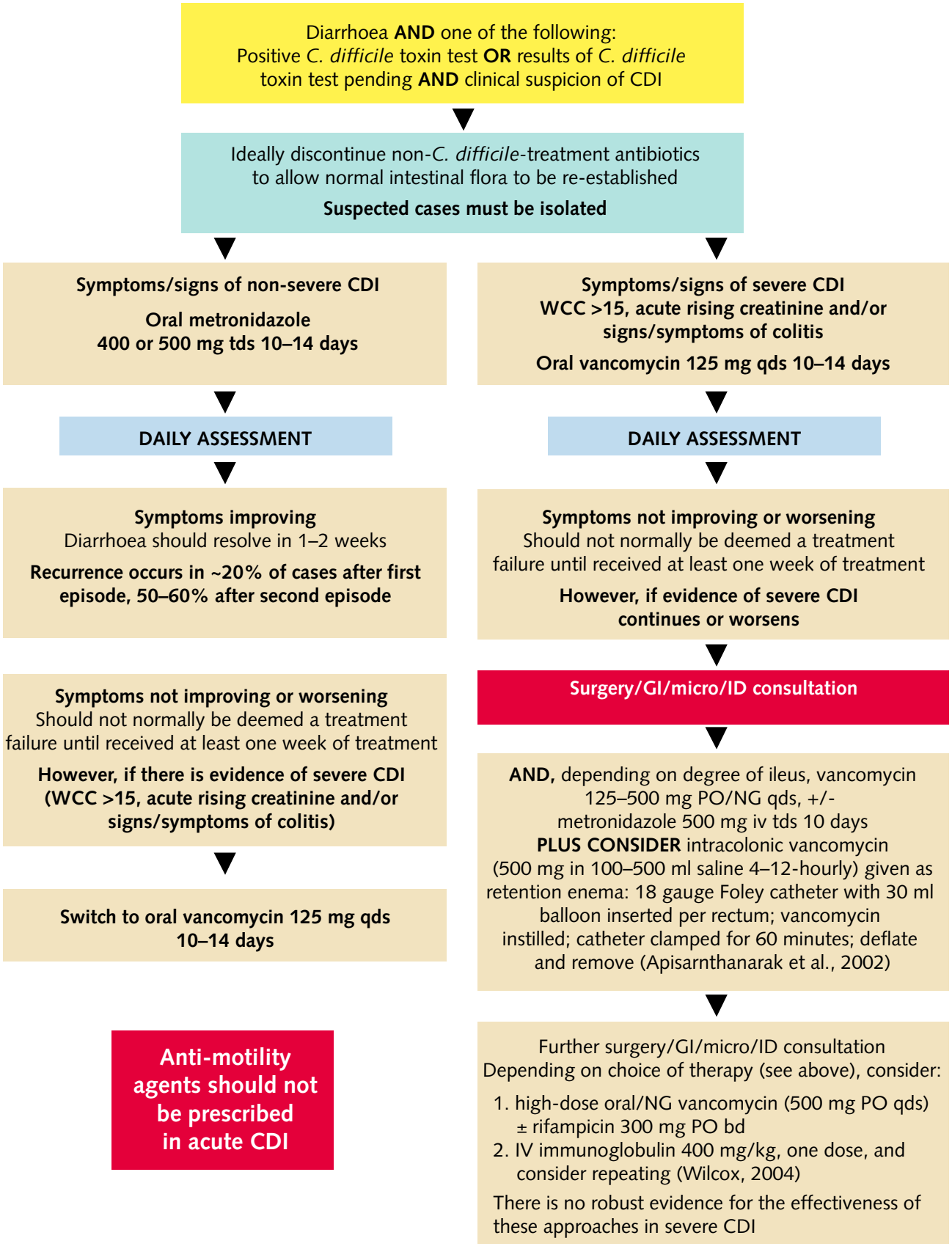
11.6 The Saving Lives programme for acute trusts (Department of Health, 2007b) specifies that a nominated doctor, nurse and manager should be responsible for infection control in each area. It states that this responsibility should be specifically included in their job descriptions, appraisals, annual individual performance reviews and knowledge and skills assessments. These individuals will have personal responsibility for control of CDI. Clinical directors, lead clinicians, the directorate and ward nurse managers should be included in distributions of information on CDI and should have devolved responsibility for their areas of management. **(Code: Duties 2c, 11f; Annex 1)** B

11.7 Trusts should comply fully with Duty 2e of the Code to ensure that they have a programme of audit of the key guidelines for the control of CDI, such as those specified in recommendations 1.2 and 1.3 (submission and processing of faecal samples), 4.8 (antibiotic prescribing), 5.7 (isolation), 6.3 (environmental cleaning), 7.4 and 7.5 (hand hygiene and protective clothing use) and 8.6 (restricting movement of patients). These should be registered with the trust's clinical audit department. **(Code: Duty 2e)** B

11.8 Trusts should ensure full compliance with Duties 11c, d and e of the Code to provide induction and training of new staff, and education and updating of guidance for existing staff that includes prevention and control of CDI. Attendance at these sessions should be a routine part of staff appraisal or personal development plans and be included in job descriptions. This training should include the results of relevant audits. By complying with the HCC's recommendation (Healthcare Commission, 2007a) that trusts should ensure that each clinical area is covered by an infection control link practitioner, trusts will facilitate compliance with both the training and audit duties of the Code. **(Code: Duties 11c, 11d, 11e, 11f)** B

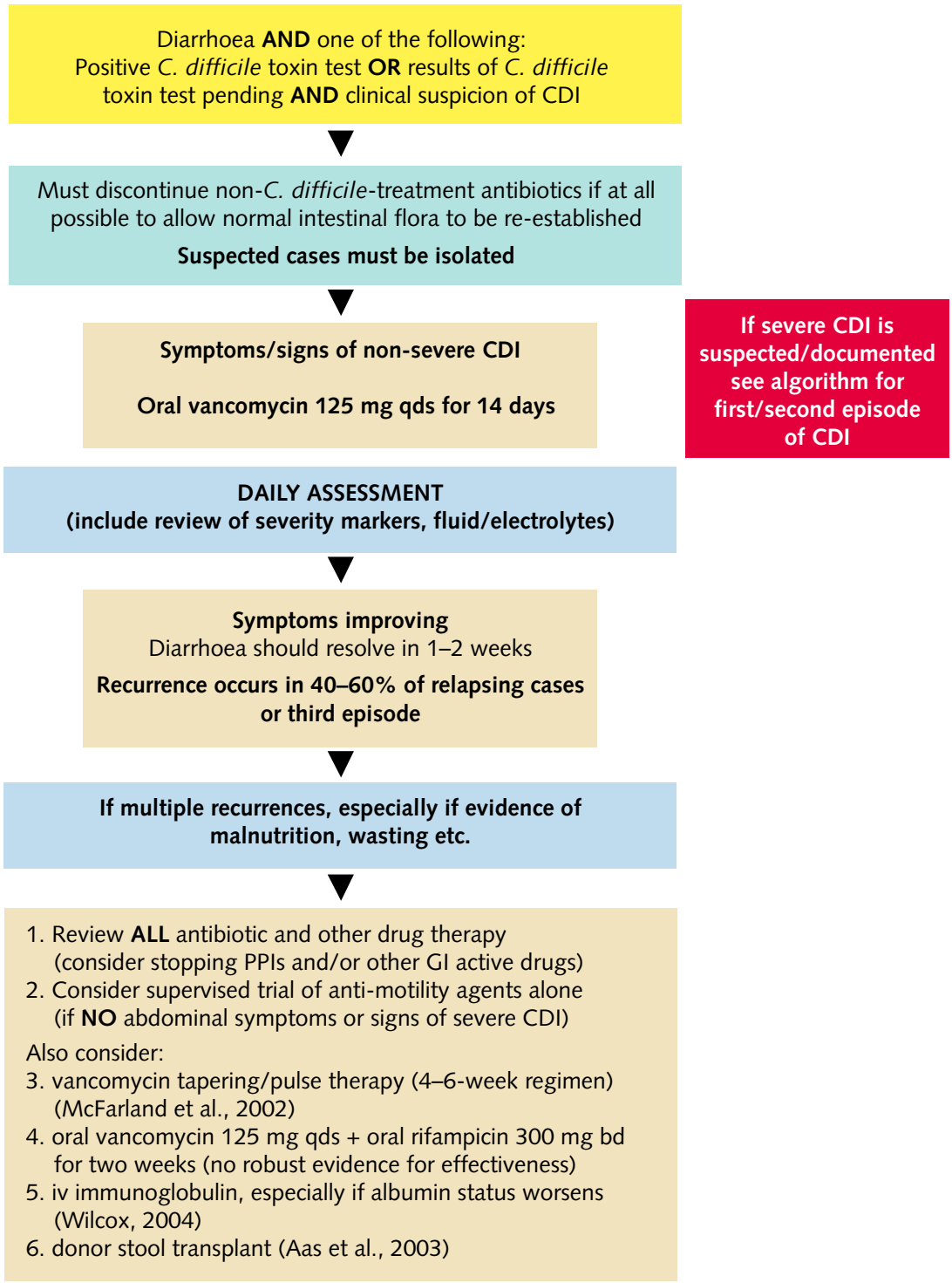
Treatment algorithms

Figure 3: First or second episode of *C. difficile* infection



Treatment algorithms

Figure 4: Recurrent *C. difficile* infection (third or subsequent episode)



Extended Guidance

The Extended Guidance provides the detailed rationale and evidence behind each of the healthcare recommendations presented in the Core Guidance.

1. Clinical definitions and laboratory diagnosis

Case and outbreak definitions

1.1 To help in identifying and managing incidents of *Clostridium difficile* infection (CDI), the following definitions are recommended, which are modified from examples provided in the literature (Department of Health, 1994; Jernigan et al., 1998; Lee, 2006; Healthcare Commission, 2006a; Musher et al., 2006):

- ***C. difficile* infection**: one episode of diarrhoea, defined either as stool loose enough to take the shape of a container used to sample it or as Bristol Stool Chart types 5–7 (Appendix 1), that is not attributable to any other cause, including medicines (Appendix 2) and that occurs at the same time as a positive toxin assay (with or without a positive *C. difficile* culture) and/or endoscopic evidence of pseudomembranous colitis (PMC).
- **A period of increased incidence (PII)** of CDI: two or more new cases (occurring >48 hours post admission, not relapses) in a 28-day period on a ward.
- **An outbreak of *C. difficile* infection**: two or more cases caused by the same strain related in time and place over a defined period that is based on the date of onset of the first case.

1.2 The incidence of CDI may differ markedly from one hospital to another. A trust should actively manage levels of CDI, whether there is an outbreak against a background of low incidence or there is hyperendemic CDI. It is not acceptable for trusts with many CDI cases to set a high threshold for response. The development of more accurate and rapid epidemiological typing methods will certainly be of assistance.

1.3 It is also important to be aware of the 'background rate' of diarrhoea in each ward, particularly wards with elderly patients, since loose stools are common in this group. An annual rate of 30–35% for episodes among patients in nursing and care homes has been observed. Infection control teams (ICTs) need to be cautious in declaring an outbreak, as the real cause of the apparent change in rate may lie elsewhere. For example, an increased awareness and ascertainment of cases by clinicians, or a change in case mix, resulting in increased numbers of susceptible patients being admitted, may give rise to pseudo-outbreaks or clusters (Department of Health, 1994; Musher et al., 2007).

1.4 Anecdotal and published evidence shows that during outbreaks of viral gastroenteritis, such as norovirus infection, there may be an associated rise in CDI. This partly explains the highly significant increase in numbers of faecal sample submissions when wards are closed as the outbreak of viral gastroenteritis is managed (Wilcox and Fawley, 2007). However, CDI should be actively excluded in all cases of diarrhoeal illness, or outbreaks of CDI will be missed.

Recent practice

1.5 The joint Healthcare Commission (HCC)/Health Protection Agency (HPA) survey (Health Protection Agency, 2006) found that the above definition of an outbreak, which is the same as that proposed in the 1994 guidelines (Department of Health, 1994) and the National Standards Group in 2004 (National *Clostridium difficile* Standards Group, 2004), was applied inconsistently by trusts.

1.6 When the survey asked directors of infection prevention and control (DIPCs) for their definitions of a CDI outbreak, none of the responses specifically mentioned the local background rate. Their responses varied widely in terms of the number of cases required to declare a local outbreak, as did the methods for deciding whether cases were linked in time and space.

Laboratory diagnosis

Evidence base

1.7 Toxin-producing *C. difficile* can be cultured from faeces of individuals of all ages, who do not have any obvious symptoms.

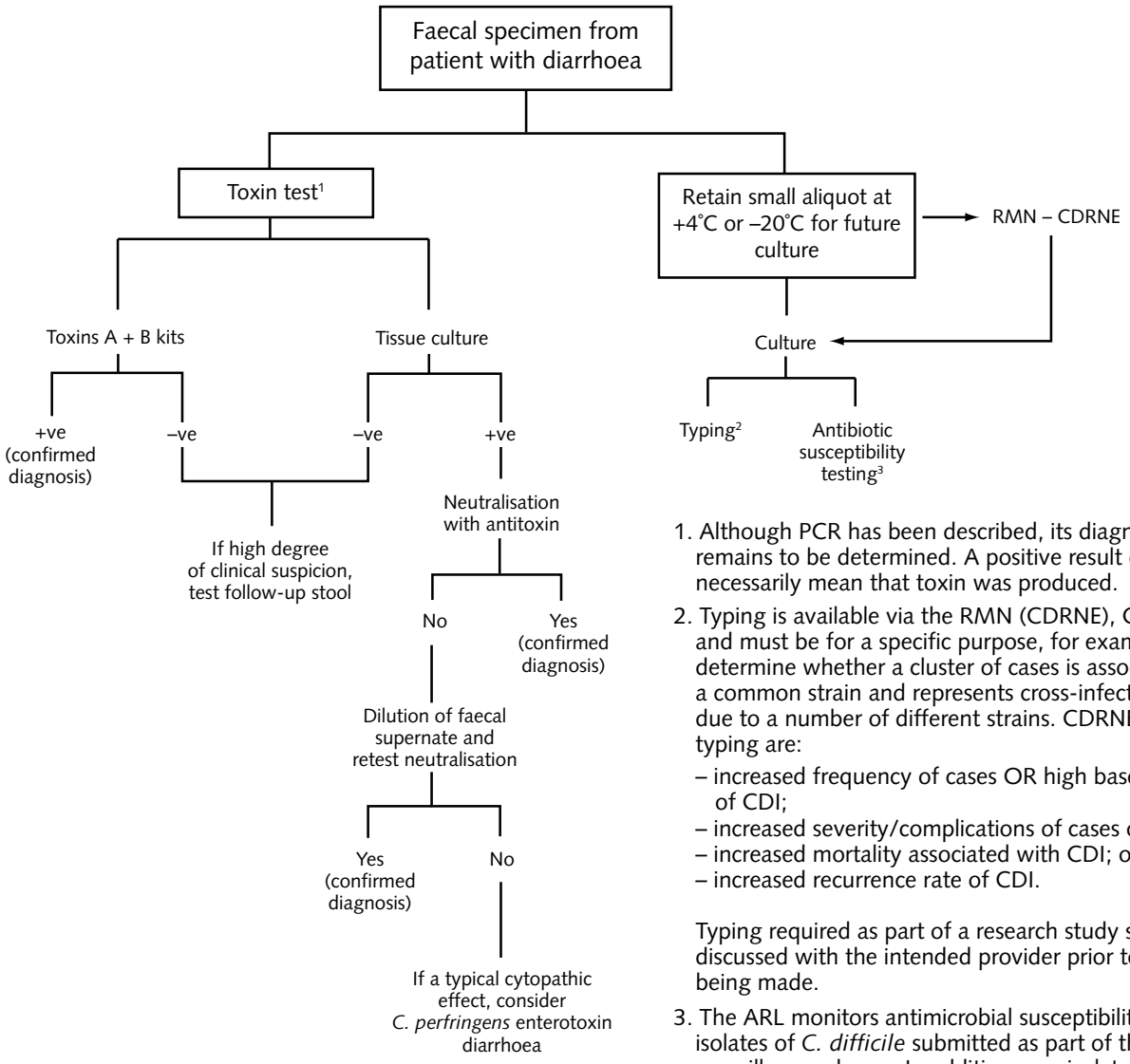
1.8 The accepted method for diagnosing CDI is therefore based on detection of either or both of the major virulence factors, toxins A and B, in the stool of a symptomatic patient (Brazier, 1998).

1.9 The typing of single isolates from severe or fatal cases rarely reveals useful data; patients can get severe and even fatal CDI with strains other than polymerase chain reaction (PCR) ribotype 027.

Current practice

1.10 Two principal methods are used for detection of faecal *C. difficile* toxin. A cytotoxin assay is the 'gold standard' for detection of both toxins, whereas kit-based tests are designed to detect toxin A (enterotoxin) only or both A and B toxins.

Figure 1: Sequence for laboratory testing for CDI



1. Although PCR has been described, its diagnostic role remains to be determined. A positive result does not necessarily mean that toxin was produced.
2. Typing is available via the RMN (CDRNE), Cfl and ARL and must be for a specific purpose, for example to determine whether a cluster of cases is associated with a common strain and represents cross-infection or is due to a number of different strains. CDRNE criteria for typing are:
   – increased frequency of cases OR high baseline rates of CDI;
   – increased severity/complications of cases of CDI;
   – increased mortality associated with CDI; or
   – increased recurrence rate of CDI.

   Typing required as part of a research study should be discussed with the intended provider prior to requests being made.
3. The ARL monitors antimicrobial susceptibility of isolates of *C. difficile* submitted as part of the DH/HPA surveillance scheme. In addition, any isolate tested elsewhere which appears to be resistant to either vancomycin or metronidazole should be sent to the ARL or Leeds General Infirmary Microbiology Department for confirmatory testing.

1.11 Two main formats of kit-based toxin detection are used: enzyme immunoassays (EIAs), which give a coloured reaction in a microtitre well for a positive test, and immunochromatography assays, which give a coloured line or band in the substrate strip. Some kits include an additional test for the enzyme glutamate dehydrogenase as an indicator of *C. difficile* in the stool.

1.12 Although considered the most sensitive method for toxin B detection in faeces, the cytotoxin assay that uses Vero, HEP2 or MRC5 cell lines is gradually falling out of favour with UK clinical diagnostic microbiology laboratories. Reasons for this include the need to maintain a cell line that may require the support of a virology department, the requirement to neutralise a positive cytopathic effect to prove it was due to *C. difficile* and, most importantly, the length of time taken to obtain a result. Speed of diagnosis can be very important in instigating necessary infection control procedures and hence in preventing a symptomatic patient putting others at risk of infection. A rapid result such as is obtainable with certain kits can give a same-day diagnosis, whereas the cytotoxin assay will be slower. However, the reduced performance in sensitivity and specificity of kits is still reason enough for some laboratories to continue using cytotoxin assays. For example, one commercial kit assay for *C. difficile* toxin was found in a recent study to have a positive predictive value of only 51% in detecting CDI (Delmee et al., 2005; van den Berg et al., 2007).

1.13 Storage temperature and multiple cycles of freezing/thawing have minimal effects upon the viability of *C. difficile* or its spores. Storage at 4°C has no discernible effect on *C. difficile* cytotoxin. However, storage at –20°C has a detrimental effect on the cytotoxin, and multiple cycles of freezing/thawing may adversely affect toxin titres (Freeman and Wilcox, 2003).

1.14 Since the 1994 guidelines were issued, there has been much progress in the application of molecular typing methods to understand the epidemiology of *C. difficile*. PCR ribotyping, developed at the Anaerobe Reference Laboratory in Cardiff, has been used since the mid-1990s to investigate outbreaks in UK hospitals and to monitor the strains that cause CDI in English hospitals.

1.15 Since the well-publicised outbreak in Stoke Mandeville Hospital that was primarily due to type 027 (Commission for Healthcare Audit and Inspection, 2006), there has been an unprecedented demand to know whether other UK hospitals have this so-called 'hypervirulent' strain. Regional support for *C. difficile* typing was established in a number of HPA laboratories around England in 2007 (the HPA *Clostridium difficile* Ribotyping Network for England, CDRNE) to provide more typing facilities for NHS trusts (see Appendices 5 and 6). The Laboratory of Healthcare Associated Infection at the HPA Centre for Infections (CfI) can also provide strain differentiation.

1.16 Typing should not influence initial measures for managing infected patients and preventing transmission, but it will provide an understanding of the epidemiology of any apparent increase in cases. Sudden increases in the number and/or severity of cases detected in a ward or across several units within a hospital are legitimate reasons for requesting typing. However, this is best undertaken in a planned way, following discussion with the relevant HPA regional laboratory or reference laboratory.

1.17 The application of other subtyping methods to subdivide ribotypes is not available as a routine service but is being investigated. The results of typing investigations undertaken locally or regionally should be available centrally to build up the national picture. Culturing *C. difficile* by alcohol shock methodologies that depend on spore survival (as currently recommended in national standard methods) may be less sensitive than conventional culture on selective agars and consequently require processing of larger amounts of faeces.

1.18 Selective agars have not been improved for a number of years, and enterococcal overgrowth can reduce isolation rates in known cases. Improvement in such media and methods are required.

1.19 Although the literature is available (Sloan et al., 2008; Peterson et al., 2007; van den Berg et al., 2007), real-time PCR methods for detection of *C. difficile* toxin genes in stools have yet to become widely used. Early evaluation studies suggest that they may be useful and the availability of commercial, random access, real-time PCR assays is likely to drive uptake. Their role in the diagnosis of CDI needs evaluation in routine clinical practice.

Recommendations

1.20 A simple grading system for our recommendations is given in Table 1 below. A grade of A, B or C appears in brackets after each recommendation. Reference is also given to the Code, highlighting, where applicable, the specific duties.

Table 1: Graded strength of evidence underlying the recommendations

Grade	Strength of evidence
A	Strongly recommended and supported by systematic review of randomised controlled trials (RCTs) or individual RCTs
B	Strongly recommended and supported by non-RCT studies and/or by clinical governance reports and/or the Code
C	Recommended and supported by group consensus and/or strong theoretical rationale

1.21 The ICT should:

i. adhere to the following definitions for use in identifying and managing incidents of CDI:

- ***C. difficile* diarrhoea**: one episode of diarrhoea, defined either as stool loose enough to take the shape of a container used to sample it or as Bristol Stool Chart types 5–7 (Appendix 1), that is not attributable to any other cause, including medicines (Appendix 2), and that occurs at the same time as a positive toxin assay (with or without a positive *C. difficile* culture) and/or endoscopic evidence of PMC.
  (Code: Duty 10l; Annex 2) 

- **A period of increased incidence (PII)** of CDI: two or more new cases (occurring >48 hours post admission, not relapses) in a 28-day period on a ward.
- **An outbreak of *C. difficile* diarrhoea**: two or more cases caused by the same strain related in time and place over a defined period that is based on the date of onset of the first case. **(Code: Duty 2c; Annex 1)** B

ii. draw up comprehensive local guidelines for the diagnosis and management of CDI, including PII (see recommendation 2.5) and outbreaks (see section 8). **(Code: Duties 2c, 10c, 10l; Annex 1; Annex 2)** C

1.22 As speed of diagnosis is important for the efficient use of isolation facilities, clinicians should, in line with the SIGHT protocol (see 3.21), ensure that stool specimens are sent for toxin testing as soon as infective diarrhoea is suspected. **(Code: Duty 1b)** B

1.23 Laboratories should ensure that:

- toxin testing is available seven days a week;
- intervals between requests for samples (for hospital in-patients) and their delivery to the laboratory should be minimised; and
- results are communicated to the ward as soon as they are available.

Performance of the above should be audited. **(Code: Duty 9; Annex 1)** B

1.24 If a commercial *C. difficile* kit is used, this should have a dual toxin A and B formulation (as toxin A negative/B positive strains exist). The kit should offer the best performance criteria in terms of sensitivity, specificity and negative and positive predictive values. Manufacturers list values for specificity and sensitivity, but independent evaluations (once common in the literature in the 1990s) are now rare (Barbut et al., 2003). Several new products have yet to be independently evaluated. **(Code: Duty 9)** B

1.25 Only test stools from symptomatic patients, i.e. only liquid/loose stools that take the shape of the container (Bristol Stool Chart types 5–7) should be examined. In suspected cases of 'silent' CDI, such as ileus, toxic megacolon or PMC with diarrhoea, other diagnostic procedures, such as colonoscopy, white cell count (WCC), serum creatinine and abdominal CT scanning, may be required. B

1.26 Do not retest for *C. difficile* toxin (CDT)-positive cases if patients are still symptomatic within a period of 28 days unless symptoms resolve and then recur and there is a need to confirm recurrent CDI. B

1.27 More than one test per patient may be required if the first test is negative but where there is a strong clinical suspicion of CDI. Retest a second sample 24 hours later. Further tests might be necessary in light of clinical evidence. B

1.28 Generally, it is not advisable to test children under the age of 2 years in whom toxigenic strains of *C. difficile* and toxins A and B may be present in the absence of symptoms. **B**

1.29 Sudden increases in the number and or severity of cases detected in a ward or across several units within a hospital are legitimate reasons for typing requests. However, this is best undertaken in a planned way, following discussion with the relevant regional laboratory or reference laboratory. **C**

2. Surveillance

Evidence base

2.1 Surveillance is 'information for action'. It provides information for:

- early recognition of changes in patterns of infection against the baseline;
- identifying the size of the problem;
- monitoring trends and comparing rates;
- evaluating the effectiveness of interventions;
- identifying areas for further investigation or research;
- reinforcing good practice; and
- influencing key hospital staff and decision-makers.

2.2 Surveillance, especially when accompanied by feedback to clinicians, has long been established as an effective tool to lower hospital-acquired infections (Haley et al., 1985).

2.3 This has been shown to be true for CDI in individual studies (Stone et al., 2000; Fowler et al., 2007). Furthermore, the recent HCC report on healthcare-associated infections (HCAIs) found that trusts that widely disseminated and fed back the results of CDI surveillance had lower rates of CDI (Healthcare Commission, 2007a).

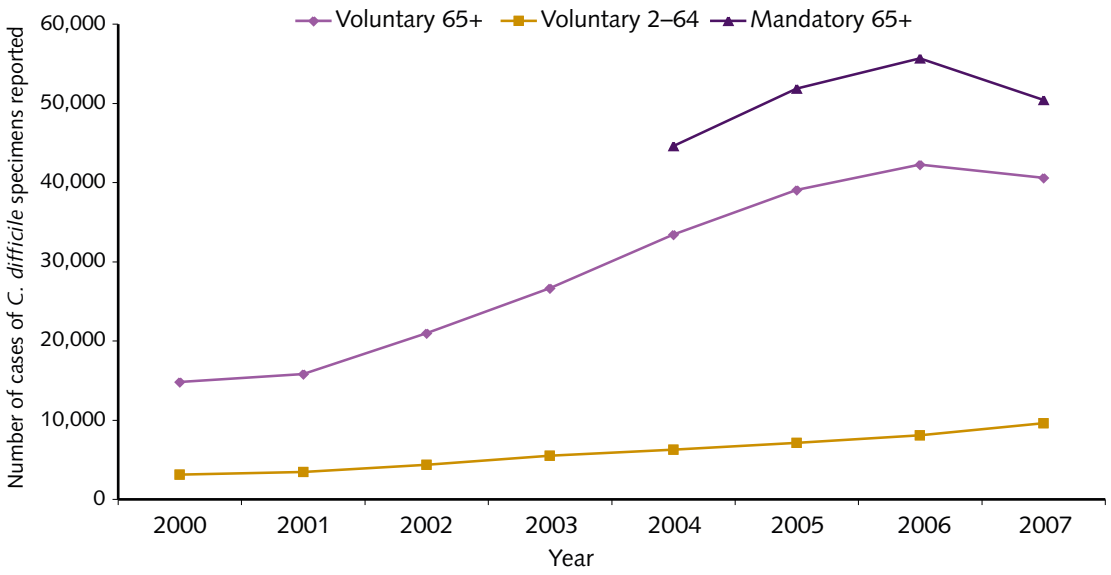
National policy

2.4 Surveillance of CDI in England is currently undergoing a significant change, the latest step being the introduction of a national target for a 30% reduction from the 2007/08 numbers by 2010/11 (HM Government, 2007).

2.5 This surveillance has been built on traditional laboratory reporting of cases of CDI since 1990, but concerns about rates of HCAI resulted, in 2004, in surveillance of CDI being included in the Government's mandatory programme for the surveillance of HCAI (Figure 2). This comprised quarterly reporting by NHS acute trusts of all cases of CDI in patients aged 65 years and over that were diagnosed in the trust's laboratories, wherever the infection was acquired.

2.6 Cases were defined as all diarrhoeal specimens that test positive for CDT where the patient has not been diagnosed with CDI in the preceding four weeks. The criteria for testing for infection and reporting cases were defined by the National *Clostridium difficile* Standards Group (National *Clostridium difficile* Standards Group, 2004). The mandatory surveillance also includes investigation of a sample of isolates from trust hospitals for a defined period in accordance with the random sampling programme. This is in order to obtain information on prevalent epidemiological types and susceptibilities, given that few isolates were being referred to the National Reference Laboratory.

Figure 2: CDI cases in patients aged 2–64 years and 65+ years



2.7 In order to have better and more informed monitoring of the progress towards meeting local targets, in April 2007 the Department of Health required changes to the CDI surveillance system. This included the establishment of web-based reporting for individual cases of infection and extension of the dataset to include patients aged 2 years and older. This policy was restated in a letter in January 2008 from the Chief Medical Officer and Chief Nursing Officer, together with restoration of the use of a 28-day de-duplication interval (Chief Medical Officer and Chief Nursing Officer, 2008).

2.8 The national CDI surveillance system has the following components:

- mandatory surveillance of all cases diagnosed in patients aged >2 years that have been reported individually to a national web-enabled surveillance system (trust-based);
- mandatory surveillance of a sample of *C. difficile* isolates by ribotyping – the random sampling programme (trust-based); and
- voluntary laboratory reporting of cases (laboratory-based).

2.9 All the above components should contribute to an understanding of the local, regional and national trends and the epidemiology of CDI. Information from these surveillance schemes is key to identifying changing trends against earlier baselines and the occurrence and extent of hospital outbreaks or hyperendemicity. Recognising ward, unit or hospital increases in the number of infected patients against a baseline is the key factor in initiating local outbreak control measures. This includes the reporting of outbreaks as serious untoward incidents (SUIs) to those responsible for performance management (strategic health authorities (SHAs) and Monitor).

2.10 Use of statistical tools such as statistical process control (SPC) charts may help ICTs to distinguish between natural and unexpected variation and to identify when numbers of cases are exceeding normal expectations for that unit (Gustafson, 2000). However, SPC limits should be regularly reviewed and adjusted in line with control targets, as levels of CDI need to be managed whether there is an outbreak against a background of low incidence or whether there is hyperendemic CDI.

2.11 There has been criticism that SPCs may not be as appropriate for biological systems as they are for manufacturing systems. Risk-adjusted charts that use the standardised infection ratio have performed better than simple charts in identifying episodes of HCAI (Gustafson, 2000).

2.12 In terms of 'information for action' at the local level, core components of the dataset should include:

- patient, laboratory, unit/ward and hospital identifiers;
- patient demographics (address, age, sex);
- date of admission and the patient's other admissions in previous six weeks;
- date of onset of infection;
- date when specimen was taken; and
- where the infection was diagnosed (hospital, community, specialty, etc.) and whether it was part of an outbreak.

2.13 Other desirable items include:

- the primary diagnosis;
- an assessment of the severity of prior and current (at diagnosis) underlying illnesses;
- antimicrobial therapy;
- total number of stool specimens processed by the laboratory against those tested for *C. difficile*; and
- possible risk factors for infection and patient outcome, including death within 30 days of diagnosis.

2.14 With decreasing lengths of hospital stay as a result of day care and keyhole surgery and changes in the healthcare economy, the need to identify whether an infection was acquired in hospital or in the community, or whether antibiotics were prescribed in hospital or the community, is becoming stronger.

2.15 It is not always possible to determine whether a CDI was acquired in the community or in hospital or when it was acquired, but the place of onset of symptoms of CDI should be identified. Separate reporting of cases with diarrhoea on admission by using hospital CDI data will help to ascertain local epidemiological trends and quantify the challenge to the institution from the community (Cooper et al., 2004b; Stone et al., 2007a, b).

2.16 Interpretation of the overall national picture is affected by complex biases in how CDI is identified. It is clear that there is much local variation in testing, as CDI is not yet routinely considered in the diagnosis of all cases of diarrhoea. This is further complicated by variations in the sensitivity and specificity of the toxin immunoassays.

2.17 This variation means that the interpretation of local surveillance and comparing local results with the national dataset is complex in terms of:

- the factors affecting CDI ascertainment;
- the wide variation in numbers and rates in the different types of acute care facility; and
- the extent that investigation of diarrhoea in all age groups, within the acute healthcare setting and in the community, is shaped by clinical suspicion and local practice (rather than any systematic epidemiological criteria).

2.18 There are clearly acute trusts that are numerically distant from the rest in terms of both high numbers of cases and higher than average rates, but the latter figures are distorted by marked variations in length of patients' stay in hospital. Comparing international surveillance results is relevant but currently limited by the variation in the diagnostic methods used in different European laboratories.

2.19 As already noted, mandatory surveillance of CDI includes a sampling programme for strains of *C. difficile* that cause disease in English hospitals. The aim of this programme, established in 2005/06, is to identify changing epidemiological types and antimicrobial susceptibilities.

2.20 Secondary care trusts were randomly allocated a week in which to send the first 10 non-duplicate positive *C. difficile* specimens to the ARL in Cardiff for typing and susceptibility testing. In the first sampling schedule, 881 isolates of *C. difficile* were obtained.

2.21 Typing investigations revealed that three main PCR ribotypes of *C. difficile* accounted for approximately 75% of the isolates obtained from symptomatic patients in roughly equal proportions: types 106, 027 and 001. However, there was some variation in the proportions of types recovered from different regions.

2.22 The remaining 220 isolates were a mixture of 22 other, rarer PCR ribotypes. Susceptibility testing (E test method) revealed that there was universal susceptibility to metronidazole and vancomycin. Resistance to quinolones and carbapenems was found at high rates, which may relate to selection of *C. difficile* in the gut. Recent studies in both the US and Europe confirm these findings. The US study looked at isolates from 1983 to 2004 and failed to find any evidence for the emergence of resistance to either metronidazole or vancomycin (Barbut et al., 2007; Hecht et al., 2007). The sampling programme has since undergone changes to reflect more accurately the size of contributing secondary care trusts. A programme dealing with cases in primary care trusts (PCTs) and their associated hospitals needs to be initiated.

2.23 Aside from the sampling programme, which forms part of the mandatory surveillance, information is also collected on isolates otherwise referred for typing by trust laboratories (see paragraph 1.13).

2.24 The 1994 guidelines did not cover either national or local surveillance. However, the report of the National Standards Group (National *Clostridium difficile* Standards Group, 2004), the HCC/HPA survey (Healthcare Commission, 2006) and the Healthcare Commission report on HCAI (Healthcare Commission, 2007a) clearly recommend good local surveillance and feedback to clinicians, as well as reporting to national surveillance.

2.25 It is important to catch information that gives early warning of changes in the epidemiology of *C. difficile*, such as trends in community-acquired disease, overall mortality, severity and strain type. Data on death and severity should also be collected. Both the HCC/HPA survey and the Healthcare Commission report on HCAI reinforce the requirement of the Department of Health to report outbreaks to external agencies.

Recent practice

2.26 The HCC/HPA survey found widespread deviations from the recommended national policy on testing and mandatory reporting by laboratories:

- 21% did not test all diarrhoeal samples for *C. difficile*.
- Non-diarrhoeal samples were tested in 20% of laboratories.
- Community-acquired samples were not tested in 24% of laboratories, and results of community-acquired samples were not reported in 23%.
- 73% did not report results from patients admitted to hospitals in other trusts.

2.27 Samples from care homes, private patients within a trust, independent healthcare facilities and GPs were not reported in 43%, 32%, 28% and 16% of trusts respectively. The same proportions of Trusts were unable to supply information on the healthcare source for these groups of patients.

2.28 The survey found widespread breaches of the Department of Health's requirement to report outbreaks. Only 39% of trusts always reported outbreaks to the health protection unit (HPU) and 35% never did so. Only 27% of trusts informed their SHA and 41% never did so. Only 60% always informed the consultant in communicable disease control (CCDC). The criteria used in the earlier guidance for defining an outbreak were not adequate.

2.29 The HCC/HPA survey found that 93% of trusts carried out some form of local surveillance. A local database was maintained by 30% of trusts, usually recording the ward or specialty where the case was diagnosed. Only 15% linked surveillance to clinical review by an infection control nurse (ICN) or an infection control doctor (ICD). Only a third of trusts carried out a regular review of CDI rates, whether the review was of yearly, quarterly, monthly, weekly or daily rates.

2.30 Only 4% of trusts routinely collected data on clinical severity, although 23% thought it would be possible to provide data on this, with 20% and 29% stating that data could be provided on colectomy and death rates respectively.

Example of good practice

2.31 A protocol for the rapid investigation of occurrence of PII of CDI is being used at the Heart of England Foundation Trust. This protocol has incorporated the recommendations made in paragraph 2.36, and the universal application of the protocol across the trust has been a key factor in its work to meet local CDI targets.

Recommendations

2.32 All NHS trusts in England are required to participate in the Department of Health's mandatory CDI reporting system and to report all cases of CDT-positive diarrhoea in patients over 2 years of age. The Department will continue to work with the HPA and Connecting for Health (CfH) and investigate the uploading of patients' demographic data from laboratory computer systems to avoid transcription errors and improve reporting consistency.
(Code: Duties 2c, 10k, 10l; Annex 1; Annex 2; Appendix 2i) B

2.33 Trusts should be strict in adhering to the criteria for testing and reporting. Only diarrhoea samples should be tested.
(Code: Duties 9, 10k; Annex 1; Appendix 2i) B

2.34 All samples (hospital and wider community) should be tested for all patients aged 65 years and above and for those less than 65 years if this is clinically indicated. Diagnostic laboratories should provide information that differentiates clearly between hospital-associated and community-associated specimens. They should clearly state the location of the patient at the time of sample submission and, if known, any previous hospital in which they were in-patients in the last four weeks. **(Code: Duty 10k)** B

2.35 There should be continuous local surveillance of cases of CDI:

- Hospitals or trusts should record and report each month all cases (in all age groups) to directorates, wards and units, with analysis of trends and exceptional events. Review of these reports should be a standing item on the agenda for directorate meetings, for example.
  (Code: Duties 2c, 10l; Annex 1; Annex 2; Appendix 2i) B
- Quarterly, or more frequent, reports of CDI should be returned to ICTs and those accountable for HCAI in specific areas or units, as well as being a standing item on the agenda of infection control committee meetings and board meetings. **(Code: Duties 2c, 10l; Annex 1; Annex 2; Appendix 2i)** B

2.36 Trusts should adhere to the standard definition of a PII and outbreak (see 1.21). The following actions are to be taken if a PII is identified on a ward (see Figure 3):

i. Urgently inform the clinical director, matron, ward manager and directorate manager.

ii. Conduct a weekly *C. difficile* ward audit using the Department of Health's *C. difficile* High Impact Intervention (HII) tool by infection control nurse or infection control doctor to continue until the weekly score is >90% in three consecutive weeks and there have been no further >48 hours cases of CDI on the ward during that period. Feed back the audit results to the matron or ward manager.

iii. Carry out a weekly antibiotic review in each ward, (using local tools); this is the responsibility of the antibiotic pharmacist.

iv. Clean the whole ward with chlorine-containing agent until no further symptomatic patients are present on the ward. Emphasise that each bed space needs to be cleaned separately with separate cloths.

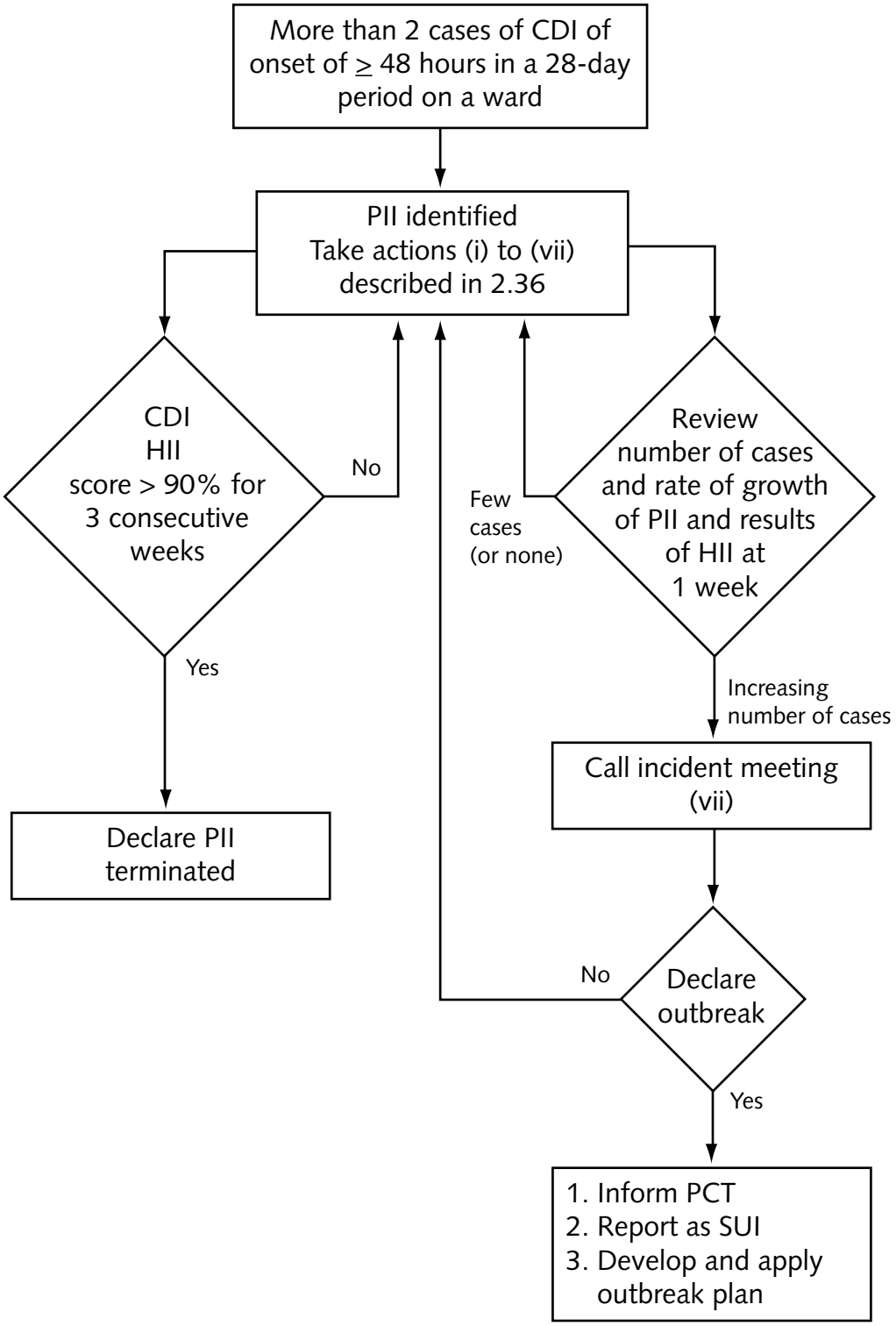
v. Use HPA CDRNE or CfI to undertake PCR ribotyping of all isolates from patients in the ward.

vi. The ICT should carry out an automatic review of ward PIIs each week.

vii. An incident meeting should be held as determined by the size and rate of growth of the PII by assessment of the situation by the DIPC and/or the duty microbiologist with the clinical director and consultants, depending on the number of cases.

2.37 Trusts should report all outbreaks as SUIs to the PCT and the SHA and subject them to a root cause analysis. This includes all ward closures that are due to diarrhoea shown to be associated with *C. difficile*.
(Code: Duties 10c, 10k; Annex 2) B

Figure 3: Algorithm for the management of PII and outbreaks of CDI, to be used together with recommendation 2.36



2.38 Local surveillance should include the number of patients with severe infection, the number requiring surgery and the number dying, where CDI caused or contributed to the death. A regular review should be conducted of deaths within 30 days of diagnosis of CDI to ensure that a common standard of assessment of cause of death or contribution to death is being applied. This will be facilitated by compliance with recommendation 3.33 to establish a multidisciplinary clinical review team. **(Code: Duty 2c; Annex 1)** B

2.39 Frozen storage of small aliquots of toxin-positive stool samples (e.g. a small Eppendorf tube full at –20°C for a rolling year) is recommended. This is so that a retrospective culture can be made should it become apparent that an outbreak of CDI or a change in incidence has taken place that might warrant culture of the organism for typing (Brazier and Duerden, 1998). Obtaining isolates is also advisable in order to monitor antimicrobial susceptibility, especially the emergence of resistance to the current first-line treatment options of metronidazole and vancomycin. C

3. Management and treatment of CDI

Evidence base

3.1 Following the outbreak of CDI at the Maidstone and Tunbridge Wells Hospital in 2006, the Healthcare Commission report (Healthcare Commission, 2007b) was critical of the general care of CDI patients at the hospital. It focused on the lack of regular review and lack of multidisciplinary assessment of patients prone to electrolyte imbalance, dehydration, malnutrition and pressure sores.

3.2 Supportive care should be given, including attention to hydration, electrolytes and nutrition. Antiperistaltic agents should be avoided in acute infection. This is because of the theoretical risk of precipitating toxic megacolon by slowing the clearance of *C. difficile* toxin from the intestine (Novak et al., 1976; Poutanen and Simor, 2004; Aslam et al., 2005; Bouza et al., 2005). The precipitating antibiotic should be stopped wherever possible; agents with less risk of inducing CDI can be substituted if an underlying infection still requires treatment.

Mild disease

3.3 Patients with mild disease may not require specific *C. difficile* antibiotic treatment. If treatment is required, oral metronidazole is recommended (dose: 400–500 mg tds for 10–14 days) as it has been shown to be as effective as oral vancomycin in mild to moderate CDI (Zar et al., 2007; Louie et al., 2007; Bouza et al., 2008).

Moderate disease

3.4 For patients with moderate disease, a 10- to 14-day course of oral metronidazole is the recommended treatment (dose: 400-500 mg tds). This is because it is cheaper than oral vancomycin and there is concern that overuse of vancomycin may result in the selection of vancomycin-resistant enterococci (HICPAC, 1995; American Society of Health-System Pharmacists, 1998; Gerding, 2005).

Severe disease

3.5 For patients with severe CDI, there is evidence that oral vancomycin is preferred (dose: 125 mg qds for 10–14 days). This is because of relatively high failure rates of metronidazole in recent reports and a slower clinical response to metronidazole compared with oral vancomycin treatment (Wilcox and Howe, 1995; Musher et al., 2005; Lahue and Davidson, 2007; Zar et al., 2007). Two recent double-blind randomised studies have reported that vancomycin was superior to metronidazole in severe cases of CDI (Louie et al., 2007; Bouza et al., 2008).

3.6 CDI due to ribotype 027 strains is more likely to be complicated and to require switching from metronidazole to vancomycin (Ellames et al., 2007), although a recent large retrospective cohort study reported no superiority of vancomycin over metronidazole. This suggests that both treatments are suboptimal for at least some strains of this ribotype (Pépin et al., 2007).

3.7 Worryingly, there is new evidence of the emergence of reduced susceptibility to metronidazole in some *C. difficile* isolates, with evidence for clonal spread (Health Protection Agency, 2008a). There is also new evidence of inferior microbiological efficacy of metronidazole in comparison with vancomycin (Al-Nassir et al., 2008; Kuijper and Wilcox, 2008).

3.8 There are, however, no definitive markers of severity. The three most frequently recognised risk factors for severe CDI are age, peak leukocytosis and blood creatinine (Pépin et al., 2004; Loo et al., 2005; Pépin et al., 2007). However, such observations are retrospective and age is too non-specific to be used as a predictor of severe CDI.

3.9 No single parameter alone is highly predictive of severe CDI, with the possible exception of very high WCCs. Zar et al. (2007) used a score based on age, WCC, temperature, albumin, endoscopy findings and admission to an intensive therapy unit to define severe cases. Louie et al. (2006) used number of stools, WCC and abdominal pain to define severe CDI. Importantly, a definition of severe CDI based on number of diarrhoeal stools may suffer from difficulties in recording such episodes, especially in elderly patients with faecal incontinence. Furthermore, severe CDI may occasionally be characterised by ileus with no diarrhoea. A prospectively validated severity score is needed. Until such time as this is available, clinicians need to be alert to the possibility of severe CDI.

3.10 We recommend using any of the following to indicate severe CDI and so to use oral vancomycin in preference to metronidazole:

- WCC >15 $\times$ 10^9/L;
- acutely rising blood creatinine (e.g. >50% increase above baseline);
- temperature >38.5°C; and
- evidence of severe colitis (abdominal signs, radiology).

3.11 A conservative WCC threshold of 15 has been chosen, as higher cut-off values may miss severe cases and relative immune paresis is common in the frail elderly who are most at risk of severe CDI. Elevated blood lactate >5 mmol/L is associated with extremely poor prognosis, even with colectomy (Lamontagne et al., 2007).

3.12 In severe CDI cases not responding to oral vancomycin 125 mg qds, high-dosage oral vancomycin (up to 500 mg qds, if necessary administered via a nasogastric tube) plus intravenous (iv) metronidazole 500 mg tds are recommended. The addition of oral rifampicin (300 mg bd) or iv immunoglobulin (400 mg/kg) may also be considered. Although there are no robust data to support these recommendations, the very poor prognosis may justify aggressive therapy.

3.13 Life-threatening disease (i.e. hypotension, partial or complete ileus or toxic megacolon, or CT (computerised tomography) evidence of severe disease) can be treated by vancomycin given via a nasogastric tube (which is then clamped for one hour) and/or by rectal installation (Apisarnthanarak et al., 2002).

3.14 Colectomy is required in some patients with megacolon (dilatation >10 cm), perforation or septic shock, and should be done before the blood lactate rises above 5 mmol/L (Lipsett et al., 1994; Longo et al., 2004; Koss et al., 2006). Patients should have a total or subtotal colectomy rather than a hemicolectomy or a caecostomy. It may be preferable to preserve the rectal stump for subsequent ileo-rectal anastomosis. The rectocolonic stoma can then be perfused with vancomycin liquid if necessary.

3.15 Recurrent disease occurs in about 20% of patients treated initially with either metronidazole or vancomycin (Teasley et al., 1983; Bartlett, 1985; Wenisch et al., 1996). The same antibiotic that had been used initially can be used to treat the first recurrence (Pépin et al., 2006). This is because the majority of recurrences are reinfections as opposed to relapses (Wilcox et al., 1998).

3.16 After a first recurrence, the risk of another infection increases to 45–60% (McFarland et al., 1999). Vancomycin is preferable to metronidazole in second and subsequent recurrences (Bolton and Culshaw, 1986). It should be noted that there is no evidence of a benefit of using metronidazole or vancomycin to prevent CDI (in patients receiving antibiotic therapy); indeed this approach may actually increase risk.

3.17 Tapering followed by pulsed doses of vancomycin may be of value. There are various regimens, such as 125 mg qds for one week, 125 mg tds for one week, 125 mg bd for one week, 125 mg od for one week, 125 mg on alternate days for one week, 125 mg every third day for one week (six weeks in total) (Tedesco et al., 1985). Clearly, this may provide a considerable selective pressure for vancomycin resistance, e.g. in enterococci.

Agents other than metronidazole or vancomycin

Probiotics

3.18 Meta-analyses have failed to demonstrate statistically any significant efficacy in treating or preventing CDI (Dendukuri et al., 2005; Pillai and Nelson, 2008). A recent randomised, double-blind, placebo-controlled trial showed a beneficial effect of using a proprietary yoghurt as prophylaxis in patients receiving antibiotics (Hickson et al., 2007), but suffered from major methodological flaws threatening the validity and generalisablity of the study (Wilcox and Sandoe, 2007). Crucially, only 7% of those screened for inclusion were recruited to the study, and controls received a milkshake as placebo, which may have increased the risk of diarrhoea because of lactose intolerance (Wilcox and Sandoe, 2007). Thus, we cannot at present recommend the use of probiotics for the prevention of CDI.

Saccharomyces boulardii

3.19 This is not available as a licensed product in the UK. It has been studied extensively but with conflicting results. Subset analysis suggested possible benefit in some recurrent cases (McFarland et al., 2002). It has caused fungaemia in immunocompetent and immunosuppressed patients, and is not recommended for widespread usage (Enache-Angoulvant and Hennequin, 2005).

Intravenous immunoglobulin

3.20 Several case reports and small series have been published regarding the use of this method to treat refractory disease (Leung et al., 1991; Warny et al., 1995; Salcedo et al., 1997; Beales, 2002; Wilcox, 2004; McPherson et al., 2006; Murphy et al., 2006). A dosage of 400 mg/kg given intravenously as a stat dose has been beneficial in about two-thirds of intractable cases. No randomised, controlled clinical trials have been performed to evaluate the efficacy of immunoglobulin in recurrent or severe CDI.

Anion exchange resin

3.21 Oral cholestyramine (4 g packet tds) has been used in the treatment of refractory CDI because it is thought to bind *C. difficile* toxins. There is no robust evidence to support the use of cholestyramine as an adjunctive agent, and there is a risk that it may bind antibiotics used to treat CDI. It is not recommended.

Non-toxigenic *C. difficile*

3.22 Two patients who had multiple relapses were given non-toxigenic *C. difficile* immediately following treatment, with successful interruption of relapse, but this is not recommended on such scant evidence (Seal et al., 1987).

Faecal transplant

3.23 There is evidence for efficiency of faecal transplant in animal models (Professor P Borriello, HPA, personal communication). The use of faecal bacteriotherapy in humans has been reviewed and it was concluded that although the number of studies reported is small (17), the results are promising for relapsing CDI (Borody et al., 2004). A fresh stool (30–50g) from a healthy donor is administered in normal saline by enema, slurries via nasogastric tube, or colonoscopy. Several case reports describe some success in cases of refractory disease (Bowden et al., 1981; Schwan et al., 1984; Tvede and Rask-Madsen, 1989; Aas et al., 2003). This is used as a last resort as there are no comparative studies to verify its effectiveness in CDI, and concerns remain about the safety of the approach. There is a randomised trial of this approach under way in the Netherlands (Keller, 2008).

Fusidic acid

3.24 The response rates in a prospective randomised, double-blind trial comparing metronidazole 400 mg tds (n=55) with fusidic acid 250mg tds 7 days (n=59) showed no significant difference (Noren et al., 2006). Recurrence rates were similar, but development of fusidic acid resistance was seen in 55% of recipients who remained culture-positive. Fusidic acid should not be used as a first-line treatment in CDI; its role in treating recurrences is unclear but resistance is likely to limit this use.

Rifampicin

3.25 No randomised, controlled trials have been reported; there is no robust evidence to support the use of rifampicin as an adjunctive agent. There are many other agents under development and these are listed in Appendix 4.

Examples of good practice

3.26 A weekly review of current symptomatic *C. difficile* in-patients is undertaken at Stoke Mandeville Hospital by a microbiologist, a gastroenterologist, a dietician and an infection control nurse. In view of the high mortality associated with CDI, a check is made to ensure that each patient is not deteriorating, that the infection is optimally treated and that the patient is receiving all necessary types of support. This weekly review should reduce the risk of patients developing complications and offers an opportunity to discuss individual cases with ward staff.

3.27 Vancomycin preparation for injection is now licensed for oral use and is cheaper than the capsules (£32 versus £90 for a 10- to 14-day course). It is also easier to swallow. The contents of vials for parenteral administration may be used for oral administration. After initial reconstitution of the vial, the selected dose may be diluted in 30 ml of water and given to the patient to drink, or the diluted material may be administered by a nasogastric tube.

Recommendations

3.28 Clinicians (doctors and nurses) should apply the following mnemonic protocol (SIGHT) when managing suspected potentially infectious diarrhoea:

S	Suspect that a case may be infective where there is no clear alternative cause for diarrhoea **(Code: Introduction)** B
I	Isolate the patient and consult with the infection control team (ICT) while determining the cause of the diarrhoea **(Code: Duties 8, 10d)** B
G	Gloves and aprons must be used for all contacts with the patient and their environment **(Code: Duty 10; Annex 2)** B
H	Hand washing with soap and water should be carried out before and after each contact with the patient and the patient's environment **(Code: Duties 4e, 10; Annex 2)** A
T	Test the stool for toxin, by sending a specimen immediately **(Code: Duty 1b)** B

3.29 Patients should be monitored daily for frequency and severity of diarrhoea using the Bristol Stool Chart (see Appendix 1). B

3.30 All antibiotics that are clearly not required should be stopped, as should other drugs that might cause diarrhoea (see Appendix 2). **(Code: Duty 10j; Annex 2)** B

3.31 CDI should be managed as a diagnosis in its own right, with each patient reviewed daily regarding fluid resuscitation, electrolyte replacement and nutrition review. Monitor for signs of increasing severity of disease, with early referral to ITU as patients may deteriorate very rapidly. B

3.32 PCTs should ensure that trusts establish a multidisciplinary clinical review team consisting of a microbiologist, an infectious diseases or infection prevention and control doctor, a gastroenterologist or surgeon, a dietician, and an infection prevention and control nurse.

3.33 The team should review all CDI patients at least weekly to ensure that the infection is being treated optimally and that the patient is receiving all necessary supportive care. B

3.34 Assess severity of CDI each day as follows:

- **Mild CDI** is not associated with a raised WCC; it is typically associated with <3 stools of type 5–7 on the Bristol Stool Chart per day. B
- **Moderate CDI** is associated with a raised WCC that is $<15 \times 10^9$/L; it is typically associated with 3–5 stools per day. C

- **Severe CDI** is associated with a WCC >15 × 10^9/L, or an acute rising serum creatinine (i.e. >50% increase above baseline), or a temperature of >38.5°C, or evidence of severe colitis (abdominal or radiological signs). The number of stools may be a less reliable indicator of severity. C
- **Life-threatening CDI** includes hypotension, partial or complete ileus or toxic megacolon, or CT evidence of severe disease. B

3.35 Treat according to severity (see also the treatment algorithms, Figures 4 and 5):

- **Mild and moderate CDI** – oral metronidazole 400–500 mg tds for 10–14 days. A
- **Severe CDI** – oral vancomycin 125 mg qds for 10–14 days. A In severe CDI cases not responding to oral vancomycin 125 mg qds, high-dosage oral vancomycin (up to 500 mg qds, if necessary administered via a nasogastric tube), +/- iv metronidazole 500 mg tds is recommended. The addition of oral rifampicin (300 mg bd) or iv immunoglobulin (400 mg/kg) may also be considered. C
- **Life-threatening CDI** – oral vancomycin up to 500 mg qds for 10–14 days via naso-gastric tube or rectal installation plus iv metronidazole 500 mg tds. Such patients should be closely monitored, with specialist surgical input, and should have their blood lactate measured. Colectomy should be considered, especially if caecal dilatation is >10 cm. Colectomy is best performed before blood lactate rises > 5 mmol/L, when survival is extremely poor (Lamontagne et al., 2007). B

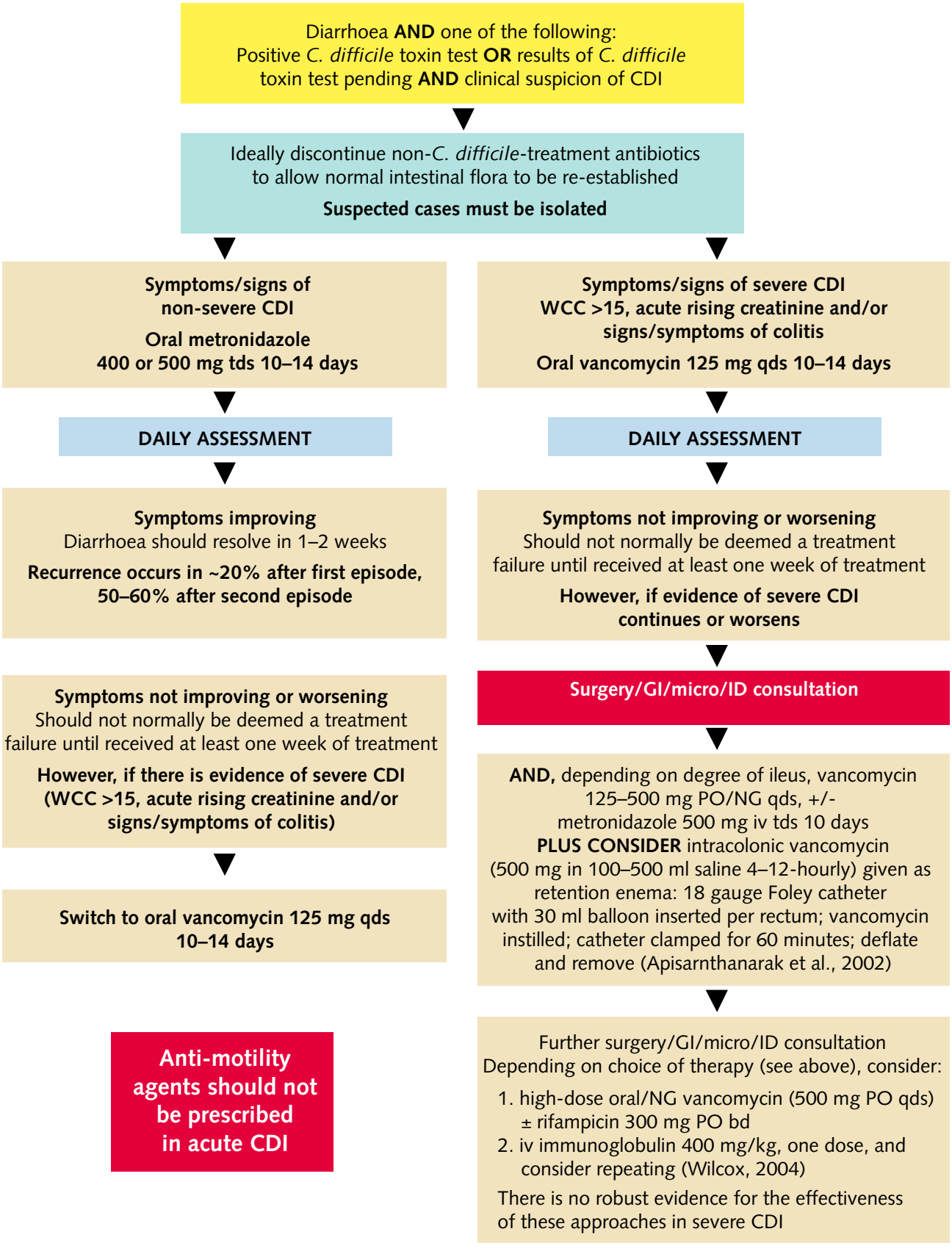
3.36 If diarrhoea persists despite 20 days' treatment but the patient is stable and the daily number of type 5–7 motions has decreased, the WCC is normal, and there is no abdominal pain or distension, the persistent diarrhoea may be due to post-infective irritable bowel syndrome. The patient may be treated with an anti-motility agent such as loperamide 2mg prn (instead of metronidazole or vancomycin). The patient should be closely observed for evidence of a therapeutic response and to ensure there is no evidence of colonic dilatation. C

3.37 **For first recurrence**, repeat the same antibiotic used to treat the initial episode (unless the first episode was treated with metronidazole and the recurrence is severe CDI, in which case vancomycin should be used). B

3.38 **For subsequent recurrences**, use vancomycin 125 mg qds. Consider the alternatives listed in the treatment algorithms (see Figures 4 and 5). C

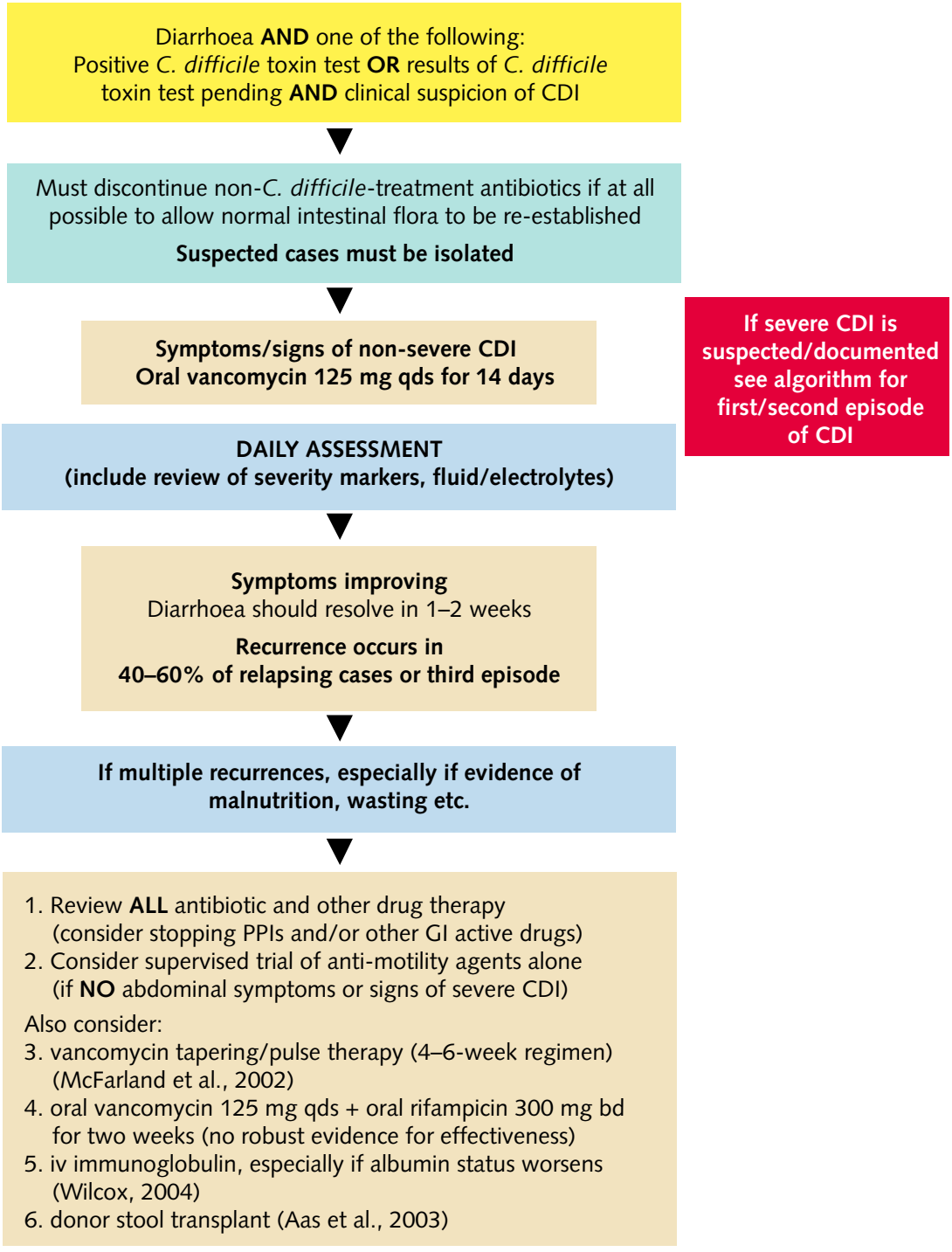
Treatment algorithms

Figure 4: First or second episode of *C. difficile* infection



Treatment algorithms

Figure 5: Recurrent *C. difficile* infection (third or subsequent episode)



4. Prevention of CDI through antibiotic prescribing

Evidence base

4.1 Use of broad-spectrum antibiotics has been strongly associated with CDI, especially third-generation cephalosporins given to the elderly, as well as clindamycin and prolonged use of aminopenicillins (National *Clostridium difficile* Standards Group, 2004; Davey et al., 2006).

4.2 Recent evidence has shown an association with carbapenems in surgical patients receiving prophylactic antibiotics (Itani et al., 2006).

4.3 Fluoroquinolones may have contributed to the recent spread of strain 027, although there are conflicting data (Biller et al., 2007; Valiquette et al., 2007; Saxton et al., 2007; Goorhuis et al., 2007; Loo et al., 2005).

4.4 Systematic review (Thomas et al., 2003) has questioned the quality of many studies relating specific antibiotics to CDI; other factors may also operate, such as:

- duration of treatment;
- polypharmacy (administration of more than one agent at a time and/or multiple courses);
- administration of prophylactic antibiotics for more than 24 hours (www.sign.ac.uk/guidelines/fulltext/45/index.html); and
- exposure to *C. difficile* (National *Clostridium difficile* Standards Group, 2004).

4.5 Nearly all antibiotics may predispose towards *C. difficile*, including clarithromicin and other macrolides (National *Clostridium difficile* Standards Group, 2004), but some appear to be much less likely to do so (gentamicin, penicillin, and anti-pseudomonal penicillins, with or without a beta-lactamase inhibitor, vancomycin).

4.6 There is a lack of easily comparable data on CDI selection by different agents. Studies are hard to do (patients rarely receive single agents, they may have had prior exposure etc.), but CDI risk should be included in licensing studies and be reported via the yellow card scheme.

4.7 There is systematic review evidence to show that restricting use of broad-spectrum antibiotics, specifically cephalosporins or clindamycin, can reduce *C. difficile*, even though most studies are methodologically flawed (Davey et al., 2006). Two crossover studies and a follow-on surveillance study on acute elderly wards showed that effective restriction of third-generation cephalosporins was associated with a reduction in *C. difficile* (Settle et al., 1998; Stone et al., 2000; Wilcox et al., 2004).

4.8 Systematic review of studies of the effectiveness of interventions to change antibiotic prescribing shows most studies to be methodologically poor (Davey et al., 2005; Stone et al., 2007a, b). However, there is evidence that a wide variety of interventions can significantly restrict use, although it is not possible to say which is the most effective. Many interventions involve pharmacists. In one trust, a well-designed study showed that daily review of antibiotic prescriptions by ward pharmacists reduced broad-spectrum antibiotic prescription (Ansari et al., 2003).

4.9 The impact of the Department of Health's Hospital Clinical Pharmacy initiative to improve antibiotic management has been reviewed (Wickens and Jacklin, 2006). It appears to have facilitated greater local multidisciplinary working between pharmacy and microbiology/infectious diseases departments, mainly through the appointment of antimicrobial pharmacists. This has resulted in activities to promote good antimicrobial control, education and monitoring, and there have been significant cost savings in a number of trusts (Wickens and Jacklin, 2006).

4.10 The evidence-based guidelines to improve antibiotic use, published in 2007 by the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA), favour such multidisciplinary working. They strongly recommend 'antimicrobial teams', consisting of an antimicrobial pharmacist, a microbiologist (along with an infectious diseases physician if available) and an information specialist (Dellit et al., 2007).

4.11 Systematic reviews of cluster RCTs (CRCTs) (Grimshaw et al., 2004; Jamtvedt et al., 2006) suggest that audit and feedback may change the implementation of evidence-based guidelines by healthcare workers. One crossover study used audit and feedback to prescribers to reduce cephalosporin use and *C. difficile* (Stone et al., 2000). A later study used it to reduce broad-spectrum and increase narrow-spectrum antibiotic use, with an associated fall in the incidence of CDI (Fowler et al., 2007). Indeed, audit and feedback have been given more prominent roles in the latest guidelines for control of meticillin-resistant *Staphylococcus aureus* (MRSA) (Coia et al., 2006) and are strongly recommended by the IDSA/SHEA guidelines to improve antibiotic management (Dellit et al., 2007).

4.12 Good antibiotic stewardship includes reviewing the use of iv antibiotics in the light of microbiology results, after 48 hours in the first instance. A switch should be made to oral medication thereafter, unless clinically indicated or unless this would result in prescription of broader-spectrum antibiotics orally. One advantage of early switch from intravenous to oral administration is earlier discharge of the patient from an environment potentially contaminated with *C. difficile*. There is no need for the initial doses of antibiotics to be given intravenously as a matter of routine. In general, no more than 5–7 days of total prescription is required, although in some situations such as lower urinary tract

infections in women, less will be required. Automatic and/or prospective stop dates should be encouraged, although these can only be implemented by a doctor (not a pharmacist) under the Medical Act.

4.13 Most surgical prophylaxis should be limited to single-dose regimens, administered as close as possible to operation (Kreisel et al., 1995). Polypharmacy should be avoided where clinically unjustified. Guidelines should be reviewed at least annually, but more frequently if changes in sensitivity, clinical presentation or local *C. difficile* rates necessitate.

4.14 New versions of guidelines should be clearly identifiable and all staff made aware of the existence of new versions (e.g. by printing them in a different colour). Guidelines should be made easily available to medical staff through means that include:

- using portable formats such as laminated cards or explanatory leaflets;
- printing of guidelines on admission proformas;
- affixing copies to notes trolleys; and
- making guidelines available on hospital intranets.

National policy

4.15 The 1994 guidelines (Department of Health, 1994) and the National *Clostridium difficile* Standards Group (2004) called for restrictive antibiotic guidelines to reduce inappropriate use of broad-spectrum antibiotics, especially that of third-generation cephalosporins in the elderly, and to increase the use of narrow-spectrum drugs. Methods suggested to achieve this are:

- monitoring by ward pharmacists;
- automatic stop dates;
- electronic prescribing; and
- production of clear guidelines that also address the need for short-course surgical prophylaxis.

4.16 Development of "an overall perspective" towards national or local prescribing guidelines for antibiotics, which considers the risk of *C. difficile* and incorporates audit, is favoured (National *Clostridium difficile* Standards Group, 2004).

4.17 The HCC has also called for restrictive antibiotic guidelines limiting inappropriate use of broad-spectrum agents (Healthcare Commission, 2006), as has the Chief Medical Officer (Chief Medical Officer and Chief Nursing Officer, 2005). In addition, the HCC has recommended the use of audit and feedback to prescribers (Healthcare Commission, 2006).

4.18 This is consistent with the recommendations of the National Audit Office's report and of the *Winning Ways* document that clinicians be involved in infection control (National Audit Office, 2000; Chief Medical Officer, 2003). The HCC/HPA survey recommended the strengthening of recommendations on restricting the use of particular antibiotics.

4.19 The annex to the Code calls for all trusts to have antibiotic guidelines which restrict broad-spectrum antibiotic use. This is particularly aimed at reducing use of extended-spectrum cephalosporins and fluoroquinolones, avoiding their empirical or definitive overuse, and ensuring their prescription only when indicated by the clinical condition of the patient or the results of microbial investigation (Department of Health, 2008a).

4.20 Duty 10j and Annex 2 also call for antibiotic guidelines to limit iv regimens to 48 hours; to provide guidance on iv–oral switch, with automatic stop dates facilitating 48-hour iv and 5-day oral regimens; and to limit most surgical prophylaxis to a single dose.

4.21 The annex further states that there should be regular audit of compliance with all aspects of antibiotic guidelines, and sees a major role for the pharmacist with specific responsibility for antibiotics in implementation of guidelines (Department of Health, 2008a). While early switch to oral antibiotics might reduce hospital length of stay and therefore exposure to CDI, there is no evidence that oral antibiotics are less selective for *C. difficile* than intravenous ones.

Recent practice

4.22 The HCC surveyed practice in NHS acute trusts in 2005 (Healthcare Commission, 2006) and found that, while 89% had written guidelines for the management of *C. difficile*, 38% had placed no restrictions on broad-spectrum antibiotic use and 18% did not audit use of antibiotics. In addition, 55% thought that improved antibiotic prescribing would be the most practical measure to help reduce CDI.

4.23 An independent survey of UK trusts in 2001/02 (Woodford et al., 2004) showed that:

- 7% had no documents relating to antibiotic control;
- 76% had a formulary;
- 56% had a written policy setting out general strategy;
- 87% had guidelines for specific drugs and diseases;
- 32% had all three of the above; and
- only 60% had both an antibiotic formulary and guidelines.

4.24 About 40% of trusts had electronic versions of the documents. Annual review took place in 56% of trusts. The survey noted that there had been little change since the previous survey in 1990.

4.25 In 2003, more than 90% of trusts took up the offer of 'pump priming' via PCTs to employ antimicrobial pharmacists. *Clean, Safe Care* (Department of Health, 2008b) supports this announced funding for specialist staff.

4.26 Although many hospitals can provide figures for total hospital usage or expenditure, some are able to provide only the latter, while many hospitals cannot provide consultant, ward or unit level data, which would facilitate feedback to prescribers.

4.27 Recent work by the HCC and the Specialist Advisory Committee on Antimicrobial Resistance has recommended that quantitative data be obtained for acute trusts (Cooke, 2007) but patient- and consultant-specific data can currently only be obtained through specific audits and not routinely.

4.28 Electronic prescribing and medicines administration programmes will ultimately provide the means for combining patient-specific data with diagnostic, surveillance and antimicrobial utilisation information. There is a need for SHAs to develop and support the provision of such data quarterly for secondary care trusts, and for PCTs to provide such data to their local microbiology departments. However, delays are likely in implementing such advances.

Examples of good practice

4.29 In a well-designed study in Tayside, a trust agreed guidelines to restrict the use of antibiotics, reinforced by daily review of drug charts conducted by ward pharmacists. This succeeded in steadily reducing broad-spectrum antibiotic use over two years (Ansari et al., 2003).

4.30 At Stoke Mandeville Hospital, Buckinghamshire, all doctors have a pocket-sized laminated card printed with the hospital guidelines, that gives prescription options in settings with and without *C. difficile*. Antibiotic use and *C. difficile* rates are fed back to wards and directorates every month.

4.31 At the Royal Free Hospital, London, the antibiotic guidelines are distributed to all doctors in leaflet form. The guidance is printed on the general medical admission proforma and is available on the intranet. Doctors on the acute care of the elderly unit carry a pocket-sized laminated card with the guidelines, and receive feedback which has reduced both cephalosporin use and *C. difficile* over many years (Stone et al., 2000; Fowler et al., 2007).

4.32 At Southampton University Hospital, an antimicrobial team ward round reduced expenditure substantially, either stopping or modifying antibiotic use in 40% of cases. The University Hospital of South Manchester has developed electronic formularies and guidelines that can be downloaded to hand-held personal digital assistants. Poster campaigns have been conducted, and algorithms for best antimicrobial selection have been put onto mouse mats and on the back of each British National Formulary issued (Williams et al., 2005).

4.33 In Leeds General Infirmary, removal of cephalosporins from routine use in elderly medicine, with substitution of piperacillin-tazobactam, was associated with a significant reduction in incidence of CDI (Wilcox et al., 2004).

Recommendations

4.34 All trusts should establish an AMT or equivalent. This should consist of an antimicrobial pharmacist, a consultant microbiologist or infectious diseases specialist, and an information technology specialist. Antimicrobial pharmacists have a valuable role in AMTs and PCTs, and providers should actively encourage their involvement and, where necessary, support recruitment to these posts. **(Code: Duty 2c; Annex 1)** B

4.35 Restrictive antibiotic guidelines should be developed by the trusts through the AMT, stressing the following recommendations:

- Use narrow-spectrum agents for empirical treatment where appropriate.
- Avoid use of clindamycin and second- and third-generation cephalosporins, especially in the elderly.
- Minimise the use of fluoroquinolones, carbapenems and prolonged courses of aminopenicillins. **(Code: Duties 10j, 10l)** B

4.36 Guidance should be given on repeated antibiotic prescription for the same or sequential infections and should be easy to understand and follow. **(Code: Duties 10j, 10l)** B

4.37 Restricted broad-spectrum antibiotics should be used when indicated by the patient's clinical condition, results of microbiological testing or local susceptibility results. **(Code: Duties 10j, 10l)** B

4.38 Guidelines should:

- name specific antibiotics for specific infections;
- give guidance on therapeutic courses of antibiotic dosage, duration (in general 5–7 days), automatic stop dates (which can only be written by doctors) and dates for iv–oral switch;
- minimise polypharmacy;

- include surgical prophylaxis (mostly limited to one dose administered as near as possible to the operation);
- be regularly reviewed;
- be easily available; and
- be easy to understand and follow.

(Code: Duty 10j) B

4.39 All consultants should be responsible for reviewing antibiotic prescriptions on all their ward rounds, and should stop unnecessary prescriptions and change those that do not comply with guidelines. Juniors should do the same on their own ward rounds. **(Code: Duty 10j)** C

4.40 Antibiotics should only be prescribed when there is clinical evidence of bacterial infection. Evidence of infection (i.e. the reason for administering antibiotics) should be clearly documented in the clinical record. **(Code: Duty 10j)** C

4.41 Antibiotics started inappropriately or without sufficient evidence should be stopped. Antibiotics should be stopped where microbiology results do not support the diagnosis of bacterial infection in the suspected site or elsewhere. Antibiotic prescriptions that depart from guidelines without justified clinical or microbiological indications should be changed or stopped. The traditional approach of completing a course of antibiotics once it has been started is no longer appropriate in these circumstances. **(Code: Duty 10j)** C

4.42 Trusts should, through the AMT, develop programmes to capture and feed back data on both antibiotic use (in defined daily doses per 1,000 bed days, with differentiation between out-patient and in-patient prescription) and *C. difficile* rates (as cases per 1,000 admissions) for the hospital as a whole. Wards and directorates should be provided with data on antibiotic prescription and *C. difficile* cases each month. **(Code: Duties 2c, 2e; Annex 1)** B

4.43 It is not always possible to define place or time of acquisition of CDI and the influence of prior antibiotic use. Cases with diarrhoea on admission or within 48 hours of admission should be carefully assessed with regard to recent admissions in order to interpret local epidemiological trends. Cases in the community should be assessed for past hospitalisation and antibiotic use.

4.44 **Clinical directors** should ensure that good antimicrobial practice becomes embedded at the patient level through one or more of the following:

- Designated 'link physicians' for units where there is local concern about the level of CDI, such as units for the care of the elderly. Such link physicians should be responsible to their directorate's medical infection control lead, and should be the person with whom the AMT liaises regarding antibiotic guidelines, audit, and feedback of antibiotic use and CDI rates to junior staff. B

- Daily review of drug charts by ward pharmacists to check compliance with antibiotic guidelines and to discuss deviations with the ward or prescribing doctor, with support from the AMT. B
- AMT ward rounds and audits to review antibiotic prescriptions, changing prescriptions where necessary and giving verbal feedback to the ward doctor and written feedback in a letter or report to the consultant. The frequency of rounds and the wards attended will vary with local circumstances. B
- In a critical care environment, joint daily rounds between intensivist, microbiologist and pharmacist should be considered.

(Code: Duties 2c, 2e, 10j, 11d; Annex 1; Annex 2; Annex 3; Appendix 2i)

4.45 Trusts should, in consultation with the AMT, liaise with organisations responsible for postgraduate training to co-ordinate teaching of antibiotic prescribing to doctors, pharmacists and nurses as part of their formal in-house training programme.

4.46 There should be mandatory core training in prudent antibiotic use for doctors, pharmacists and nurses, in addition to an introductory session on each induction programme. Post-registration, this should be repeated every three years and should specifically cover those antibiotics that provoke CDI. **(Code: Duty 11d; Annex 3)** C

5. Prevention through isolation

Evidence base

5.1 The National *Clostridium difficile* Standards Group examined individual studies to assess the impact of isolation of patients with CDI. The evidence from these studies, where isolation was either the main intervention, or part of a package of interventions, indicates that early isolation helps to both control outbreaks and reduce endemic levels of CDI (National *Clostridium difficile* Standards Group, 2004).

5.2 Although such studies share the weaknesses of infection control studies in general (Stone et al., 2007a, b), RCTs may be neither feasible nor ethical. No systematic review exists, but a systematic review of isolation in the hospital management of MRSA found evidence that isolation, as part of a package of measures, can reduce MRSA levels even in endemic settings (Cooper et al., 2003, 2004a).

5.3 Evidence was also found for the effectiveness of isolation wards with designated staff, isolation in single rooms, and isolation measures with cohorting of nursing staff. Given that *C. difficile* is an infectious disease with very high levels of hand and environmental contamination but not staff carriage as with MRSA, we consider it highly likely that isolation of suspected and proven cases is effective.

National policy

5.4 The Department of Health/Public Health Laboratory Service guidelines (Department of Health, 1994) recommended that symptomatic patients should be isolated until formed stools have been obtained, whether they remain toxin or culture positive or negative. Those guidelines also recommend that, wherever possible, affected patients (including patients with diarrhoea who have not yet been confirmed as *C. difficile*-positive) should be transferred to an isolation ward. If an isolation ward is not available, the patients should be managed in single rooms.

5.5 The National *Clostridium difficile* Standards Group reiterated this guidance in 2004 (National *Clostridium difficile* Standards Group, 2004) and the HCC/HPA survey promoted adherence to it in 2006 (Healthcare Commission, 2006), as did Saving Lives in 2007.

5.6 In a large outbreak, it may not be possible to isolate affected patients in single rooms and it may then be necessary to cohort nurse them in a dedicated area of a ward. Negative-pressure ventilation is not required for CDI patients in isolation wards or single rooms.

Recent practice

5.7 Despite strong recommendations regarding isolation of patients with CDI having existed since 1994, the survey (Healthcare Commission, 2006) found that 40% of trusts did not routinely isolate patients with CDI and only 11% had an isolation ward specifically for CDI.

5.8 The HCC's investigations into the outbreaks at Stoke Mandeville (Commission for Healthcare Audit and Inspection, 2006) and Maidstone (Healthcare Commission, 2007b) highlight lessons for other trusts.

5.9 Chief among these is the need for rapid isolation of patients with diarrhoea as well as restriction of the movement of infected patients between wards. The HCC "prioritises the management of patient risk" and is unequivocal in "reiterating to NHS Boards that the safety of patients is not to be compromised under any circumstances".

5.10 The HCC report stated that trusts need to ensure that the safety of patients is not compromised in the pursuit of other strategic objectives, such as financial and other targets and service reconfigurations. It specifically criticised the Stoke Mandeville and Maidstone boards for not immediately following the advice of the ICTs and HPUs to open an isolation ward with self-contained toilet facilities, when isolation capacity in the hospitals was exceeded.

Examples of good practice

5.11 *C. difficile* isolation wards set up at Stoke Mandeville Hospital and Royal Devon and Exeter Hospital were associated with a decline in the incidence of *C. difficile* in these hospitals.

5.12 Strict criteria for de-isolation were introduced at Stoke Mandeville Hospital, and these also helped. Birmingham Heart of England, Shrewsbury and Telford NHS Trust, Kettering, King's College London and West Hertfordshire are trusts which have recently and successfully introduced isolation wards, and this approach is strongly supported by all microbiologists on the working group (see Appendix 9) (Professor PM Hawkey and Sheldon Stone, personal communications).

Recommendations

5.13 Patients with potentially infective diarrhoea (at least one episode) should ideally be moved immediately into a single room with a self-contained toilet and its own hand basin. Stool specimens should be sent immediately for *C. difficile* toxin test. (For more information see the SIGHT protocol.) If the room does not have its own toilet facilities then a commode should be arranged. **(Code: Duties 4e, 8, 10d; Annex 2)** B

5.14 The Bristol Stool Chart (Appendix 1) should be used to monitor the patient's diarrhoea. B

5.15 All staff or visitors entering a single room/isolation ward should use disposable gloves and aprons for all contact with the patient and the patient's environment, and wash their own hands with soap and water before and after patient contact (see SIGHT protocol). **(Code: Duty 10a; Annex 2)** A

5.16 The patient should remain isolated until there has been no diarrhoea (types 5–7) for at least 48 hours, and a formed stool has been achieved (types 1–4). **(Code: Duties 8, 10d; Annex 2)** C

5.17 If isolation in a single room is not possible because the single room capacity is exceeded, patients with confirmed CDI should be nursed in a dedicated *C. difficile* ward. An alternative is cohort nursing in a bay with a solid partition, including a door, separating it from the rest of the ward. However, this requires rigorous supervision to maintain cleanliness in toilets/commodes and to ensure staff contact precautions in such bays are observed. A dedicated cohort ward is therefore preferable.

5.18 Where single-room isolation or cohort nursing in a bay is not halting or reducing spread of infection and the advice of the ICT is to open or create a designated isolation ward, this should be done. If necessary, take external advice from the HPU. **(Code: Duties 8, 10d)** B

5.19 Confirmed cases should be transferred to a single room or isolation ward as soon as possible after diagnosis and no later than the end of the day of diagnosis. An audit should be done of the number of patients isolated and the percentage of suspected and confirmed cases isolated during the working day. The infection control link practitioner will have a key role in this process. Minimising the movement of patients between wards will reduce the exposure of other patients to *C. difficile* when a case of CDI is recognised. **(Code: Duties 2e, 2f)** B

5.20 Transfer and movement of patients should be reduced to an operationally effective minimum. Where patients need to attend departments for essential investigations, they should be 'last on the list' unless earlier investigation is clinically indicated. In advance of the transfer, the receiving area should be notified of the patient's CDI status. Arrangements should be put in place to minimise the patient's waiting time and hence contact with other patients. Transfer to other healthcare facilities should, if possible, include notification of the patient's CDI status and be appropriate, i.e. the patient should be called for when the facility is ready for them and their transfer planned so that they are not held in communal waiting areas. Staff, including ambulance personnel, should adopt infection control precautions when in contact with the patient. **(Code: Duties 2f, 6, 10a; Annex 1; Annex 2)** **B**

5.21 After transport of the patient with CDI, the risk of cross-infection to other patients is minimal. Good infection control practices and cleaning should suffice to prevent cross-infection. Faecal soiling should be cleaned then treated using chlorine-containing agents.
(Code: Duties 2f, 3, 5, 7, 10i; Annex 1; Annex 2) **B**

5.22 All clinical waste and linen from patients with CDI, including bedding and adjacent curtains, should be considered contaminated and should be managed in accordance with local guidelines and national guidance.
(Code: Duties 4f, 4g; Annex 1; Appendix 2f) **B**

5.23 Infection control precautions for handling deceased patients are the same as those used when patients are alive. Faecal soiling around the cadaver should be cleaned first with detergent and then with a chlorine-containing cleaning agent. Plastic body bags are not necessary, but may be used as part of general practice in accordance with standard precautions for all patients. There is negligible risk to mortuary staff or undertakers provided that standard infection control precautions are used. **(Code: Duty 10i; Annex 2; Appendix 2d)** **B**

6. Prevention through environmental cleaning and disinfection

Evidence base

6.1 *C. difficile* spores can survive in the environment for months or years and unless removed by assiduous cleaning can be found on multiple surfaces in healthcare settings (Fekety et al., 1981; McFarland et al., 1989; O'Neill et al., 1993).

6.2 Not surprisingly, the heaviest contamination is often on floors, commodes, toilets, bedpans and bed frames, which are subject to faecal contamination. One good retrospective cohort study showed statistically significant reductions in CDI rates in a bone marrow transplant unit following the introduction of the following infection control interventions:

- education;
- hand washing;
- glove wearing; and
- environmental cleaning with unbuffered 1:10 hypochlorite solution (Apisarnthanarak et al., 2004).

6.3 A range of studies show that improvements in environmental cleaning, such as the introduction of hypochlorite or other sporicidal agents, will lead to an associated reduction in CDI rates.

6.4 A simple educational intervention to change the way cleaning was undertaken by house cleaning staff, using bleach disinfection, dramatically reduced environmental contamination with *C. difficile* and vancomycin-resistant enterococci (Eckstein et al., 2007). It is essential that fabrics and carpets from environments such as floors and chairs, which may otherwise be damaged by bleach, are removed.

6.5 The rate of environmental contamination with *C. difficile* has been shown to increase according to the carriage and symptom status of the patients. Contamination is lowest in rooms of culture-negative patients and highest in symptomatic patients (Kim et al., 1981; McFarland et al., 1989).

6.6 However, possibly because of confounding factors, the incidence of CDI can correlate significantly with the prevalence of environmental *C. difficile* on one hospital ward but not on another (Fawley and Wilcox, 2001).

6.7 Samore and colleagues showed that the environmental prevalence of *C. difficile* correlated with the extent of contamination of healthcare workers' hands by this bacterium (Samore et al., 1996).

6.8 Environmental contamination has been linked to spread of *C. difficile* via contaminated commodes (McFarland et al., 1989; Samore et al., 1996; Fawley and Wilcox, 2001), blood pressure cuffs (Manian et al., 1996), and oral and rectal thermometers (Brooks et al., 1992; Brooks et al., 1998; Jernigan et al., 1998).

6.9 Replacement of electronic thermometers with single-use disposable thermometers has been associated with significant reductions in CDI incidence (Brooks et al., 1992; Brooks et al., 1998; Jernigan et al., 1998). There is no published evidence of colonoscopies acting as vectors, but failure of disinfection will result in a potent vector for cross-infection, as occurred in the UK in 1978 (Professor P Borriello, unpublished data).

6.10 Effective cleaning of the environment has been demonstrated to reduce the incidence of *C. difficile* (Kaatz et al., 1988; Wilcox et al., 2003). Cleaning by detergent alone has been shown to be insufficient to decontaminate and studies have demonstrated there is a need for a sporicidal product.

6.11 In a study by Mayfield et al. (2000), introduction of hypochlorite-based cleaning was associated with reduced incidence of CDI in a bone marrow transplant unit, but incidence increased to the baseline level following the reintroduction of the original quaternary ammonium cleaning agent. A significant correlation has been demonstrated between the use of a chlorine-containing agent (1,000 ppm available chlorine) and reduction in the incidence of CDI on one of two hospital wards examined.

6.12 Various disinfectants are available, but non-chlorine-containing products are often not sporicidal and may actually enhance sporulation (Fawley et al., 2007).

6.13 A report published in 2007 highlighted the use of hydrogen peroxide vapour (HPV) to reduce environmental contamination with *C. difficile* (Boyce, 2007). In this study, *C. difficile* was isolated from 2.4% of swab cultures and 25.6% of sponge cultures before the use of HPV, and both figures were reduced to zero after the use of HPV. The incidence of new nosocomial cases decreased from 1.36 cases per 1,000 patient days to 0.84 cases per 1,000 patient days. The decrease could not be attributed to changes in antimicrobial usage patterns.

6.14 However, the viability of this method is limited both by its cost and by the practical considerations of the room/area that needs to be vacated by patients and staff, left empty for several hours and/or sealed.

6.15 A wide range of disinfectants suitable for instrument (e.g. endoscope) or environment decontamination show in vitro activity against *C. difficile* spores (Rutala et al., 1993; Shetty et al., 1999; Wullt et al., 2003; Block, 2004; Perez et al., 2005; Fawley et al., 2007). With the exceptions noted above, comparative in situ efficacy data for these disinfection options are lacking.

6.16 The efficacy of cleaning is critical to the success of decontamination in general, and therefore the acceptability of disinfection regimens to their users is a key issue. Endoscopes have not been implicated in the transmission of *C. difficile*, but the potential for spread via this mechanism is preventable by careful cleaning and disinfection as recommended by the manufacturer.

National policy

6.17 In March 2004, the *NHS Healthcare Cleaning Manual* was published to act as a benchmark for cleaning within NHS trusts (Department of Health, 2004a). It gives clear guidance on how to clean but does not detail the cleaning products that should be used or the frequencies with which items should be cleaned.

6.18 In July 2004, a Department of Health action plan, *Towards Cleaner Hospitals and Lower Rates of Infection*, was published, which aimed to bring good practice to all areas of the NHS (Department of Health, 2004b). As part of this, the Matrons' Charter, entitled 'An action plan for cleaner hospitals', was introduced, setting out 10 broad commitments around cleanliness and cleaning for which matrons were to act as the lynchpins.

6.19 In December 2004, the Department released guidance (Department of Health and NHS Estates, 2004) on contracting for cleaning, which sets out quality standards. It also outlines the frequencies with which different areas should be cleaned depending on risk, but again does not include recommendations on which cleaning products to use or detail how cleaning should differ during outbreak situations.

6.20 In an effort to reduce the risk of cross-infection due to use of cleaning materials in multiple areas, the National Patient Safety Agency introduced a colour-coding scheme in January 2007 (National Patient Safety Agency, 2007a).

6.21 In view of concerns that a rapid turnover of patients might compromise the cleaning of beds, the HCC stated in 2007 that trusts should ensure that they have guidelines in place specifying the protocol for cleaning between changeover of patients, and that checks are made to ensure that these guidelines are maintained.

Recent practice

6.22 The profile of cleanliness within hospitals has risen over recent years, and there is now an increased awareness of the issue. Since 2000, patient environment action teams (PEATs) have assessed the patients' hospital environment within each NHS trust. The number of trusts that have acceptable or good results for cleanliness has increased over the years. Many trusts also assess their own cleaning by means of monthly visual inspections. However, there is often little correlation between visible and microbiological cleanliness; the use of culture and adenosine triphosphate (ATP) bioluminescence would provide better information to manage cleaning. At present hospitals should have their own cleaning schedules and recommendations regarding cleaning solutions, both for routine cleaning and for enhanced cleaning during outbreaks of *C. difficile*.

6.23 The HCC report on HCAI (Healthcare Commission, 2007a) found a high correlation in trusts between high PEAT scores and lower rates of CDI.

6.24 The correlation between bathroom and toilet cleanliness and lower CDI rates was especially significant. In trusts where meetings to discuss PEAT results were held by infection control and cleaning staff and matrons.

Examples of good practice

6.25 At Buckinghamshire Hospitals NHS Trust and Heart of England NHS Foundation Trust, a whole ward is cleaned with chlorine if there has been evidence of transmission occurring on the ward. Evidence of transmission is defined as two or more cases of hospital-acquired *C. difficile* diarrhoea in one week, or three cases within three weeks. Chlorine is used throughout the ward and the cleaning regimen includes a complete change of curtains. Anecdotal evidence suggests that this helps to reduce further transmission of *C. difficile* within the ward, but further studies are required.

6.26 At the Royal Free Hampstead NHS Trust, four infection control link practitioners are attached to the infection prevention and control team. The teams each cover a clinical directorate and provide audit and training on cleaning, hand hygiene, personal protective clothing and isolation practices. PEAT assessments are conducted monthly on all wards and discussed at monthly multidisciplinary team meetings, attended by the infection prevention and control team, matrons, ward sisters and facilities and domestic staff. In addition, domestic services carries out a weekly cleaning check, using a modified Infection Control Nurses Association audit tool, which also assesses cleanliness of clinical equipment.

Recommendations

6.27 Environmental cleaning of rooms or bed spaces of CDI patients should be carried out at least daily using chlorine-containing cleaning agents (at least 1,000 ppm available chlorine). **(Code: Duties 4, 10i; Annex 2)** B

6.28 All commodes, toilets and bathroom areas of CDI patients should be cleaned after each use with chlorine-containing cleaning agents (at least 1,000 ppm available chlorine). **(Code: Duty 10i; Annex 2)** B

6.29 Trusts should ensure that all clinical areas assess cleanliness and ensure that they have introduced the National Specifications for Cleanliness (National Patient Safety Agency, 2007c). In particular, they should ensure that an appropriate auditing process (which is designed to ensure monitoring is at its most intense in areas of very high and high risk) is in place and fully complied with. The results of this should be discussed at regular (at least monthly) meetings of matrons, and infection prevention and control and cleaning staff. **(Code: Duties 2e, 4, 10i, 10l, 11d; Annex 2; Annex 3)** B

6.30 Terminal cleaning of a mattress, bed space, bay or ward area after the discharge, transfer or death of a patient with CDI, should be thorough. All areas should be cleaned using chlorine-containing cleaning agents (at least 1,000 ppm available chlorine) and curtains changed. To provide total disinfection of the environment/equipment in single rooms/isolation wards, consideration should be given to the use of vaporised hydrogen peroxide. Trusts should have a specific protocol for this and should carry out an audit of compliance with it. **(Code: Duties 4, 10i; Annex 2)** B

6.31 The ward environment should not be cluttered. The recent Releasing Time to Care: The Productive Ward initiative by the NHS Institute promotes this (www.institute.nhs.uk). Medical equipment should ideally be for single patient use, but if this is not possible it should be thoroughly cleaned before and after each new patient use. This process should be recorded and audited together with regular checks of the integrity of surfaces including mattress covers. **(Code: Duty 4f; Annex 1)** B

6.32 Chlorine-containing cleaning agents should be made up to the correct concentration and stored only in accordance with manufacturers' instructions, with particular attention being paid to compliance with health and safety regulations (HM Government, 1974; Health and Safety Executive, 2005). **(Code: Duty 10i; Annex 2)** B

6.33 Routine environmental screening for *C. difficile* is not recommended, but may be useful to ascertain whether cleaning standards are suboptimal, notably in an outbreak or hyperendemic setting.

6.34 Trusts should ensure, through their directors of nursing and human resources, that each clinical area is covered by an infection control link practitioner whose role and job description should include training, auditing and feeding back to staff on cleaning, isolation, hand hygiene and personal protective clothing practices. This could be either a member of the clinical team, or one of a number of designated posts attached to the infection prevention and control team, each covering several clinical teams or a clinical directorate full time. **(Code: Duties 2e, 11d; Annex 3)** B

7. Hand hygiene in the prevention of CDI

Evidence base

7.1 Contamination of hands of healthcare workers and patients by *C. difficile* is a well-established route of transmission. There is a strong correlation between hand-carriage of organisms and the intensity of environmental contamination and this is high and persistent in the rooms of those patients with both symptomatic and asymptomatic faecal carriage of the organism (McFarland et al., 1989; Samore et al., 1996). Wearing vinyl gloves significantly reduces but does not prevent hand contamination (Johnson et al., 1990).

7.2 Hand hygiene by washing with liquid soap and water effectively decontaminates hands from both the spore and vegetative forms of the organism. Alcohol handrub or other disinfecting agents are effective in removing the vegetative form. Although alcohol handrub and disinfecting agents reduce spore contamination, they do not do so as effectively as soap and water, as they leave more spores on the hands to be ingested or transmitted (Boyce and Pittet, 2002; National *Clostridium difficile* Standards Group, 2004; Leischner et al., 2005). Alcohol handrub does not remove norovirus (Boyce and Pittet, 2002) – a fact which further strengthens the case for using soap and water in cases of suspected infective diarrhoea.

7.3 There are no definitive trials on the effect of improved use of hand washing with soap and how this affects levels of CDI. However, there is systematic and critical review evidence of RCTs. This shows that interventions leading to increased hand washing compliance significantly reduced the incidence of diarrhoeal illness in community settings (Curtis and Cairncross, 2003; Stone et al., 2001). A trial is under way, which has *C. difficile* as one of the secondary outcomes (National Patient Safety Agency, 2007b).

7.4 Compliance by healthcare workers with hand hygiene guidance is known to be poor (Boyce and Pittet, 2002). Systematic reviews suggest that audit and feedback may be the most effective ways to improve compliance (Naikoba and Hayward, 2001; Grimshaw et al., 2004; Jamtvedt et al., 2006). The core recommendations in the WHO consensus guidelines suggest a multimodal intervention strategy consisting of system change, training and education, audit, promotion and culture change (WHO, 2005). Available measures to audit hand hygiene are methodologically limited (Gould et al., 2007; Haas and Larson, 2007), although a reliable method with clear standard operating procedures and evidence of sensitivity to change is available on the *clean**your**hands* website (www.npsa.nhs.uk/cleanyourhands).

7.5 The risk of cross-transmission to healthcare workers appears to be very low (Delmee, 1989). *C. difficile* is widely distributed in the environment and thus may be encountered in many ways without resulting infection.

7.6 A large proportion of adults have evidence of an immune response to *C. difficile* without having suffered overt disease. A very small number of cases of CDI in healthcare workers have been reported (Strimling et al., 1989; Arfons et al., 2005), despite the huge potential for exposure of this population to *C. difficile*. Good personal hygiene and adherence to infection-control precautions will minimise this risk still further. Anecdotal reports concerning HCWs who refuse to work on wards with cases of CDI (e.g. staff supplied from locum agencies) have no basis in fact.

National policy

7.7 Hand hygiene before and after each patient contact, after environmental contact and when moving between 'clean' and 'dirty' sites on the same patient, is enshrined in the WHO Five Moments for Hand Hygiene (World Health Organization, 2006), and in clinical governance across the NHS through the *clean**your**hands* campaign, the Saving Lives programme (Department of Health, 2005) and the Code (Department of Health, 2008a).

7.8 The Healthcare Commission emphasises hand washing, rather than use of alcohol handrubs, for all cases of infective diarrhoea (Teare et al., 2001), as does the *clean**your**hands* campaign (National Patient Safety Agency, 2007b).

7.9 This hand-washing guidance to prevent the spread of *C. difficile* is in line with:

- international guidelines (World Health Organization, 2005); and
- Saving Lives (Department of Health, 2006a) – hand washing is included in the sixth High Impact Intervention.
- Trusts should in addition comply with the NHS dress code (Department of Health, 2007c).

7.10 Saving Lives also recommends the use of disposable gloves and aprons for all contact with patients and their body fluids as well as an audit of hand hygiene compliance.

Recent practice

7.11 Hand hygiene compliance among healthcare workers is poor. Compliance rates of 40% are commonplace (Boyce and Pittet, 2002). The pilot study for the *clean**your**hands* campaign reported pre-intervention compliance of 25% (www.npsa.nhs.uk/site/media/documents/692_final_evaluation.pdf).

7.12 The National Observational Study to Evaluate the *clean**your**hands* Campaign reports that the campaign appears to have increased usage of soap and alcohol handrubs two-and-a-half-fold (Stone et al., 2007c), a rise that has been sustained over 2005/06 and then doubled again during 2007 (www.idrn.org/nosec.php).

7.13 Almost 90% of trusts have near-patient alcohol handrubs in almost all wards, with 76% of trusts reporting that the campaign is still a top trust priority and two-thirds of trusts auditing hand hygiene compliance on wards every six months (www.idrn.org/nosec.php).

7.14 The HCC has found that nearly all trusts have hand hygiene guidelines in place for *C. difficile* (Healthcare Commission, 2006). However, healthcare workers have become aware that alcohol handrubs are not as effective as soap and water for removal of *C. difficile* spores, and as a consequence there is confusion as to what is expected of healthcare workers with regard to hand decontamination in preventing spread of *C. difficile*.

7.15 For this reason, the *clean**your**hands* campaign, which emphasised the use of alcohol handrubs because for most organisms they are more effective and take less time than soap (Teare et al., 2001), has issued guidance that soap is to be used when dealing with patients with CDI. This has been recognised in the Patient Safety Alert (National Patient Safety Agency, 2008) which highlights the role of hand hygiene in prevention and control of infection and emphasises the need to use soap and water when caring for patients with CDI. Saving Lives also makes it clear that the use of alcohol handrub in a *C. difficile* outbreak situation is ineffective (Department of Health, 2007b). However, evidence shows that CDI outbreaks can be controlled while still promoting handrubs for non-diarrhoeal patients (Pittet, personal communication).

Examples of good practice

7.16 Kingston Hospital, Surrey set a target of 95% hand hygiene compliance. It achieved this by introducing weekly hand hygiene auditing by a team of matrons and senior nurses or therapists across the trust, with board-level support. This has produced clinical engagement and a spirit of competition between staff groups and wards. The results by ward and staff group are published weekly on the intranet and the internet (www.kingstonhospital.nhs.uk/news/trust_board/2006). For infective diarrhoea, the hospital recommends hand washing, thorough drying, then alcohol handrub, with use of gloves and aprons for all patient contact.

7.17 St Helier Hospital, Surrey, includes patients in its hand hygiene programmes, requiring them to wash before they eat and drink, with a soap-based hand wipe used by those who are bed-bound.

7.18 At the Royal Free Hospital, London, 25 senior managers audit hand hygiene compliance using a standardised tool (www.npsa.nhs.uk/cleanyourhands/resources) (McAteer et al., 2008), as part of a weekly walkabout. Managers discuss results with staff and challenge poor practice.

Recommendations

7.19 All healthcare workers should wash their hands with soap and water before and after contact with patients with suspected or proven CDI or any other infective diarrhoea, and after contact with the patient's immediate environment or body fluids, in line with the SIGHT protocol. Hands should be dried thoroughly thereafter. **(Code: Duty 10a; Annex 2)** **A**

7.20 All healthcare workers must use disposable gloves and aprons for any physical contact with such patients and the patient's immediate environment and body fluids, in line with the SIGHT protocol. Gloves and aprons should be removed after use and disposed of in line with infection control directives or guidance, before washing hands as above. **(Code: Duty 10a; Annex 2)** **B**

7.21 Alcohol handrub **must not** be used as an alternative to soap and water. It can be applied **after** washing to rid hands of remaining non-clostridial organisms. **(Code: Duty 10a; Annex 2)** **B**

7.22 Trusts should audit hand hygiene and disposable glove and apron use among staff caring for patients with suspected or proven infective diarrhoea. This audit should occur as soon as ICTs become aware of such cases, in line with the seventh High Impact Intervention of Saving Lives (Department of Health, 2007b). Infection control link practitioners have a key role in this. **(Code: Duties 2e, 10a, 11d; Annex 2; Annex 3)** **B**

7.23 Trusts should implement the *clean**your**hands* campaign at all times, making it a top priority within their clinical governance framework, and ensure widespread and frequent audit and feedback, using standardised measures (www.npsa.nhs.uk/cleanyourhands/resources) (McAteer et al., 2008). Infection control link practitioners have a key role in this. **(Code: Duties 2e, 10a, 11d; Annex 2; Annex 3)** **B**

8. Coping with high prevalence

Evidence base

8.1 Observational, mainly retrospective, time-series studies report the success of multiple measures (antibiotic restriction, cleaning, isolation, hand washing and use of gloves and aprons) in reducing epidemic or high endemic levels of CDI.

8.2 These studies, although often methodologically flawed (Davey et al., 2006; Stone et al., 2007a, b), largely replicate the findings of the better-quality studies that have looked at how isolation measures as part of a multifaceted intervention can reduce high endemic levels of MRSA (Cooper et al., 2004b).

8.3 Such combined interventions require institutional commitment, senior leadership and a multidisciplinary approach. A 24-month study in Florida (Whitaker et al., 2007) showed the successful effect of introducing a jointly developed protocol with clinical and nursing teams and an ICT.

8.4 The intervention involved the following:

- environmental cleaning, lapses of which were quickly identified by daily visits from the ICT;
- an educational tool for patients and visitors;
- automated reporting; and
- standardised local surveillance combined with a standardised nursing unit isolation procedure.

8.5 Weekly reports by the nursing director and daily rounds by nursing leadership kept the direct line supervisors informed of changes in rates and the emergence of local peaks of infection. The authors comment that these peaks were invariably associated with lapses in procedure. This underlines the great importance in the endemic CDI situation of maintaining clear, effective infection control protocols, which are independently supervised and enforced.

8.6 The results of such studies are reinforced by the findings of the Healthcare Commission investigations into the CDI outbreaks at Stoke Mandeville (Commission for Healthcare Audit and Inspection, 2006) and Maidstone and Tunbridge Wells (Healthcare Commission, 2007b).

8.7 These reports emphasise the role to be played by co-ordinated implementation of the following:

- antibiotic restriction;
- cleaning;
- surveillance;
- hand washing;

- isolation;
- early toxin testing; and
- restricting the movements of patients between wards.

8.8 The reports state unambiguously the need for clear operational policies, good communication with patients, relatives and the general public, and reciprocal proactive relationships with regional HPUs. They criticise delays in opening isolation wards resulting from financial, access and other targets being given priority over patient safety. The lessons to be learnt in the wider NHS from these reports have informed our recommendations, which have also been influenced by the highly successful structured approach adopted to bring the Stoke Mandeville outbreak under control.

8.9 The HCC report on HCAI (Healthcare Commission, 2007a) reported significantly lower CDI rates in trusts that had policies restricting bed movement and in those where the ICT regularly attended bed management meetings.

8.10 The same report also established that there were lower rates of CDI where infection control link practitioners were widespread across the trust. Although 86% of trusts had these in at least 50% of clinical areas, only 23% had them in all areas.

National policy

8.11 Neither the 1994 *C. difficile* guidelines (Department of Health, 1994) nor those of the National *Clostridium difficile* Standards Group (2004) define high prevalence, nor do they specify measures to deal with it. The implication is, however, clear in both documents: that measures to prevent or control outbreaks (isolation, cleaning, hand washing, gloves and aprons, restricting patient movement and antibiotic guidelines) apply to this situation.

8.12 The HCC/HPA survey (Health Protection Agency, 2006) notes that where high or rising levels of CDI have become the norm it can be difficult to detect new outbreaks. It recommends that the definition of an outbreak given in this report (see chapter 1) is applied consistently and that outbreaks are reported to the SHA or Monitor as required by the Department of Health.

8.13 The HPA Regional Microbiology Network has defined high prevalence as more than 60–80 cases a year, and has issued to London chief executives a good practice guide, a rapid audit tool and an isolation ward checklist, with the aim of reducing hospital-wide levels. Intervention at a lower level in a low-incidence background is desirable and this guidance suggests a pragmatic definition of a PII with the attendant action required to ensure further transmission does not occur (see paragraphs 1.21 and 2.36).

Recommendations

8.14 Increase the activity of the ICT:

- Institute at least weekly meetings involving all aspects of bed and estates management within the trust.
- Institute daily review of new and existing cases of CDI (review clinical condition of patient and adhere to infection control precautions).
- Ensure that the infection control link practitioner (see 6.34) covers all affected areas.

(Code: Duties 4a, 10c; Annex 1; Annex 2) B

8.15 Review and maximise isolation procedures:

- Depending on availability of single rooms, consideration should be given to establishing an isolation ward(s).
- Draw up a detailed operational plan for both clinical management and estates/bed/nursing support.
- The use of cohort nursing in bays may be considered, but the difficulties in maintaining cleanliness in toilets/commodes and supervising staff contact precautions may render this action ineffective, and it is not evidence based.

(Code: Duties 4a, 8; Annex 1) B

8.16 Institute intensive local surveillance:

- All ICTs should routinely report cases of CDI back to wards and senior trust management on a monthly basis (see 2.35).
- In the event of an outbreak declared by the DIPC on advice from the microbiologist, which should be endorsed by management and formally recorded in publicly available documents. The DIPC should ensure collection of information on cases every day and keep senior management informed.

(Code: Duty 10l; Annex 2; Appendix 2i) B

8.17 Optimise ward cleaning and disinfection:

- In the absence of clear biological indicators of the persistence of *C. difficile* spores in the environment, adhere tightly to cleaning protocols using sporicidal agents.
- Obvious soiling with faeces (particularly on touch points) and dirty linen are potent sources for cross-infection and should be removed immediately.

(Code: Duties 4, 10i; Annex 2) B

8.18 Communicate diagnostic microbiology results as rapidly as possible:

- Ribotyping of representative isolates should be undertaken using one of the specialist laboratories listed in Appendix 5, which can be accessed via the regional microbiologist.
- The AMT should ensure that the guidance on antibiotic usage is strictly followed.

(Code: Duties 10j, 10k) B

8.19 Reduce the movement of patients and staff to an operationally effective minimum:

- Movement of patients with diarrhoea both within and between wards will lead to the spread of CDI.
- Isolation wards and cohort bays should have minimal contact with uninfected ward areas.
- Great care should be given to identifying and preventing the movement of beds, commodes, trolleys and other equipment between areas.
- Compliance with guidelines should be audited.

(Code: Duty 6; Annex 1) B

8.20 Enhance communications with all parties and staff:

- Review communication of the situation to, and advice from, the HPU, regional microbiologist, CfI and SHA each day, as appropriate;
- Establish timely and relevant communication to all sections of the trust, including patients, and to PCTs.
- Ensure that patient information leaflets are given out.
- Provide feedback on progress with CDI control to affected wards.
- Consider issuing press statements and information to the media and general public.

(Code: Duties 5, 10k) B

9. CDI in the community

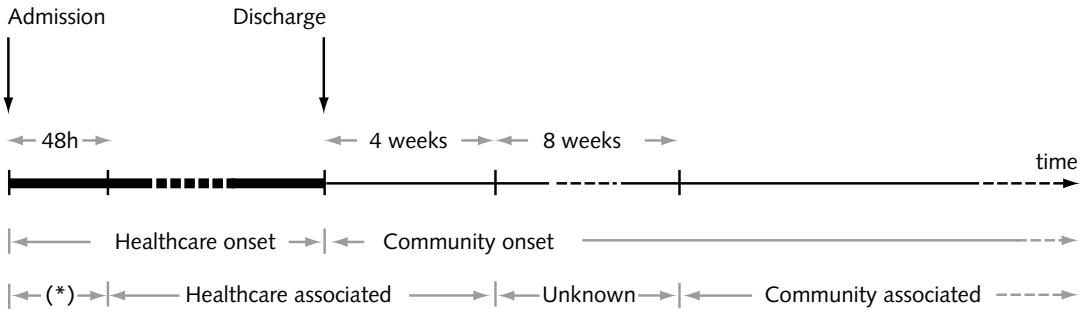
Evidence base

9.1 A 2007 US study investigated cases of community-onset CDI, and concluded that a 30-day cut-off should be used to define community-onset healthcare-associated cases (Chang et al., 2007).

9.2 The final sentence of this study noted that "This definition is consistent with the recently published recommended definition, which gives the cut-off of 4 weeks after discharge from a healthcare facility." This US recommended definition (McDonald et al., 2007) concurs with 2006 European consensus definitions of CDI (Kuijper et al., 2006), as shown in Figure 6.

9.3 Thus, healthcare-associated CDI is defined as that occurring up to four weeks after discharge from a healthcare unit (i.e. a hospital). There is a grey period of eight weeks after this time (i.e. from one to three months after hospital discharge) where it is uncertain whether a CDI case is hospital or community associated.

Figure 6: Relationship between healthcare-associated and community-associated CDI (Kuijper et al., 2006)



(*): May be community or healthcare associated, depending on case history; if healthcare associated, may have been acquired in the same facility or imported from another.

9.4 The exact incidence of true community-acquired CDI is not clear, and this situation is not helped by the use of different definitions (see above for preferred terminology). A Swedish study reported 28% of all CDI to be community acquired (Karlström et al., 1998). A recent German study revealed an incidence of 9.3% among 703 patients with diarrhoea who were visiting the general practitioner (Weil et al., 2007).

9.5 The Healthcare Commission report on Maidstone and Tunbridge Wells NHS Trust (Healthcare Commission, 2007b) reported that 10% of CDI was community acquired. In a prospective case-control UK study in two geographically distinct locations (Leeds and Truro), the proportions of randomly selected community-derived faecal samples positive for *C. difficile* cytotoxin was 2.1% in both cohorts (Wilcox et al., 2008).

9.6 The calculated annual incidences were 29.5 cases per 100,000 individuals in the urban setting of Leeds and 20.2 cases per 100,000 individuals in Truro. Exposure to antibiotics in the previous four weeks, particularly multiple agents ($P < 0.001$), aminopenicillins ($P < 0.05$) and oral cephalosporins ($P < 0.05$), was significantly more frequent among cases than controls. Hospitalisation in the preceding six months was significantly associated with CDI (45% v. 23%; $P= 0.022$). However, approximately one-third of the patients had neither exposure to antibiotics nor recent hospitalisation. Contact with infants aged 2 years and younger was significantly associated with CDI (14% v. 2%; $P = 0.02$).

9.7 Prior exposure to any or specific gastrointestinal acting drugs (proton pump inhibitors (PPIs), H2 antagonists or non-steroidal anti-inflammatory drugs) was not significantly more common in CDI cases. Potential risk factors for community-associated CDI should be explored further to explain cases not linked to recent antibiotic therapy or hospitalisation.

9.8 The HCC/HPA survey (Healthcare Commission, 2006) found that 36% of trusts reported that 6% of CDI came from community hospitals, with 50% reporting that an identical proportion came from GP cases. Chapter 2 of this report has however documented the widespread failure to test or report community and care home samples.

9.9 Studies in the US show that CDI may be endemic in nursing homes, with rates as high as 33%. There are no comparable studies in the UK, although a study in the old NHS long-stay ward setting reported that CDI was endemic (Bender et al., 1986).

9.10 According to US and Canadian studies, care homes are not the only settings associated with considerable antibiotic use, much of it inappropriate (Simor et al., 2002; Quinn et al., 2007); they are also settings which receive residents from hospital who have suffered from CDI in hospital. There is the potential for two-way transmission of CDI between hospital and care home, the so-called "two-way street" (Rosenberg, 1995).

9.11 The extent and appropriateness of antibiotic use in UK care homes have not been studied, nor have the transmission dynamics between care homes and hospitals.

9.12 There are reports that some cases of CDI in the community may be associated with the use of PPIs. There is an unresolved controversy concerning PPIs as a potential risk factor in CDI.

9.13 Two retrospective studies have suggested that community-associated CDI in England is associated with use of PPIs (Dial et al., 2005, 2006). A hospital-based case-control study in Wales also found that CDI was independently associated with antibiotic use, acid suppression therapy and female sex (Yearsley et al., 2006). However, two large series reviews and review of the literature have failed to demonstrate such an association.

9.14 Data confounding, which is inherent in retrospective studies, is likely to affect risk factor analyses, and prospective studies are needed to resolve this issue (Pépin et al., 2005; Lowe et al., 2006). The Leeds and Truro study (see paragraph 9.5) found no association between CDI and PPIs in the community (Wilcox et al., 2008).

9.15 Patients who have had CDI and become asymptomatic are not a risk to others, even if they continue to excrete *C. difficile* in their stools and/or remain toxin positive, provided that they observe the normal personal hygiene precaution of hand washing after using the toilet.

9.16 However, a recent study identified that environmental contamination was significantly commoner around asymptomatic carriers than non-carriers (Riggs et al., 2007). This may reflect poor toilet capacity or environmental cleaning or both. This observation should not be interpreted as a reason to isolate or test asymptomatic individuals for evidence of toxin excretion or *C. difficile* carriage, but rather as a reason to maintain a high standard of environmental cleaning and hand hygiene with soap and water.

9.17 There is no value in using antibiotics such as metronidazole or vancomycin to attempt to clear patients of *C. difficile*. Indeed, in comparison with placebo, metronidazole has no clearance benefit and there is a trend to increased long-term *C. difficile* carriage in vancomycin recipients (Johnson et al., 1992).

National policy

9.18 The Department of Health's *Infection Control Guidance for Care Homes* (Department of Health, 2006b) states that "the registered manager has the responsibility to report suspected outbreaks to the local HPU as soon as this is recognised". Also, "if more than two cases, suspected or known to be infectious [of diarrhoea and vomiting] occur within a few days, the local HPU/CCDC should be notified".

9.19 Recommended good practice on antimicrobial prescribing in primary care is available at www.hpa.org.uk/infections/topics_az/primary_care_guidance/Antibioticguide

9.20 Techniques are available to reduce antimicrobial prescribing, such as giving patients a prescription but asking them not to use it unless symptoms do not improve.

9.21 The *clean**your**hands* campaign has now been rolled out to the community, including care homes (www.npsa.nhs.uk/cleanyourhands).

9.22 Saving Lives (Department of Health, 2007b) has prevention and management of CDI as one of the High Impact Interventions.

9.23 From 2010/11, a revised version of the Code covering independent healthcare and social care will be prepared in line with the provisions of the Health and Social Care Act 2008.

Recommendations

9.24 All cases of diarrhoea among people in the community aged 2 years and above should be investigated for CDI unless there are good clinical or epidemiological reasons not to do so. Testing for CDI should be included in laboratory protocols for the investigation of diarrhoea. Laboratories should report back positive results as a matter of urgency. Samples should indicate clearly who should be informed of the result. Mandatory reporting applies to all cases where the patient is aged over 2 years. B

9.25 In the first instance, NHS acute trusts should identify where the patient was when the specimen was taken (e.g. GP surgery or ward). Cases in which specimens were taken before admission of the patient to hospital or within 48 hours of admission should be termed community-onset CDI. This categorisation will not allow a true measure of community acquisition, but it will separate those cases acquired during the current admission period from those acquired before then (either in the same trust or in another setting). B

9.26 There is a consensus across Europe and the US that healthcare-associated CDI should be defined as that occurring up to four weeks after discharge from a healthcare unit (e.g. hospital). There is a grey period of eight weeks after this time (i.e. from one to three months after hospital discharge) where it is uncertain whether a CDI case is hospital or community associated. C

9.27 If there is a significant number of cases of community-onset CDI, further investigations should be undertaken to assess whether they reflect true community-acquired infections or recent discharges from hospital. Understanding the source and causes of infection will help in targeting efforts to reduce infections. C

9.28 An outbreak is defined as "two or more cases caused by the same strain related in time and place over a defined period based on the date of onset of the first case". Institutions such as care homes should therefore maintain a log of cases by date and location, to aid recognition of an outbreak. B

9.29 If more than two cases of diarrhoea that are suspected or known to be infectious occur within a few days at a care home or other community institution, the registered manager is responsible for reporting this to the local HPU or CCDC. B

9.30 Outbreaks of CDI in institutional settings should be investigated in the same way as in the acute hospital setting. B

9.31 Those in the community who have contact with people with diarrhoea should wear disposable gloves and aprons for all contact with them and their environment. After contact they should dispose of these items and wash their own hands with liquid soap and water, whether or not their hands are visibly soiled. Alcohol handrub can be used after this. A

9.32 Staff in the community who have diarrhoea should not work unless they have been symptom-free for 48 hours or the diarrhoea has been shown to be non-infectious and not a risk to others. Staff with continuous severe diarrhoea should be investigated and followed up. B

9.33 The PCT, HPU and DIPC in a locality should jointly prepare local protocols on the investigation and management of cases according to national guidance and should define out-of-hours arrangements between relevant parties. C

9.34 Guidance on prescribing antibiotics in the community should be followed. PPIs should be used only when there is a clear clinical indication. C

9.35 There should be no restriction on institutions such as care homes receiving patients who have had CDI and are now clinically asymptomatic. Care should be taken to communicate the individual's infections status clearly to staff and GPs, issuing a proforma letter such as the one in Appendix 3. C

10. Death certification

Evidence base

10.1 The HCC report into the Maidstone and Tunbridge Wells outbreak found that in approximately 12% of patients death was mainly due to CDI (Healthcare Commission, 2007b). Despite this, death certificates did not mention CDI in 65% of cases where it was considered to be a definite or probable cause of death.

10.2 Similar statistics were reported for deaths in patients with MRSA in a confidential study of deaths published in November 2007, indicating a widespread misreporting of deaths due to HCAI (Health Protection Agency, 2007).

10.3 Published data suggests 30-day all-cause mortality of *C. difficile* to be 21% (Morgan et al., 2008) and secondary care trusts should maintain comparative data on this. Assessment of criteria for attributing death to CDI is urgently needed.

10.4 Comparative studies with other or matched hospital populations are needed, and given the recurrent nature of the illness a systematic analysis is also required of the period of time over which excess mortality in *C. difficile* patients is sustained.

10.5 Trusts should consider urgent medical action to manage cases if their audited 30-day mortality rate approaches 20%.

National policy

10.6 Death certification is an important source of information about the mortality associated with different diseases, both for clinicians and for those responsible for planning and managing health services and recognising priorities for medical research (Chief Medical Officer, 2007). It is also an important source of information for the relatives of those who have died.

10.7 The medical profession has a legal responsibility to ensure that the certificate accurately reflects the sequence of events leading to death (Chief Medical Officer, 2007). The consultant in charge of the patient's care is ultimately responsible for making sure that the information is accurate.

10.8 The underlying cause of death is defined as "the disease or injury which initiated the train of morbid events leading directly to death". This wording should appear on the lowest completed line of Part 1 of the death certificate.

10.9 For any death from an infectious disease, the following should be documented on the death certificate (General Register Office/ONS's Death Certification Advisory Group, 2007):

- the place of death;
- the infecting organism (if known);
- the presence of any antibiotic resistance; and
- the route or source of infection.

10.10 If the source of the infectious disease is healthcare associated, this should be stated clearly on the certificate.

10.11 If an HCAI was part of the sequence of events leading to death, it should appear in Part 1 of the certificate. If it was not part of the direct sequence but contributed to the death, it should be mentioned in Part 2 (Chief Medical Officer, 2007; General Register Office/ONS's Death Certification Advisory Group, 2007). Appendix 7 gives examples of correct entries for CDI and other HCAIs.

10.12 Guidance is required on later attribution of death after retrospective review subsequent to the issue of death certificates.

Example of good practice

10.13 In Shrewsbury, all patients with *C. difficile* are matched against the national database and any death occurring within 30 days is identified. A progressive centrally initiated audit and report, covering all death certification relevant to *C. difficile*, are being conducted by a gastroenterologist and the medical director.

Recommendations

10.14 If a patient with CDI dies, the death certificate should state whether CDI was part of the sequence of events leading directly to death or whether it was the underlying cause of death. If either case applies CDI should be mentioned in Part 1 of the certificate. **(Code: Duty 5)** B

10.15 If CDI was not part of the sequence of events leading directly to death but contributed in some way to it, this should be mentioned in Part 2. **(Code: Duty 5)** B

10.16 If a doctor is in doubt about the circumstances of death when writing the certificate, they should consult with the trust's multidisciplinary clinical review team for CDI. B

10.17 Doctors have a legal duty to mention CDI on a death certificate if it was part of the sequence of events directly leading to death or contributed in some way. **(Code: Duties 11c, 11d, 11e)** B

10.18 Medical directors should ensure that training is provided on death certification and should audit certificates to check that they accurately record HCAI. **(Code: Duties 11c, 11d, 11e)** B

11. Governance, audit and performance indicators

Background

11.1 The Health Act 2006 Code of Practice (Department of Health, 2006c; 2008a), referred to as the Code, states unambiguously that prevention and control of HCAI should be a high priority for all parts of the NHS and for healthcare providers in the independent and voluntary sectors.

11.2 The Code considers that "effective prevention and control should be embedded into everyday practice and applied consistently by everyone". It calls for "a high awareness of the possibility of HCAI in both patients and healthcare workers" and states that its purpose is to "help NHS bodies plan and implement how they can prevent and control HCAIs". It sets out "criteria by which managers of NHS organisations are to ensure that patients are cared for in a clean environment, where the risk of HCAI is kept as low as possible".

11.3 Failure to observe the Code renders NHS bodies liable to various sanctions such as Improvement Notices being issued by the HCC.

11.4 The Code lists 11 'duties' of care that NHS bodies owe to their patients in this context, and describes in annexes detailed ways in which these duties might be met, grouping them under three headings: "Management, Organisation and the Environment" (Duties 1–9), "Clinical Protocols" (Duties 10a–l) and "Healthcare Workers" (Duty 11).

11.5 CDI is singled out for special attention under Duty 10l, but nearly all the other duties are central to the control of CDI. Many of our recommendations in preceding chapters are either mandated in their entirety by specific duties of the Code or provide a way to comply with certain duties, and we have indicated which is the case for each recommendation.

11.6 The HCC report on HCAI (Healthcare Commission, 2007a) was based on data on practice collected six months before the Code came into effect. It highlighted different practices associated with reduced levels of CDI, such as:

- widespread coverage of clinical areas by infection control link practitioners;
- higher PEAT scores;
- regular meetings between ICTs and bed management teams;
- regular discussion of PEAT scores with cleaning and infection control staff; and
- compliance with guidelines restricting patient movement.

11.7 It also found that trusts which had formally assessed the skills of their DIPCs against those set out by the Department of Health, had lower rates of CDI. Trusts which included prevention and control of infection in appraisal and personal development plans for the majority of clinical staff also had lower CDI rates.

11.8 The HCC recommended that:

- audits of HCAI should be registered with clinical audit departments;
- trusts should ensure that essential training of staff takes place;
- training should include information from audits;
- arrangements should be in place to assess the performance of all units of management; and
- indicators should include not only outcomes such as CDI but compliance with key guidelines such as hand hygiene and cleanliness. These indicators are listed in Table 2.

11.9 The HCC report into the outbreak in Maidstone and Tunbridge Wells (Healthcare Commission, 2007b) noted that infection control reports to the board tended to be retrospective annual reports rather than prospective planning documents requiring board input. There was also no monitoring of CDI levels by the HPU, whose approach, in common with that of many HPUs, was reactive rather than proactive.

11.10 The SHA did not performance-manage CDI levels until near the end of the outbreak. The PCT service level agreements with the trust included two indicators for HCAI, but these were not monitored. The PCT was criticised for focusing on finance and the number of patients treated, while paying scant attention to the quality of care, including infection control.

11.11 The HCC report into the Stoke Mandeville outbreaks (Commission for Healthcare Audit and Inspection, 2006) noted the lack of ring-fenced time for infection control link practitioners. Its report into HCAI (Healthcare Commission, 2007a) found that a third of trusts had insufficient protected time for such practitioners.

11.12 Compliance with the requirements of the Code will be assessed by the HCC and when it is asked to investigate specific incidents or complaints (Healthcare Commission Criteria for Assessment). The requirements of the Code will be fulfilled if trusts have guidelines and procedures in place based upon this guidance document and other guidance and requirements issued by the Department of Health. The performance of NHS trusts will be assessed by the HCC through inspection and a combination of primary performance indicators and indicators of outcome and implementation of processes and procedures (Table 2). Evidence of progress in reduction of incidence and appropriate target setting will be sought.

11.13 The recommendations below concern organisational and management arrangements not covered explicitly in previous chapters. They also deal with training and education of healthcare workers in prevention and control of CDI, as required under Duty 11 of the Code, as this is not explicitly dealt with elsewhere. The recommendations also provide an overview of audit and performance indicators for prevention and control of CDI for trusts to consider in their clinical governance framework.

Recommendations

11.14 Trusts should ensure that they comply with Duty 2b of the Code in respect of the appointment of a DIPC and their role. In addition, the DIPC should report at least quarterly on CDI to the chief executive and trust board. More frequent reporting on action is necessary if the incidence of infection is comparatively high or there is evidence of an outbreak. **(Code: Duties 2b, 10c)** B

11.15 The DIPC should have the qualifications and experience required for the post, as detailed in the DIPC role profile. A trust board member should take specific responsibility for regular liaison with the DIPC and also with consultant microbiologists and the infection prevention and control team, especially if the DIPC is not from an infection-related specialty. **(Code: Duties 2a, 2b)** B

11.16 Trusts and PCTs should work closely together when monitoring CDI against the targets. Web-based surveillance data will be used to monitor progress in reducing CDI. Relevant stakeholders (e.g. the Department of Health, PCTs, SHAs) should have access to the data. **(Code: Duty 10k; Appendix 2i)** B

11.17 The HPA should provide PCTs with information on reported cases to the PCT where it has responsibility for monitoring a local acute trust or health economy. B

11.18 Acute trusts should ensure that information analysts and specialists are available to give adequate local support to the DIPC and AMT in monitoring antibiotic use. This is made clear in recommendation 4.34, and the requirement for adequately resourced information technology is a duty under the Code. Ideally, automated processes should be set up in SHAs to facilitate the development of accurate databases on antibiotic use, and data should be collated nationally. **(Code: Duty 2c; Annex 1)** B

11.19 The Saving Lives programme for acute trusts (Department of Health, 2007b) specifies that a nominated doctor, nurse and manager should be responsible for infection control in each area. It states that this responsibility should be specifically included in their job descriptions, appraisals, annual individual performance reviews and knowledge and skills assessments. These individuals will have personal responsibility for control of CDI. Clinical directors, lead clinicians, the directorate and ward nurse managers should be included in distributions of information on CDI and should have devolved responsibility for their areas of management. **(Code: Duties 2c, 11f; Annex 1)** B

11.20 Trusts should comply fully with Duty 2e of the Code to ensure that they have a programme of audit of the key guidelines for the control of CDI such as those specified in recommendations 1.23 (submission and processing of faecal samples), 4.42 (antibiotic prescribing), 5.20 (isolation), 6.29 (environmental cleaning), 7.22 and 7.23 (hand hygiene and protective clothing use) and 8.19 (restricting movement of patients). These should be registered with the trust's clinical audit department. **(Code: Duty 2e)** B

11.21 Trusts should ensure full compliance with Duties 11c, d and e, of the Code to provide induction and training of new staff, and education and updating of guidance for existing staff that includes prevention and control of CDI. Attendance at these sessions should be a routine part of staff appraisal or personal development plans and be included in job descriptions. This training should include the results of relevant audits. By complying with the HCC's recommendation (Healthcare Commission, 2007a) that trusts should ensure that each clinical area is covered by an infection control link practitioner, trusts will facilitate compliance with both the training and audit duties of the Code. **(Code: Duties 11c, 11d, 11e, 11f)** B

Table 2: Performance indicators likely to be assessed by the Healthcare Commission to demonstrate compliance with the Code

A. Primary outcome indicators required for the mandatory national surveillance and for monitoring local reduction targets by PCTs

i. Number of cases in patients aged 2–64 and over 65 years (mandatory national surveillance); in relation to trust plans for reduction targets
ii. Number of cases in each age group (may be part of local target monitoring)
iii. Number of cases requiring surgery
iv. SUI reports of CDI

B. Indicators of process and monitoring of outcome (all or several of these may be required by the Healthcare Commission)

i. Guidelines on CDI management and evidence of compliance
ii. Infection control committee reports on CDI incidence
iii. Quarterly DIPC reports to trust board
iv. Appropriate cleaning and hand hygiene guidelines approved by trust board
v. Inclusion in cleanliness and DIPC reports of information on commodes, bedpans, ward toilets, bathrooms and sluices. Evidence that results are discussed by ICT, matrons and cleaning teams regularly (at least monthly)
vi. Monthly information on CDI for infection control leads, wards and units
vii. Evidence of containment isolation of cases of diarrhoea and *C. difficile* and evidence that this matches demand
viii. Evidence of sufficient, timely and appropriate laboratory testing for *C. difficile*.
ix. Evidence of typing of an appropriate selection of isolates of *C. difficile*
x. Reports of AMTs, consisting of antimicrobial pharmacists and infection specialists, to drug and therapeutic committees, including *C. difficile* cases per 1,000 daily defined doses of specific antibiotics used
xi. Evidence of regular review of antibiotic usage by drug and therapeutics committees
xii. Presence of an AMT undertaking appropriate activity, including feedback to clinicians
xiii. Antibiotic and laboratory investigation guidelines that appropriately restrict broad-spectrum agents for therapy and prophylaxis, and include advice on duration of use and narrowing of spectrum of agent after microbiological investigation
xiv. Antibiotic use audits assessing compliance with guidelines
xv. Evidence of infection control link practitioners with ring-fenced time covering all clinical areas
xvi. Evidence of training of medical staff on antibiotic use and death certification and of all staff in control of infection and management of *C. difficile*
xvii. Audit of outcome of CDI, including information on mortality associated with the diagnosis of CDI

Appendices

1: Research recommendations

2: The Bristol Stool Form Scale (Bristol Stool Chart) and example of stool record chart

3: Medicines that can produce diarrhoea

4: Example of a proforma letter to GPs

5: Treatments for CDI under investigation

6: Accessing national microbiological services for strain typing

7: Criteria for ribotyping isolates from the HPA *Clostridium difficile* Ribotyping Network for England (CDRNE)

8: Examples of death certification for CDI patients

9: Abbreviations

10: Members of the working group

Appendix 1:
Research recommendations

The following areas have been identified by the working group as needing further research to fill gaps in the evidence base. It is hoped that they will inform the research community and also the various research funders.

1. Clinical definitions and laboratory diagnosis

1.1 To avoid reliance on manufacturers' data, independent evaluations of specificity and sensitivity of different enzyme immunoassays for toxin detection are required. These should be available as assays are marketed.

1.2 To define criteria for attribution of diarrhoea to *C. difficile* and declaration of outbreaks, specific study should be made of faecal submission rates in hospital and their relationship to norovirus and *C. difficile* outbreaks.

1.3 Technologies such as micro-array methods need stringent evaluation in terms of their specificity and sensitivity compared with current rapid methods. For example, it is important to note, especially for a spore former, that presence of the genes does not automatically equate to production of toxins. New sub-typing methods such as VNTR or MLVA will probably add an extra dimension to our understanding of the epidemiology of *C. difficile* outbreaks at a local level.

2. Surveillance

2.1 Research is required to investigate whether the incidence of CDI in younger age groups and the community is increasing and, if so, why.

2.2 Research is required to investigate whether disease severity is increasing and whether this is linked to changes in strain type or not. Such research will be facilitated by the creation of multidisciplinary clinical review teams to manage CDI as a diagnosis in its own right.

2.3 Methods to test antimicrobial susceptibility and characterise molecular mechanisms of resistance need to be improved.

3. Management and treatment of CDI

3.1 Prospective markers of severity or prognostic risk scores will require development and validation. This will be facilitated by development of multidisciplinary clinical review teams who will be able to recruit and monitor patients with a range of disease severity.

3.2 The exact titre of *C. difficile* toxin antibodies in immunoglobulin preparations required to treat disease needs to be determined and then subjected to evaluation through randomised, controlled trials.

3.3 New therapeutic options for the treatment of CDI need to be explored to help reduce the rate of recurrence and provide better treatment for severe disease. The use of donor faecal transplantation needs to be properly explored through suitable multi-centre trials (Keller, 2008).

3.4 No research has been carried out on agents that block toxin formulation by ribosomal blockade. By analogy with accepted practice in other diseases caused by actively forming microbial toxins, such research should be undertaken.

4. Prevention of CDI through antibiotic prescription

4.1 Evidence is required as to the best method of reducing broad-spectrum antibiotic use and CDI in the elderly and other hospital populations without increasing the infection-specific mortality. A well-designed cluster randomised controlled trial (CRCT) comparing different strategies is required (Medical Research Council, 2000; Stone et al., 2007a, b).

4.2 Large-scale, high-quality prospective studies of the relative risks of acquiring CDI through exposure to different antibiotics are required, and these should address the weaknesses of earlier studies (Thomas et al., 2003).

4.3 Feasibility studies are required that will develop and evaluate electronic prescribing and audit systems suitable for use throughout the NHS. These will enable the local relationships between prescribing patterns and *C. difficile* to be explored.

5. Prevention through isolation

5.1 Studies are required to define how the relative contributions of isolation strategies, environmental cleaning and antibiotic prescription contribute to help control the spread of CDI.

5.2 High-quality observational studies (Stone et al., 2007a, b) or CRCTs are required to determine the efficacy of different isolation strategies. These will need to be informed by the Medical Research Council (2008) framework for complex interventions. The studies should be able to address barriers to carrying out isolation strategies at individual healthcare worker, ward and institution level.

5.3 Faecal management systems can be used in patients with faecal incontinence to prevent the soiling of garments and bed linen. Further research is needed to investigate whether this approach is of practical value to patients with CDI and a possible aid to reducing the spread of *C. difficile*.

6. Prevention through environmental cleaning and disinfection

6.1 Improved methods for both surface and clinical area decontamination should be developed and evaluated.

6.2 High-quality observational studies, leading to CRCTs or other high-quality experimental design studies, are required to show the relative efficacy of different cleaning regimens.

6.3 The importance of either changing or cleaning (e.g. using steam) on fabrics such as curtains in clinical areas needs to be understood through research.

6.4 The use of microfibre products for effective decontamination of the healthcare environment from *C. difficile* requires further evaluation. There is evidence that not all microfibre cleaning products are equally effective at removing bacteria from surfaces. Furthermore, some microfibre cloths are associated (in vitro) with significantly increased risk of surface recontamination (Moore and Griffith, 2006). Many microfibre cleaning products are incompatible with disinfectants.

6.5 Further research and guidance is needed to investigate how successful laundry cleaning methods and associated detergents/disinfectants are in removing and killing *C. difficile*.

7. Hand hygiene in the prevention of CDI

7.1 Research is required on the frequency and appropriate use of gloves in healthcare settings, along with appropriately designed trials (Stone et al., 2007a, b) of behaviourally grounded interventions to improve this (Michie et al., 2005).

7.2 Similar trials are required of interventions to improve the quality of, as well as compliance with, hand hygiene.

7.3 A standardised, valid, reliable measure or combination of measures of hand hygiene compliance, such as direct observation and mechanical counters or consumables usage, needs to be developed.

7.4 Further research is needed on compounds or wipes to remove spores from contaminated hands.

8. Coping with high prevalence

8.1 Characterisation of the genetic and phenotypic properties associated with strains capable of causing epidemics of CDI is required.

8.2 A well-designed randomised controlled trial (Medical Research Council, 2000; Stone et al., 2007a, b) of isolation ward versus cohort nursing by designated nurses of CDI patients on general wards is required.

9. CDI in the community

9.1 Further prospective studies of the risk factors for community-associated CDI (including family spread) are required to investigate the large proportion of cases that are not linked to recent antibiotic therapy or hospitalisation.

9.2 The extent and appropriateness of the use of antibiotics in UK care homes require study.

9.3 The incidence, prevalence and transmission dynamics of CDI in UK care homes need to be determined.

9.4 The extent of occurrence and epidemiology of *C. difficile* in foodstuffs needs to be determined.

Appendix 2:
The Bristol Stool Form Scale (Bristol Stool Chart)

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces, a mushy stool
Type 7		Watery, no solid pieces ENTIRELY LIQUID

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Example of stool record chart

STOOL RECORD CHART

Name: .....Date of birth/Hospital no:.....

Date sample sent: .....

Date	Time	Type no.	Description/comments (please refer to chart overleaf)

Appendix 3:
Medicines that can produce diarrhoea

Diarrhoea is a common adverse drug reaction (ADR) with many medicines. Antimicrobials account for about 25% of drug-induced diarrhoea though most cases are benign (Lee, 2006).

While diarrhoea has been seen with most medicines, the ones that are most commonly implicated are:

- acarbose;
- antimicrobials;
- biguanides;
- bile salts;
- colchicine;
- cytotoxics;
- dipyridamole;
- gold preparations;
- iron preparations;
- laxatives;
- leflunomide;
- magnesium preparations, eg antacids;
- metoclopramide;
- misoprostol;
- non-steroidal anti-inflammatory drugs (NSAIDS), e.g. aspirin, ibuprofen;
- olsalazine;
- orlistat;
- proton pump inhibitors; and
- ticlopidine.

Alternative diagnoses for the diarrhoea are important; therefore, careful attention should be paid to the temporal relationship between the time that the medicine is first taken and when the diarrhoea first appears.

Further information on adverse effects is available from local medicines information centres or by using the 'search by section' facility at http://emc.medicines.org.uk/

Appendix 4:
Example of a proforma letter to GPs

Date:

Dear Doctor

Re:

The above was recently an in-patient on Ward .....

During their hospitalisation, your patient was diagnosed as having *Clostridium difficile* infection and was treated with.....

This infection is almost exclusively associated with the use of antibiotics. Infection may become manifest while on antibiotics, but a significant number of cases occur following cessation of therapy, the incubation period extending to several weeks. Symptoms may include fever, abdominal pain and diarrhoea (with/without blood or mucus).

We are therefore writing to inform you that there is a small chance following discharge that:

- your patient could relapse with the infection. If this happens, please discuss their treatment with the medical microbiologist. If concerned about the severity of infection, hospital admission should be considered; and
- future administration of broad-spectrum antibiotics could precipitate infection.

(If antibiotics are required, a short course of a narrow-spectrum agent is preferable.)

Once the patient has recovered, follow-up samples for clearance are not required.

For further advice, contact the medical microbiologist on extension xxx or via the switchboard outside working hours.

Yours sincerely

Appendix 5: Treatments for CDI under investigation

The following agents are not yet licensed for the treatment of *Clostridium difficile* infection (CDI) in the UK. Improved therapies for CDI are urgently needed and fast-track licensing should be considered by the Medicines and Healthcare products Regulatory Agency, European Medicines Agency and National Institute for Health and Clinical Excellence.

Tolevamer

This is a novel polystyrene agent to bind *C. difficile* toxin A and B and effectively treats mild to moderate CDI (Louie et al., 2006). It is generally well tolerated but an early formulation was associated with an increased risk of hypokalaemia. Unfortunately, results from the two large phase III randomised studies in comparison with metronidazole and vancomycin have been very disappointing. Tolevamer failed to meet the primary endpoints of non-inferiority versus vancomycin (or metronidazole) (Louie et al., 2007; Bouza et al., 2008). Recurrent CDI was more frequent with vancomycin or metronidazole than tolevamer, but the disappointing primary response rate with the latter (47%) brings into question the clinical utility of this finding.

Ramoplanin

This is an oral, non-absorbable lipoglycodepsipeptide antibiotic which blocks peptidoglycan synthesis. It has been found to be equivalent in efficacy to vancomycin in phase II trials.

Rifaximin

Rifaximin is a rifampicin-like antibiotic which remains in the gut following oral administration. It is licensed in some countries (not in the UK at present) for the treatment of travellers' diarrhoea caused by *Escherichia coli*. This has been found to be equivalent in efficacy to vancomycin in phase II trials. Eight patients with multiple recurrences of CDI were given a two-week course of rifaximin when they were asymptomatic, immediately after completing a course of vancomycin. Seven of the eight patients experienced no further diarrhoea recurrence (Johnson et al., 2007). Controlled studies of rifaximin in CDI are needed. Rifaximin-resistant strains have been reported and are associated with treatment failure. Rifampicin resistance is predictive of resistance to rifaximin.

Nitazoxanide

This is a new thiazolide antiparasitic agent. It has been found to be equivalent in efficacy to metronidazole in phase II trials (dose of 500 mg 12-hourly for 7–10 days) (Musher et al., 2006).

C. difficile vaccines

Trials have commenced using a toxoid vaccine (Acambis; phase II) and monoclonal antibodies to toxin A and toxin B (Medarex; phase II). The vaccine is given in three doses (days 1, 8 and 30) and has a favourable side-effect profile (Kotloff et al., 1996). The vaccine is highly immunogenic.

Anti-CDI colostrum and bovine whey

These have undergone phase I studies. Bovine whey demonstrates a reduction in relapse rate (van Dissel et al., 2005).

Appendix 6: Accessing national microbiological services for strain typing

ENGLAND

The Health Protection Agency (HPA) Regional Microbiology Network provides ribotyping on a regional basis, free of charge, on faeces samples. The regional microbiologist or *Clostridium difficile* Ribotyping Network for England (CDRNE) laboratory (see list below) will assess the request using the criteria shown in Appendix 6.

- Leeds (Reference Laboratory)
- Leeds (Leeds General Infirmary)
- Birmingham (Heartlands Hospital)
- London (HPA Collaborating Centre at University College Hospital)
- Manchester (Manchester Royal Infirmary)
- Newcastle (Newcastle General Hospital)
- Southampton (Southampton General Hospital)

Details of the contacts to access CDNRE can be found on the HPA website at: www.hpa.org.uk/webw/HPAweb&Page&HPAwebAutoListName/Page/1208417851521?p=1208417851521

CENTRE FOR INFECTIONS

C. difficile isolates can be ribotyped by the Laboratory of Healthcare-Associated Infection (HPA Centre for Infections, 61 Colindale Avenue, London NW9 5EQ).

WALES

Anaerobe Reference Laboratory
NPHS Microbiology Cardiff
University Hospital of Wales
Heath Park
Cardiff CF14 4XW
Tel: 02920 742378 or 742171
Web: www.hpa.org.uk/cfi/arl
Email: brazier@cf.ac.uk

SCOTLAND

Scottish Salmonella Reference Laboratory
Microbiology Department
Stobhill Hospital
Glasgow G21 3UW
Tel: 0141 201 3013
Fax: 0141 558 5508
Web: www.ssrl.scot.nhs.uk

Appendix 7:
Criteria for ribotyping isolates from the HPA *Clostridium difficile* Ribotyping Network for England (CDRNE)

Guidance to help NHS colleagues to access *Clostridium difficile* ribotyping through the CDRNE laboratories (Leeds, Birmingham, London, Manchester, Newcastle, Southampton).

Key issues to access the services:

1. **Has my hospital got a high baseline rate, or could my hospital have a problem with a hypervirulent strain?**

   Evidence:

   High baseline rate, or
   Increase in frequency or severity or cases of *C. difficile* infection, or
   Increase in mortality, or
   Increase in the recurrence rate.

2. **My hospital has a problem with hypervirulent strain because some of the isolates (e.g. from DH mandatory surveillance) are ribotype 027.**

   How bad is the problem?

   How many cases per week?
   Severity mortality data
   Recurrence rates.

3. **What do I need to do to access the *C. difficile* ribotyping service?**

   Discuss the situation with your regional microbiologist (RM) or the CDRNE laboratory.

   Agree to provide clinical information minimum data set including outcome data.

   Send faecal samples, the number of which will be decided following discussions with the CDRNE laboratory.

   Complete the referral form to access the service after agreement with the RM or the CDRNE laboratory.

4. **Environmental screening**

   'Routine' ribotyping of environmental spores is not necessary.

   The main measures to control *C. difficile* infections are case isolation, enhanced environmental cleaning, and good antibiotic prescribing, in addition to optimising hand hygiene and use of personal protective equipment. Ribotyping environmental spores is not necessary for control, and therefore the CDRNE laboratories will not entertain such requests.

www.hpa.org.uk/webw/HPAweb&Page&HPAwebAutoListName/Page/1208417851521?p=1208417851521

Appendix 8:
Examples of death certification for CDI patients

(Modified from the November 2007 version of *Guidance for doctors certifying cause of death in England and Wales*, www.gro.gov.uk/medcert.)

If a healthcare-associated infection (HCAI) was part of the sequence leading to death, it should be in Part 1 of the certificate, and you should include all the conditions in the sequence of events back to the original disease being treated.

Examples:

Ia. Clostridium difficile pseudomembranous colitis
Ib. Multiple antibiotic therapy
Ic. Community-acquired pneumonia with severe sepsis

II. Immobility, polymyalgia rheumatica, osteoporosis

If your patient had an HCAI which was not part of the direct sequence, but which you think contributed at all to their death, it should be mentioned in Part 2 of the certificate.

Examples:

Ia. Bronchopneumonia
Ib. Carcinomatosis and renal failure
Ic. Adenocarcinoma of the prostate

II. Clostridium difficile infection secondary to antibiotic therapy for recurrent bronchopneumonia

Appendix 9: Abbreviations

ADR	Adverse drug reaction
AHR	Alcohol handrub
AMT	Antimicrobial management team
ARL	Anaerobe Reference Laboratory
CCDC	Consultant in communicable disease control
CDI	*Clostridium difficile* infection
CDRNE	*Clostridium difficile* Ribotyping Network for England
CDT	*Clostridium difficile* toxin
CfH	Connecting for Health
CfI	Centre for Infections (Health Protection Agency)
CMO	Chief Medical Officer
CNO	Chief Nursing Officer
CRCTs	Cluster randomised controlled trials
DH	Department of Health
DIPCs	Directors of infection prevention and control
GI	Gastrointestinal
HCAI	Healthcare-associated infection
HCC	Healthcare Commission
HCW	Healthcare worker
HICPAC	Healthcare Infection Control Practices Advisory Committee
HII	High Impact Intervention
HPA	Health Protection Agency
HPU	Health protection unit
HPV	Hydrogen peroxide vapour
ICD	Infection control doctor
ICN	Infection control nurse
ICT	Infection control team
IDSA	Infectious Disease Society of America
IV	Intravenous
MLVA	Multiple locus variable
MRSA	Meticillin-resistant *Staphylococcus aureus*
NAP1	North American pulso-type 1
NCDSG	National *Clostridium difficile* Standards Group
NG	Naso-gastric
NHS	National Health Service
NPHS	National Public Health Service (Wales)
NRL	National Reference Library
PCR	Polymerase chain reaction
PCT	Primary care trust
PEAT	Patient Environment Action Team
PII	Period of increased incidence
PMC	Pseudomembranous colitis
PPI	Proton pump inhibitor
RCT	Randomised controlled trial
RMN	Regional microbiology network
SHA	Strategic health authority
SHEA	Society for Healthcare Epidemiology of America
SPC	Statistical process control
SUI	Serious untoward incident
UK	United Kingdom
US	United States
VNTR	Variable number tandem repeats
WCC	White cell count
WHO	World Health Organization

Appendix 10: Members of the working group

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