American Journal of Infection Control 46 (2018) 998-1002

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major Article

Overreporting healthcare-associated *C. difficile*: A comparison of NHSN LabID with clinical surveillance definitions in the era of molecular testing

Kathryn Albert RN, BSN, MPH, CIC [a,*], Barbara Ross RN, MS, CIC, FAPIC [a], David P. Calfee MD, MS [a,b], Matthew S. Simon MD, MS [a,b]

[a] *Department of Infection Prevention & Control, New York- Presbyterian Weill Cornell Medical Center, New York, NY*
[b] *Department of Medicine, Division of Infectious Diseases, Weill Cornell Medicine, New York, NY*

Key Words:
Clostridium difficile
Healthcare-associated infections
Surveillance
Infection control
Public reporting

Background: *Clostridium difficile* infection (CDI) is the most common healthcare-associated gastrointestinal infection. Hospitals are required to report cases of healthcare facility-onset CDI (HO-CDI) using the National Healthcare Safety Network's CDI laboratory-identified (LabID) event definition. The aim of this study was to determine the extent of potential over-reporting due to the exclusion of important clinical data within LabID reporting definitions.

Methods: In 2015, retrospective chart review was performed on 212 HO-CDI cases reported from a large urban medical center. Cases had positive polymerase chain reaction test for the *C. difficile* toxin B gene from an unformed stool specimen collected >3 days after admission and >8 weeks after most recent LabID event. Cases were categorized into "clinical surveillance" groups: community-acquired infection, recurrence/relapse, asymptomatic colonization, colonization with self-limited symptoms, possible HO-CDI, and probable HO-CDI.

Results: Of the infections, 13.6% were community acquired, 2.8% were recurrent/relapse, 1.9% were asymptomatic colonization, 18.4% were symptomatic colonization, 38.7% were possible HO-CDI, and 24.5% were probable HO-CDI. Within 24 hours of testing, 34.1% of patients had received a stool softener and/or laxative.

Conclusions: Laxative use and failure to identify community-onset infection may contribute to misclassification of HO-CDI. Only 62% of reported cases met clinical surveillance criteria.

Clostridium difficile is a toxin-producing bacterium that has become a leading cause of healthcare-associated diarrhea in the United States.[1] Each year, *C. difficile* infects approximately 250,000 people and leads to 14,000 deaths.[2,3] The U.S. healthcare system also pays an estimated $5.4 billion per year to manage this ongoing public health problem.[4] Between 2000 and 2009, the incidence rate for *C. difficile* infection (CDI) doubled in the United States,[5] and a recent report from the Centers for Disease Control and Prevention (CDC) showed only an 8% decrease between 2011 and 2014.[6] CDI has traditionally been associated with hospitalization and antibiotic use, but an increasing number of cases are being attributed to the community setting and to people without prior exposure to healthcare facilities or antibiotics.[7,8]

In 2009, the CDC's National Healthcare Safety Network (NHSN) introduced a laboratory-identified (LabID) infection reporting module that identifies healthcare facility-onset CDI (HO-CDI). NHSN defines HO-CDI as a positive laboratory test result for *C. difficile* toxin A and/or B from an unformed stool specimen >3 days after admission and >8 weeks after the most recent CDI LabID event.[9] LabID surveillance replaced the more labor-intensive form of surveillance that involves chart review of clinical symptoms in relation to lab results.[10,11] Introduction of the LabID surveillance method was intended to simplify and standardize surveillance for CDI.[11]To help guide infection prevention efforts and measure their effect, surveillance for and reporting of HO-CDI using the LabID definition became mandatory in 2013 for all hospitals participating in the Centers for Medicare and Medicaid Services (CMS) Inpatient Prospective Payment System Quality Reporting Program.[9]

Although LabID surveillance has provided hospitals with an easier alternative for reporting HO-CDI cases, misclassification exists due

* Address correspondence to Kathryn Albert, RN, BSN, MPH, CIC, Department of Infection Prevention & Control, New York- Presbyterian Weill Cornell Medical Center, 525 East 68th St, New York, NY 10065.
E-mail address: kaa9041@nyp.org (K. Albert).
Conflicts of interest: None to report.

0196-6553/
https://doi.org/10.1016/j.ajic.2018.03.001

to its lack of clinical assessment.[1,12-14] Recent studies show that 10%-15% of patients are asymptomatically colonized with *C. difficile* upon admission to the hospital.[15,16] Distinguishing this carriage state from CDI is challenging when *C. difficile* polymerase chain reaction (PCR)-based technology is used for diagnostic testing.[13,15-17] PCR assays are less able to distinguish asymptomatic colonization from true *C. difficile* disease compared with toxin-based assays, which are more specific for the detection of toxin production.[15] Therefore, a positive PCR *C. difficile* test in the context of other etiologies for loose stools, such as stool softeners and/or laxatives, chemotherapy, underlying disease, and enteral feeding, may represent colonization, not HO-CDI.[1,14,18] CDI cases originating from the community may be misclassified as HO-CDI because of delays in recognition and/or specimen collection that result in testing on hospital day 4 or later despite an earlier onset of symptoms.[1,9,12-14] The objective of this study was to determine the extent of potential overreporting of HO-CDI using the LabID event reporting definition.

METHODS

Case selection and data collection

Retrospective chart review was performed on all patients age 18 years or older who were hospitalized in 2015 at a large urban medical center and identified as a case of HO-CDI using NHSN LabID definitions. At the study hospital, CDI is diagnosed using the Cepheid (Sunnyvale, California) Xpert *C. difficile* PCR for the toxin B gene, and all positive tests are reported to the NHSN. The electronic medical record for each case was reviewed for various clinical events that contributed to *C. difficile* testing and was entered into a REDCap database. The presence of fever, abdominal pain, and diarrhea was recorded from each case along with the timing and duration of symptoms. Diarrhea was determined to be present under the following conditions: documentation of 3 or more loose bowel movements within a 24-hour period or >1000 ml of output from a stoma within a 24-hour period. If the numeric quantity of diarrheal episodes was not provided, diarrhea was presumed if clinician documentation described "multiple" or "several" episodes of diarrhea within a 24-hour period. Documentation was reviewed for alternative reasons that may have contributed to the development of diarrhea (tube feeding, gastrointestinal bleeding, inflammatory bowel disease, or chemotherapy), along with a known positive test for *C. difficile* at an outside facility. The medication administration record of each case was also reviewed for stool softeners and laxatives given to the patient within 24 hours of *C. difficile* testing, along with antibiotic treatment for presumed CDI (metronidazole, vancomycin [administered by the oral or rectal route], and/or fidaxomicin).

Categorizing "clinical surveillance" groups

Using the collected clinical information, each HO-CDI case was categorized into 6 "clinical surveillance" groups: community-acquired infection, recurrent/relapsed infection, asymptomatic colonization, colonization with self-limited symptoms, possible HO-CDI, and probable HO-CDI (Table 1). Criteria for the community-acquired and recurrent/relapse infection groups were diarrhea onset ≤3 days after admission and diarrhea onset ≤8 weeks after the most recent LabID event, respectively. The asymptomatic-colonized group was composed of cases that lacked any documentation of clinical symptoms.[13,19,20] Cases where diarrhea resolved within 24 hours of testing, regardless of whether they received CDI treatment, were classified as colonization with self-limited symptoms.[18,21] Cases that demonstrated clinical symptoms compatible with CDI that persisted for more than 24 hours but had diagnoses or treatment that mimic symptoms of CDI (e.g., tube feeding, gastrointestinal bleeding, inflammatory bowel disease, and chemotherapy) were classified as possible HO-CDI.[13,18,22] Probable HO-CDI cases were those that did not meet criteria for the other CDI categories. This study was approved by the institutional review board at Weill Cornell Medicine.

Table 1
Clinical surveillance groups

Category	Definition
Community-acquired infection	Diarrhea onset ≤ 3 days after admission
Recurrent/relapse infection	Diarrhea onset ≤ 8 weeks after most recent LabID event
Asymptomatic colonization	Positive specimen without documentation of diarrhea
Colonization with self-limited symptoms	Diarrhea resolved within 24 hours of positive specimen
Possible HO-CDI	Positive specimen in the setting of diarrhea with a potential alternative clinical explanation
Probable HO-CDI	Positive specimen not belonging to other categories.

HO-CDI, healthcare facility-onset *Clostridium difficile* infection

RESULTS

In 2015, 212 adult cases of HO-CDI were identified at the study facility based on NHSN LabID criteria (Table 2). Of the cases, 60% were women, and the median age was 66 years (range: 19-96 years). The median length of time from hospital admission to the date of a positive *C. difficile* test was 9 days (range: 4-225 days). Of all the HO-CDI cases, 51 (24 %) met the probable HO-CDI clinical surveillance definition. Eighty-one (38.2%) were considered possible HO-CDIs cases, as they had alternative clinical explanations for symptoms.

Thirty-nine cases (18.4%) had diarrhea that resolved within 24 hours of sending a specimen for testing and were classified as colonized with self-limited symptoms. The asymptomatic-colonizer group had 4 cases (1.9%) that lacked documentation of any clinical symptoms of CDI. Cases classified as recurrent/relapse CDI infections included 4 patients who tested positive as outpatients at our facility and 2 who had documentation of a positive test at an outside healthcare facility (2.8%). Thirty-one cases (14.6%) were classified as community-acquired CDI since they had documented symptom onset of CDI 3 or fewer days after admission. All but 2 of the reported HO-CDI cases (99%) received antibiotic treatment for presumed CDI. One patient had a stool sample sent for testing but died shortly after the test was sent. The other patient did not receive antibiotic treatment because the clinician decided it would be inappropriate due to a lack of clinically significant symptoms.

Of all the reported cases, 73 (34.4%) received stool softeners and/or laxatives within 24 hours of being tested (Table 2). Docusate (n = 56, 26.4%) and senna (n = 32, 15%) were most frequently given before testing, followed by polyethylene glycol (n = 19, 8.9%), bisacodyl (n = 8, 3.7%), lactulose (n = 5, 2.3%), and magnesium hydroxide (n = 2, 1%). Of the cases using stool softeners and/or laxatives prior to testing, most were classified in the colonization with self-limited symptoms (n = 20) or possible HO-CDI (n = 34) groups (Fig 1).

DISCUSSION

Based on our study, only 62.2% of the cases reported to NHSN in 2015 met our clinical definition of probable or possible HO-CDI. We estimate that the remaining reported cases may have been misclassified due to delays in testing, inappropriate testing, and/or use of stool softeners and laxatives. These results support previous studies that examined the effect of testing practices on CDI rates. Kwon et al.[23] and Kelly et al.[13] demonstrated how inappropriately

Table 2
Demographic and clinical characteristics of HO-CDI cases according to surveillance group (n = 212)

Characteristics	n (%) or median (range)						
	Overall (n = 212)	Community-acquired infection (n = 31)	Recurrent/ relapse infection (n = 6)	Asymptomatic colonization (n = 4)	Colonization with self-limited symptoms (n = 39)	Possible HO-CDI (n = 81)	Probable HO-CDI (n = 51)
Age (years)	66 (19-96)	71 (26-96)	65 (28-82)	70 (60-95)	67 (26-87)	66 (26-92)	64 (19-90)
Women	128 (60.3)	17 (54.8)	3 (50)	4 (100)	16 (41)	45 (55.5)	38 (74.5)
Time from admission to symptom onset (days)	8 (0-399)	2 (0-2)	8 (0-30)	N/A	10 (4-371)	8 (4-53)	7 (4-398)
Time from admission to positive specimen (days)	9 (4-225)	3 (3-22)	10 (3-34)	4 (3-8)	10 (4-224)	9 (4-54)	8 (19-90)
White blood cell count (x10^3/uL)	8.75 (0.1-59)	9.4 (0.7- 27.8)	7.5 (0.1-18.7)	10.8 (4.9-22.7)	9.9 (0.1-47.2)	7.4 (0.1-59)	9 (0.1-32.8)
Fever > 38°C within 24 hours of positive specimen	40 (18.8)	5 (16.1)	1 (16.6)	0 (0)	7 (17.9)	18 (22.2)	9 (17.6)
Diarrhea within 24 hours of positive specimen	182 (85.8)	28 (90.3)	5 (83.3)	0 (0)	28 (71.7)	73 (90.1)	51 (100)
Received stool softeners or laxatives within 24 hours before positive specimen	73 (34.4)	7 (22.5)	0 (0)	2 (50)	20 (51.2)	34 (41.9)	10 (19.6)
Tube feeds	30 (27.5)	5 (16.1)	0 (0)	0 (0)	5 (12.8)	20 (24.6)	0 (0)
Gastrointestinal bleeding	13 (11.9)	1 (3.2)	0 (0)	0 (0)	1 (2.5)	11 (13.5)	0 (0)
Inflammatory bowel disease	28 (25.7)	7 (22.5)	1 (16.6)	0 (0)	3 (7.6)	17 (20.9)	0 (0)
Chemotherapy	32 (29.4)	0 (0)	1 (16.6)	0 (0)	6 (15.3)	24 (29.6)	1 (1.9)
Received antibiotic treatment for CDI	210 (99)	31(100)	6 (100)	3 (75)	39 (100)	81 (100)	50 (98)

CDI, *Clostridium difficile* infection; *HO-CDI*, healthcare facility-onset *Clostridium difficile* infection

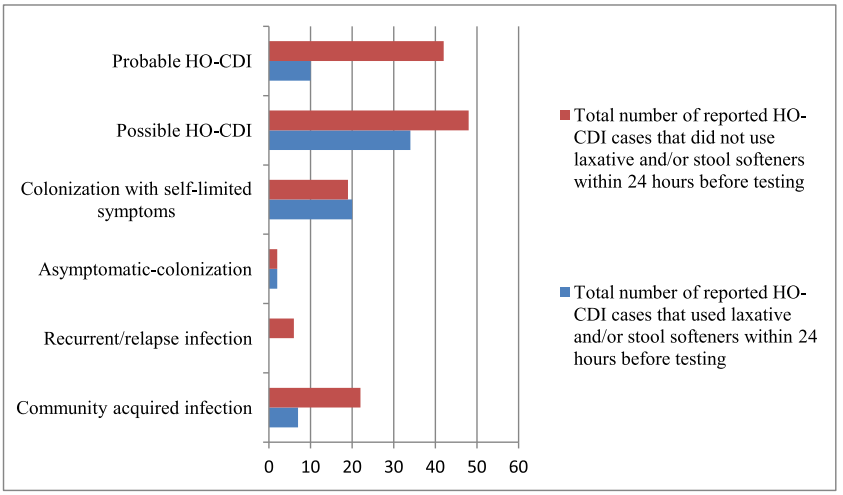

Fig 1. Laxative and/or stool softener use among clinical surveillance groups

testing patients for CDI either too late or without clinically significant diarrhea contributes to overdiagnosis and overreporting of HO-CDI. We found a greater proportion of cases that may have been misclassified compared with Kelly et al., who found potential misclassification in 15% of cases.

Of the various clinical surveillance groups, possible HO-CDI was the most frequent classification (38.2%). This group was composed of patients with underlying medical conditions that may mimic symptoms of CDI, highlighting challenges in distinguishing colonization from active disease. Of the reported HO-CDI cases, 103 had documentation of inflammatory bowel disease, chemotherapy, tube feedings, or gastrointestinal bleeding. While *C. difficile* colonization is well described in the literature,[19,24-26] there is no NHSN surveillance definition that distinguishes colonization from infection. As a result, complicated clinical scenarios are not accounted for in HO-CDI reporting, leading to potential misclassification, particularly among patients with alternative diarrheal etiologies.

PCR has become the most widely used method for CDI testing due to the benefits of a quick turnaround time and high sensitivity.[22,23,27] In New York State in 2015, 59.4% of healthcare facilities reporting to NHSN used PCR alone for CDI testing, which was a 3% increase from 2014 (V. Haley, PhD, New York State Department of Health). Due to its detection of the *C. difficile* toxin B gene and not direct toxin detection, a positive test result may indicate active infection or symptomatic colonization with diarrhea due to other causes.[13,23,27] Extrapolating our findings to New York State inpatient facilities, where a total of 18,646 cases of CDI were reported in 2015,[28] approximately 2200 (12%) may be attributed to colonization. Testing clinically significant diarrhea is crucial not only for accurate HO-CDI reporting but also for appropriate diagnosis and treatment.[13,23] Given that 34.1% of our reported HO-CDI cases used stool softeners and/or laxatives shortly before testing, it is possible that clinicians were unaware either of these testing features or their patients' stool softener and/or laxative use. Electronic systems designed to help clinicians and laboratories improve testing practices may be beneficial. A study by White et al. demonstrated how a *C. difficile* order set decreased inappropriate testing by reminding clinicians of a patient's recent stool softener and/or laxative use

prior to ordering *C. difficile* PCR tests.[29] A similar study was done by Truong et al. where the laboratory used an electronic tracking system to successfully enforce compliance with appropriate testing practices.[30] Our findings support the need for interventions to improve *C. difficile* testing practices in the era of molecular diagnostics.

This study also demonstrated that clinicians tend to be liberal about treating patients for CDI once there is a positive test result and that there are difficulties in clearly distinguishing true CDI from colonization. Of our cases, 98.6% received antibiotic treatment for CDI, and only 1 clinician withheld treatment due to lack of clinically significant symptoms. We estimate that 20% of the reported HO-CDI cases were patients with colonization and without active infection (asymptomatic-colonization and colonization with self-limited symptoms groups combined). Treating colonized patients with antibiotics is not a recommended practice and may predispose them to colonization with multidrug-resistant organisms.[1,13,31]

This study had several limitations. Our study subjects were inpatients at a single urban academic medical center and were most likely sicker than the general population. CDI is also most commonly seen in adult populations, and the selected age group for participation in this study was 18 years or older. However, CDI is now being recognized as a growing problem within the pediatric population, and rates are rising among hospitalized children.[24,25] Children were not represented in this study, although similar challenges exist in both the hospital and community setting with respect to testing practices in this population.[24] Inconsistent chart documentation of gastrointestinal symptoms was also a limitation in the setting of a retrospective study design. While a retrospective chart review was more feasible than a prospective study, inconsistent documentation practices made it difficult to determine the presence of diarrhea. Clinicians would frequently document that the patient experienced diarrhea prior to testing, but the actual number of diarrheal episodes was not always recorded in the intake and output flow sheet by nursing staff members. Alternatively, nursing staff members would sometimes document multiple episodes of diarrhea, whereas clinicians would document "no complaints of diarrhea" or not even mention the presence of diarrhea at all. Documentation of bowel movement consistency was also missing at times. It is also possible that misclassification within the 6 groups occurred due to discharge or death shortly after testing. The colonization with self-limited symptoms group in particular could be underestimated, as this group was composed of patients whose diarrhea resolved within 24 hours of specimen collection. The presence of pseudomembranous colitis may have also prompted CDI testing; however, in this study, imaging tests and colonoscopies were not reviewed.

Healthcare facilities nationwide continue to struggle with high HO-CDI rates despite substantial efforts to improve infection control practices. The NHSN LabID surveillance definition lacks clinical criteria and, therefore, may be overestimating the true incidence of HO-CDI. This is supported by a whole-genome sequence study of isolates that demonstrated that a minority (38%) of cases were the result of in-hospital transmission.[26] While this overestimation is undesirable, the lack of clinical criteria in LabID surveillance does give healthcare facilities incentive to improve the process of care for patients with CDI. Currently, CMS uses HO-CDI as part of its hospital-acquired conditions program, which penalizes the reimbursement of hospitals falling into the bottom quartile.[32] To avoid financial penalties of inflated case reporting, healthcare facilities are incentivized to reduce delays in testing and ensure that testing is performed for appropriate clinical indications. Not only can these process improvements reduce inaccurate reporting, but, more importantly, they can potentially improve the quality of care for patients through timely diagnosis and reductions in unnecessary antibiotic use. *C. difficile* colonization in the setting of other plausible etiologies of diarrhea also presents a challenge to accurate reporting. There are no standardized surveillance definitions to distinguish colonization from infection, and further study to validate clinical criteria is needed to improve the accuracy of HO-CDI surveillance. Incorporating clinical criteria into a new *C. difficile* surveillance definition must be balanced against the labor-intensive process of conducting clinical case reviews and the challenges of ensuring consistent application of the definition across all institutions. An ideal situation would harness data from the electronic medical record to not only detect LabID cases but also to identify recent laxative use, episodes of diarrhea from the flow sheet, and alternative reasons for diarrhea, such as tube feedings or chemotherapy. However, barriers to such an approach include variability in clinical documentation of the frequency and characteristics of bowel movements, access to electronic documentation, and information technology resources to capture and analyze data.

In summary, we found that a significant proportion (38%) of HO-CDI cases reported to the NHSN using LabID definitions did not meet our clinical surveillance definition of HO-CDI. Ongoing review of reported HO-CDI cases is critical for guiding efforts to improve the diagnosis, treatment, and control of *C. difficile* and to ensure the reliability of HO-CDI surveillance as a meaningful quality metric.

Acknowledgements

We would like to thank Preeti Pathela, DrPH, MPH, from the Graduate Program in Public Health at Mount Sinai for her support during this study.

References

1. Cohen S, Gerding D, Johnson S, Ciaran K, Loo V, McDonald C, et al. Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the infectious diseases society of America (IDSA). Infect Control Hosp Epidemiol 2010;31:431-55.
2. The Centers for Disease Control. Antibiotic resistance threats in the United States, 2013. Available from: https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf. Accessed December 13, 2016; 2013.
3. The White House. National Action Plan For Combating Antibiotic Resistant Bacteria. Available from: https://obamawhitehouse.archives.gov/sites/default/files/docs/national_action_plan_for_combating_antibotic-resistant_bacteria.pdf. Accessed February 11, 2017; 2015.
4. Desai K, Gupta SB, Dubberke ER, Prabhu VS, Browne C, Mast TC. Epidemiological and economic burden of Clostridium difficile in the United States: estimates from a modeling approach. BMC Infect Dis 2016;16:303.
5. Marra AR, Edmond MB, Ford BA, Herwaldt LA, Algwizani AR, Diekema DJ. Failure of Risk-Adjustment by Test Method for C. difficile Laboratory-Identified Event Reporting. Infect Control Amp Hosp Epidemiol 2017;38:109-11.
6. Centers for Disease Control and Prevention. National and State Healthcare-Associated Infections Progress Report. Available from: https://www.cdc.gov/HAI/pdfs/progress-report/hai-progress-report.pdf. Accessed August 1, 2017; 2016.
7. Chitnis AS, Holzbauer SM, Belflower RM, Winston LG, Bamberg WM, Lyons C, et al. Epidemiology of community-associated clostridium difficile infection, 2009 through 2011. JAMA Intern Med 2013;173:1359-67.
8. Kuntz JL, Chrischilles EA, Pendergast JF, Herwaldt LA, Polgreen PM. Incidence of and risk factors for community-associated Clostridium difficile infection: a nested case-control study. BMC Infect Dis 2011;11:194.
9. Surveillance for C. Diff and MDRO | NHSN | CDC. Available from: https://www.cdc.gov/nhsn/ltach/cdiff-mrsa/index.html. Accessed December 29, 2016.
10. McDonald C, Bruno C, Dubberke E, Song X, Horan T, Kutty P. Recommendations for surveillance of Clostridium difficile-associated disease. Infect Control Hosp Epidemiol 2007;28:140-5.
11. Gase KA, Haley VB, Xiong K, Antwerpen CV, Stricof RL. Comparison of 2 Clostridium difficile surveillance methods: National Healthcare Safety Network's laboratory-identified event reporting module versus clinical infection surveillance. Infect Control Hosp Epidemiol 2013;34:284-90.
12. Baier R, Morphis B, Marsella M, Mermel L. Clostridium difficile surveillance: a multicenter comparison of LabID events and use of standard definitions. Infect Control Hosp Epidemiol 2013;34:653-5.
13. Kelly SG, Yarrington M, Zembower TR, Sutton SH, Silkaitis C, Postelnick M, et al. Inappropriate clostridium difficile testing and consequent overtreatment and inaccurate publicly reported metrics. Infect Control Hosp Epidemiol 2016;37:1395-400.

14. Durkin M, Baker A, Dicks K, Lewis S, Chen L, Anderson D, et al. A comparison between national healthcare safety network laboratory-identified event reporting versus traditional surveillance for clostridium difficile infection. Infect Control Hosp Epidemiol 2015;36:125-31.
15. Leekha S, Aronhalt KC, Sloan LM, Patel R, Orenstein R. Asymptomatic Clostridium difficile colonization in a tertiary care hospital: admission prevalence and risk factors. Am J Infect Control 2013;41:390-3.
16. Alasmari F, Seiler SM, Hink T, Burnham C-AD, Dubberke ER. Prevalence and risk factors for asymptomatic clostridium difficile carriage. Clin Infect Dis 2014;59:216-22.
17. Polage CR, Solnick JV, Cohen SH. Nosocomial diarrhea: evaluation and treatment of causes other than clostridium difficile. Clin Infect Dis Off Publ Infect Dis Soc Am 2012;55:982-9.
18. Polage CR, Gyorke CE, Kennedy MA, Leslie JL, Chin DL, Wang S, et al. Overdiagnosis of clostridium difficile infection in the molecular test era. JAMA Intern Med 2015;175:1792.
19. Furuya-Kanamori L, Marquess J, Yakob L, Riley TV, Paterson DL, Foster NF, et al. Asymptomatic Clostridium difficile colonization: epidemiology and clinical implications. BMC Infect Dis 2015;15:516.
20. Nissle K, Kopf D, Rösler A. Asymptomatic and yet C. difficile-toxin positive? Prevalence and risk factors of carriers of toxigenic Clostridium difficile among geriatric in-patients. BMC Geriatr 2016;16:185.
21. Su W-Y, Mercer J, Hal SJV, Maley M. Clostridium difficile testing: have we got it right? J Clin Microbiol 2013;51:377-8.
22. Dubberke ER, Burnham C-AD. Diagnosis of clostridium difficile infection: treat the patient, not the test. JAMA Intern Med 2015;175:1801.
23. Kwon JH, Reske KA, Hink T, Burnham CA, Dubberke ER. Evaluation of correlation between pretest probability for clostridium difficile infection and clostridium difficile enzyme immunoassay results. J Clin Microbiol 2017;55:596-605.
24. Antonara S, Leber AL. Diagnosis of clostridium difficile infections in children. J Clin Microbiol 2016;54:1425-33.
25. Nicholson MR, Crews JD, Starke JR, Jiang Z-D, DuPont H, Edwards K. Recurrent clostridium difficile infection in children: patient risk factors and markers of intestinal inflammation. Pediatr Infect Dis J 2017;36:379-83.
26. Eyre DW, Cule ML, Wilson DJ, Griffiths D, Vaughan A, O'Connor L, et al. Diverse sources of C. difficile infection identified on whole-genome sequencing. N Engl J Med 2013;369:1204-8.
27. Burnham C-AD, Dubberke ER, Kociolek LK, Polage CR, Riley TV. Clostridium difficile—diagnostic and clinical challenges. Clin Chem 2016;62:310-4.
28. New York State Department of Health. Hospital-Acquired Infections in New York State, 2015 Part 2:Technical Report. Available from: https://www.health.ny.gov/statistics/facilities/hospital/hospital_acquired_infections/2015/docs/hospital_acquired_infection_p2.pdf. Accessed October 17, 2017; 2017.
29. White DR, Hamilton KW, Pegues DA, Hanish A, Umscheid CA. The impact of a computerized clinical decision support tool on inappropriate clostridium difficile testing. Infect Control Amp Hosp Epidemiol 2017;38:1204-8.
30. Truong CY, Gombar S, Wilson R, Sundararajan G, Tekic N, Holubar M, et al. Real-time electronic tracking of diarrheal episodes and laxative therapy enables verification of clostridium difficile clinical testing criteria and reduction of clostridium difficile infection rates. J Clin Microbiol 2017;55:1276-84.
31. Johnson S, Homann S, Bettin K, Quick J, Calbots C, Peterson L, et al. Treatment of asymptomatic Clostridium difficile carriers (fecal excretors) with vancomycin or metronidazole. A randomized, placebo-controlled trial. Ann Intern Med 1992;117:297-302.
32. Patient Protection and Affordable Care Act. Sect. Payment adjustment for conditions acquired in hospitals, 111-148. Available from: https://www.gpo.gov/fdsys/pkg/PLAW-111publ148/pdf/PLAW-111publ148.pdf; 2015. Accessed October 6, 2017.