

What is Clostridium difficile?

Clostridium difficile is a spore-forming anaerobic bacterium that is widely distributed in soil and the intestinal tracts of animals. C. difficile may also form part of the normal gut flora in humans. It is particularly uncommon in infants aged less than two years of age, who lack receptors for the enterotoxin produced by pathogenic strains. Therefore, testing for C. difficile in infants aged less than 2 years is not recommended. C. difficile infection (CDI) in humans is mediated by the production of two enterotoxins. Not all strains of C. difficile are toxin-producers.

C. difficile infection is not confined to hospitals and is increasingly common in community and nursing home settings. This is outlined later in this article.

What factors predispose patients to C. difficile infection?

Overall, the most common risk factors are exposure to antibiotics, advanced age and hospitalisation.

- **Intrinsic risk factors** for CDI include increasing age, severity of underlying disease, co-morbidity, immunosuppression, cognitive and functional impairment.
- **Other risk factors** for CDI include use of anti-microbial agents, length of hospitalisation, use of cancer chemotherapy agents, receipt of gastro-intestinal procedures and surgery, tube-feeding, the use of acid-suppressant medications, laxatives or stool softeners.
- **Environmental risk factors** include high C. difficile burden in a unit/ward/healthcare facility, high frequency of admissions and discharges to long term care, residence in close or shared quarters, use of shared toilet facilities and limited ability to isolate infected patients
- **Risk factors for recurrence of CDI** include re-exposure to antibiotics, age greater than 65 years, severe underlying disease, low serum albumin level (<2.5g/dL), ICU stay, prolonged hospitalisation and poor immune response following exposure to C. difficile toxin.

How does Clostridium difficile infection (CDI) present?

Typically, CDI presents with the following symptoms as early as several days and to up to 10 weeks after administration of antibiotic therapy

- diarrhoea
- abdominal cramps
- fever
- elevated white cell count

Pseudo-membranous colitis (PMC) is the most severe manifestation of disease. PMC usually manifests as pan colitis; however, a right-sided colitis is also described, featuring fever, pain, and decreased gut motility often with only mild diarrhoea. It is important to note that severely ill patients may have little or no diarrhoea due to dilation of the colon (toxic megacolon) and paralytic ileus that may result from a loss of colonic muscular tone. CDI-associated mortality varies depending on the population studied and has been reported as high as 30%.

Recurrence of CDI following treatment is very common occurring in 8-50% of cases. Recurrent CDI is defined as a patient with an episode of CDI that occurs within eight weeks following the onset of a previous episode. Recurrences can correspond to either a relapse of

infection due to the original strain of *C. difficile* or re-infection with a different strain. The risk of recurrence increases with each recurrence. If a patient has two or more episodes of CDI, the risk of additional recurrences increases to 50-65%.

What should I do if I suspect my patient has CDI?

The following mnemonic protocol (SIGHT) provides a useful framework 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 if in a healthcare facility (e.g., a nursing home). Consult with the infection prevention and control team where available while determining the cause of the diarrhoea
G	Gloves and aprons must be used for all contacts with the patient and their environment. Instruct the patient and carers/family members in hand hygiene and when they need to use PPE (see below)
H	Hand washing with soap and water should be carried out after each contact with the patient and the patient’s environment
T	Test the stool for <i>C. difficile</i> toxin, by sending a specimen immediately. If the patient is unwell/unstable, contact the consultant microbiologists/ID physician for advice.

What do I do if CDI is confirmed?

The first approach in the treatment of CDI should be, if possible, to stop the precipitating antibiotic(s). If antibiotics must be continued for clinical reasons, antibiotic(s) with a lower propensity to induce CDI should be substituted. Supportive therapy with replacement of fluids and electrolytes is also crucial at the early stage for these patients. The specific management of CDI depends on disease severity and whether this is the first episode or a recurrence (Fig 1)

How does *C. difficile* spread?

C. difficile can be transmitted from patient-to-patient, via contaminated hands, or via environmental (including healthcare equipment) contamination. *C. difficile* is also a spore-forming organism, a property which makes it more resistant to standard disinfectants and facilitates its persistence in the environment, often for several months.

Why should I not use alcohol hand rub for hand hygiene when caring for patients with CDI?

Alcohol hand rub should not be used as an alternative to soap as *C. difficile* spores are known to be highly resistant to killing by alcohol. None of the agents used in antiseptic hand-wash or antiseptic hand-rub preparations are reliably sporicidal against *Clostridium* species. The physical action of rubbing and rinsing is the only way to remove spores from hands as WHO (2009) recommends hand washing with soap and water when exposure to potential spore-forming pathogens is suspected. The type of soap to use (i.e., non-antimicrobial/ antimicrobial) is an unresolved issue with guidelines recommending either can be used.

Fig 1: Management of patient with C. difficile infection in primary care

Positive Laboratory result for C. difficile toxin

- Is this the first episode of *C. difficile* infection (CDI)? If yes see below
- If not and this diagnosis is recurrent CDI (patient previously diagnosed with CDI within the past 8 weeks) , contact the Consultant Microbiologist / Infectious Disease Physician for advice

Assess the patient for severity * (will affect management)

Indicators of severity may include fever, hypotension, abdominal pain, dehydration, raised white cell count and/or inflammatory markers, low serum albumin.

IF SEVERE* C. difficile infection:

- Refer patients with severe infection to hospital
- Inform the hospital of potential severe CDI diagnosis

IF NON SEVERE C. difficile infection:

1. Wash your hands before and after examining the patient
2. Review antimicrobials - Immediately discontinue unnecessary antimicrobial therapy
3. Review the requirement for and dose of proton pump inhibitors
4. Avoid antimotility medications
5. If symptoms have resolved – observe.
6. If the patient is symptomatic (i.e., diarrhoea) commence antibiotics for *C. difficile*
 - Oral metronidazole 400 mg TDS for 10 to 14 days).
 - Inability to take oral medication, metronidazole intolerance or contraindication, contact the Consultant Microbiologist / Infectious Disease Physician for advice.

- Download the patient information leaflet from the HPSC website.
<http://www.hpsc.ie/hpsc/A-Z/Gastroenteric/Clostridiumdifficile/Factsheets/>
- Advise the patient with regards to good hygiene and the importance of suitable and adequate fluids.
- Advise the patient to contact the GP surgery if symptoms persist. If GP surgery requires advice on treatment contact Consultant Microbiologist /ID physician for advice

STOOL SAMPLES FOR CLEARANCE ARE NOT REQUIRED

How should patients with confirmed CDI be managed in a nursing home?

The control of CDI is best achieved by the use of Standard and Contact Precautions. (See: <http://www.hpsc.ie/hpsc/A-Z/Gastroenteric/Clostridiumdifficile/Factsheets/File,2947,en.pdf>).

- Standard Precautions should be used when exposure to blood, body fluids, non-intact skin or mucous membranes is anticipated.
- Contact Precautions are designed to reduce the risk of transmitting *C. difficile* by direct or indirect contact. Direct contact transmission occurs when microorganisms are transferred from one colonised/infected person to another person, e.g. direct patient-to-patient contact. Indirect contact transmission involves the transfer of an infectious agent to a contaminated intermediate object or person, e.g., hands of healthcare personnel or patient care equipment, such as commodes.

In healthcare facilities (hospitals and nursing homes), it is recommended that patients with confirmed or suspected CDI are isolated in a single room to prevent spread to other patients.

- If ensuite facilities are not available, it is essential that the patient/resident with CDI has a dedicated toilet or commode and is not permitted to use the general toilet facilities on the ward/unit.
- Hand washing should be performed with soap (antimicrobial or non-antimicrobial) and water during patient/resident care according to the World Health Organisation (WHO) 'My Five Moments for Hand Hygiene'. The physical action of rubbing and rinsing is the only way to remove spores from hands. Alcohol hand rub must not be used as an alternative to soap as spores are known to be highly resistant to killing by alcohol. It can be applied after washing to rid hands of remaining non-clostridial organisms.
- Patients/residents should be advised and if needed assisted, to wash their hands with soap and water and dry with paper towel after using the bathroom and before eating.
- Personal protective equipment (PPE) (i.e. gloves and aprons) should be donned prior to, and subsequently removed, following each period of care activity for a patient/resident with CDI: Gloves and apron/gown should be worn when entering a room for all interactions that may involve contact with the patient/resident or potentially contaminated areas in the patient/residents' environment.
- Care equipment, e.g. blood pressure cuffs, thermometers, hoist slings should be dedicated to a single patient with CDI.
- Environmental and equipment decontamination should be performed as outlined in these guidelines.

How should patients with confirmed CDI be managed at home?

In the home, the following precautions are advised:

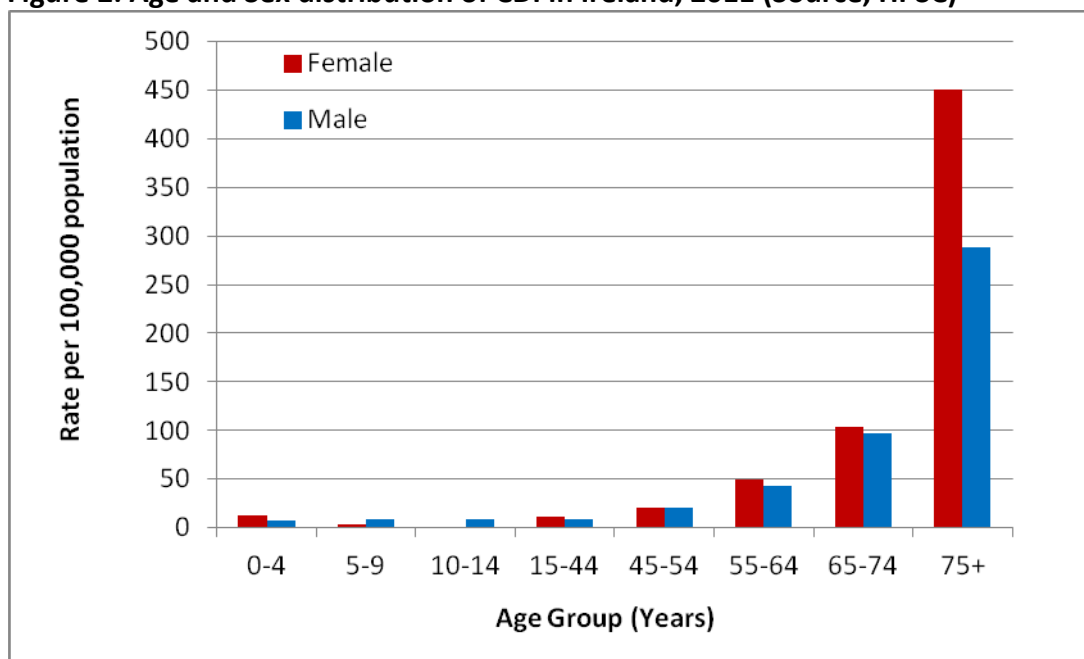
- Hand hygiene is the single most important infection control measure.
 - Carers, including family and healthcare workers, should wash their hands thoroughly with soap and water and dry, if assisting with personal care.

- The person with CDI should wash their hands thoroughly with soap and warm water and dry them after using the bathroom, before preparing food and before eating.
- Disposable gloves and aprons should be worn by healthcare workers when attending to a patient who has diarrhoea. These should be removed and disposed of immediately after the episode of care. Hand hygiene should then be carried out as described above.
- Waste soiled with diarrhoea (e.g. incontinence wear) should be disposed of in a safe manner (i.e. the waste bag should be sealed to ensure that the bag will not leak or that the outside of the bag should not become contaminated).
- The person with CDI should be facilitated and encouraged to maintain good personal hygiene standards:
 - Personal items such as towels and face cloths should not be shared.
 - Persons with CDI should avoid using the same toilet as other family members if possible.
 - If this is not possible, after an episode of diarrhoea, the bathroom should be first cleaned with detergent and water and then disinfected with a mixture of bleach and water as instructed on the container. Special attention should be paid to frequently touched sites (e.g., sink taps, flush handle, toilet seats) and the toilet bowl.
- The immediate environment of the person with CDI should be cleaned with detergent and water, paying particular attention to hand contact surfaces (e.g., bedside table, hand rails). If soiled, following cleaning, the area should then be disinfected as above.
- Used laundry should be machine-washed separately from other washing on the hottest wash cycle suitable for linen and clothing.
- Laundry soiled with diarrhoea should first be machine washed using a cold pre-wash cycle and then washed using detergent powder/liquid at the hottest wash cycle tolerated for the clothing.
- Patients and their families should receive an information leaflet. The risk of household contacts acquiring *C. difficile* once a patient has been discharged is considered very low but this risk may be higher for those household contacts receiving antibiotic therapy. (Grade C)

What information is available in Ireland on *C. difficile*?

The Health Protection Surveillance Centre (HPSC) has published weekly reports of new CDI cases since May 2008. In 2011, 1,511 cases of CDI were reported (92.5% new and 7% recurrent CDI). Most patients were female (61%) and in the over 65 age group (69%). Twenty patients (13%) had severe CDI; three patients requiring surgery and intensive care unit (ICU) admission, five requiring surgery only and 13 requiring ICU admission without surgery. Forty-three deaths were reported, of which two were directly attributed to CDI and 24 were not directly attributed to CDI. The cause of death for the remainder of patients was either unknown or not specified.

Figure 2: Age and Sex distribution of CDI in Ireland, 2011 (Source, HPSC)



* Rates calculated using 2011 census data

In 2011, eight outbreaks of *C. difficile* infection, all healthcare-associated and involving 35 patients were notified to Public Health Departments (**Table 1**). Four were linked to hospitals, two to nursing homes and two to long-term care facilities.

Table 1. CDI outbreaks reported in Ireland in 2011 by HSE area (Source, HPSC)

HSE Region	Outbreak location	Total number ill
East	Residential Home	3
East	Community Hospital/ Long Stay Unit	4
East	Hospital	6
East	Residential Home	2
East	Hospital	8
North East	Community Hospital/ Long Stay Unit	2
South	Hospital	2
West	Hospital	8

What information do we have on *C. difficile* infection outside acute hospitals?

C. difficile infection is not confined to hospitals and is increasingly common in community and nursing home settings. During 2011 and 2010, 20% of all CDI cases were associated with the community and 10% of cases were associated with nursing homes, an increase from 8% in 2010. Moreover, 27% of all patients with CDI had onset of symptoms in the community, consistent with the figure reported in 2010. Figure 3 outlines the data from 2011.

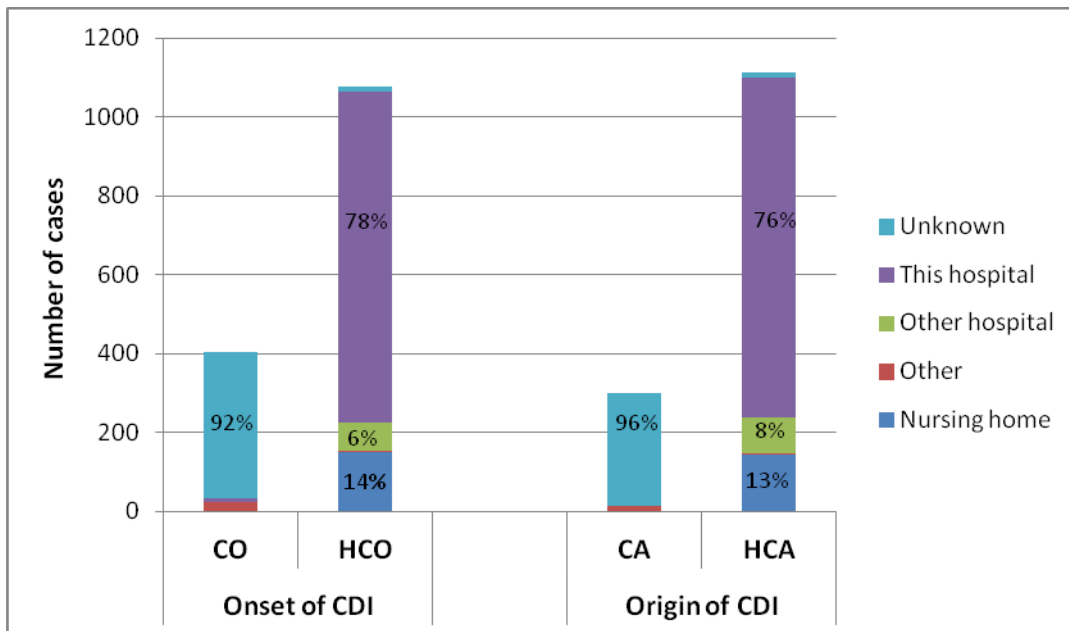


Figure 3. CDI Origin and Onset by Location where CDI Case Originated, 2011

CO: Onset of CDI symptoms occurred in the community

HCO: Onset of CDI symptoms occurred in a healthcare facility (hospital/nursing home)

CA: The patient acquired their CDI infection in the community

HA: The patient acquired their CDI infection in a healthcare facility

What is Clostridium difficile 027?

In specialist reference laboratories, *C. difficile* isolates can be further classified into over 150 polymerase chain reaction (PCR) ribotypes. A changing pattern of disease severity was observed in Canada between 1991 and 2003. The number of patients with complicated CDI (defined as having any of toxic megacolon, colonic perforation, colectomy, shock requiring vasopressor therapy or death) rose significantly (7% in 1991-1992 to 18% in 2003). CDI due to an emerging ribotype 027 was responsible for an epidemic in the Quebec region of Canada during 2003-2004. Between one and three thousand deaths due to CDI may have occurred during this epidemic. In Europe, *C. difficile* ribotype 027 outbreaks have been recognised in a number of countries, including the UK and Ireland. *C. difficile* 027 is thought to result in more severe CDI due to production of more toxins than other strains and it is also associated with resistance to the increasingly-prescribed fluoroquinolone class of antibiotics.

Where can I get further information (factsheets/guidelines etc)?

- *C. difficile* infection: www.hpsc.ie/hpsc/A-Z/Gastroenteric/Clostridiumdifficile/
- Antibiotic Prescribing in Primary Care: www.antibioticprescribing.ie/
- Public Information on Antibiotics: www.hse.ie/go/antibiotics