

# Prevention Strategies of Clostridium Difficile Infection, Review

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**Abstract:** The main objective of this review was to highlight the different prevention strategies that used by different health organization or countries to control the infection of Clostridium difficile, and the protocols used in these strategies, also to discuss and summarize the effective of these strategies in reducing the spread of this infectious disease. Comprehensive search method was conducted using several electronic databases including; Medline/PubMed, and Embase, for relevant articles concerning the prevention strategies toward Clostridium difficile which were published up to June, 2017. Effective prevention of CDI requires a multidisciplinary approach that includes leaders in hospital administration, clinicians, the infection control department, pharmacy, and the clinical laboratory, as well as environmental services. Hand hygiene is an important component of most hospital infection control and prevention programs. Hospitalists, as front-line caregivers, physician leaders in their hospitals, and coordinators of patient care, can play a key role in these regards. Care when deciding when and which antimicrobial to use to treat non-CDI infections; being attuned to symptoms that may be due to CDI, and prompt diagnosis and treatment of CDI; adhering to infection control policies; awareness of cleaning practices; and also being an active member of the infection control committee are all ways that hospitalists may take active roles in preventing CDI.

**Keywords:** Clostridium Difficile Infection (CDI), electronic databases including.

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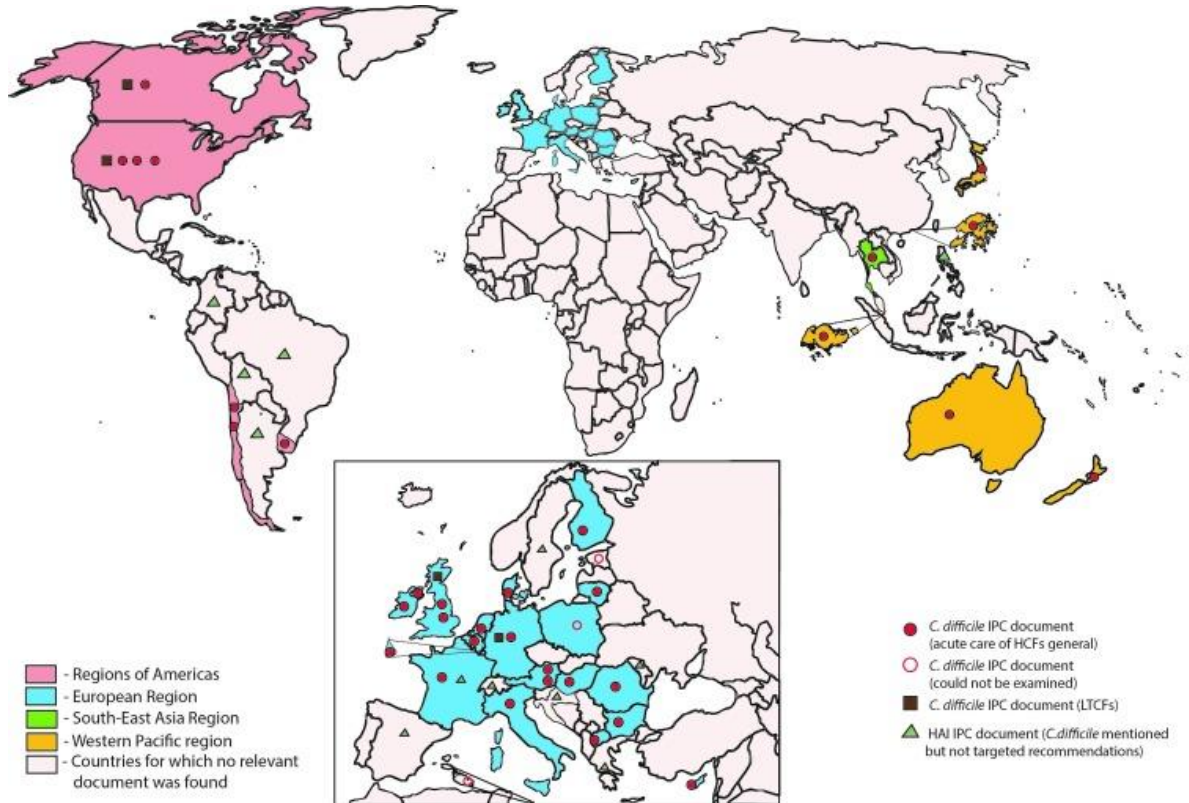
## 1. INTRODUCTION

*Clostridium difficile* is a Gram-positive, anaerobic, spore-forming, toxin-producing bacillus that causes antibiotic-associated diarrhea and colitis. It is transferred through the fecal-- oral path amongst people. It was first separated in 1935 by Hall and also O'Toole from the stool of healthy and balanced neonates <sup>(1)</sup>. Clostridium difficile infection (CDI) is a leading cause of hospital-associated gastrointestinal illness and reason for healthcare associated infections (HAI) worldwide impacting especially the elderly and also hospitalized individuals <sup>(2,3,4)</sup>. The concern of CDI remains under-identified and difficulties related to case discovery hinder avoidance.

Over the past 20 years, the incidence as well as intensity of CDI have actually raised significantly. This microorganism is now associated with a much greater incidence of hospital stays compared to a lot more widely publicized methicillin-resistant Staphylococcus aureus <sup>(2)</sup>. CDI can trigger a range of disease varying from asymptomatic carriage to light looseness of the bowels to pseudomembranous colitis with blood poisoning, harmful megacolon, body organ failing, and fatality. The price of US healthcare facility discharges with CDI listed as a diagnosis doubled from 31/100,000 populace in 1996 to 61/100,000 in 2003. The price was sevenfold higher face to faces > 65 years of age compared with the 45- 64 years' age group <sup>(2,3)</sup>. Mortality prices pertaining to CDI likewise enhanced during the same time period, rising from 5.7 fatalities each million populace in 1999 to 23.7 fatalities per million population in 2004, a rise of regarding 35% annually <sup>(5)</sup>. From 1999 to 2004, CDI was reported as a cause of death in 20,642 persons in the United States, virtually 7 times the price of all other intestinal tract infections combined <sup>(5)</sup>.

There are vast variants in the schedule or degrees of execution of effective Infection Prevention and also Control (IPC) steps for CDI. A national study in Canada recognized a comprehensive absence of antimicrobial stewardship programs, less than 25% of the 33 taking part healthcare facilities <sup>(6)</sup> in 2005. Extra recently, interest was attracted to the lack of professional understanding and also testing <sup>(7)</sup>, differences in the stamina of recommendations across various IPC guidelines <sup>(8)</sup>, as well as the lack of knowledge on the independent effects of common IPC strategies <sup>(9,10)</sup>.

Around the world, 42 files with targeted IPC recommendations for CDI were determined (**Figure 1**) <sup>(8)</sup>. These documents defined guidance from 28 different countries/territories in 4 WHO regions <sup>(8)</sup>.



**Figure 1: Geographic distribution of CDI-targeted IPC guidance reviewed. Countries with documents included in the review are colored by WHO regions <sup>(8)</sup>.**

The main objective of this review was to highlight the different prevention strategies that used by different health organization or countries to control the infection of *Clostridium difficile*, and the protocols used in these strategies, also to discuss and summarize the effective of these strategies in reducing the spread of this infectious disease.

## 2. METHODS AND MATERIALS

Comprehensive search method was conducted using several electronic databases including; Medline/PubMed, and Embase, for relevant articles concerning the prevention strategies toward *Clostridium difficile* which were published up to June, 2017. In our search method a Mesh terms were used included “*difficile*” “*clostridium difficile infection (CDI)*”, “prevention”, “strategies”, “control”, and “protocol.” We further screened references of included studies in this review for more relevant studies to be included in this review. Restrictions were applied to English language published studies with human subject.

## 3. DISCUSSION

### ▪ Transmission and clinical presentation of *C. difficile*:

The life cycle of *C. difficile* begins in the spore kind. These spores are conveniently transferred as they are immune to warm, acid, as well as antibiotics. The spores could continue to be sensible for months outside of the human body. In the healthcare facility, they can be discovered on bed linens, furnishings, clinical equipment, in addition to on the skin as well as jewelry of caregivers <sup>(11)</sup>. When consumed, the spores go through the upper digestion tract into the intestinal tracts

where they can germinate as well as conquer the colon. A research study showed that 21% of patients getting prescription antibiotics as well as admitted to a general clinical ward were colonized by this bacterium<sup>(12)</sup>. Healthy people are usually secured from CDI by the normal microbial flora of the gut, which withstands *C. difficile*'s colonization as well as growth. Interruption of the typical microflora by prescription antibiotics allows *C. difficile* to proliferate, generate toxic substances, as well as cause condition<sup>(13)</sup>. *C. difficile* causes looseness of the bowels and colitis through the release of two healthy protein exotoxins, toxic substance An and contaminant B. Greater than 60% of the populace has lotion as well as colonic antibody reactions to these toxic substances<sup>(14,15)</sup>. Absent or reduced concentrations of serum IgG antibody against *C. difficile* toxic substances has actually been shown to provide a greater threat of CDI among hospitalized individuals that come to be colonized by this microorganism<sup>(16)</sup>. Toxigenic *C. difficile* can be identified in greater than 95% of pseudomembranous colitis cases and in 15%-- 25% of antibiotic-associated diarrhea situations<sup>(17,18)</sup>.

Healthcare workers are a primary mode of *C. difficile* transmission. *C. difficile* spores wind up on several hospital surfaces as well as infect health care worker hands and medical tools (stethoscopes, thermometers, etc) made use of on multiple clients. One research study located that after caring for a client with CDI, 59% of healthcare workers had hand contamination despite whether or not they actually touched the individual<sup>(12)</sup>. Numerous researches have actually revealed that people in adjacent spaces are at equal or greater threat of acquiring CDI as clients admitted to the same space<sup>(19,20)</sup>. A recent study discovered that admission to an intensive care unit room that formerly housed a person for CDI was a risk aspect for establishing CDI, 89% of patients that in fact developed CDI did not have this risk element<sup>(21)</sup>. The two toxic substance genetics are found on the pathogenicity locus a 5-gene area that includes the genes for toxic substance A (*tcdA*) and also toxic substance B (*tcdB*) as well as 3 regulatory or supplementary genes (*tcdC*, *tcdE*, and also *tcdR*) (Figure 2).

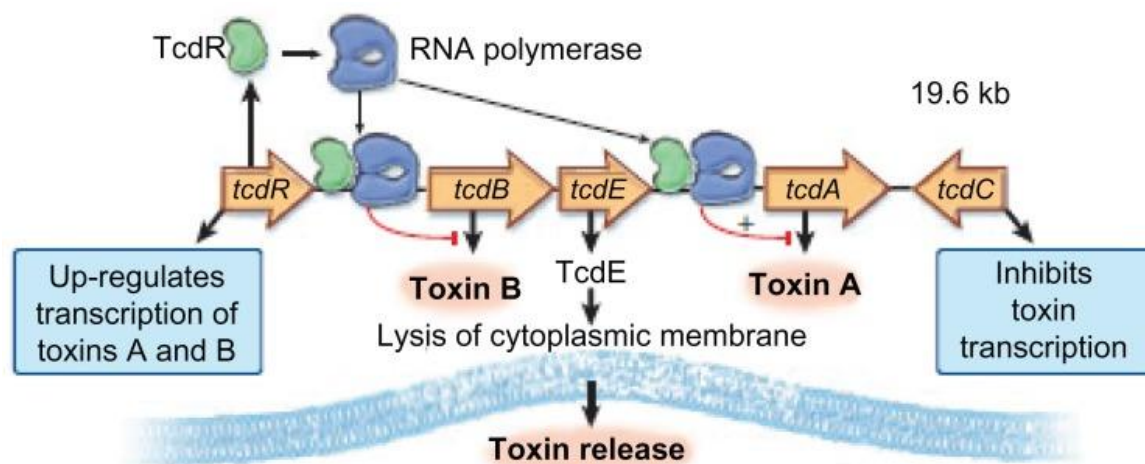


Figure 2: The pathogenicity locus of *Clostridium difficile*.

#### ▪ Infection Prevention and also Control (IPC) steps for CDI in clinical setting:

No details referrals were identified for CDI patients in experienced professional facilities, such as residential care and assisted living facility, outpatient treatment, rehab, as well as long-- term care centers (LTCFs). *C. difficile* targeted IPC strategies generally drew from proof from intense treatment settings. 4 guidance documents were specific to LTCFs and in various other nine, advised strategies were integrated with support for acute medical facilities. Pertinent issues and also challenges for the prevention of CDI in LTCFs were highlighted consisting of: the vulnerable wellness condition of citizens which may position problems in keeping precautions; eg, cognitively damaged patients<sup>(22)</sup>, regular stool incontinence<sup>(23)</sup>, the positioning of CDI situations in LTCFs in shared spaces due the minimal number of solitary rooms<sup>(23)</sup>; and also the absence of hassle-free hand-- cleaning facilities<sup>(24)</sup>. The significance of surveillance, monitoring of outbreaks, and communication in between rescue services and staff in intense care centers (when residents with CDI should be transferred) was talked about<sup>(22)</sup>, particularly in the light of the under-- identified worry of CDI and incomplete adherence to IPC guidelines in LTCFs<sup>(25)</sup>.

Early discovery of CDI need to lead to earlier therapy as well as earlier introduction of infection control procedures. The Association for Professionals in Infection Control and Epidemiology recommends numerous monitoring steps<sup>(26,27)</sup>: (A) a high index of uncertainty in clients with risk factors for CDI (recent or present antimicrobials, use of anti-neoplastic

representatives, progressed age, current hospitalization, or home in a LTCH, previous CDI); (B) doctor advocacy for the use of the most effective *C. difficile* analysis examinations with a quick turn-around time and a high sensitivity as well as specificity for detection of toxigenic *C. difficile*; and also (C) making sure that suitable personnel are informed quickly concerning positive *C. difficile* outcomes, to make sure that proper therapy and also get in touch with preventative measure measures can be initiated. A previous report defines one institution's detailed efforts to control an episode of CDI caused by the hyper virulent strain (NAP1/ BI/ 027) utilizing a *C. difficile* infection control" bundle ", including education, boosted as well as very early case finding, expanded infection control actions, growth of a *C. difficile* monitoring team, and also antimicrobial stewardship. Healthcare facility rates of *C. difficile* decreased from 7.2 situations per/ 1,000 discharges throughout the year prior to organization of these steps to 4.8 situations each/ 1,000 discharges in the subsequent 5 years<sup>(28)</sup>.

▪ **Isolation strategy of CDI patients:**

Most data released on CDI prevention are from single-center before-after researches performed in action to outbreaks or elevated CDI prices. Often numerous concomitant treatments are done, making it tough to determine the relative importance of one intervention relative to another. Before-after researches are additionally restricted by time-related prejudices that are challenging to readjust for in the lack of a control team or correctly carried out analyses, such as disturbed time-series evaluation (29,30). Nevertheless, a number of researches have used these methods, showing the relevance of antimicrobial stewardship as well as its function in stopping CDI<sup>(31,32,33,34)</sup>. A current intensive care unit-based study discovered admission to an area of a person with CDI to be a danger aspect for CDI, however 90% of patients who established CDI did not have this danger aspect<sup>(35)</sup>. Various other researches that have analyzed sharing a space with a person detected with CDI or being confessed to a room after a client with CDI was discharged from that space have not located these direct exposures to be risk elements for CDI<sup>(36,37,38)</sup>. Furthermore, use of sporicidal techniques to clean the environment outside of episode setups has not continually showed a reduction in CDI with these techniques<sup>(39,40)</sup>.

Isolation of CDI situations, presumed and also verified, was commonly advised along with making use of en-suite restrooms or individual bedpans. Guidelines additionally advised cohorting CDI individuals, if necessary. The factors to consider and also advantages stated, past avoiding the spread of *C. difficile* spores, consisted of effective allocation of human as well as financial sources and also the growth of details experience amongst dedicated staff handling the separated patient/cohort. Maintaining contact preventative measures till at least after diarrheal episodes have actually quit (most commonly for 48 hours or longer) was normally suggested. However, extended contact precautions up until the discharge of the CDI situation were additionally advised<sup>(41,42)</sup>. Management assistance and also interaction were highlighted as key aspects considered that isolation of cases can incur managerial difficulties and also expenses.

Challenges to elucidate the impact of seclusion treatments as a means to stop transmission of CDI will certainly be influenced by each center's ability to detect CDI situations immediately, accessibility of isolation rooms, as well as period of actions. Recent efforts have been made to offer an estimate of the result of separating CDI situations. As an example, a retrospective associate study reported a 43% (95% CI 7- 65%) drop in *C. difficile* acquisition price in a center with solitary-- areas in its ICU wards compared to multi-- bed rooms<sup>(43)</sup>. A raised threat of reoccurrence (chances ratio OR: 3.77 95% CI 1.37- 10.35) among previously cohorted individuals has actually also been reported<sup>(44)</sup>. Shedding of *C. difficile* spores as well as evidence of contamination after resolution of diarrhea has actually been found<sup>(45,46)</sup>, the effect of longer isolation periods and seclusion on the occurrence of CDI or threat of transmission stays inadequately comprehended.

▪ **Hand hygiene as an effective method for IPC-CDI:**

The importance and challenges related to efficient hand health in the context of *C. difficile* IPC were discussed in all documents. Unique interest was attracted to constraints of sanitation hand with alcohol-- based hand rubs (ABHR) as they are non-sporicidal as well as do not remove *C. difficile* spores from polluted hands. Assistance on ideal techniques differed and also included the special use soap and water when taking care of patients with CDI, specifically throughout episodes, raising recognition and also advising health care carriers about the restrictions of ABHRs<sup>(47,48)</sup>, or emphasizing the WHO hand hygiene recommendations as well as the primary use of ABHR to prevent confusing messages<sup>(48)</sup>.

The proof on the impact of different hand health practices was reported to be of modest high quality and also the effectiveness as well as effectiveness of sanitation over hand-- washing for hand hygiene purposes was reported as an area of conflict<sup>(41)</sup>. These differences in reporting the value of hand hygiene practices come from study revealing that hand-- cleaning with soap and also water is the most effective way to eliminate *C. difficile* spores. While the usage of ABHR

alone is not efficient, its use does not appear to be damaging in terms of affecting straight on CDI rates<sup>(9)</sup>. It is noteworthy that there is a dependence on proof from research studies of multidrug- immune microorganisms to prevent CDI with client - care methods and also a paucity in research studies that have actually examined their efficiency during native to the island durations<sup>(9,49,50)</sup>.

Hand hygiene and appropriate use PPE is important for HAI avoidance. Although the use of ABHRs is inadequate to remove *C. difficile* spores as well as hand washing is liked (a message communicated in many standards), problems exist concerning compliance and detrimental results of blended guidelines for hand health<sup>(9)</sup>. Recently, a study found that compliance with WHO - advised methods by health care workers caring for individuals with CDI was observed to be about 60 - 70%, with no hand hygiene conducted inside seclusion areas. A higher compliance was observed for making use of hand wear gloves (~ 85- 90%) and also gowns (~ 88- 97%)<sup>(51)</sup>. Clearly more research is required, particularly for the result of different hand hygiene practices on CDI occurrence during endemic durations<sup>(9)</sup>, but a more powerful emphasis on the use of gloves has actually been emphasized as an important, economical, and also possibly more effective procedure to prevent *C. difficile* transmission<sup>(52)</sup>.

▪ **Management approaches to recurrent CDI:**

The administration of reoccurring CDI stays a significant challenge due to a paucity of clinical tests and thus evidence-based management guidelines. Frequent CDI is specified as the reoccurrence of CDI signs within 8 weeks after signs and symptom resolution, verified with a positive feces examination. The danger of recurrence after a preliminary episode of CDI is 20% and increased as much as 60% after the 3rd episode<sup>(53)</sup>. The risk of reappearance is higher with older age, concomitant antibiotic exposure, presence of comorbidities and dead levels of serum IgG anti-toxin A<sup>(54)</sup>. The initial reappearance is treated the same as the first episode, stratified by extent. A 2nd recurrence is treated with a 6 - week taper of oral vancomycin. Several treatment options are offered for future reappearances, that include FMT, vancomycin followed by rifaximin chaser or IVIG (**Table 1**). An instance series of three people showed that fidaxomicin might be an option for individuals with numerous reoccurrences of CDI that have failed other therapies<sup>(55)</sup>. Although these options have not been contrasted in randomized medical trials, fecal transplant appears to be the most effective modality for persistent CDI.

**Table 1: Management options for recurrent *C. difficile* infection.**

<b><i>First recurrence:</i></b>
Mild to moderate
Oral metronidazole 500 mg 3 times a day for 10–14 days
Mild to moderate CDI (no response to oral metronidazole / severe CDI previously)
Severe CDI
Oral vancomycin 125 mg 4 times a day for 10–14 days
<b><i>Second recurrence:</i></b>
Oral vancomycin tapered over 7 weeks
125 mg 4 times daily for 14 days
125 mg twice daily for 7 days
125 mg once daily for 7 days
125 mg once every other day for 8 days
125 mg once every third days for 15 days
<b><i>Future recurrences</i></b>
Fecal microbiota transplantation
Oral vancomycin 125 mg 4 times a day for 14 days, followed by rifaximin 400 mg twice daily for 14 days
Consider intravenous immunoglobulin, 400 mg/kg, repeated up to 3 times at 3-week intervals
Consider combination therapy with oral vancomycin and oral rifaximin

#### 4. CONCLUSION

Effective prevention of CDI requires a multidisciplinary approach that includes leaders in hospital administration, clinicians, the infection control department, pharmacy, and the clinical laboratory, as well as environmental services. Hand hygiene is an important component of most hospital infection control and prevention programs. Hospitalists, as front-line caregivers, physician leaders in their hospitals, and coordinators of patient care, can play a key role in these regards. Care when deciding when and which antimicrobial to use to treat non-CDI infections; being attuned to symptoms that may be due to CDI, and prompt diagnosis and treatment of CDI; adhering to infection control policies; awareness of cleaning practices; and also being an active member of the infection control committee are all ways that hospitalists may take active roles in preventing CDI.

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