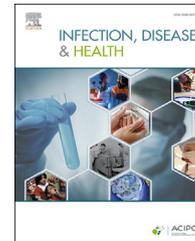




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Guidelines

ASID/ACIPC position statement – Infection control for patients with *Clostridium difficile* infection in healthcare facilities

Rhonda L. Stuart ^{a,*}, Caroline Marshall ^{b,c}, Glenys Harrington ^d,
Louisa Sasko ^{e,f}, Mary-Louise McLaws ^g, John Ferguson ^{h,i,j}

^a Monash Infectious Diseases, Monash Health and Centre for Inflammatory Diseases, School of Clinical Sciences, Monash University, Melbourne, Vic, Australia

^b Infection Prevention and Surveillance Service and Victorian Infectious Diseases Service, Royal Melbourne Hospital, Department of Medicine, University of Melbourne, Melbourne, Australia

^c The Peter Doherty Institute for Infection and Immunity, Vic, Australia

^d Infection Control Consultancy (ICC), Melbourne, Vic, Australia

^e Infection Control and Physical Health Care, Macquarie Hospital, North Ryde, NSW, Australia

^f School of Medicine, Western Sydney University, Campbelltown, NSW, Australia

^g Epidemiology, Hospital Infection and Infectious Diseases Control, School of Public Health and Community Medicine, Faculty of Medicine, UNSW Sydney, Sydney, NSW, Australia

^h Health Pathology, NSW, Australia

ⁱ Hunter New England Health, NSW, Australia

^j School of Medicine, University of Newcastle, Newcastle, NSW, Australia

Received 20 September 2018; received in revised form 8 October 2018; accepted Oct 8, 2018

Available online 17 November 2018

KEYWORDS

Clostridium difficile;
Infection prevention;
Hand hygiene;
Environmental cleaning

Abstract *Background:* In 2011, the Australasian Society for Infectious Diseases (ASID) and the Australian Infection Control Association (AICA), now known as the Australasian College of Infection Prevention and Control (ACIPC), produced a position statement on infection control requirements for preventing and controlling *Clostridium difficile* infection (CDI) in healthcare settings. *Methods:* The statement updated in 2017 to reflect new literature available. The authors reviewed the 2011 position statement and critically appraised new literature published between 2011 and 2017 and relevant current infection control guidelines to identify where new evidence had become available or best practice had changed.

Results: The position statement was updated incorporating the new findings. A draft version of the updated position statement was circulated for consultation to members of ASID and ACIPC. The authors responded to all comments received and updated the position statement.

* Corresponding author.

E-mail address: Rhonda.Stuart@monashhealth.org (R.L. Stuart).

Conclusions: This updated position statement emphasizes the importance of health service organizations having evidence-based infection prevention and control programs and comprehensive antimicrobial stewardship programs, to ensure the risk of *C. difficile* acquisition, transmission and infection is minimised.

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Highlights

- Antimicrobial stewardship.
 - The use of standard and contact precautions.
 - Environmental and equipment cleaning and disinfection.
 - Staff, patient and visitor education.
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Introduction

Process of position statement development

In 2011, the Australasian Society for Infectious Diseases (ASID) and the Australian Infection Control Association (AICA), now known as the Australasian College of Infection Prevention and Control (ACIPC), produced a position statement on infection control requirements for preventing and controlling *Clostridium difficile*¹ infection (CDI) in healthcare settings [1].

In 2017, the authors reviewed the 2011 position statement as well as critically appraising new literature published between 2011 and 2017 and relevant current infection control guidelines to identify where new evidence had become available or best practice had changed. The position statement was then updated accordingly. A draft version of the updated position statement was circulated for consultation to members of ASID and ACIPC. The authors responded to all comments received and updated the position statement as necessary.

C. difficile (*Clostridioides difficile*) infection

Clostridium difficile is a Gram-positive, anaerobic, spore-forming, potentially toxigenic bacterium. In the United States, *C. difficile* now rivals methicillin-resistant *Staphylococcus aureus* (MRSA) as the most common cause of healthcare-associated infection (HAI), accounting for \$3.2 billion in excess costs annually [2–4].

CDI may present with varying severity, from mild diarrhoea to pseudomembranous colitis, toxic megacolon and can result in death. Since 2000, there has been an increase in the rates of CDI in some healthcare facilities in the United States, Canada and Europe that has been associated with an epidemic strain of *C. difficile*. This strain (BI/NAP1/027, toxinotype III or PCR ribotype 027) is characterised by binary

toxin production and increased sporulation [2,5]. Other virulent strains associated with severe disease in Europe have also emerged, including PCR ribotypes 015, 018 and 056 [6]. Australian surveys concerning isolates obtained from 2012 to 2014 indicated that the most common ribotypes were 014/020, 002, 056 and 070 [7,8]. Small numbers of virulent ribotypes 078 and 244 were found. Few isolates of ribotype 027 were identified in these surveys despite documented detections in Victoria, WA and NSW [9–11].

Epidemiology of *C. difficile* infection

While the national prevalence of CDI is unknown, some Australian states have reported rates between 2.49 and 16.3 per 10,000 bed days [12–14]. The rate of CDI in the United Kingdom has declined from 14.9 cases per 10,000 patient days in 2007/8 to 3.67 cases per 10,000 patient days in 2016/17 [15]. The most recent reported rate of CDI in the United States was 14.9 cases per 10,000 people in the population in 2015 [16]. Most cases have been in hospitalised individuals; however, increasing numbers of community-associated cases are being reported in Australia [7,12,17], as well as in the United States and Europe [16,18–22]. The prevalence of community-associated CDI (CA-CDI) in Australia is considered to be less than 30% of all CDI cases [7,12].

CA-CDI is an emerging concern of public health significance. Risk factors for CA-CDI include antimicrobial exposure, with the strongest associations found with prior use of clindamycin, fluoroquinolones and cephalosporins [23]. Whilst there are associations with similar comorbidities to hospital associated CDI, CA-CDI cases are frequently younger and lack traditional risk factors. The epidemiology of and specific risk factors for CA-CDI requires further study. The available evidence suggests close contacts (including children < 2 years old), the environment, animals (particularly production animals) and food as potential sources of this infection in the community [29].

Surveillance

In 2013 the Australian Commission for Safety and Quality in Healthcare (ACSQHC) established a national definition and surveillance method for hospital-identified CDI (HI-CDI)

¹ Reclassified in 2016 as *Clostridioides difficile* (see Lawson PA, Citron DM, Tyrrell KL, Finegold SM. Reclassification of *Clostridium difficile* as *Clostridioides difficile* (Hall and O'Toole 1935) Prévot 1938. *Anaerobe*. 2016; 40:95–9).

[30]. This national approach is consistent with surveillance definitions and recommendations that have been previously endorsed and used in Europe and the United States [31,32]. The national definition for HI-CDI specifies that a CDI case is defined as a case of diarrhoea (that is, an unformed stool that takes the shape of the container) where the stool sample yields a positive result in a laboratory assay for *C. difficile* toxin A and/or B, or toxin-producing *C. difficile* is detected in the stool sample by culture or other means. Data collection only includes new HI-CDI cases. Cases to be excluded are those who test positive within the last eight weeks of their previous positive test and patients who are <2 years of age. Paediatric carriage of *C. difficile* is highest in infants and declines markedly after the first year [33]. However, disease is uncommon at this age and therefore national surveillance usually do not include children <2 years of age. A surveillance implementation guide to support health service organisations (HSO) to implement hospital-based surveillance of CDI is also available [34]. This guide provides guidance on applying standard exposure classification criteria in line with international expert consensus on the categorisation of CDI associated with healthcare and community exposure [31].

Since January 2013, each HSO is required to undertake surveillance of CDI as part of the National Safety and Quality Health Service (NSQHS) Standards, Standard 3 – Preventing and Controlling Healthcare–Associated Infection. This requirement will continue with the release of the 2nd edition of the NSQHS Standards and the Preventing and Controlling Healthcare–Associated Infection Standard in November 2017 for implementation in January 2019. In addition, CDI surveillance is a specific requirement of the national Performance and Accountability Framework (PAF) [35], which is the reporting instrument for the National Health Reform Agreement. In the majority of Australian states and territories, surveillance is undertaken at the individual hospital level and is reported centrally at the jurisdictional level either as incidence data or as aggregate data by individual hospitals. Given that private pathology providers usually do not link in with current jurisdictional reporting systems, it is likely that the burden of CDI in the community is underestimated using hospital-based surveillance methods.

The ACSQHC has recently undertaken work to examine the usefulness of patient administrative data as a means to monitor the national CDI burden. Coding data for ICD-10 code A04.7 (Enterocolitis due to *C. difficile*) was compared against traditional clinical epidemiological surveillance data provided by the individual states [36]. Despite a high level of comparability being observed, there is still a time lag between the time of diagnosis and when administrative data become available for analysis at a national level. Further work also needs to be done to confirm case validity. Access to administrative data is more timely at the hospital level and individual hospitals can use their own patient administrative data systems to complement traditional clinical epidemiological surveillance methods and other evaluation strategies to broadly monitor the effectiveness of local infection control and antimicrobial strategies and identify the need for practice improvement.

Patient identification and diagnostic testing

Laboratory testing and diagnosis should be carried out consistent with the Public Health Laboratory Network Laboratory Case definition for CDI [37]. In particular:

- Tests for toxigenic *C. difficile* should only be performed on unformed stool specimens (or gut contents from patients with diarrhoea), unless ileus is suspected. Positive test results from formed stools should be disregarded.
- All adults and children ≥ 2 years old, who have been hospitalised for ≥ 48 h and develop diarrhoea (≥ 3 unformed stools in a 24-hour period) should be tested for CDI.
- All adults and children ≥ 2 years old, in whom diarrhoea has persisted for >48 h and no other enteropathogen has been identified should be tested for CDI.
- Repeat testing of faecal specimens during the same episode of diarrhoea is not recommended:
 - a) within 4 weeks of a positive test (response to treatment is determined by clinical criteria) or
 - b) following a negative test – unless CDI is strongly suspected and a more sensitive method (e.g. nucleic acid amplification testing) is used after a negative immunoassay.

Tests for *C. difficile* in children <2 years old should only be performed in consultation with a paediatrician.

Diarrhoea is defined as loose stools that take the shape of a receptacle or that correspond to Bristol Stool Chart types 5–7 [38]. Diarrhoea is ≥ 3 loose or unformed stools in 24 h or fewer consecutive hours or occurs more frequently than what is normal for the individual [38,39].

Infection prevention and control professionals and clinicians must be informed of CDI cases promptly in order to implement effective infection control precautions. Routine identification of asymptomatic carriers is not recommended [32].

Hospitals should also be alert to the possibility of CDI presenting in patients from the community, including residential aged care facilities. It is reasonable to consider testing outpatients >65 years presenting with diarrhoea, as defined above, and those patients with one or more risk factors for CDI (see Table 1).

Routes of transmission

The period between exposure to *C. difficile* and the occurrence of symptoms has been estimated to be a median of 2–3 days [40]. The primary mode of transmission of *C. difficile* is person-to-person via the faecal-oral route. *C. difficile* can exist in a vegetative or spore form. These spores can persist on environmental surfaces or portable equipment for several months and place patients at risk from contamination of healthcare workers' (HCWs) hands and fomites [40–43]. In heavily contaminated environments spores may be aerosolised by movement of HCWs and patients, allowing widespread dissemination [44,45]. Spores are resistant to the bactericidal effects of alcohol

Table 1 Risk factors for *Clostridium difficile* infection.

Antimicrobial exposure [23,24]
Advanced age [5,25]
Prolonged hospitalisation [5]
Residence in aged care facilities/nursing homes [26]
Immunosuppression/chemotherapy [5]
Gastrointestinal surgery or manipulation of the gastrointestinal tract [5], nasogastric tube insertion [27]
Gastric acid suppressive therapy [28]

and most hospital disinfectants [46,47]. A prior room occupant with CDI is a significant risk factor for CDI acquisition [48,49], independent of established CDI risk factors as shown by a single centre intensive care study [50]. Of patients who acquired CDI after admission to the ICU, 4.6% had a prior occupant without CDI, whereas 11.0% had a prior occupant with CDI ($P = 0.002$).

The use of molecular technology such as multilocus variable number of tandem repeats analysis and whole genome sequencing has increased our understanding of the transmission dynamics of *C. difficile*. It is now clear that symptomatic patients do not account for all episodes of *C. difficile* transmission and infection [51,52]. One systematic review that included 8725 patients reported the colonisation rate was more than 8% and colonisation on hospital admission was significant risk for subsequent *C. difficile* disease compared with non-colonised patients (RR 5.86, 95% CI 4.21–8.16) [53].

Infection prevention and control precautions.

It is likely that there are many more individuals colonised with *C. difficile* than those who have been identified with the disease (CDI) [43,54,55], making a targeted focus on this pathogen (i.e. vertical control strategies) relatively less important than broad based horizontal strategies that focus on all infections due to all pathogens, such as antimicrobial stewardship, hand hygiene and adequate environmental cleaning [56]. A summary of the recommended measures for the prevention and control of *C. difficile* in Australian hospitals is included in Table 2.

Antimicrobial stewardship

Antibiotic use increases the risk for developing CDI by seven to ten fold during and up to one month after treatment and by approximately threefold for two months thereafter [57,58]. Targeted restriction of a particular antibiotic agent or class of agents can reduce CDI rates in the community and in healthcare settings [59]. Virtually all antibiotics have been associated with CDI [60], with certain agents having higher risks, including clindamycin [61–63], amoxicillin-clavulanic acid [63], cephalosporins [63,64], and fluoroquinolones [63,65,66].

Interventional trials examining the impact of antimicrobial restriction on CDI have been summarised [59,67]. These have involved restriction of clindamycin, fluoroquinolones and third and fourth generation

cephalosporins. Two of the trials also included changes to IC practice, with almost all demonstrating significant reductions in CDI rates [49,56]. Seven studies restricted multiple agents, including quinolones [59,67,68], making it impossible to determine the impact of isolated quinolone restriction. A country-wide study was recently reported from Scotland, showing that community-wide antibiotic restriction focused around the '4C' antibiotics (clindamycin, ciprofloxacin, amoxicillin-clavulanic acid and cephalosporins of any class) was associated with changes to both healthcare and community CDI incidence with reductions of 68% and 45%, respectively. The time course of the changes was not associated with implementation of key infection control measures [69,70].

Prevention and control of CDI should include an antimicrobial stewardship program [71] that is aimed at minimising the frequency and duration of antibiotic use and promoting a narrow-spectrum antibiotic policy [72]. The program must address usage across hospital and community sectors. Many antimicrobial stewardship programs now include stewardship of gastric acid suppressive therapy given its independent association with CDI risk and profligate use [73]. It is important that wherever possible, individual patients with CDI should cease all antecedent antibiotic or gastric acid suppressive therapy once a diagnosis of CDI is made.

Probiotics

The role of probiotics for CDI prevention is an evolving area of study. Some meta-analyses suggest that use of probiotics may be beneficial for prevention of CDI [74,75]. The recent SHEA/IDSA CDI guideline assessed that there was still inadequate evidence to support a recommendation for use of probiotics for primary prevention of CDI [76].

Standard precautions (including hand hygiene)

Whilst this statement focuses on the importance of standard precautions [84] including hand hygiene, other precautions include close attention to the avoidance/management of potential fomites – e.g. personal clothing, lanyards, mobile phones and reused patient equipment including adhesive tape rolls.

Point-of-care hand hygiene when bundled with other infection prevention strategies has been associated with reductions in HAIs [77–79]. Hands should be washed with soap and water or an antiseptic wash when hands are visibly dirty/soiled and should be disinfected with alcohol based hand rub (ABHR) when hands are visibly clean [32,80]. While the evidence suggests that ABHR is not as effective at destruction of spores [85], it is very effective in reducing the bioburden of vegetative forms of *C. difficile* from hands while hand hygiene with soap and water is more effective at removing both the organism and spores. Importantly, studies have not shown an increase in CDI during outbreaks with the use of ABHR [3,81].

Because there are very few studies showing the effectiveness of hand washing over the use of ABHR and glove use for the control of CDI outside outbreaks [81,82], this Position Statement recommends the primary use of ABHR

Table 2 Summary of the recommended measures for the prevention and control of *Clostridium difficile* in Australian healthcare facilities.

Measure	Key points
Antimicrobial stewardship	<ul style="list-style-type: none"> • Focus on minimising antibiotic use, with particular attention to high risk antimicrobials • Promote the use of narrow-spectrum antibiotics, where possible
Apply standard precautions at all times	<ul style="list-style-type: none"> • Include stewardship of gastric acid suppressive therapy. • Use alcohol based hand rub (ABHR) when hands are visibly clean • Use soap and water or an antiseptic wash when hands are visibly dirty/soiled.
Apply contact precautions in addition to standard precautions	<ul style="list-style-type: none"> • Use personal protective equipment (PPE) (gowns/aprons^a and gloves) on entry to patient rooms • Isolate suspected or known case in a single room with dedicated toilet/ensuite. • If single room isolation is not possible: <ul style="list-style-type: none"> – contact precautions within the bed space – dedicate toilet/ensuite or commode • Dedicate re-useable patient care equipment, such as thermometers, blood pressure cuffs, wheelchairs and stethoscopes, to each patient • Minimise patient transfers • Maintain contact precautions for 48 h after the last episode of diarrhoea.
Ensure environmental and equipment cleaning and disinfection	<ul style="list-style-type: none"> • Use a detergent and sporicidal agent for all cleaning • Clean and disinfect all horizontal surfaces and all touchable surfaces in the patient area, including the toilet/bathroom/ensuite, daily and on discharge or transfer • Shared patient care equipment must be cleaned and disinfected after each patient use
Staff education	<ul style="list-style-type: none"> • Audit and provide feedback on cleaning and disinfection compliance. • Provide all staff with information on CDI and the measures to prevent and control transmission • Provide all clinical staff with training on antibiotic prescribing, standard precautions and contact precautions.
Patients and visitor education	<ul style="list-style-type: none"> • Educate patients and visitors on the importance of hand hygiene • Advise visitors who are assisting with care of the patient to wear gowns/aprons and gloves to protect their clothing.
The bundling of supplemental control measures is recommended in the event of an outbreak	<ul style="list-style-type: none"> • Supplementary control measures include: <ul style="list-style-type: none"> – re-doubled efforts to reduce/modify antimicrobial use – strict enforcement of standard and contact precautions – enhanced cleaning and disinfection procedures, with regular auditing and feedback to cleaning staff.

^a Choice depends on the specific clinical situation and local policies and procedures.

for hand hygiene when caring for patients with CDI [83]. The rationale for this is given as follows.

Asymptomatic carriage of toxigenic *C. difficile* is common in hospitalised patients and skin contamination can be detected on 50% of patients with CDI up to 7 days after resolution of diarrhoea [84]. The vegetative form of *C. difficile* is highly sensitive to the action of ABHR [85]. Although the spore form is resistant to ABHR [85], the recovery of vegetative forms was as high as 10-fold greater compared with the recovery of spore forms in the faeces of 26 patients with CDI [86]. This suggests that reducing transmission of vegetative forms may be crucial in CDI control. The importance of reducing the vegetative forms is also supported by studies demonstrating that exposure to gastric acid suppressive therapy is an independent risk factor for CDI [86].

Given the risk of spread of *C. difficile* will be much larger than estimates based only on passive case detection [55], there is unlikely to be a marked additional impact provided by hand hygiene with ABHR for *visibly clean* hands before and after care of recognised CDI cases. It is, therefore, important not to confuse HCWs with mixed messages about the use of ABHR as this may be detrimental to any hand hygiene compliance program.

Contact precautions

The risk of colonisation for inpatients increases with hospitalisation [87] and the median time from exposure to *C. difficile* to infection is short (2–3 days) which supports the

importance of rapid isolation of patients with CDI [87]. Yet, strong epidemiologic evidence for the efficacy of patient isolation and cohorting is limited and is only in the context of an outbreak setting [88].

Isolation as a strategy for the containment of endemic CDI has been only been explored in limited reports [67,89]. A useful modelling study identified that adherence to a bundle of isolation and screening strategies reduced the spread of CDI by 19% and colonisation by 36% [90]. The reduction when antimicrobial stewardship was added to the CDI bundle was 62% and 56% for colonisation [90].

Any patients with three or more loose stools within a 24-hour period should preferably be placed in a single room with dedicated toileting facilities [3,91,92]. If healthcare facilities are unable to isolate the patient in a single room with ensuite facilities then implement contact precautions within the bed space and allocate a dedicated toilet/bathroom or commode to the patient with a daily cleaning and disinfecting regimen using a sporicidal agent [32,93,94].

Clear signage should be used to indicate when contact precautions are required [3]. Contact precautions includes the use of personal protective equipment (PPE) including donning of gowns/aprons and gloves on entry to patient rooms. These precautions are based on the evidence of high contamination of surfaces in rooms of CDI patients [95] and evidence for contamination of HCW hands and clothing with *C. difficile* when caring for patients with CDI [32,40,82,92,93]. However, there are no data per se to show that gown/apron use reduces CDI transmission [67,92,96]. Nevertheless, gowns/aprons are recommended because PPE use is likely to reduce contamination of HCWs clothes and hands. Gowns/aprons should be removed and hand hygiene performed on exiting the room.

When patients are in contact precautions transfers should be kept to a minimum. If patients require transport to another clinical area, ensure that the receiving area is aware of the transfer and that wheelchairs, trolleys and patient areas are appropriately cleaned and disinfected with a suitable sporicidal agent (see *Environmental and equipment cleaning and disinfection below*) after use. The presence of CDI should not delay the provision of healthcare services.

Glove use

Based on precautionary principles, glove use has been previously recommended to minimise the level of contamination with vegetative forms and spores on hands of HCWs when caring for patients with known CDI. However, only one observational study has examined the importance of glove use [82]. Several important potential confounders may not have been controlled for in this study, including the level of hand hygiene compliance, which was not reported. Although healthcare-associated CDI rates in the ward where gloves were introduced declined from 7.7 to 1.5 per 1000 patient discharges (Relative Risk = 0.16, $p = 0.015$), the overall difference in CDI incidence compared with the control wards was not statistically significant due to the small number of cases ($p = 0.14$).

Glove use is 'strongly recommended' in many international guidelines during any care episode of patients with CDI [76,97]. Gloves should be routinely employed when caring for patients with CDI as there is good evidence that demonstrates the protective effect of gloves when exposure to diarrhoea or blood or body fluid is likely [82,103]. Gloves must be changed and hand hygiene performed when moving from dirty to clean tasks or when changing between procedures for the same patient. If gloves are contaminated, correct and careful removal is required to prevent hand and/or wrist contamination and hand hygiene should be performed immediately after removal. All gloves and gowns/aprons should be removed and hand hygiene performed on exiting the room.

Ceasing contact precautions

For patients with *C. difficile*, contact precautions and isolation must remain in place for a further 48 h after the last episode of diarrhoea [95]. The rationale is based on the possibility that *C. difficile* may still be shed from patients despite symptom resolution [84,98]. Careful assessment must be made before removing a patient from contact precautions if bowel motions have failed to return to normal. Onset of ileus/toxic megacolon may be associated with an unexpected reduction in bowel motions. In these circumstances the patient would still require contact precautions. When patients have been treated for CDI but continue to have diarrhoea, their need for ongoing contact precautions should be assessed on a case by case basis in discussion with infection prevention and control staff.

Environmental and equipment cleaning and disinfection

The environment is an important source of healthcare-associated CDI [99]. *C. difficile* spores can be found on multiple surfaces in the healthcare setting and can survive for months [43,100]. Spores are resistant to cleaning and disinfection with many of the currently used cleaning and disinfection agents. Thus any *C. difficile* contaminated surfaces or fomites should be cleaned and disinfected with a sporicidal agent.

In *C. difficile*-contaminated patient care areas, all horizontal surfaces and all touchable (hand contact) surfaces in the patient area, including the bathroom/ensuite, should be cleaned and disinfected daily and on discharge or transfer (i.e. terminal clean). Cleaning should take place with a method that has been validated to deal effectively with environmental spore contamination.

Many authorities recommend using a cleaning agent that contains chlorine, however, in recent years, new products with sporicidal activity have become available. These include peracetic acid and accelerated hydrogen peroxide containing agents [101,102].

When selecting new agents the user should be familiar with the Therapeutic Goods Administration (TGA) summary of disinfectant regulations in Australia (<http://www.tga.gov.au/summary-disinfectant-regulation>) and follow the

manufacturer's instructions for use. Manufacturers/suppliers of new agents should provide information to substantiate sporicidal claims (i.e. Registered TGA, Australian Register of Therapeutic Goods (ARTG) entry).

If using a chlorine based agent (i.e. household bleach) high levels of chlorine (5000 mg/L free chlorine) have been shown to have consistent efficacy against *C. difficile* spores however lower dilutions of chlorine (1000 and 3000 mg/L free chlorine) show varying capacity to eradicate spores [103].

Sporicidal agent contact times recommended by the manufacturer/supplier need to be practical for healthcare settings. Long contact times (the time the surface needs to remain wet) of 10–30 min may be an occupational health and safety hazard and are not practical for a healthcare setting.

Patient care equipment, such as thermometers, blood pressure cuffs, wheelchairs and stethoscopes, should be dedicated to each patient with *C. difficile*. If they are removed from the patient zone they must be cleaned and disinfected with a sporicidal agent. Shared patient care equipment should be cleaned and disinfected using a sporicidal agent after each patient use.

New no-touch cleaning technologies, such as hydrogen peroxide vapour (HPV) and ultraviolet (UV–C) light may be used as an adjunct to routine discharge/transfer terminal cleaning and disinfecting procedures [104]. Both of these no-touch technologies are effective in reducing *C. difficile* in the environment and reducing disease in patients in observational studies and one randomised controlled trial of ultraviolet (UV) light [105]. HPV has been associated with greater reduction in spore forming organisms than ultraviolet (UV) light [106], although the clinical impact of this has not been tested. A recently published systematic review on the impact of no-touch disinfection methods to decrease healthcare associated infections has shown that use of ultraviolet (UV) light systems was associated with a statistically significant reduction in *C. difficile* infections, particularly in studies with high baseline rates of *C. difficile* [107]. Use of a HPV system was not associated with a statistically significant reduction in *C. difficile* infections in this review. Both systems have advantages and disadvantages and users should choose only devices with

demonstrated bactericidal and sporicidal capabilities and preferably select a device that has been shown to reduce hospital associated infections. Routine environmental screening for *C. difficile* is not recommended [32].

Education and quality improvement

All HSOs, including residential aged care facilities, should give CDI prevention and control the highest priority, even when the incidence of CDI is low. Analysis of individual cases of CDI can provide useful guidance for antimicrobial stewardship programs, quality improvement and educational processes.

Education programs should focus on antibiotic prescribing as the primary preventative strategy for CDI. HSO staff (including administration, cleaning staff, food services and maintenance staff) should be provided with information on CDI and the measures to prevent and control transmission. All clinical staff should receive training on standard precautions including the importance of hand hygiene and glove use in caring for patients with CDI. They should also be trained in the appropriate use of personal protective equipment (PPE) and be able to demonstrate correct donning and removal of PPE. Cleaning staff require training, audit, feedback and encouragement to ensure that environmental cleaning and disinfection is optimal [108].

Monitoring of CDI rates and reporting to relevant committees is required as a quality process indicator.

Patients and their visitors

Patients and their visitors should be educated about CDI, contact precautions and hand hygiene. If the visitor is assisting with care of the patient, gowns/aprons and gloves should be worn to protect their clothing and hands. Hand hygiene should be performed on completion of care. Visitors should be advised not to use the patient's bathroom or visit other patients' rooms.

Cluster investigation and outbreak management

An increase in the number of patients with CDI above the usual number in the healthcare institution should prompt

Table 3 Epidemiological steps of an outbreak investigation [110].

Verify diagnosis of all CDI cases by ensuring laboratory confirmation.
Establish the outbreak. Identify that additional cases constitute an outbreak by comparing the number against previous case numbers.
Construct a working case definition. For the purpose of control in the early stages of the outbreak until laboratory confirmation is available for all cases, a case definition may be based on clinical presentation, such as episodes of diarrhoea, and an epidemiological risk factor (e.g. contact of a CDI laboratory confirmed patient).
Communicate the outbreak to ward/unit/residential aged care facility staff and encourage early reporting of potential/suspected cases.
Search for additional cases , passively through the laboratory and actively with the help of ward/unit staff.
Implement control and prevention measures.
Develop and test a hypothesis for the outbreak.
Reevaluate hypothesis and if necessary based on data, reconsider/refine and re-evaluate the hypothesis.
Reevaluate the implementation of control and prevention measures
Communicate final findings

an epidemiological investigation. The aim of the epidemiological investigation is to assist in the identification of the source of the outbreak, implementing the most effective strategies for control and preventing continuation of the outbreak [109]. The steps in Table 3 performed during an investigation are provided as a guide only and reflects an initial investigation [110]. As cases increase and further analysis and information becomes available the order of steps may change [111]. Testing for the genetic relatedness of isolates may assist in providing information in relation to transmission of CDI from known symptomatic patients [52].

Supplementary control measures

In the case of an outbreak, consider the following supplementary control measures [108]:

- re-doubled efforts to reduce/modify antimicrobial and proton pump inhibitor use
- strict enforcement of standard and transmission-based precautions with auditing and appropriate feedback to relevant clinicians
- enhanced cleaning and disinfection procedures using a sporicidal agent, with attention paid to detail. Regular monitoring of cleaning, using methods such as fluorescent marking audits, with feedback to cleaning staff should be employed.

Compliance with control strategies should be monitored and audited with feedback to relevant clinical staff and key stakeholders along with reporting within the organisation as required until the number of cases returns to pre-outbreak levels.

Conclusion

All health service organizations should have in place an evidence-based infection prevention and control program and a comprehensive antimicrobial stewardship program to ensure the risk of *C. difficile* acquisition, transmission and CDI is minimised. Further research is required to determine the most effective combination of control strategies.

Ethical considerations

As this is an evidence-based position statement, ethical approval is not required.

Authorship statement

All authors were involved in the draft and revision of this paper.

Conflicts of interest

GH has received consulting fees from Rapid Sterilisation and hence abstained from reviewing and updating the section on environmental and equipment cleaning and disinfection.

All other authors have no potential conflicts of interest to declare.

Provenance and peer review

Not commissioned; externally peer reviewed.

Funding

No funding.

Key national resources

Australian Commission on Safety and Quality in Health-care: Implementation Guide for Surveillance of *C. difficile* infection (2013): https://www.safetyandquality.gov.au/wp-content/uploads/2012/02/1303-CDI-Implementation_Guide-_V10.pdf.

National definition and calculation of Hospital identified *C. difficile* infection (2013): <https://www.safetyandquality.gov.au/our-work/healthcare-associated-infection/national-hai-surveillance-initiative/national-definition-and-calculation-of-hospital-identified-clostridium-difficile-infection/>

Public Health Laboratory Network: *C. difficile* infection laboratory case definition (2016): [http://www.health.gov.au/internet/main/publishing.nsf/Content/FA6E8CED3C4D067FCA257FC30009EBF8/\\$File/Clostridium-difficile-infection-LCD-May2016.pdf](http://www.health.gov.au/internet/main/publishing.nsf/Content/FA6E8CED3C4D067FCA257FC30009EBF8/$File/Clostridium-difficile-infection-LCD-May2016.pdf).

Australasian Society for Infectious Diseases: Australasian Society of Infectious Diseases updated guidelines for the management of *C. difficile* infection in adults and children in Australia and New Zealand (2016): <http://onlinelibrary.wiley.com/doi/10.1111/imj.13027/full>.

National Health and Medical Research Council: NHMRC (2010) Australian Guidelines for the Prevention and Control of Infection in Healthcare. Commonwealth of Australia. <https://www.nhmrc.gov.au/guidelines-publications/cd33>.

References

- [1] Stuart RL, Marshall C, McLaws ML, et al. ASID/AICA position statement – infection control guidelines for patients with *Clostridium difficile* infection in healthcare settings. *Healthc Infect* 2011;16:33–9.
- [2] McDonald LC, Owings M, Jernigan DB. *Clostridium difficile* infection in patients discharged from US short-stay hospitals, 1996-2003. *Emerg Infect Dis* 2006;12:409–15.
- [3] Dubberke ER, Carling P, Carrico R, Donskey CJ, Loo VG, McDonald LC, et al. Strategies to prevent *Clostridium difficile* infections in acute care hospitals: 2014 update. *Infect Hosp Epidemiol* 2014;35:S48–65.
- [4] O'Brien JA, Lahue BJ, Caro JJ, Davidson DM. The emerging infectious challenge of *Clostridium difficile*-associated disease in Massachusetts hospitals: clinical and economic consequences. *Infect Control Hosp Epidemiol* 2007;28:1219–27.
- [5] Bartlett JG. Narrative review: the new epidemic of *Clostridium difficile*-associated enteric disease. *Ann Intern Med* 2006;145:758–64.

- [6] Bauer MP, Notermans DW, van Benthem BH. 0157. Epidemiology and control of *C. difficile* infection. Vienna: European Congress of Clinical Microbiology and Infectious Diseases; 2010.
- [7] Collins DA, Putsathit P, Elliott B, Riley TV. Laboratory-based surveillance of *Clostridium difficile* strains circulating in the Australian healthcare setting in 2012. *Pathology* 2017;49:309–13.
- [8] Knight DR, Giglio S, Huntington PG, Korman TM, Kotsanas D, Moore CV, et al. Surveillance for antimicrobial resistance in Australian isolates of *Clostridium difficile*, 2013–14. *J Antimicrob Chemother* 2015;70:2992–9.
- [9] Riley TV, Thean S, Hool G, Golledge CL. First Australian isolation of epidemic *Clostridium difficile* PCR ribotype 027. *Med J Aust* 2009;190:706–8.
- [10] Richards M, Knox J, Elliott B, Mackin K, Lyras D, Waring LJ, et al. Severe infection with *Clostridium difficile* PCR ribotype 027 acquired in Melbourne, Australia. *Med J Aust* 2011;194:369–71.
- [11] Cheng AC, Collins DA, Elliott B, Ferguson JK, Paterson DL, Thean S, et al. Laboratory-based surveillance of *Clostridium difficile* circulating in Australia. September–November 2010. *Pathology* 2016;48:257–60.
- [12] Worth LJ, Spelman T, Bull AL, Brett JA, Richards MJ. Epidemiology of *Clostridium difficile* infections in Australia: enhanced surveillance to evaluate time trends and severity of illness in Victoria, 2010–2014. *J Hosp Infect* 2016;93:280–5.
- [13] Foster NF, Collins DA, Ditchburn SL, Duncan CN, van Schalkwyk CL, Keed ABR, et al. Epidemiology of *Clostridium difficile* infection in two tertiary-care hospitals in Perth, Western Australia: a cross-sectional study. *New Microbes New Infect* 2014;2:64–71.
- [14] Slimings C, Armstrong P, Beckingham WD, Bull AL, Hall L, Kennedy KJ, et al. Increasing incidence of *Clostridium difficile* infection, Australia, 2011–2012. *Med J Aust* 2014;200:272–6.
- [15] Public Health England. *C. difficile* infections: quarterly counts by acute trust and CCG, and financial year counts and rates by acute trust and CCG, up to financial year 2016 to 2017 (Table 8a: Financial year counts and rates of *C. difficile* infection (patients aged 2 years and over)) - all reported cases [Internet]. 2017 [cited 19 January 2018]; Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/625307/C_difficile_annual_tables_2017 ods.
- [16] Centers for Disease Control and Prevention. *Clostridium difficile* infection (CDI) Tracking [Online]. 2015 [cited 13 February 2018]; Available from: <https://www.cdc.gov/hai/eip/clostridium-difficile.html>.
- [17] Collins DA, Selvey LA, Celenza A, Riley TV. Community-associated *Clostridium difficile* infection in emergency department patients in Western Australia. *Anaerobe* 2017;48:121–5.
- [18] Bauer MP, Goorhuis A, Koster T, Numan-Ruberg SC, Hagen EC, Debast SB, et al. Community-onset *Clostridium difficile*-associated diarrhoea not associated with antibiotic usage—two case reports with review of the changing epidemiology of *Clostridium difficile*-associated diarrhoea. *Neth J Med* 2008;66:207–11.
- [19] Centers for Disease Control and Prevention. Severe *Clostridium difficile*-associated disease in populations previously at low risk—four states, 2005. *Morb Mortal Wkly Rep* 2005;54:1201–5.
- [20] Kotila SM, Mentula S, Ollgren J, Virolainen-Julkunen A, Lytikainen O. Community- and healthcare-associated *Clostridium difficile* infections, Finland, 2008–2013(1). *Emerg Infect Dis* 2016;22:1747–53.
- [21] Banks A, Brown DJ, Mather H, Coia JE, Wiuff C. Sentinel community *Clostridium difficile* infection (CDI) surveillance in Scotland, April 2013 to March 2014. *Anaerobe* 2016;37:49–53.
- [22] Lessa FC, Mu Y, Bamberg WM, Beldavs ZG, Dumyati GK, Dunn JR, et al. Burden of *Clostridium difficile* infection in the United States. *N Engl J Med* 2015;372:825–34.
- [23] Deshpande A, Pasupuleti V, Thota P, Pant C, Rolston DD, Sferra TJ, et al. Community-associated *Clostridium difficile* infection and antibiotics: a meta-analysis. *J Antimicrob Chemother* 2013;68:1951–61.
- [24] Slimings C, Riley TV. Antibiotics and hospital-acquired *Clostridium difficile* infection: update of systematic review and meta-analysis. *J Antimicrob Chemother* 2014;69:881–91.
- [25] Chen Y, Glass K, Liu B, Riley TV, Korda R, Kirk MD. A population-based longitudinal study of *Clostridium difficile* infection-related hospitalization in mid-age and older Australians. *Epidemiol Infect* 2017;145:575–82.
- [26] Fisher A, Varendran R. Letter: clinical predictors of *Clostridium difficile* infection – advanced age and residential status are important factors for prediction and prevention. *Aliment Pharmacol Ther* 2014;41:232–7.
- [27] Wijarnpreecha K, Sornprom S, Thongprayoon C, Phatharacharukul P, Cheungpasitporn W, Nakkala K. The risk of *Clostridium difficile* associated diarrhea in nasogastric tube insertion: a systematic review and meta-analysis. *Dig Liver Dis* 2016;48:468–72.
- [28] Trifan A, Stanciu C, Girleanu I, Stoica OC, Singeap AM, Maxim R, et al. Proton pump inhibitors therapy and risk of *Clostridium difficile* infection: systematic review and meta-analysis. *World J Gastroenterol* 2017;23:6500–15.
- [29] Bloomfield LE, Riley TV. Epidemiology and risk factors for community-associated *Clostridium difficile* infection: a narrative review. *Infect Dis Ther* 2016;5:231–51.
- [30] Australian Commission on Safety and Quality in Health Care. National definition and calculation of Hospital identified *Clostridium difficile* infection [Internet]. 2012 [cited 23 October 2017]; Available from: <https://www.safetyandquality.gov.au/our-work/healthcare-associated-infection/national-hai-surveillance-initiative/national-definition-and-calculation-of-hospital-identified-clostridium-difficile-infection/>.
- [31] McDonald LC, Coignard B, Dubberke E, Song X, Horan T, Kuty PK. Recommendations for surveillance of *Clostridium difficile*-associated disease. *Infect Control Hosp Epidemiol* 2007;28:140–5.
- [32] Cohen SH, Gerding DN, Johnson S, Kelly CP, Loo VG, McDonald L, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA). *Infect Control Hosp Epidemiol* 2011;31:431–55.
- [33] Viscidi R, Willey S, Bartlett JG. Isolation rates and toxigenic potential of *Clostridium difficile* isolates from various patient populations. *Gastroenterology* 1981;81:5–9.
- [34] Australian Commission on Safety and Quality in Healthcare. Implementation guide for surveillance of *Clostridium difficile* infection [Online]. 2013 [cited 1 August 2017]; Available from: https://www.safetyandquality.gov.au/wp-content/uploads/2012/02/1303-CDI-Implementation_Guide_V10.pdf.
- [35] Australian Institute of Health and Welfare. Performance and accountability Framework [Online]. 2011 [cited 1 August 2017]; Available from: <http://www.aihw.gov.au/health-performance/performance-and-accountability-framework/>.
- [36] Gralton J. 2017, senior project officer, Australian commission on safety and quality in health care. Personal Communication; 2017.

- [37] Public Health Laboratory Network. *Clostridium difficile* infection laboratory case definition [Online]. 2016 [cited 22 March 2017]; Available from: [http://www.health.gov.au/internet/main/publishing.nsf/Content/FA6E8CED3C4D067FCA257FC30009EBF8/\\$File/Clostridium-difficile-infection-LCD-May2016.pdf](http://www.health.gov.au/internet/main/publishing.nsf/Content/FA6E8CED3C4D067FCA257FC30009EBF8/$File/Clostridium-difficile-infection-LCD-May2016.pdf).
- [38] Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. *Scand J Gastroenterol* 1997;32: 920–4.
- [39] World Health Organization. Diarrhoea [Online]. 2017 [cited Available from: <http://www.who.int/topics/diarrhoea/en/>.
- [40] McFarland LV, Mulligan ME, Kwok RY, Stamm WE. Nosocomial acquisition of *Clostridium difficile* infection. *N Engl J Med* 1989;320:204–10.
- [41] Mayfield JL, Leet T, Miller J, Mundy LM. Environmental control to reduce transmission of *Clostridium difficile*. *Clin Infect Dis* 2000;31:995–1000.
- [42] Brooks SE, Veal RO, Kramer M, Dore L, Schupf N, Adachi M. Reduction in the incidence of *Clostridium difficile*-associated diarrhea in an acute care hospital and a skilled nursing facility following replacement of electronic thermometers with single-use disposables. *Infect Control Hosp Epidemiol* 1992;13:98–103.
- [43] Dumford 3rd DM, Nerandzic MM, Eckstein BC, Donskey CJ. What is on that keyboard? Detecting hidden environmental reservoirs of *Clostridium difficile* during an outbreak associated with North American pulsed-field gel electrophoresis type 1 strains. *Am J Infect Contr* 2009;37:15–9.
- [44] Best EL, Fawley WN, Parnell P, Wilcox MH. The potential for airborne dispersal of *Clostridium difficile* from symptomatic patients. *Clin Infect Dis* 2010;50:1450–7.
- [45] Roberts K, Smith CF, Snelling AM, Kerr KG, Banfield KR, Sleight PA, et al. Aerial dissemination of *Clostridium difficile* spores. *BMC Infect Dis* 2008;8:7.
- [46] Wilcox MH, Fawley WN. Hospital disinfectants and spore formation by *Clostridium difficile*. *Lancet* 2000;356:1324.
- [47] Wilcox MH, Fawley WN, Wigglesworth N, Parnell P, Verity P, Freeman J. Comparison of the effect of detergent versus hypochlorite cleaning on environmental contamination and incidence of *Clostridium difficile* infection. *J Hosp Infect* 2003;54:109–14.
- [48] Mitchell BG, Dancer SJ, Anderson M, Dehn E. Risk of organism acquisition from prior room occupants: a systematic review and meta-analysis. *J Hosp Infect* 2015;91:211–7.
- [49] Chang VT, Nelson K. The role of physical proximity in nosocomial diarrhea. *Clin Infect Dis* 2000;31:717–22.
- [50] Shaughnessy MK, Micielli RL, DePestel DD, Arndt J, Strachan CL, Welch KB, et al. Evaluation of hospital room assignment and acquisition of *Clostridium difficile* infection. *Infect Control Hosp Epidemiol* 2011;32:201–6.
- [51] Curry SR, Muto CA, Schlackman JL, Pasculle AW, Shutt KA, Marsh JW, et al. Use of multilocus variable number of tandem repeats analysis genotyping to determine the role of asymptomatic carriers in *Clostridium difficile* transmission. *Clin Infect Dis* 2013;57:1094–102.
- [52] Eyre DW, Cule ML, Wilson DJ, Eyre DW, Cule ML, Wilson DJ, et al. Diverse sources of *C. difficile* infection identified on whole-genome sequencing. *N Engl J Med* 2013;369: 1195–205.
- [53] Zacharioudakis IM, Zervou FN, Pliakos EE, Ziakas PD, Mylonakis E. Colonization with toxinogenic *C. difficile* upon hospital admission, and risk of infection: a systematic review and meta-analysis. *Am J Gastroenterol* 2015;110:381–90.
- [54] Mutters R, Nonnenmacher C, Susin C, Albrecht U, Kropatsch R, Schumacher S. Quantitative detection of *Clostridium difficile* in hospital environmental samples by real-time polymerase chain reaction. *J Hosp Infect* 2009;71:43–8.
- [55] Riggs MM, Sethi AK, Zabarsky TF, Eckstein EC, Jump RL, Donskey CJ. Asymptomatic carriers are a potential source for transmission of epidemic and non-epidemic *Clostridium difficile* strains among long-term care facility residents. *Clin Infect Dis* 2007;45:992–8.
- [56] Septimus E, Weinstein RA, Perl TM, Goldmann DA, Yokoe DS. Approaches for preventing healthcare-associated infections: go long or go wide? *Infect Control Hosp Epidemiol* 2014;35: 797–801.
- [57] Hensgens MP, Goorhuis A, Dekkers OM, Kuijper EJ. Time interval of increased risk for *Clostridium difficile* infection after exposure to antibiotics. *J Antimicrob Chemother* 2012; 67:742–8.
- [58] Centers for Disease Control and Prevention. Vital signs: preventing *Clostridium difficile* infections. *Morb Mortal Wkly Rep* 2012;61:157–62.
- [59] Feazel LM, Malhotra A, Perencevich EN, Kaboli P, Diekema DJ, Schweizer ML. Effect of antibiotic stewardship programmes on *Clostridium difficile* incidence: a systematic review and meta-analysis. *J Antimicrob Chemother* 2014;69: 1748–54.
- [60] Thomas C, Stevenson M, Riley TV. Antibiotics and hospital-acquired *Clostridium difficile*-associated diarrhoea: a systematic review. *J Antimicrob Chemother* 2003;51:1339–50.
- [61] Climo MW, Israel DS, Wong ES, Williams D, Coudron P, Markowitz SM. Hospital-wide restriction of clindamycin: effect on the incidence of *Clostridium difficile*-associated diarrhea and cost. *Ann Intern Med* 1998;128:989–95.
- [62] Pear SM, Williamson TH, Bettin KM, Gerding DN, Galgiani JN. Decrease in nosocomial *Clostridium difficile*-associated diarrhea by restricting clindamycin use. *Ann Intern Med* 1994; 120:272–7.
- [63] Kavanagh K, Pan J, Marwick C, Davey P, Wiuff C, Bryson S, et al. Cumulative and temporal associations between antimicrobial prescribing and community-associated *Clostridium difficile* infection: population-based case-control study using administrative data. *J Antimicrob Chemother* 2017;72: 1193–201.
- [64] Carling P, Fung T, Killion A, Terrin N, Barza M. Favorable impact of a multidisciplinary antibiotic management program conducted during 7 years. *Infect Control Hosp Epidemiol* 2003;24:699–706.
- [65] Gaynes R, Rimland D, Killum E, Lowery HK, Johnson TM, Killgore G, et al. Outbreak of *Clostridium difficile* infection in a long-term care facility: association with gatifloxacin use. *Clin Infect Dis* 2004;38:640–5.
- [66] Biller P, Shank B, Lind L, Brennan M, Tkatch L, Killgore G, et al. Moxifloxacin therapy as a risk factor for *Clostridium difficile*-associated disease during an outbreak: attempts to control a new epidemic strain. *Infect Control Hosp Epidemiol* 2007;28:198–201.
- [67] Hsu J, Abad C, Dinh M, Safdar N. Prevention of endemic healthcare-associated *Clostridium difficile* infection: reviewing the evidence. *Am J Gastroenterol* 2010;105:2327–39.
- [68] Price J, Cheek E, Lippett S, Cubbon M, Gerding DN, Sambol SP, et al. Impact of an intervention to control *Clostridium difficile* infection on hospital- and community-onset disease; an interrupted time series analysis. *Clin Microbiol Infect* 2010;16:1297–302.
- [69] Graber CJ. *Clostridium difficile* infection: stewardship's lowest hanging fruit? *Lancet Infect Dis* 2017 Feb;17(2): 123–4
- [70] Lawes T, Lopez-Lozano JM, Nebot CA, Macartney G, Subbarao-Sharma R, Wares KD, et al. Effect of a national 4C antibiotic stewardship intervention on the clinical and molecular epidemiology of *Clostridium difficile* infections in a region of Scotland: a non-linear time-series analysis. *Lancet Infect Dis* 2017;17:194–206.
- [71] Baur D, Gladstone BP, Burkert F, Carrara E, Foschi F, Döbele S, et al. Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-

- resistant bacteria and *Clostridium difficile* infection: a systematic review and meta-analysis. *Lancet Infect Dis* 2017;17:990–1001.
- [72] Fowler S, Webber A, Cooper BS, Phimister A, Price K, Carter Y, et al. Successful use of feedback to improve antibiotic prescribing and reduce *Clostridium difficile* infection: a controlled interrupted time series. *J Antimicrob Chemother* 2007;59:990–5.
- [73] Kandel CE, Gill S, McCreedy J, Matelski J, Powis JE. Reducing co-administration of proton pump inhibitors and antibiotics using a computerized order entry alert and prospective audit and feedback. *BMC Infect Dis* 2016;16:355.
- [74] Shen NT, Maw A, Tmanova LL, Pino A, Ancy K, Crawford CV, et al. Timely use of probiotics in hospitalized adults prevents *Clostridium difficile* infection: a systematic review with meta-regression analysis. *Gastroenterology* 2017;152:1889–900.
- [75] Johnston BC, Ma SS, Goldenberg JZ, Thorlund K, Vandvik PO, Loeb M, et al. Probiotics for the prevention of *Clostridium difficile*-associated diarrhea: a systematic review and meta-analysis. *Ann Intern Med* 2012;157:878–88.
- [76] McDonald LC, Gerding DN, Johnson S, Bakken JS, Carroll KC, Coffin SE, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults and children: 2017 update by the infectious diseases society of America (IDSA) and society for healthcare epidemiology of America (SHEA). *Clinical Infectious Diseases*; 2018 [ePub].
- [77] Grayson ML, Jarvie LJ, Martin R, Johnson PDR, Jodoin ME, McMullan C, et al. Significant reductions in methicillin-resistant *Staphylococcus aureus* bacteraemia and clinical isolates associated with a multisite, hand hygiene culture-change program and subsequent successful statewide roll-out. *Med J Aust* 2008;188:633–40.
- [78] Pittet D, Allegranzi B, Boyce J. The world health organization guidelines on hand hygiene in health care and their consensus recommendations. *Infect Control Hosp Epidemiol* 2009;30:611–22.
- [79] McLaws ML, Pantle AC, Fitzpatrick KR, Hughes CF. More than hand hygiene is needed to affect methicillin-resistant *Staphylococcus aureus* clinical indicator rates: clean hands save lives, part IV. *Med J Aust* 2009;191:S26–31.
- [80] National Health and Medical Research Council and Australian Commission on Safety and Quality in Health Care. Australian guidelines for the prevention and control of infection in healthcare [Online]. 2010 [cited 9 October 2017]; Available from: <http://www.nhmrc.gov.au/guidelines/publications/cd33>.
- [81] Jabbar U, Leischner J, Kasper D, Gerber R, Sambol SP, Parada JP, et al. Effectiveness of alcohol-based hand rubs for removal of *Clostridium difficile* spores from hands. *Infect Control Hosp Epidemiol* 2010;31:565–70.
- [82] Johnson S, Gerding DN, Olson MM, Weiler MD, Hughes RA, Clabots CR, et al. Prospective, controlled study of vinyl glove use to interrupt *Clostridium difficile* nosocomial transmission. *Am J Med* 1990;88:137–40.
- [83] World Health Organization. WHO guidelines on hand hygiene in health care [Internet]. 2009 [cited 23 October 2017]; Available from: http://apps.who.int/iris/bitstream/10665/44102/1/9789241597906_eng.pdf.
- [84] Bobulsky GS, Al-Nassir WN, Riggs MM, Sethi AK, Donskey CJ. *Clostridium difficile* skin contamination in patients with *C. difficile*-associated disease. *Clin Infect Dis* 2008;46:447–50.
- [85] Wullt M, Odenholt I, Walder M. Activity of three disinfectants and acidified nitrite against *Clostridium difficile* spores. *Infect Control Hosp Epidemiol* 2003;24:765–8.
- [86] Jump RLP, Pultz MJ, Donskey CJ. Vegetative *Clostridium difficile* survives in room air on moist surfaces and in gastric contents with reduced acidity: a potential mechanism to explain the association between proton pump inhibitors and *C. difficile*-associated diarrhea? *Antimicrob Agents Chemother* 2007;51:2883–7.
- [87] Chalmers JD, Akram AR, Singanayagam A, Wilcox MH, Hill AT. Risk factors for *Clostridium difficile* infection in hospitalized patients with community-acquired pneumonia. *J Infect* 2016;73:45–53.
- [88] Ratnayake L, McEwen J, Henderson N, Nathwani D, Phillips G, Brown D, et al. Control of an outbreak of diarrhoea in a vascular surgery unit caused by a high-level clindamycin-resistant *Clostridium difficile* PCR ribotype 106. *J Hosp Infect* 2011;79:242–7.
- [89] Longtin Y, Paquet-Bolduc B, Gilca R, Garenc C, Fortin E, Longtin J, et al. Effect of detecting and isolating *Clostridium difficile* carriers at hospital admission on the incidence of *C. difficile* infections: a quasi-experimental controlled study. *JAMA Intern Med* 2016;176:796–804.
- [90] Grigoras CA, Zervou FN, Zacharioudakis IM, Siettos CI, Mylonakis E. Isolation of *C. difficile* carriers alone and as part of a bundle approach for the prevention of *Clostridium difficile* Infection (CDI): a mathematical model based on clinical study data. *PLoS One* 2016;11:e0156577.
- [91] Vonberg RP, Kuijper EJ, Wilcox MH, Barbut F, Tüll P, Gastmeier P, et al. Infection control measures to limit the spread of *Clostridium difficile*. *Clin Microbiol Infect* 2008;14:2–20.
- [92] Weber DJ, Rutala WA, Miller MB, Huslage K, Sickbert-Bennett E. Role of hospital surfaces in the transmission of emerging health care-associated pathogens: norovirus, *Clostridium difficile*, and *Acinetobacter* species. *Am J Infect Contr* 2010;38:S25–33.
- [93] Siegel JD, Rhinehart E, Jackson M, Chiarello L. Management of multidrug-resistant organisms in health care settings, 2006. *Am J Infect Control* 2007;35:S165–93.
- [94] Orenstein R, Aronhalt KC, McManus JE, Fedraw LA. A targeted strategy to wipe out *Clostridium difficile*. *Infect Contr Hosp Epidemiol* 2011;32:1137–9.
- [95] Kundrapu S, Sunkesula VC, Jury LA, Sethi AK, Donskey CJ. Utility of perirectal swab specimens for diagnosis of *Clostridium difficile* infection. *Clin Infect Dis* 2012;55:1527–30.
- [96] Surawicz CM, Brandt LJ, Binion DG, Ananthakrishnan AN, Curry SR, Gilligan PH, et al. Guidelines for diagnosis, treatment, and prevention of *Clostridium difficile* infections. *Am J Gastroenterol* 2013;108:478–98.
- [97] Fehér C, Mensa J. A comparison of current guidelines of five international societies on *Clostridium difficile* infection management. *Infect Dis Ther* 2016;5:207–30.
- [98] Sethi AK, Al-Nassir WN, Nerandzic MM, Bobulsky GS, Donskey CJ. Persistence of skin contamination and environmental shedding of *Clostridium difficile* during and after treatment of *C. difficile* infection. *Infect Control Hosp Epidemiol* 2010;31:21–7.
- [99] Weber DJ, Anderson DJ, Sexton DJ, Rutala WA. Role of the environment in the transmission of *Clostridium difficile* in health care facilities. *Am J Infect Contr* 2013;41:S105–10.
- [100] Kramer A, Schwebke I, Kampf G. How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. *BMC Infect Dis* 2006;6:130.
- [101] Doan L, Forrest H, Fakis A, Craig J, Claxton L, Khare M. Clinical and cost effectiveness of eight disinfection methods for terminal disinfection of hospital isolation rooms contaminated with *Clostridium difficile* 027. *J Hosp Infect* 2012;82:114–21.
- [102] Perez J, Springthorpe VS, Sattar SA. Activity of selected oxidizing microbicides against the spores of *Clostridium difficile*: relevance to environmental control. *Am J Infect Control* 2005;33:320–5.
- [103] MacLeod-Glover N, Sadowski C. Efficacy of cleaning products for *C. difficile*: environmental strategies to reduce the spread

- of *Clostridium difficile*–associated diarrhea in geriatric rehabilitation. *Can Fam Physician* 2010;56:417–23.
- [104] Weber DJ, Rutala WA, Anderson DJ, Chen LF, Sickbert-Bennett EE, Boyce JM. Effectiveness of ultraviolet devices and hydrogen peroxide systems for terminal room decontamination: focus on clinical trials. *Am J Infect Contr* 2016;44:e77–84.
- [105] Anderson DJ, Chen LF, Weber DJ, Moehring RW, Lewis SS, Triplett PF, et al. Enhanced terminal room disinfection and acquisition and infection caused by multidrug-resistant organisms and *Clostridium difficile* (the Benefits of Enhanced Terminal Room Disinfection study): a cluster-randomised, multicentre, crossover study. *Lancet* 2017;389:805–14.
- [106] Havill NL, Moore BA, Boyce JM. Comparison of the microbiological efficacy of hydrogen peroxide vapor and ultraviolet light processes for room decontamination. *Infect Control Hosp Epidemiol* 2012;33:507–12.
- [107] Marra AR, Schweizer ML, Edmond MB. No-touch disinfection methods to decrease multidrug-resistant organism infections: a systematic review and meta-analysis. *Infect Control Hosp Epidemiol* 2017;16:1–12.
- [108] Carling PC, Briggs JL, Perkins J, Highlander D. Improved cleaning of patient rooms using a new targeting method. *Clin Infect Dis* 2006;42:385–8.
- [109] Gregg MB, editor. *Field epidemiology*. 2nd ed. Oxford: Oxford University Press; 2003.
- [110] Dicker R, Coronado F, Koo D, Parrish RG. *Principles of epidemiology in public health practice*. 3rd ed. Atlanta: Centers for Disease Control and Prevention; 2006.
- [111] Centers for Disease Control and Prevention. *Principles of epidemiology in public health practice. An introduction to applied epidemiology and biostatistics* [Online]. 2006 [cited 15 March 2018]; Available from: <https://www.cdc.gov/ophss/csels/dsepd/ss1978/SS1978.pdf>.