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## Infection Prevention in Practice

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## Short Report

# Prospective Review of *Clostridioides difficile* Testing Indications to Inform Local Laboratory Stewardship Initiatives

Noah Reich<sup>a</sup>, Michael Payne<sup>a,b,c</sup>, Azra Sharma<sup>c</sup>, Sylvie Champagne<sup>a,b</sup>,  
 Marc G. Romney<sup>a,b</sup>, Michelle Hinch<sup>d</sup>, Victor Leung<sup>a,b,c,d</sup>,  
 Christopher F. Lowe<sup>a,b,c,\*</sup>

<sup>a</sup> Faculty of Medicine, University of British Columbia, Canada

<sup>b</sup> Division of Medical Microbiology, St. Paul's Hospital, Vancouver, BC, Canada

<sup>c</sup> Infection Prevention and Control, Providence Health Care, Vancouver, BC, Canada

<sup>d</sup> Antimicrobial Stewardship Program, Providence Health Care, Vancouver, BC, Canada

## ARTICLE INFO

## Article history:

Received 2 July 2019

Accepted 29 July 2019

Available online 5 August 2019

## Keywords:

*Clostridioides difficile*

Infections

Diagnostic Stewardship

Pre-analytical

Laxative



## SUMMARY

We conducted a prospective chart review to determine the prevalence of and reasons for inappropriate *Clostridioides difficile* test-ordering at a tertiary care hospital. Inappropriate orders accounted for 54% of all tests. The two primary aetiologies of inappropriate test-ordering were an alternative reason for diarrhoea (34%) and an asymptomatic patient (20%). These results highlight the need to focus diagnostic stewardship of *C. difficile* testing on pre-analytical factors.

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## Background

*Clostridioides difficile*, a spore-forming Gram-positive bacillus, is the most common cause of healthcare-associated diarrhoea in North America [1]. Following the NAP1 outbreak in the early 2000's, the incidence of *C. difficile* in Canada has

been decreasing since 2009, in particular the NAP1/Ribotype 027 strain incidence has decreased [2].

Diagnostic testing for *C. difficile* in the microbiology laboratory is primarily based on molecular testing (polymerase chain reaction; PCR) or toxin enzyme immunoassay. The optimal laboratory diagnostic strategy continues to evolve, with algorithms including both testing modalities favoured over standalone testing [3]. Utilization of PCR testing alone cannot differentiate colonization from infection, and has been associated with overdiagnosis and unnecessary treatment of

\* Corresponding author. Christopher Lowe, MD, FRCPC, St. Paul's Hospital, Virology Laboratory, 1081 Burrard St., Vancouver, V6Z 1Y6 BC, Canada. Tel.: +604 806 8422.

E-mail address: [clowe@providencehealth.bc.ca](mailto:clowe@providencehealth.bc.ca) (C.F. Lowe).

*C. difficile* [4]. This may be further exacerbated by the declining prevalence of *C. difficile* infections (CDIs).

Given the imperfect testing methods, an emphasis on diagnostic stewardship is imperative to avoid unwanted outcomes associated with over-testing of *C. difficile* and over-diagnosis of CDIs. Prioritizing the pre-analytical process of laboratory testing avoids excess cost associated with testing, delays in reporting a result (even if the laboratory cancels) and over-reporting of positive *C. difficile* results. However, prior to implementing *C. difficile* diagnostic stewardship within our facilities, it was important to understand the underlying motivations for testing by clinicians to target stewardship initiatives. Therefore, we sought to determine the prevalence of and reasons for inappropriate CDI testing at a Canadian tertiary care hospital.

**Material and methods**

A pilot prospective chart review was conducted for all inpatients admitted to our tertiary care hospital with a *C. difficile* test ordered and accepted for testing in the microbiology laboratory from April 26<sup>th</sup> to May 28<sup>th</sup>, 2018. Data collected in the chart review included clinical history, symptoms, vital signs, laboratory data (WBC, creatinine), alternative reasons for diarrhoea (laxative use within 48 hours of testing, nasogastric tube or enteral feed, current chemotherapy), type of ordering clinician and *C. difficile* test results. *C. difficile* testing at our laboratory is based on the reverse algorithm as previously described [5]. Rejection criteria included testing only unformed stool samples. If repeat testing was ordered, the microbiology laboratory would only test samples on the same patient after four days with a previous negative test result and after 30 days with a previous positive test result.

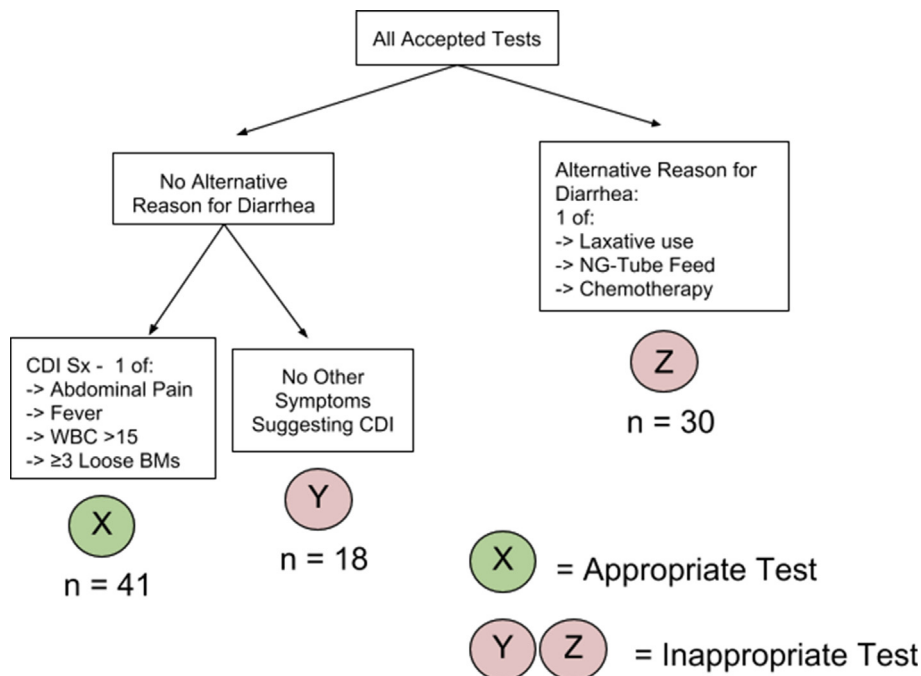
*C. difficile* orders were categorized as appropriate or inappropriate based on clinical presentation and identification of alternative reasons for diarrhoea (Figures 1 and 2). Statistical analysis of categorical variables was performed with the Chi-square method [6]. Research ethics board approval was obtained.

**Results**

A total of 89 charts were reviewed. The median length of stay prior to *C. difficile* test was three days (mean seven days). The order location was distributed as follows: Medicine (51), Surgery (12), Critical Care (14), Emergency (11) and Palliative Care (1). Overall, 41 (46%) tests were considered appropriate, while 48 (54%) tests were assessed as inappropriate. Physicians ordered 68 (76.4%) tests and nurses initiated 21 (23.6%) tests. A discrepancy in appropriateness of testing between the two groups was observed with 85.7% of nurse-initiated tests being inappropriate while 44.1% of physician-initiated tests were inappropriate (p = 0.00083).

Determination of inappropriateness was analyzed two different ways, based on which factor was assessed first in the chart review (presence of an alternative reason for diarrhoea or presence of ≥3 loose bowel movements). If alternative reasons for diarrhoea were reviewed first (Figure 1), 34% had an alternate reason for diarrhoea (category Z), with further review of clinical symptoms identifying 20% without clinical symptoms consistent with CDI (Category Y). Of the patients with an alternative reason for diarrhoea, 16 (53%) of them were due to laxative use, 4 (13%) due to laxative use and an NG-tube feed, 7 (23%) due to an NG-tube feed only, and 3 (10%) due to recent chemotherapy. Laxative use was involved in 20 (42%) of all the inappropriate tests (n=48).

Review of the patients based on symptoms (≥3 loose bowel movements in 24 hours), is presented in Figure 2, with no



**Figure 1.** *Clostridioides difficile* test appropriateness categorization stratified by the presence of an alternative reason for diarrhoea.

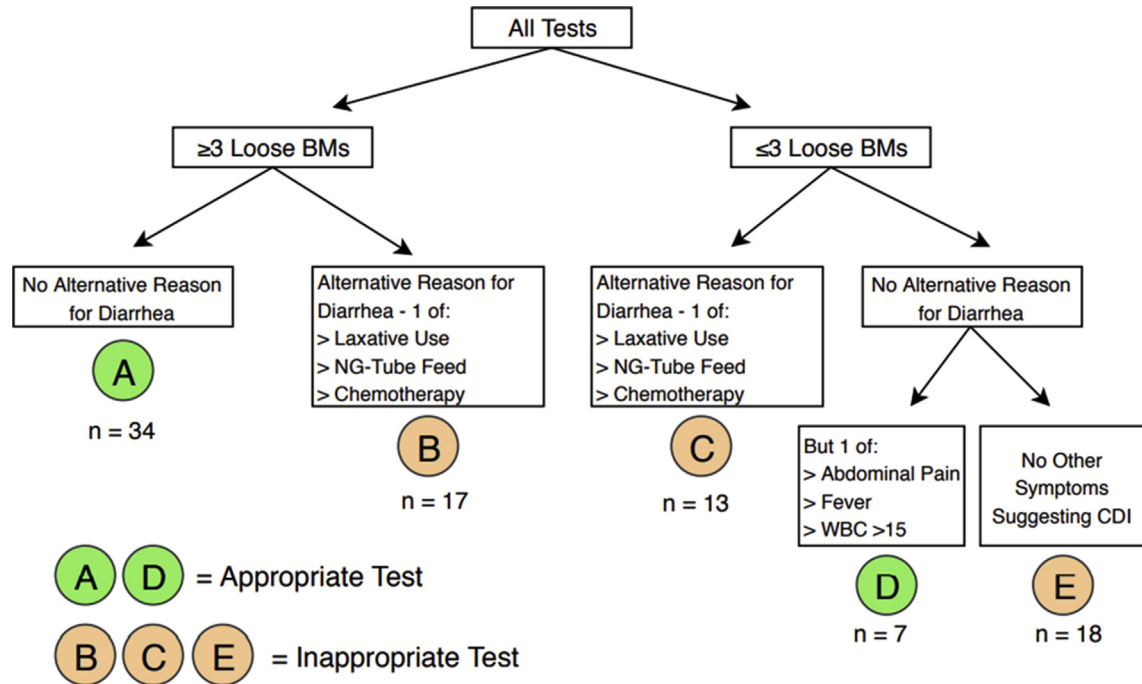


Figure 2. *Clostridioides difficile* test appropriateness categorization stratified by the presence of  $\geq 3$  loose bowel movements.

difference in the number of appropriate and inappropriate tests compared to Figure 1. Initial review of bowel movements identified 57% (51/89) patients with  $\geq 3$  loose bowel movements, with 33% (17/51) associated with an alternative reason. For patients with  $< 3$  bowel movements, 82% (31/38) were considered inappropriate while 18% (7/38) had a sign or symptom of a possible CDI.

One of the consequences of inappropriate test-ordering is excess costs to the laboratory. The direct laboratory costs associated with unnecessary testing in this 31-day study was estimated at \$2347.68 CAD (48 inappropriate tests at \$48.91/test based on provincial billing) [7]. Extrapolation of these costs to one year gives the estimate of excess costs to be \$27,642.04 CAD.

## Discussion

Inappropriate *C. difficile* test ordering was prevalent in our hospital, representing 54% of all *C. difficile* tests ordered during the evaluation. Similar results have been reported at other facilities, with inappropriate testing estimated to represent 9–44% of tests [8,9]. A primary driver of inappropriate ordering is related to concurrent laxative administration within the previous 48 hours of ordering a *C. difficile* test [10]. Hospitals and laboratories have utilized technology to try to address this pre-analytical issue, specifically with electronic medical records (EMR) and computerized physician order entry. Reduction in *C. difficile* testing has been achieved, either by prompting clinicians to confirm appropriate testing or restriction of test ordering unless specific criteria were met ( $> 2$  loose bowel movements in 24 hours, no recent laxative use) [9,10]. With laxatives being a primary driver of inappropriate testing, healthcare facilities can potentially utilize electronic order entry to improve test ordering. Implementing automated order restrictions or reminders in EMR, such as a review of the

medication administration record when a *C. difficile* test is ordered, despite recent laxative administration, can be a useful tool in prompting the clinician to consider alternatives prior to ordering *C. difficile* testing.

The 2018 SHEA/IDSA *C. difficile* guidelines continue to recommend that testing should only be conducted in patients who have three or more loose stools in a 24 hour period [3]. In our review, 20% of testing was considered inappropriate based on the lack of symptomatology. At our facility, clinicians (nurses and physicians) can collect and order *C. difficile* testing. In discussion with frontline providers, stool might be collected by a frontline nurse if they notice a patient has a loose stool, as there is a fear that they may not get an adequate sample later on. In addition, the number of loose stools is a highly subjective measure. Historically, the number of loose stools required to meet the definition of diarrhoea has varied from  $\geq 3$  episodes to  $> 6$  [3]. At an individual level, assessing the number of stools by a patient is dependent on factors such as patient reliability, frequency in which a HCW assesses the patient and consistency of documentation in the patient's chart. Our chart review indicated that categorizing inappropriateness initially by either number of loose stools or alternate reason for diarrhoea were similar, and perhaps education around reducing inappropriate tests may be more effective by focusing HCW's on an objective measure (i.e. laxative use) rather than a subjective measure (number of loose stools).

Limitations of this study included that it was performed only in a single center over a relatively short period of time. During this study period, the clear majority of tests were negative by PCR method (82/89) and there were four cases of colonization and only three cases of infection. This lowered the pre-test probability of *C. difficile* and potentially affected appropriateness of testing. However, the rates of inappropriate test were similar to previous reports [8,9]. Lastly, the medication review for each patient was not all-inclusive, but based on

available medical records; this could have underestimated the number the patients having alternative reasons for diarrhoea in the study.

Our review of *C. difficile* test indications identified that the majority of samples submitted and tested were considered inappropriate. Laxative administration was a frequent contributor to inappropriate testing. Diagnostic stewardship initiatives targeting such issues will depend on local infrastructure and resources, and in the absence of a technological upgrade in EMR, targeted education for clinicians ordering the test (physicians and nurses) is still required. Highlighting laxative administration in education sessions may be a useful and objective supplemental message to the traditional focus on number of bowel movements.

## Acknowledgments

We would like to acknowledge the microbiology laboratory staff for their dedication to providing quality laboratory testing, as well as the physicians at our facility for their openness to having a discussion regarding *C. difficile* testing and management.

## Conflict of Interest

None.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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