It Is Not about the Assay: Preanalytical Screening Is the Key to Reducing *Clostridioides difficile* Infection

Siu-Kei Chow,[a] Azita Naderpour,[b] Julianna Van Enk[c]

[a]Department of Microbiology, Laboratories Northwest, MultiCare Health System, Tacoma, Washington, USA
[b]Office of Infection Control, MultiCare Health System, Tacoma, Washington, USA
[c]Department of Pharmacy Services, MultiCare Health System, Tacoma, Washington, USA

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Clostridioides difficile (formerly *Clostridium difficile*) infection (CDI) is one of the most common health care-associated infections in the United States, resulting in significant morbidity, deaths, and economic burdens (1). Whether a *C. difficile* nucleic acid amplification test (NAAT) alone or a two-step algorithm involving a toxin enzyme immunoassay (EIA) should be used for better diagnosis of CDI is still controversial (2). Here we describe the achievement of reducing the hospital-onset CDI (HO-CDI) rate by 61% by implementing a simple computerized support tool (CST) coupled with education to enforce preanalytical screening for *C. difficile* testing.

We conducted a retrospective study at four hospitals (total capacity of 1,048 beds) of the MultiCare Health System, reviewing the laboratory-identified (LabID) HO-CDI events defined by the National Healthcare Safety Network (NHSN) (onset on hospital day >3) and *C. difficile* test volumes before and after the introduction of a CST coupled with education. The preintervention period spanned 12 months (January 2015 to December 2015), the intervention period spanned 3 months (January 2016 to March 2016), and the postintervention period spanned 24 months (April 2016 to March 2018). The diarrheal episodes, laxatives administered, and treatment for the LabID HO-CDI events were analyzed. In this study, true HO-CDI was defined as clinically significant diarrhea (≥3 unformed stools within 24 h) with onset on hospital day >3, without laxatives administered within 48 h prior to *C. difficile* testing (3). The laboratory uses a standalone *C. difficile* NAAT (BD MAX Cdiff assay; Becton, Dickinson, Franklin Lakes, NJ) for unformed stool specimens rating 6 or 7 on the Bristol stool scale. The CST was built in our hospital information system (Epic, Verona, WI) for use prior to the placement of a *C. difficile* test order. The ordering provider is prompted to answer 2 or 3 questions, depending on the age of the patient. No *C. difficile* testing is allowed for children <1 year of age; therefore, such orders cannot be processed in Epic. For patients >2 years of age, the ordering provider must indicate (i) whether the patient had ≥3 unformed stools in the past 24 h and (ii) whether the patient has severe ileus or toxic megacolon. For patients 1 to 2 years of age, the ordering provider must answer a third question about obtaining test approval from an infectious diseases specialist, a gastroenterologist, or the director of microbiology. In addition to the mandatory questions, a best practice alert appears for all *C. difficile* test orders, reminding the provider not to test if the patient has received laxative or stool softener in the past 48 h. Data analyses were performed using the t test for continuous variables, the Z test for proportions, and the χ^2 test for categorical variables. All statistical tests were 2 tailed, with P values of ≤0.05 being considered statistically significant.

Between January 2015 and March 2018, a total of 377 LabID HO-CDI events were reported. Upon review, 7 events were excluded from this study; 3 events not meeting the NHSN criteria were misclassified as HO-CDI, and 4 events involved severe ileus or
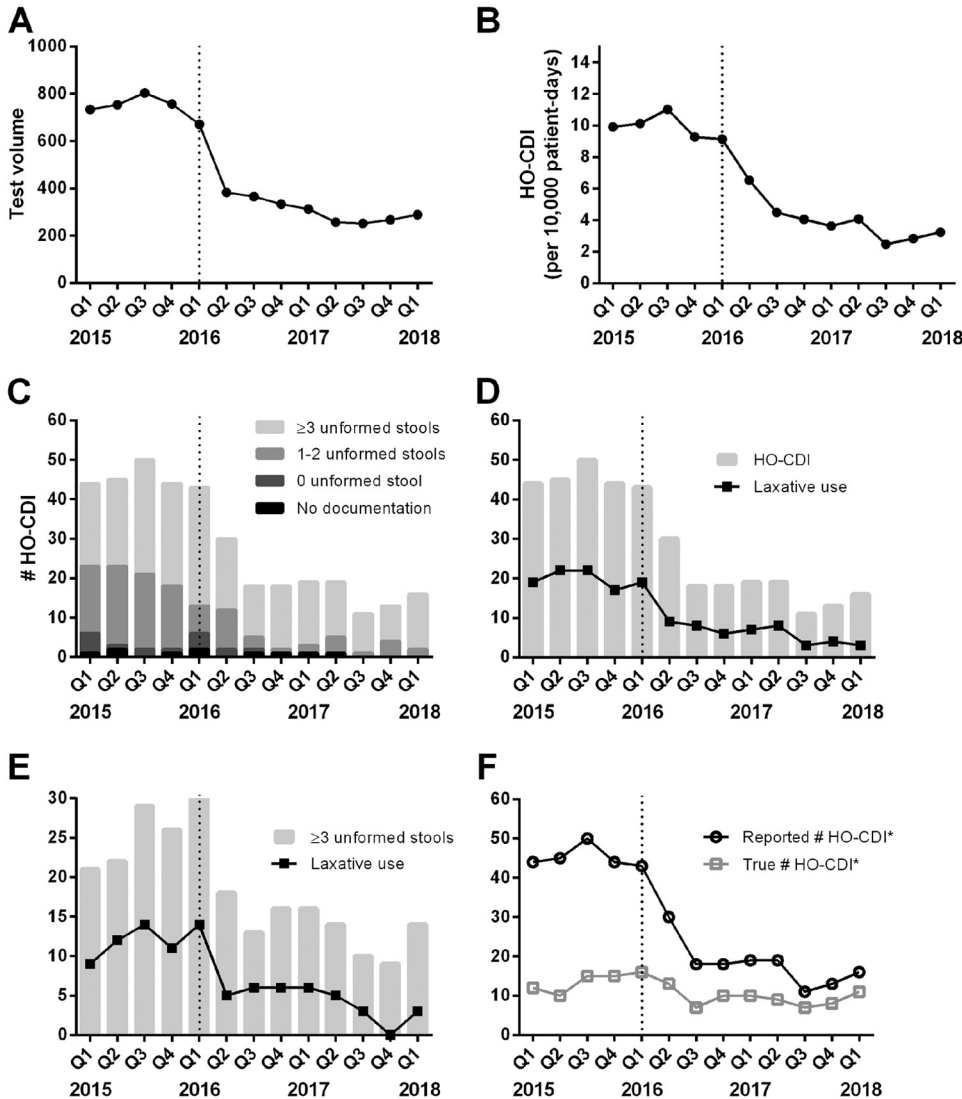
FIG 1 Changes in *Clostridioides difficile* tests and CDI cases from January 2015 to March 2018, divided into quarters, with the dotted line indicating 2016 quarter 1 as the intervention period. (A) *C. difficile* test volumes for inpatients. (B) Reported HO-CDI rates. (C) Distribution of diarrheal episodes among LabID HO-CDI events. (D) Laxative use among LabID HO-CDI events. (E) Laxative use among LabID HO-CDI events with clinically significant diarrhea, defined as ≥3 unformed stools within 24 h prior to testing. (F) Numbers of reported HO-CDI events and true HO-CDI events, after removal of events with laxative use and/or insignificant diarrhea (<3 unformed stools within 24 h). The asterisks indicate the exclusion of 3 cases of non-HO-CDI events and 4 cases involving ileus or the use of a rectal tube throughout the study period.

the use of a rectal tube, such that the typical definition of clinically significant diarrhea (≥3 unformed stools within 24 h) did not apply. During the study period, *C. difficile* test volumes decreased by 60% (mean ± standard deviation, 762 ± 30 tests/quarter pre-intervention versus 308 ± 50 tests/quarter postintervention; $P < 0.001$) (Fig. 1A). The HO-CDI rate decreased by 61% (10.1 cases/10,000 patient days preintervention versus 3.9 cases/10,000 patient days postintervention; $P < 0.001$) (Fig. 1B). Tests in cases with ≥3 unformed stools increased from 53% to 78% (from 98 of 183 cases to 110 of 144 cases; $P < 0.001$) (Fig. 1C). Tests in cases with prior laxative use decreased from 44% to 33% (from 80 of 183 cases to 48 of 144 cases; $P = 0.003$) (Fig. 1D). Among the events with clinically significant diarrhea, the percentage of cases with prior laxative use decreased from 47% to 31% (from 46 of 98 cases to 34 of 110 cases; $P = 0.002$) (Fig. 1E). After removal of events with insignificant diarrhea (<3 unformed stools within 24 h) and pretest laxative use, the numbers of true HO-CDI events were 13.0 ± 2.4 events/
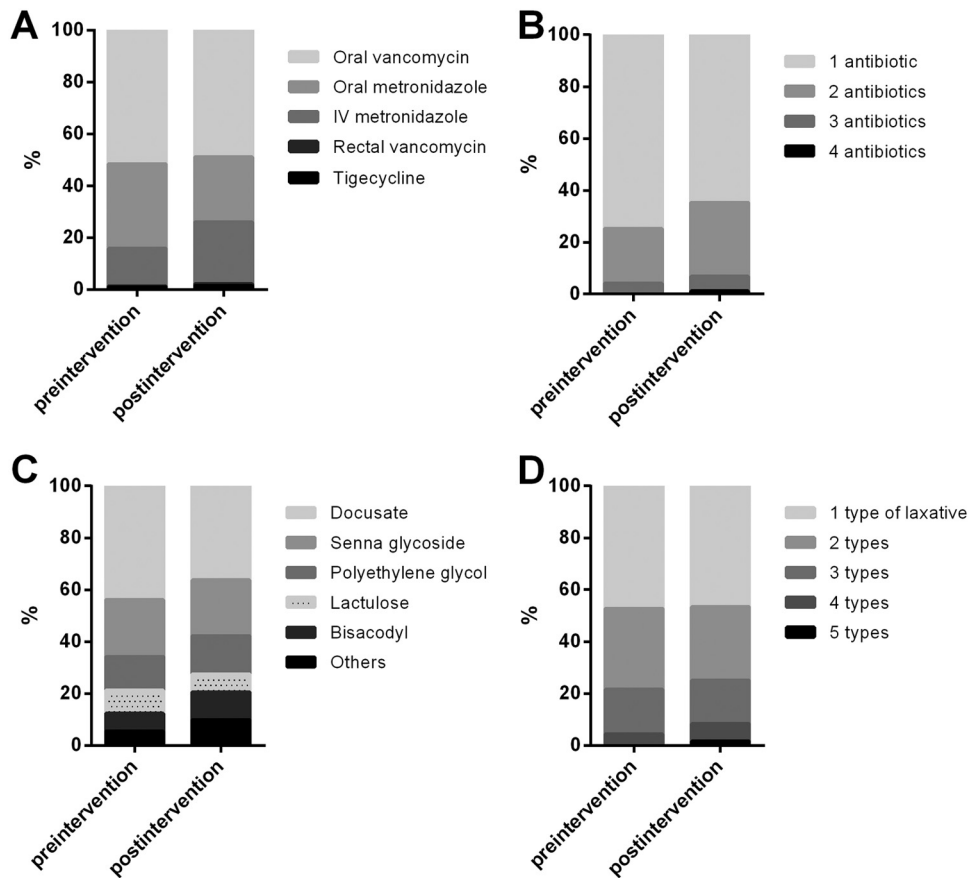
FIG 2 Treatment for cases with positive *C. difficile* results and laxative use preintervention (January 2015 to December 2015) and postintervention (April 2016 to March 2018). (A) Type and route of antibiotics for *C. difficile* treatment (preintervention, $n = 221$; postintervention, $n = 270$). IV, intravenous. (B) Number of different types/ routes of antibiotics per patient (preintervention, $n = 171$; postintervention, $n = 141$). (C) Type of laxatives administered within 48 h prior to *C. difficile* testing (preintervention, $n = 146$; postintervention, $n = 102$). (D) Number of different types of laxatives, administered within 48 h prior to *C. difficile* testing, per patient (preintervention, $n = 80$; postintervention, $n = 48$).

quarter preintervention and 9.4 ± 2.1 events/quarter postintervention ($P = 0.02$) (Fig. 1F). During the preintervention period, there was a 71% difference in the overall number of reported HO-CDI cases, compared to true HO-CDI cases; this difference was reduced by 23% postintervention ($P < 0.001$) (Fig. 1F). The percentage of patients who received treatment increased insignificantly, from 93% to 98% (from 171 of 183 patients to 141 of 144 patients; $P = 0.1$), whereas 95% of patients with inappropriate testing were treated. The variety and type of antibiotics that patients received did not change significantly during the study period ($P > 0.1$) (Fig. 2A and B). The variety and type of laxatives showed no significant changes before versus after the intervention ($P > 0.2$) (Fig. 2C and D).

This study demonstrates the effectiveness of a CST coupled with education to reduce HO-CDI. We highlight that testing of patients without clinically significant diarrhea or with prior laxative use accounted for as much as 70% of reported LabID HO-CDI events. Similar to findings others have reported (3), 95% of patients with inappropriate testing received treatment. Inappropriate testing of unformed stools from patients who received laxative therapy remains a challenge (4), as this clinical parameter is seldom accessible to laboratorians except using a real-time monitoring system (5). Therefore, it is crucial to educate care providers that testing patients with a low pretest probability of disease leads to false-positive test results, unnecessary treatment, and increased costs (6, 7). One caveat of the CST is that its effectiveness

relies on the integrity of the ordering providers answering the questions in Epic. However, we anticipate the HO-CDI rate to decrease further with future implementation of a hard stop on test orders with laxative use within the previous 48 h, instead of simply having the reminder in the best practice alert.

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