***Clostridioides difficile*:**
A Public Health Threat in Plain Sight

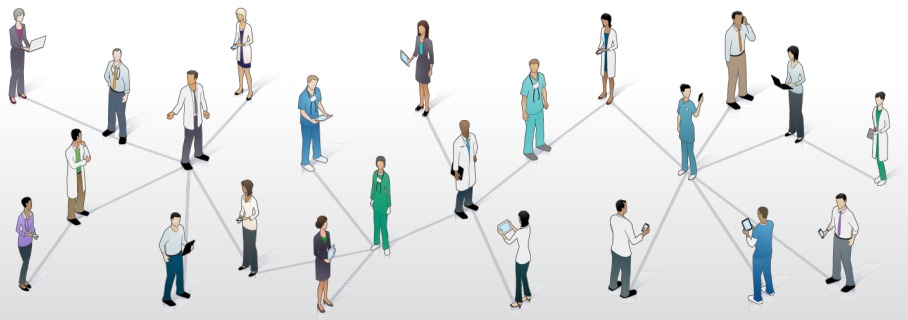
***Clostridioides difficile* (pronounced: klos-TRID-e-OY-dees dif-uh-SEEL) – or *C. difficile* – is a bacterium (germ) that can cause a serious and potentially life-threatening infection associated with symptoms from diarrhea to severe intestinal infections.[1,2]**

Recognizing the CDC defining *C. difficile* infection as an urgent public health threat, a group of experts representing a cross-section of healthcare professionals and patient organizations impacted by this infectious disease launched the *C. difficile* Awareness Initiative. Working together, and with support from Pfizer Inc., this multidisciplinary panel of experts represents infectious disease specialists, physicians, and nurses as well as representatives of patient support groups and professional organizations. They share a common mission: to build and expand public awareness of and education around *C. difficile.* The focus is to reach a broad spectrum of people who are potentially at risk of contracting this infection.

The *C. difficile* Awareness Initiative's goal is helping both the healthcare community and the general public understand three critical points surrounding this public health issue:

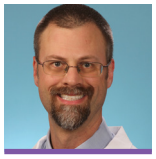
1. ***C. difficile* bacteria can be anywhere and persistent**
2. ***C. difficile* infection (CDI) is unpredictable and can occur in anyone, particularly adults**
3. **CDI can be a debilitating disease**

This Call-to-Action represents the group's broad array of experience with and understanding of the current disease state. It provides a closer examination of the issues to establish a more widespread understanding of *C. difficile* and raise awareness of the potential risks for and impact of the infection. The goal is to galvanize relevant experts and organizations to work collectively toward solutions for combatting this potentially serious infectious disease.



The Founding Committee of the *C. difficile* Awareness Initiative **includes:**

James C. Appleby, BSPharm, MPH, Chief Executive Officer, The Gerontological Society of America. www.geron.org (aging community representative)



Erik R. Dubberke, MD, MSPH, Professor of Medicine, Washington University School of Medicine. (*C. difficile*/ infectious disease expert)

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Artie L. Shelton, MD, Colonel, USA (Ret), Director of the Vietnam Veterans of America's Veterans Health Council. www.vva.org/what-we-do/outreach-programs/veterans-health-council/ (veteran representative)

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A closer look at a public health threat

C. difficile is a Gram-positive anaerobic germ that, when outside the body, forms spores that are inactive and can lie dormant for months or sometimes years.[7,8,9] When ingested, however, the spores have the ability to germinate into the pathogenic vegetative (active) form and "bloom" in the intestines of people with an imbalance of gut bacteria, such as those taking antibiotics, the elderly, and those with compromised immune systems.[7] In healthy intestines with a normal microbiome, the checks and balances of neighboring, beneficial bacteria help prevent this germination and proliferation of *C. difficile* spores.[7]

"From my experience, more people in the US are familiar with Ebola than C. difficile, even though the risk of getting Ebola is significantly lower. We need to work together and as collaboratively as possible to continue educating people and healthcare workers."

– Christian John Lillis,
Peggy Lillis Foundation

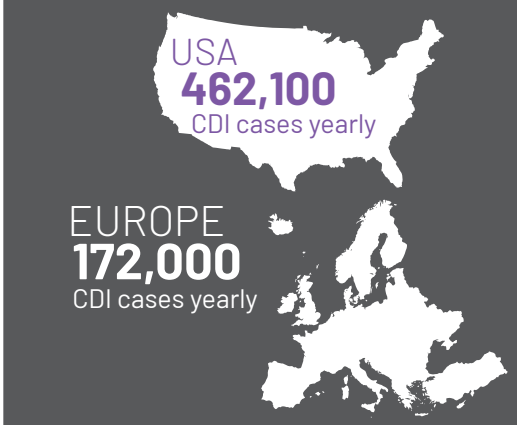
The disease-causing effects from *C. difficile* are mainly due to two exotoxins – toxin A and toxin B – though not all *C. difficile* germs are able to produce toxins.[7] These exotoxins cause the *C. difficile* infection by damaging the cells of the colon and causing inflammation, resulting in signs and symptoms that can range from mild to severe diarrhea, as well as cramping, fever, nausea, and, in severe cases, intestinal inflammation, toxic megacolon (enlargement of the colon), and even death.[10,11,12] The use of antibiotic therapy, advanced age, and having significant health problems resulting in hospitalization, are primary risk factors for the development of CDI.[10,12] In healthcare and community settings, these infections can cause antibiotic-associated diarrhea,[10] and may be responsible for an estimated 15 to 25 percent of all antibiotic-associated diarrhea in hospitalized patients in the United States (US) with the risk increasing with the severity of disease and the age of the patient.[10] Once CDI has occurred, the use of antibiotics to treat CDI further compromises the intestinal microbiota integrity and may prevent the recovery of the gut microbiome.[13]

In **2017:**

224,000 hospitalizations & **20,500** deaths associated with the infection

12,800 were directly related to ***C. difficile*** due to antibiotic-resistant infection

Despite more than a decade of intervention and notable decreases in hospital associated infections, including a 12 percent decrease in *C. difficile* infections between 2017 and 2018, the burden of *C. difficile* on both affected people and health systems remains high.[14,15] According to the most recent US Centers for Disease Control and Prevention (CDC) surveillance data, the burden of *C. difficile* infection in the US remains high and represents a critical unmet medical need.[16] A CDC study – published in April 2020 – estimated the national burden of CDI to be 462,100 cases (95 percent CI, 428,600 to 495,600) in 2017. This equates to an estimated incidence of 144 cases per 100,000 persons. When accounting for the type of laboratory assay used to determine the diagnoses, the adjusted number of cases may be lower but still substantial.[17] (see *Estimating the Burden of CDI* on page 3) In addition, nearly 70,000 people had at least one recurrence of CDI (incidence ~22 per 100,000



What's in a name? *Clostridioides* vs. *Clostridium*

First identified in 1935 and named *Bacillus difficilis*, the bacterium was originally believed to be part of normal gut microbiota.[3] The "*difficilis*" part of the name comes from the difficulty scientists had in culturing this germ. Four decades later, in the 1970s, researchers reclassified it as *Clostridium difficile* given that, like other members of the genus *Clostridium*, *C. difficile* also is anaerobic, Gram positive, and spore-forming.[4,5] Most recently in 2016, taxonomists determined that *C. difficile* had been misclassified as *Clostridium* based on improved genetic testing with 16S rRNA gene sequencing.[6] The analysis determined that the organism is actually located within the *Peptostreptococcaceae* family of Gram-positive bacteria and proposed reclassifying it as "*Peptoclostridium difficile*."[6] Noting that changing the name of this microorganism from *C. difficile*/*C. diff* to *P. difficile*/*P. diff* could create confusion and impact patient care, several microbiologists proposed renaming it *Clostridioides difficile* so that the germ could retain the commonly-used *C. difficile* name.[6]

"C. difficile can be anywhere. Spores have been cultured from dust, from livestock, and from food purchased at grocery stores. Even our pets can be colonized with C. difficile. We think of an infectious disease like C. difficile as being associated with hospitals and people who are already sick, but the spores have been found even in the homes of otherwise healthy people."

– Dr. Erik R. Dubberke,
Washington University School of Medicine

Estimating the Burden of CDI[17]

According to a recent CDC study by Alice Guh, et al (*NEJM* 2020), the overall incidence of CDI reported between 2011 and 2017 has declined, driven primarily by a decrease in the incidence of healthcare-associated cases. Using data from the CDC's Emerging Infections Program (EIP) – a population-based CDI surveillance in 10 states among a population of 12 million people – Guh and colleagues estimated that the number of laboratory-confirmed CDI cases in persons >two years of age in the US declined from 476,400 (155 per 100,000) in 2011 to 462,100 (144 per 100,000) in 2017.

CDI cases were confirmed by EIP surveillance laboratories using NAAT (nucleic acid amplification test) either alone or in combination with an enzyme immunoassay for toxins. NAAT is a highly-sensitive laboratory test that detects the gene that encodes the *C. difficile* toxin. Given that NAAT does not detect the actual presence of the *C. difficile* toxin, there are concerns that increasing reliance on this test has led to an overdiagnosis of the infection. Since 2011, NAAT rates have increased from 55 percent in 2011 to 83 percent in 2017.

When adjusting for NAAT use, the CDC estimated there were 365,200 (113 per 100,000 based on a NAAT rate of 55 percent) CDI cases in 2017, representing a net decline in CDI of 24 percent since 2011. This was mainly due to a 36 percent reduction in healthcare-associated cases during this time, which may be the result of many contributing factors such as a decreased use of fluoroquinolones, reduced prevalence of the epidemic strain (ribotype 027), and better diagnostic stewardship. After adjusting for NAAT use, the CDC also found that the number of community-associated cases remained unchanged, and there was no decline in the number of CDI recurrences or in-hospital CDI deaths from 2011 to 2017.

"When talking about the risk of C. difficile among older adults and the elderly, we also need to think about the risk among our veterans. Of the more than 19 million veterans in the US, 47 percent are 65 years or older. This is a growing population of people who are at-risk and will need to be educated."

– Dr. Artie Shelton,
Vietnam Veterans of America's Veterans Health Council

persons), there were 224,000 CDI-related hospitalizations (incidence ~70 per 100,000 persons) and 20,500 CDI-associated in hospital deaths (incidence ~6 per 100,000 persons) in 2017 in the US.[17] Of the CDI-associated deaths, at least 12,800 deaths are directly related to *C. difficile* due to antibiotic-resistant infection.[2] Outside the US, an estimated 172,000 CDI cases occur annually in Europe.[18]

Each year, more than $7 billion is spent in the US and European Union (EU) in *C. difficile*-related costs.[18,19,20] The disease also contributes to longer hospital stays,[18,21] decreased productivity,[18,22] reduced quality of life,[19,22,23] and an increased risk of disability (morbidity) and death (mortality).[19]

The CDC classified *C. difficile* at "Hazard Level—Urgent," when it published its first report in 2013 on germs that pose high antibiotic resistance threats.[2] *C. difficile* remained at this threat level in the CDC's follow-up report in 2019, signifying the difficult nature of this infectious germ.[2] According to the CDC, "Hazard Level—Urgent" threats have the potential to become widespread and therefore require urgent attention to identify and prevent transmission of infection.[2] Globally, the World Health Organization (WHO) has recognized *C. difficile* as a priority pathogen.[24]

C. difficile can be anywhere and persistent

Although *C. difficile* infections have historically been associated primarily with hospital settings, recent data have challenged this belief. While *C. difficile* may be found in the following locations, not everyone will become infected. Spores from this germ have been observed in many environments both indoors and outdoors, in healthcare facilities as well as in community settings such as outpatient clinics, dentist offices, homes, parks, supermarkets, restaurants, and playgrounds.[25] *C. difficile* spores have also been reported in food, soil, households, and water sources such as rivers, lakes, swimming pools, and wastewater treatment plants.[26] In one study of people with recurrent *C. difficile* infection, positive samples of the germ were found throughout their homes – on the vacuum cleaner, toilet, and bathroom sink and faucet, and to some extent on the microwave, refrigerator, and television remote control.[27] This is true even in homes of otherwise healthy people who have not had CDI.[25] Being highly prevalent in soil, *C. difficile* spores can be spread throughout the home by simple pathways such as dog paws and shoes.[26]

The spores can be highly resilient, persistent, and easily transmissible.[28] *C. difficile* spores are shed in feces and are found in the soil. They can survive for up to five months on hard surfaces.[29] They can potentially be detected on any surface that comes into contact with fecal matter or dirt and dust.[30] People with symptomatic infection are the main source of contagion from person to person within a healthcare setting, which may be through contamination of hands and medical equipment that come into contact with an infected patient.[28,31] Asymptomatic carriers also might contribute to the spread of the disease.[32] Typically, three percent of healthy adults are colonized by *C. difficile* strains, and they do not exhibit clinical symptoms of infection.[33] These individuals may shed *C. difficile* in their stool. If the

germ in these individuals has the ability to create toxins, then there is the risk that these people can transmit toxigenic strains to others, potentially causing an infection.[34]

C. difficile spores can survive heat and common cleaning agents like detergent, and germicides like disinfectants.[28,35,36] Commonly-used hospital cleaning agents as well as alcohol-based hand sanitizers are not sporicidal and therefore, cannot eradicate *C. difficile* spores.[28,37] Bleach-based cleaning agents are effective at eradicating *C. difficile* spores,[38] though dwelling time on contaminated surface may differ by brand.

In healthcare settings, *C. difficile* spores spread mainly on hands of infected patients and surfaces in which they may come into contact.[31,39] *C. difficile* is highly contagious. Handwashing with soap and water is recognized by the CDC as the preferred method for effectively removing *C. difficile* spores to reduce the risk of transmission, especially during outbreaks.[29,37] While these methods are important to keep *C. difficile* at bay, they may not eliminate the risk entirely. In one hospital-based study, 78 percent of hospital rooms were contaminated with *C. difficile* after cleaning, and those rates fell to 11 percent after more intensive cleaning.[40] As noted earlier, health-care associated infections overall have declined since 2011.[17]

Current guidelines recommend that affected patients be placed in isolation to decrease the chances of transmission,[41] though this precaution is not without its difficulties and burdens to both the medical institution, the staff, and the patient. This situation might worsen in the post-COVID 19 era if medical personnel continue to experience a shortage of personal protective equipment.

When considering current and future preventive measures against *C. difficile* infection, it is important to remember that the risk of coming into contact with the germ is not limited to healthcare settings. Given that the germ has been detected in a range of familiar, everyday locations, and is difficult to eradicate, people need to be more mindful of the potential risk for exposure and to take precautions to minimize their chances for infection.

"Despite being classified by the CDC as an urgent public health threat, C. difficile remains under-recognized by the public as well as by many healthcare professionals. Many patients I have met with who have a C. difficile infection say they had never heard of it until they learned they were infected."

– Dr. Erik R. Dubberke,
Washington University
School of Medicine

CDI is unpredictable and can occur in anyone, particularly adults

The risk factors associated with an increased risk for *C. difficile* infections include the use of antimicrobial therapy, advanced age, longer duration of hospitalization, and comorbidities.[2,12]

Cases of CDI are classified into three epidemiologic categories:[42]

1. **Community-associated (CA)**, which is defined as symptom onset in an outpatient setting setting or within three days of admission to a healthcare facility without a history of admission to a healthcare facility in the previous 12 weeks. According to the CDC's 2017 Annual Report for the Emerging Infection Program for *Clostridioides difficile* infection, nearly 50 percent of all cases of *C. difficile* infections are community-associated infections.[16,17]
2. **Community-onset healthcare facility-associated (CO-HCFA)**, which is defined as symptom onset in an outpatient setting or within three days after a hospital admission in someone with a documented overnight stay in a healthcare facility – such as a hospital or long-term care facility – in the 12 weeks prior to symptom onset.
3. **Healthcare facility-onset (HCFO)**, which is defined as symptom onset more than three days after admission to the hospital or in a person residing in a long-term care facility (LTCF).

According to a CDC study, of the estimated 235,700 cases of healthcare-associated CDIs in 2017, 143,600 were HCFO (87,000 hospital-onset and 56,600 LTCF-onset) and 92,400 were CO-HCFA.[17]

Antibiotic use plays a role in driving CDI epidemiology.[43] While antibiotics are essential to treat certain bacterial infections, one of the possible unintended effects is the disruption or destruction of the gut microbiota, including the beneficial germs.[44] In compromised patients who lack enough healthy bacteria to keep *C. difficile* in check, the risk of *C. difficile* infection from antibiotics increases.[43]

During a 10-year period (2001 – 2010), the occurrence of infections nearly doubled among hospitalized adults.[45] Between 2011 and 2015, the incidence of *C. difficile* infections in the healthcare setting remained relatively unchanged[46] until 2015, when the overall incidence began steadily declining.[17] According to a 2015 population-based study by the CDC, two of every three healthcare facility-associated infections in the US are among patients age 65 or older.[14]

As people age, their immune systems weaken and they often have other medical conditions, increasing their risk for infection.[19] The rise of *C. difficile* infection risk observed in older adults may be attributable to more frequent interactions with healthcare systems and increased exposure to antibiotics. Hospitalization and long-term nursing home care are considered risk factors for *C. difficile* infection.[12,47] Patients at these facilities are more susceptible to *C. difficile* infection because of diminished health, frequent antibiotic exposure, contact with healthcare workers, and exposure to other infected patients.[47] Even being in a room adjacent to an affected patient can place other patients at risk for *C. difficile* infection.[38,48] Approximately 13 out of every 1,000 hospitalized patients in the US have CDI,[49] resulting in $4.8 billion in healthcare-related costs in the US (based on 2008 data).[20]

"We are in the midst of a demographic transformation in America, in which the number of people who are age 65 or older is growing dramatically. As a result, we will have an increasing population of potentially at-risk individuals."

– Dr. James Appleby,
Gerontological Society of America

Of all patients who are treated for *C. difficile* infection in the hospital, more than half were already sick on admission, making *C. difficile* infections, according to the CDC, "a potential source of intrahospital transmission."[50] When infected patients are transferred among healthcare facilities and receive care at multiple institutions, the incidence of infection at hospitals may rise.[51] Healthcare institutions with the highest level of connections to other facilities often have significantly higher rates of infections.[51]

Healthcare-facility onset infections generally affect higher risk, older

patients while infections in the community setting may affect lower risk populations. For example, a study of more than 18,000 nonsurgical hospitalized patients found that those with confirmed *C. difficile* infection (n=390) tended to be older (median age 66 vs. 52.7 years) and more likely to have other comorbid conditions such as congestive heart failure, obstructive pulmonary disease, and cancer, than other hospitalized patients.[52] On the other hand, a separate study found that patients with community-associated infection were younger (median age of 50 years vs. 72 years) with fewer co-occurring medical conditions than patients with infections associated with healthcare facilities.[53] According to a 2017 CDC report, 55 percent of all infections reported in patients 50 to 54 years of age were community-associated.[16]

While patients with community-associated infection tend to be younger, the impact of the infection appears to be more severe with age. Older patients (≥65 years) with community-associated CDI tend to have more severe infection (43 percent versus 28 percent) and severe complicated infection (11 percent versus three percent), compared with patients under 65 years, according to one population-based study (n=385 confirmed CDI cases).[53] Older patients also were found to be twice as likely to be hospitalized for their infection.[53]

In addition to taking antibiotics, exposure to a healthcare facility is a marker for people at risk for *C. difficile* infection. About one in six patients with a healthcare-associated CDI get sick after they have been discharged from the hospital.[17] About 80 percent of patients with community-associated infection had prior contact with an outpatient health facility, such as an emergency department or family practice office, and about 65 percent had used an antibiotic in the 12 weeks before their infection.[54]

Although certain factors such as antibiotic use, exposure to healthcare facility, and advancing age, are associated with *C. difficile* infection, predicting which patients will develop an infection and when is very challenging. Affected patients continue shedding spores even after symptoms resolve. In a prospective, observational study among infected patients (n=52), 60 percent still had skin contamination and 37 percent were still shedding spores at the time diarrhea resolved.[55] Although these rates decreased by the end of treatment (32 percent skin contamination and 14 percent spore shedding), the rates increased again about one to four weeks following treatment (58 percent and 50 percent, respectively).[55]

"An important step is to make sure nurses are getting critical information on a regular basis about C. difficile so that they are always following the right precautions to protect themselves and their patients. This includes always being mindful they are properly gowned and have gloves on when caring for patients."

– Millicent Gorham,
National Black Nurses Association

CDI can be a debilitating disease

Common symptoms of CDI include three or more diarrheal bowel movements per day,[1] abdominal tenderness or pain, fever, nausea, and loss of appetite.[1,56] In more severe cases, infections can cause uncontrollable, watery diarrhea up to 10 to 15 times a day.[1] Symptoms may last two days or longer,[1] impairing patients' quality of life, work and daily activities,[57] and placing a burden on healthcare systems.[58] Severe symptoms also may include swelling or inflammation of the large intestine, toxic megacolon (a rare yet life-threatening complication of severe colon disease or infection), and even death.[1,12]

The impact of infection-related diarrhea may continue well beyond the hospital stay. Within a month of healthcare associated CDI diagnosis, one in 11 people 65 or older die.[12] Within 180 days after hospital discharge, one study found that 38 percent of patients with *C. difficile* infection died versus 12 percent among non-affected patients.[52]

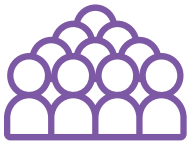
When assessing a patient's overall length of hospital stay, a retrospective cohort study of nonsurgical hospitalized patients found that 2.8 days were attributed to *C. difficile* infection.[52] A separate retrospective study (2005-2010) found that about one in four patients hospitalized for *C. difficile* infection required a prolonged stay (median 5.5 to 12.2 days) in a special care unit or a non-general hospital room.[59] In that study, more than half of the patients were isolated for at least a day, and 12 percent required nearly two weeks of intensive care.[59]

Patients may suffer emotionally during hospitalization for an infection, especially as a result of isolation. In semi-structured interviews with patients with CDI conducted in the US and France from 2011 to 2012, investigators explored the patient experience throughout the infection – from the first signs of CDI to hospitalization, and onto discharge from the hospital. Patients in this qualitative study (N=24) reported increased feelings of loneliness, leading to depression and sadness, as a result of the isolation.[22] Some patients also reported feeling shame and embarrassment, believing they were a burden to healthcare providers because of the extensive precautions taken and constant need for cleaning.[22]

"We need the courage to take away the stigma associated with having a conversation about this infection and help people feel comfortable to talk about it. I think this is especially important for older people age 65+ who use more healthcare services and need to be aware."

– Dr. James Appleby,
Gerontological Society of America

ABOUT ONE IN SIX PATIENTS with healthcare-associated CDI get sick after they have been discharged from the hospital[17]



About **80 PERCENT OF PATIENTS** with community-associated infection had prior contact with an outpatient health facility, such as an emergency department or family practice office[54]

and about **65 PERCENT** had used an antibiotic in the 12 weeks before their infection.[54]

"I believe most healthcare professionals are familiar with the risk factors for C. difficile. They know that it is more common now than it was 10 or 15 years ago. But I think where the lack of recognition occurs is how C. difficile actually impacts the patient. Many of the serious outcomes that occur as a result of the infection occur well after acute symptoms resolve, and the physicians who diagnosed the C. difficile infection sometimes are not involved with the patient at this point."

– Dr. Erik R. Dubberke,
Washington University School of Medicine

A large, global retrospective study predicting the effect of advancing age on treatment outcomes in patients after their initial or first recurrent infection concluded that treatment outcomes worsen with every subsequent decade in patients over the age of 40, compared to those younger than age 40.[60]

CDI also can have long-lasting effects on a patient's mental and emotional health, even after symptoms have subsided.[61] Following recovery, some patients who had suffered CDI reported living in fear of a recurrence, feeling too weak to resume their normal life, and distancing themselves from loved ones for fear of still being contagious, according to patient interviews (2011 to 2012).[22] Some patients also said they may stop leaving their home altogether, as they felt the need to stay close to a toilet.[22]

Recurrent CDI is a major problem for patients. Recurrence is generally defined as the re-emergence of symptoms along with a positive test for *C. difficile* within two to eight weeks of the last infection.[14,41] An estimated 18 percent of all cases of CDI involved a first episode

"I've heard people ignore diarrhea thinking it will go away, but when someone has a case that just won't go away after taking antibiotics, then they should call their doctor."

– Dr. Artie Shelton,
Vietnam Veterans of America's Veterans Health Council

of recurrence, and the risk of recurrence more than doubles after two or more infections.[62] In 2017, nearly 70,000 people experienced a first recurrence of CDI based on the CDC's latest estimates.[17] Of those who experience recurrence, an estimated 40 to 60 percent will experience multiple episodes.[63] With each recurrence, treatment options become more limited.[28] Rehospitalization for recurrent CDIs are associated with excess hospital days and costs.

A recurrent infection can be a continued burden to patients. In a 2017 phone survey of patients with a history of recurrent CDI admitted to one of seven Chicago area hospitals, nearly three in five rated their diarrhea as severe in their most recent bout of infection (n=119).[64] About one in three of these patients reported extreme exhaustion (31 percent) and severe abdominal pain (29 percent).[64] Forty-two percent of patients surveyed were very worried about getting sick again and 31 percent were worried about getting others sick.[64] Almost half of patients changed their behaviors: 47 percent began washing their hands more frequently and 45 percent increased their use of soap and water.[64] Between 22 and 32 percent also reported that they went out to eat at restaurants less, avoided public areas, and avoided certain medications.[64]

C. difficile infection is not simply an acute medical condition, but a disease that can have a long-term impact on patients and healthcare providers. The burden associated with infection can impact not only the infected individual, but also his or her family members, who may be affected both emotionally and, in some cases, financially.[61] Given the difficult nature of symptoms and the ongoing fears of recurrence, organizations have been created to provide support for people who have suffered *C. difficile* infection with the goal of encouraging people and healthcare providers to share stories and build awareness.

"I hear from people all the time who tell me they learned they had C. difficile in the emergency room but no one ever connected the dots back to their primary healthcare professional like their personal physician or even their dentist. As a C. difficile advocate, this scares me because I believe we need to make those connections across specialties and facilities."

– Christian John Lillis,
Peggy Lillis Foundation

CDI Prevention: Current Guidance

The joint **Infectious Diseases Society of America (IDSA)/Society for Healthcare Epidemiology of America (SHEA) 2017 clinical practice guidelines on CDI** – an update of the 2010 guidelines – includes recommendations for CDI prevention, listed in the table below.[41]

IDSA/SHEA Recommendations for Healthcare Providers: CDI Prevention and Control

MEASURE	RECOMMENDATION
Isolation	Accommodate patients with CDI in a private room with a dedicated toilet to decrease transmission to other patients.
Contact precautions	Use personal protective equipment, such as gloves and gowns, before entering patient rooms and wear them when in close contact with patients.
Hand hygiene	Wash with either soap and water or an alcohol-based hand-hygiene product before and after contacting a patient and after removing gloves. (Handwashing with soap and water is preferred over alcohol-based hand-hygiene products after contact with an area likely to be contaminated with fecal material.)
Bathing	Encourage patients to wash their hands and shower to reduce the number of skin spores.
Cleaning and disinfection of medical equipment	Use disposable equipment and ensure that reusable equipment is thoroughly cleaned and disinfected, preferably with a sporicidal.
Environmental cleaning	Evaluate cleaning processes to ensure quality and effectiveness of environmental cleaning.
Antibiotic stewardship	Minimize the frequency and duration of antibiotic use as well as the number of antibiotic agents.

The CDC C. difficile guidelines[65,66] corroborate many of the IDSA/SHEA prevention recommendations for healthcare providers. Additional recommendations include developing an infrastructure for multidisciplinary infection-prevention programs; cleaning room surfaces with bleach or another EPA-approved, spore-killing disinfectant; and testing for *C. difficile* if a patient has diarrhea during antibiotic therapy or within several months of taking an antibiotic(s).

In addition to CDC, the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) provides the following guidance for the prevention of CDI in acute healthcare settings:[67]

- Perform surveillance and reporting of CDI infection rates at both the hospital and ward levels
- Use contact precautions and personal protective equipment to decrease CDI acquisition/transmission
- Introduce daily environmental sporicidal disinfection and terminal disinfection of patients' rooms to decrease CDI acquisition/transmission
- Restrict overall antibiotic use and reduce the duration of use for individual therapies
- Educate healthcare providers and workers on CDI prevention strategies
- Educate patients and visitors on prevention measures

Antimicrobial Stewardship

Antibiotic resistance is a global problem. Drug-resistant infections pose a significant public health and economic burden to healthcare systems because they limit the number of remaining treatment options providers can prescribe and patients can take to fight an infectious germ. While antibiotics are often necessary to fight certain bacterial infections, their use does play a role in driving infection epidemiology, including *C. difficile*.[43] Every year, antibiotic resistance costs the US $20 billion in added healthcare costs and $35 billion in lost productivity.[68]

C. difficile isolates with reduced susceptibility, and even resistance, to antibiotics contribute to the pressing medical needs in CDIs. Clinical practice guidelines from the Infectious Disease Society of America/Society for Healthcare Epidemiology (IDSA/SHEA) note that the goal of antimicrobial stewardship is to "optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including toxicity, selection of pathogenic organisms (such as *C. difficile*), and the emergence of resistance."[69]

Proper management of antibiotic use requires an evidence-based approach, prescriptively applied to discrete health settings, and the individual patient's situation. Therefore, it is critical for everyone – from infectious disease specialists, prescribers, and pharmacists to patients and caregivers – to work together as a team to ensure that antibiotics are only used by patients who need them and for the correct duration. Monitoring antibiotic exposure may be an effective approach to control *C. difficile* infections.

As part of a global effort to promote antibiotic stewardship, more than 100 companies and trade associations within the pharmaceutical industry signed the Declaration on Antimicrobial Resistance at the World Economic Forum in Davos, Switzerland in 2016. Along with encouraging the appropriate use of new and existing antibiotic treatments, the declaration also called for coordinated action to improve infection prevention, hygiene, stewardship, and conservation measures.[70] Implementing better stewardship practices could prevent infections and save lives.[65]

Creating a call to action

We are at a crucial moment in the fight against *C. difficile* and CDI. Despite recent progress in preventive intervention, *C. difficile* infection afflicts hundreds of thousands of people across the US and Europe, and remains a widespread, potentially debilitating and in some cases fatal disease. Everyone – from healthcare professionals to policy makers to the general public – must understand the global public health threat that *C. difficile* poses and work together to educate, raise awareness, and find solutions for combatting this serious infectious disease.

To accelerate the pace of progress against CDI, the *C. difficile* Awareness Initiative has identified four key areas of focus:

- **Educate relevant healthcare allies about *C. difficile* so they recognize the seriousness of the problem.** *C. difficile* is an issue that impacts many people, from the patients who are afflicted with the infection and their loved ones to physicians, nurses, and other healthcare facility staff who care for them. This is an issue that warrants attention not only from the infectious disease specialist and gastroenterologist, but from a broader cross-section of the healthcare community representing many medical professionals and patients. This includes anyone who might prescribe an antibiotic or provide any medical care for patients who are potentially at risk, including primary care, pulmonology, urology, geriatrics, oncology, obstetrics and gynecology, dentistry, surgery, and others. It also includes any organization that supports the needs of these at-risk populations such as the elderly, veterans, and people who are immunocompromised.

"Nurses are great resources to help with education. They are often the frontlines in medical practices, healthcare facilities, and hospitals. Through the nurses, we have an opportunity to educate patients and families and even other healthcare providers. I believe nurses can play a critical role in helping to connect those dots."

– Millicent Gorham,
National Black Nurses Association

- **Enlist these allies to help drive awareness among healthcare professionals with a connection to *C. difficile*.** Given that *C. difficile* infections affect patients in many settings, we believe that education must focus on healthcare professionals from multiple disciplines. That is why the Founding Committee members of the *C. difficile* Awareness Initiative include experts who represent not only the infectious disease community but also nurses, geriatricians, and veterans' medical care professionals. Moving ahead, our goal is to create a multidisciplinary group of allies to support the Initiative's educational efforts and encourage them to make *C. difficile* awareness a priority for the communities they represent.
- **Work collaboratively and across disciplines to rally the public to become more knowledgeable.** Knowledge is the best defense against a serious health issue such as *C. difficile* infections. Simply asking about the precautions that might be taken to prevent an infection could help to minimize a person's risk. Unfortunately, for many people, the first time they hear the word *C. difficile* is when they or a loved one are being diagnosed with the infection, and we believe that is too late. As part of our effort, we will enlist support from organizations that represent many types of people to help increase awareness and put *C. difficile* on the public's radar.
- **Reach people in their everyday lives through new technologies and experiences.** While there is useful educational content available for people to learn more about *C. difficile*, there is a need for other resources that shed light on this serious public health threat in ways that are educational and factual but also grab their attention. Education should focus on diminishing the stigmas and barriers that prevent people from having a conversation about this infection, giving them the tools needed take more precautions.

This is just the start of an essential process to shed light on a critical public health issue. Going forward, we must act together to better understand *C. difficile* and the experiences and needs of people who are affected to ensure we improve outcomes across the globe. With this action and other aligned activities, the group hopes to build a broader and elevated understanding of the disease, and that further actions are taken to reduce the rates of CDI over the next decade.

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