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A national survey of testing and management of asymptomatic carriage of *C. difficile*

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Abstract

A nationwide survey indicated that screening for asymptomatic carriers of *C. difficile* is an uncommon practice in US healthcare settings. Better understanding of the role of asymptomatic carriage in *C. difficile* transmission, and of the measures available to reduce that risk, are needed to inform best practices regarding the management of carriers.

Recognized as one of the most important pathogens in healthcare settings, *Clostridioides difficile* resulted in half a million infections among US inpatients in 2011.[1] Although much is known about the contribution of symptomatic patients to transmission of *C. difficile* in healthcare settings, asymptomatic *C. difficile* colonization has recently garnered attention as a potential reservoir for transmission. Asymptomatic carriage is being increasingly recognized among hospitalized adults, which has resulted in anecdotal reports of identification and isolation of these patients despite a lack of recommendations on testing or management. We conducted a survey to assess current clinical testing practices for asymptomatic carriers of *C. difficile* and to determine whether such testing is common.

Methods

The Infectious Diseases Society of America (IDSA) Emerging Infections Network (EIN) is a provider-based emerging infections sentinel network,[2] which is funded by the Centers for Disease Control and Prevention (CDC) and sponsored by the IDSA. EIN surveyed 1,309 US-based adult infectious disease specialists from November 29 through December 23, 2017. Two reminders followed an initial invitation by e-mailed link or faxed paper copy

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to nonresponders. No incentive for participation was provided. A confidential 9-question multiple choice/open-ended survey contained questions regarding identification of patients with asymptomatic carriage of *C. difficile*, isolation, and management. Data analysis was performed with SAS version 9.4 software (SAS Institute, Cary, NC). For open-ended questions, comments were systematically reviewed, coded for relevant themes, and grouped into categories.

Results

A total of 679 EIN physician members completed the survey, for a response rate of 52%. Of these, 105 respondents (15%) indicated that they had not seen patients with symptomatic CDI in the past 6 months and were excluded from further analysis; none of these 105 respondents reported testing asymptomatic patients. The remaining 574 (85%) respondents indicated that they had seen patients with symptomatic *C. difficile* infection (CDI) in the past 6 months. Of these, 166 (29%) worked in a hospital with >600 hospital beds, and 523 (91%) indicated that the nucleic acid amplification test (NAAT) was either conducted as a single step or in multistep algorithm laboratory testing for symptomatic *C. difficile* (Table 1). Of the 574 respondents, 22 (4%) indicated testing patients for asymptomatic carriage of *C. difficile*. Of these 22 respondents, 36% practiced in university-affiliated hospitals and 32% in >600 bed hospitals (Table 1).

Of those who reported testing patients to detect asymptomatic carriers, the reasons for screening included (1) being cared for on selected units (n = 11, 50%) such as intensive care and oncology/hematopoietic cell transplant units, having a previous history of CDI (n = 5, 23%), (2) being in long-term care prior to admission (n = 4, 18%), and (3) being part of a hospital-wide nonselective screening approach (n = 4, 18%). Rectal swab (n = 11, 50%) was the most common specimen tested. Once asymptomatic carriage of *C. difficile* was detected, contact precautions were most often instituted, followed by enhanced environmental cleaning (Fig. 1). Of those who reported using antibiotic prophylaxis (n = 10) in detected asymptomatic carriers, oral vancomycin (80%) was the most commonly used antibiotic. The most common reasons for prescribing antibiotic prophylaxis included use of other antibiotics (50%) and because carriage was identified (40%). Among asymptomatic carriers who developed diarrhea (n = 18), repeat *C. difficile* testing was performed in 44%; empiric treatment without repeat testing was started in 39%.

Discussion

A nationwide survey among US infectious disease physicians indicated that screening for asymptomatic carriers for *C. difficile* among hospitalized adults was uncommon. The low occurrence of screening for asymptomatic carriers may be indicative of uncertainty regarding their contribution to transmission, lack of data on how to act on this information, and costs associated with active surveillance. In addition, at the time of the survey, the guidelines recommended neither detection nor management of such patients.[3] The current 2017 IDSA/SHEA guidelines reiterate this recommendation.[1]

Prevalence of asymptomatic colonization in the community settings has varied from 0% to 18% among healthy adults.[4,5] In acute-care settings, colonization has ranged from 5% to 21%, and in long-term care facilities colonization has ranged from 0% to 51%.[6,7] Approximately 15% of asymptomatic carriers receive the diagnosis of CDI.[1] Based on the existing but limited information, the incubation period is considered relatively short in most patients. However, the etiology of diarrhea in previously asymptomatic carriers, whether due to *C. difficile* or other causes, may be unclear. Additionally, asymptomatic carriers, including those who have recovered from CDI but remain colonized, may have developed antibodies that protect them from the effects of *C. difficile* toxins, but may still serve as a potential reservoir for transmission to others within a healthcare setting and in the community.[7,8]

The most common reasons reported for screening in this survey were concerns about CDI in vulnerable patient populations (intensive care units, oncology and/or HCT units, previous history of CDI) and the previous location where the patient resided. The survey did not ask at what point during the patient's hospital care that screening was performed. Although real-time interventional studies are scarce, mathematical modeling studies predict that screening for *C. difficile* carriage on admission could mitigate healthcare-associated CDI (HA-CDI) when bundled with other prevention measures.[8,9] A single-center quasi-experimental study by Longtin et al[8] demonstrated a 62% reduction in the rates of CDI after implementing an active surveillance protocol. In a recent study of outbreaks, the same authors did not find a difference in rates when screening was instituted.[10] Currently, patient screening either at the time of hospital admission or during hospitalization is not recommended.[1] Although rectal swabs were the most commonly reported screening specimen, often the perirectal swab is used. Perirectal swab samples have 70%–99% sensitivity for the detection of *C. difficile* colonization, which is comparable with rectal swab samples; however, perirectal swabs are less invasive and may be used in patients with neutropenia.[7]

Of concern is the use of antibiotics in carriers. As mentioned earlier, at the time of this survey, the 2014 Strategies update recommended against treatment or decolonization of asymptomatic carriers.[3] This has been reiterated in the recent IDSA/SHEA updated clinical practice guidelines, which recommend against treatment if such a patient were to be identified due to the lack of evidence.[1] Treatment of carriers failed to show benefit in eradicating disease or reducing rates of HA-CDI and studies suggest that oral vancomycin may be particularly disruptive to the microbiome and may increase the risk for CDI once stopped.[11]

The results of this survey may not be generalizable because the survey was sent to EIN members who may not be representative of the majority of infectious disease physicians. In addition, self-reported responses may be subject to bias.

Screening to detect asymptomatic carriers appears to be an uncommon practice. Future studies that improve our understanding of asymptomatic *C. difficile* carrier epidemiology (including burden), risk they pose for transmission (eg, duration of shedding, contagiousness, infectious dose), and of the effects of interventions that might prevent transmission to others (eg, transmission-based precautions, use of antibiotics, and

unintended consequences) may better inform those who identify and manage these patients, and how these patients impact transmission within healthcare settings.

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Conflicts of interest.

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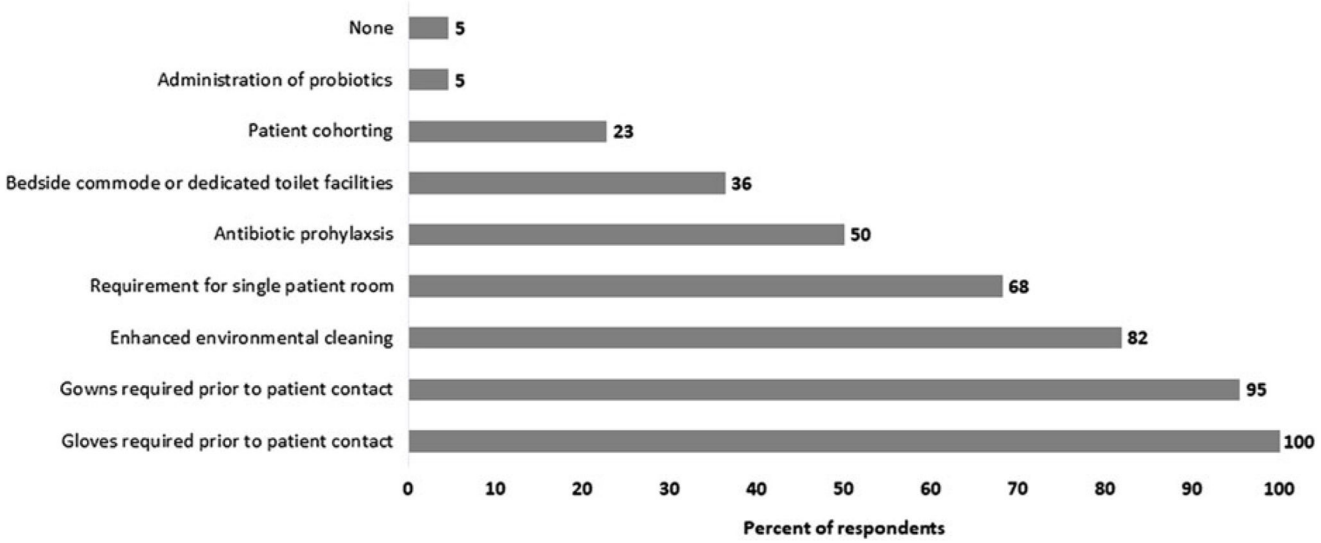

Fig. 1.

Reported interventions when asymptomatic *C. difficile* carriers were detected, Emerging infections Network Survey, 2017 (n = 22).

Table 1.

Characteristics of Respondents and Those That Responded Affirmatively to Testing for Asymptomatic Patients, EIN Survey, 2017

Variable	Respondents (n = 574), No. (%)	Responded Affirmatively to Testing for Asymptomatic *C. difficile* (n = 22), No. (%)
Practice Characteristics		
Type of Hospital		
University hospital	190 (33)	8 (36)
Community hospital	169 (29)	6 (27)
Non-university teaching hospital	148 (26)	5 (23)
VA hospital or DOD	37 (7)	1 (5)
City/Council hospital	30 (5)	2 (9)
Region		
New England	52 (9)	1 (5)
Mid Atlantic	78 (13)	2 (9)
East North Central	80 (14)	10 (45)
West North Central	55 (10)	0
South Atlantic	102 (18)	0
East South Central	30 (5)	0
West South Central	36 (6)	1 (5)
Mountain	26 (5)	2 (9)
Pacific	113 (20)	6 (27)
Puerto Rico	2 (0.4)	0
Hospital bed size		
<200	63 (11)	3 (14)
200–350	138 (24)	3 (14)
351–450	92 (16)	4 (18)
451–600	115 (20)	5 (22)
>600	166 (29)	7 (32)
Survey Answers		
Approximately how many patients with symptomatic CDI have you seen in the past 6 months?		
1–10	196 (34)	6 (27)
11–25	232 (40)	6 (27)
26–50	99 (17)	5 (23)
>50	47 (8)	5 (23)
Type of testing for symptomatic CDI		
Single test		
C. difficile included in a GI panel of multiple pathogens	8 (1)	1 (5)
NAAT only, eg, PCR or LAMP	310 (54)	11 (50)
EIA for toxin only	11 (2)	0

Variable	Respondents (n = 574), No. (%)	Responded Affirmatively to Testing for Asymptomatic *C. difficile* (n = 22), No. (%)
Multistep test		
Combination of NAAT (including GI panel) and other tests (eg, GDH, EIA, toxigenic culture)	213 (37)	7 (31)
Combined EIA for glutamate dehydrogenase (GDH) assay and toxin	15 (3)	2 (9)
GDH EIA followed by cell cytotoxicity neutralization assay or toxin	8 (1)	1 (5)
Not sure	9 (2)	0

Note. VA, Veterans Affairs; DOD, Department of Defense; NAAT, nucleic acid amplification test; PCR, polymerase chain reaction; LAMP, loop-mediated isothermal amplification EIA, enzyme immunoassay; GI, gastrointestinal; GDH, glutamate dehydrogenase.