Clostridium difficile Infection in Long-term Care Facilities: A Call to Action for Antimicrobial Stewardship

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Across the United States, the baby boomers are entering into their elderly years. As they are America’s largest generation to do so to date, their need for care will greatly affect nursing homes, long-term care facilities, and long-term acute-care hospitals (LTACHs). Unfortunately, the rise of Clostridium difficile infection (CDI), particularly in extended-care facilities, might become the biggest obstacle in their care. Elderly extended-care-facility residents are at an elevated risk of CDI simply due to their advanced age and the fact that they are receiving care in an extended-care facility. LTACHs experience a high incidence rate of CDI, and these infections can lead to major complications for a patient’s health. Other factors that contribute to higher risk for CDI include receiving multiple courses of antibiotics, longer length of antibiotic treatment, and previous CDI. Although this obstacle to proper care is great, some simple solutions are available to healthcare providers. Probiotics may help improve natural immunity in patients, and strict adherence to antimicrobial stewardship standards could help reduce this serious bacterial threat.

Keywords. C. difficile infection; long-term care facilities; antibiotic stewardship; C. difficile colonization; probiotics.

As the baby boomers of America age, the US healthcare system is tasked with providing proper care for these patients. A common choice for care is nursing homes, also called extended-care facilities, which provide both long-term residential/custodial care and short-term stay for rehabilitation or post-acute-care/skilled-care needs [1].

Sometimes patients require a specialized type of care that is found in a skilled nursing facility, or long-term acute-care hospital (LTACH) as designated under Medicaid [2]. The differentiation of different types of care facilities is complex, difficult to define, and even harder to distinguish, but LTACHs are emerging in importance in this sector. The LTACH designation is determined by both patient-level and facility-level criteria. Congress and the Secretary of Health and Human Services define LTACHs based on facility and patient criteria to ensure that patients admitted to these facilities are medically complex and have a good chance of improvement. Facility-level criteria include features such as staffing, patient evaluation and review processes, and types of patients present in the facility. Patient-level criteria should identify specific clinical characteristics and treatment modalities. Additional definitions give this designation to facilities that provide diagnostic and medical treatment or rehabilitation to patients with chronic illness or complex and serious medical conditions. Patients would need to have 3–6 concurrent active diagnoses and an acute episode on top of several comorbidities that cannot be treated effectively at an alternative level of care. The average length of stay of each patient often exceeds 25 days. These definitions are more specific and could help settle some of the confusion around these highly specialized and significantly important healthcare settings.
Within the United States, there are currently 522 identified LTACHs. Currently, 3 medical groups have the largest percentages of LTACHs in their systems: 21% (108) are part of the Select Medical group, 19% (100) are in the Kindred Healthcare group, and 7% (35) are part of the Vibra group. The other 53% of LTACHs are parts of different medical groups. Of the total, 42% (220) of all of these facilities are free-standing, meaning that they are not physically attached to another healthcare building. Seventeen percent (88) are remote or satellite campuses that operate as part of the larger group, and 41% (214) are located within a hospital, known as a hospital-in-hospital.

All of the above-mentioned LTACH groups have a total of 28,666 beds, which operate at an occupancy that can range from 40% to 84%. In 1 year’s time, there were a total of 217,380 discharges from the above-mentioned LTACHs, with 66% of patients having Medicare as their primary insurance, 6.8% using Medicaid, and 27.2% using some other type of insurance. These patients contributed 6,735,486 patient-days with an average length of stay in their respective LTACHs of 31 days. These LTACHs had a Medicare case mix index of 1.107. A case mix index with a value ≥1 indicates that patients are, on average, sicker than the average Medicare patient. This shows that all those involved with healthcare in an LTACH are dealing with a particularly delicate group of patients among whom CDI is an important health-related issue.

Diarrhea is generally associated with higher mortality in elderly compared with younger patients. In a review of mortality data collected by the National Center for Health Statistics from 1979 through 1987, it was found that elderly individuals experienced the highest percentage of deaths having diarrhea listed as either an immediate or underlying cause [3] At least 30% of diarrheal deaths in the elderly occur in nonhospital patient care settings, mainly nursing homes [3], and Clostridium difficile infection (CDI) is one of the predominant causes of infectious diarrhea in elderly residents living in nursing homes, accounting for at least 11% of cases [4]. CDI has been on the rise from 2001 through 2010. The second half of the decade saw a 47% increase in cases of C. difficile colitis compared with the first half of the decade [5]. This increase was seen in healthcare settings across the United States, and is a threat to LTACH residents. Compared with nursing homes, LTACHs may experience a higher prevalence of CDI due to a higher rate of antibiotic use [6].

Similarly, CDI is a major concern in long-term care facility (LTCF) residents. Data suggest that CDI is endemic in LTCFs and remains largely uncontrolled despite numerous efforts to manage the issue [1]. The incidence rate (2.3 cases/10,000 resident-days) and recurrence rate (1.0 case/10,000 resident-days) of CDI in LTCFs is comparable to that of acute-care hospitals [7]. Incidence of CDI differs based on the type of unit where the patient is residing. Sub-acute-care units have the highest incidence rate, whereas traditional nursing home units have the lowest incidence [1]. There have also been several reported outbreaks of CDI in LTCFs within the past 10 years [8, 9].

An epidemiologic study of CDI in a 350-bed LTCF and 280-bed adjoined chronic-care hospital found that 94 residents tested positive for C. difficile from 236 different samples. Samples were collected between 1 November 1989 and 31 October 1990 [10]. Three point prevalence surveys were conducted during this study, and 65 residents who originally tested negative in the first point prevalence survey tested positive within 12 months of follow-up, giving an incidence rate of 1.56/100 resident-months [10].

A major risk factor for CDI in LTCFs is previous antibiotic use [10, 11]. It has been reported that 50%–75% of LTCF residents receive at least 1 course of an antibiotic in a year [12–14], and an estimated 8%–33% of those treated with an antibiotic in a LTCF acquire C. difficile [10, 15]. There are many risk factors for CDI in nursing home patients, but a few of the key factors are as follows: ≥3 comorbidities, low albumin, presence of a nasogastric or gastrostomy feeding tube, fecal incontinence, and use of proton pump inhibitors [10, 15, 16–20] (Table 1). In fact, admission to an LTCF itself is a risk factor for CDI. At least 50% of CDI occurs within 4 weeks of admission to an LTCF, indicating that some of these patients are exposed to C. difficile during their acute-care hospital stay [7]. Another important risk factor for CDI acquisition is frequent transitions between hospitals and LTCFs. Patients also experience a greater risk of infection when paired with roommates or if they are admitted to a room previously occupied by a patient with CDI [21, 22].

Older adults also develop severe complications associated with CDI [23, 24]. Several factors contribute to this enhanced risk of complication from CDI. Age-related changes in fecal flora, immunosenescence, the presence of underlying diseases, frequent exposure to antibiotics, decreased antibody production to C. difficile toxins, and impaired phagocytosis all contribute to an increased risk of complications [25–27].

Table 1. Patients at High Risk of Clostridium difficile Colonization

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Other Factors With Increased Risk of Colonization</th>
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<tbody>
<tr>
<td>Antibiotic use in the previous 3 mo</td>
<td>Multiple antibiotic use</td>
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<tr>
<td>History of previous C. difficile infection</td>
<td>Duration of antibiotic therapy</td>
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<tr>
<td>Fecal incontinence</td>
<td>Renal insufficiency</td>
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<td></td>
<td>Patients receiving chemotherapy</td>
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<td></td>
<td>Recent hospitalization</td>
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<td></td>
<td>H2 blocker use</td>
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Sources: References [17–20].

* Patients in whom preemptive isolation should be implemented, especially in an outbreak situation.
Several studies reported the prevalence of *C. difficile* colonization in LTCF residents to range between 4% and 20% in endemic settings [11, 28] and 30% in the context of an outbreak [11]. A significant proportion of residents may already be carrying *C. difficile* on admission to the LTCF, and an additional 10%–20% may acquire the organism during their stay in an LTCF [29]. Residents who are colonized with *C. difficile* may be subsequently at low risk of developing clinical disease but may act as reservoirs for spreading *C. difficile* to other patients [30, 31]. Additionally, a high percentage of patients in LTCFs are colonized with toxigenic strains but do not display symptoms. This may be because they have a strong immunoglobulin G response against toxin A or toxin B, a chemical produced by *C. difficile* [32]. Previous hospital exposure, chronic dialysis steroid/immunosuppressant medication, antibiotic use, and H2 blocker use are identified as risk factors for *C. difficile* carriage [17, 28].

In a study done at an LTACH in Los Angeles, it was seen that there is a small group of patients who play a major role in the CDI problem affecting LTACHs [33]. Some of the patients in this group carry *C. difficile* and are either asymptomatic carriers or are not suspected by clinicians to have active CDI. A group of 36 patients was monitored for a 1-month period while they were receiving treatment at the Los Angeles LTACH [33]. Four patients in this group were admitted testing positive for an antigen associated with *C. difficile*; 2 having unsuspected, active disease; and 2 who were carriers and not experiencing symptoms. During the individual courses of treatment of the patients, 20 of the 36 (55.5%) patients being followed had symptoms of diarrhea, whereas 5 patients (13.8%) were eventually diagnosed with CDI [33]. Clearly, patients who are either experiencing active, unsuspected disease or those who are asymptomatic carriers are an important piece to solving the CDI puzzle. Stricter screening processes for patients being admitted to these vulnerable healthcare settings may be necessary to prevent adverse outcomes such as those seen in this LTACH.

Besides patients themselves, there are other important reservoirs for *C. difficile*. Spore-contaminated environments and objects colonized or infected with *C. difficile* can pass the bacterium along to new hosts [34]. Contaminated rectal thermometers, bedside commodes, and telephones are potential sources of infection as well. One outbreak in a nursing home was associated with transmission of *C. difficile* by the reuse of contaminated electronic thermometers [35]. Hands of healthcare workers who care for patients with CDI are transiently contaminated with *C. difficile* and may also contribute to spread [21].

Despite many efforts to destroy spores of *C. difficile*, the bacteria continue to persist in LTCFs. Detergent-based cleaners used to disinfect surfaces are ineffective in eliminating spores [36]. LTCF residents usually live in a shared space with common sleeping, eating, and restroom facilities. Because of the limited resources of LTCFs, isolating infected residents proves difficult and ultimately contributes to the spread of spores [37].

### MEASURES TO REDUCE CDI IN LTCFs/LTACHs

Any LTCF resident who develops acute diarrhea during or after completion of a course of antibiotics should be suspected of having CDI unless proven otherwise.

Long-term care facilities have limited resources in personnel, expertise, and diagnostic services, especially in laboratory assessment. All of these factors can have a considerable impact on the proper treatment of CDI [38]. Empowering midlevel providers to order a *C. difficile* test as soon as the clinical criteria are met would be beneficial. These steps can help in early implementation of infection control interventions and may reduce the spread of the organism within the LTCF.

We suggest a bundle approach with a combination of infection control and antimicrobial management strategies so as to reduce CDI rates at LTCFs [39, 40]. Components of the approach include preemptive contact isolation, preemptive treatment, hand hygiene with soap and water, and effective environmental cleaning [11, 40, 41]. Environmental cleansing with 1:10 hypochlorite solution or 10% bleach should be done after the patient is discharged [42] to ensure a clean, fomite-free environment.

Current guidelines recommend discontinuation of contact precautions after resolution of diarrhea [11]; however, some institutions continue contact precautions until discharge because patients continue to excrete *C. difficile* spores even after the resolution of symptoms.

Current antimicrobial therapies for CDI still have relapse rates of 15%–30% [43, 44]. Consequently, it is important to consider new and alternative treatments to antibiotics. An important, but not yet sanctioned, preventive measure for CDI is the use of probiotics. The outdated Infectious Diseases Society of America guidelines from 2010 do not support the use of probiotics for CDI prevention [45]. A study of probiotic use in elderly patients showed that there was an increase in total T cells, helper T cells (also known as CD4+ cells), activated T lymphocytes (CD25+ cells), and natural killer cells [46]. Specifically, *Bacillus lactis* HN019 showed an increase in the phagocytic abilities of mononuclear and polymorphonuclear lymphocytes [46]. By increasing the natural immune abilities of these patients, healthcare providers are strengthening the lines of defense that patients already have, combating the risk for opportunistic infections. Another study demonstrated that using a bundle approach, which included the use of probiotics, and proper antimicrobial stewardship led to a decrease in CDI of 73% [47]. In a study of the use of a probiotic drink containing *Lactobacillus casei*, *Lactobacillus bulgaricus*, and *Streptococcus thermophilus*, it was found that no patients using the probiotic drink developed CDI, whereas 9 of 53 patients (17%) using...
the placebo experienced CDI [48]. In a single-center study in China, Gao et al [49] treated 255 patients (average age, 60 ± 6 years) in a dose-ranging study with a probiotic, and reported a significant reduction in duration and severity of antibiotic-associated diarrhea and CDI in the probiotic-treated group compared with the placebo group. The use of probiotics in the LTACH population may provide a much-needed and simple preventive measure for CDI infection.

Finally, there is strong need for antibiotic stewardship programs in LTCFs. Current guidelines recommend surveillance of antibiotic usage in LTCFs [11]. Stewardship programs are resource intensive and may be difficult to implement in LTCFs. This is because LTCFs are often underfunded, understaffed, and overwhelmed with patients [50]. Restricting suspected antimicrobial usage along with infection control measures should be considered during an outbreak of CDI. Future research should focus on cost-effectiveness of antimicrobial stewardship programs in LTCFs, as well as the role of asymptomatically colonized patients as a potential source of CDI in LTCFs and benefit of infection control in these patients in limiting spread of C. difficile.

With CDI on the rise across the United States, it is imperative that healthcare workers and administrators in LTACHs do all they can to prevent the spread of C. difficile [5]. Because LTACHs serve a fragile population that harbors many risk factors for CDI, this increase in CDI is posing a serious threat to these patients. Proper preventive measures, screening, recognition, and action need to be taken to ensure that this problem meets its match. By providing patients with clean rooms and using sterile instruments, healthcare workers can help reduce the environmental risk for patients to acquire CDI. Physicians and other providers can practice smarter medicine by choosing more effective antibiotics and possibly stopping the problem before it happens by using probiotics.

LTACHs would also greatly benefit from properly implemented antimicrobial stewardship programs that are joined with a bundle approach to preclude future infections. A comprehensive program consisting of environmental disinfection of rooms of CDI patients, active surveillance with a sensitive diagnostic test, infection control measures consisting of hand hygiene with soap and water and contact precautions while caring for CDI patients, and antimicrobial stewardship programs minimizing the frequency and duration of antimicrobial therapy and restricting the use of clindamycin and cephalosporin resulted in a decrease in incidence of CDI by 23% at a 50-bed LTACH in the southeastern United States [51]. Similar strategies could be implemented at other LTACHs to decrease CDI rates. Although LTACHs and the patients they serve seem to be the perfect storm, an astute approach to prevention and treatment may help provide a permanent calm and stop the storm before it can ever happen.

Notes

Supplement sponsorship. This article appeared as part of the supplement “Prebiotics: Added Supplementary Value in Clostridium difficile Infection,” sponsored by Bio-K Plus International.

Potential conflicts of interest. E. J. C. G. serves on the Bio K Plus advisory board, and is on the infection control and medical advisory board for Kindred Healthcare System. T. C. reports no potential conflicts. Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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