Reductions in *Clostridium difficile* Infection (CDI) Rates Using Real-Time Automated Clinical Criteria Verification to Enforce Appropriate Testing

Clostridium difficile infection (CDI) is diagnosed in more than 450,000 patients annually.¹ *Clostridium difficile* infection rates increased 3.5-fold from 2000 to 2008, coinciding with the widespread adoption of highly sensitive polymerase chain reaction (PCR)–based testing, which cannot distinguish between colonization and active colitis.² Asymptomatic colonization can be present in 20%–40% of hospitalized patients, and inappropriate CDI testing can lead to false-positive tests and unnecessary treatment.^{2,3} While controversy over the optimal CDI testing method continues, strategies to enforce clinically appropriate testing are urgently needed.^{4–6}

We created a real-time computer physician order entry (CPOE) alert to enforce appropriate *C. difficile* testing and to reduce CDI rates.

METHODS

We conducted a pre- versus postintervention cohort study to evaluate C. difficile testing in adults hospitalized at a 417-bed academic hospital between April 1, 2015, and June 30, 2017. The baseline period (April 1, 2015, through March 31, 2016) and the intervention period (June 1, 2016, through June 30, 2017) were compared, excluding a 3-month phase-in period (April 1, 2016, through June 30, 2016). The PCR-based CDI testing method remained unchanged throughout the study period. The intervention involved automated real-time CPOE verification to enforce appropriate CDI testing criteria: (1) diarrhea (\geq 3 liquid/watery stools in 24 hours), (2) no alternate cause for diarrhea, (3) no laxative use within 24 hours, (4) no previous CDI test result within 7 days, and (5) age >1 year.^{5,6} Clinicians were required to attest to criteria 1 and 2; criteria 3-5 were programmed to autopopulate the ordering screen, including laxative name and time administered if given within 24 hours. Any contraindication to testing resulted in a "hard stop" prompt instructing prescribers to either exit the order or to submit the name of an approving infectious diseases (ID) or gastrointestinal (GI) physician to override hospital protocol (see Supplemental Figure 1).

To ensure adherence, infection preventionists reviewed overrides weekly. Approving ID and/or GI physician names were verified, and physicians placing orders without appropriate approval received a warning e-mail signed by ID and/or GI leadership and the Chief Medical Officer (CMO) that reiterated protocol criteria and reminded physicians that orders without approval are being monitored. An e-mail with the following text was sent to physicians who did not seek proper approval for *C. difficile* testing when ordering criteria were not met: "We received notification that you have input false or non-ID/GI physician names for approval of *C. difficile* testing in patients who were either (1) already tested within 7 days or (2) had received laxatives within 24 hours. Testing outside of these parameters requires careful clinical consideration and approval from ID/GI specialists. Ordering without approval is being monitored. Repeat inappropriate orders will be reported to your Division Chief, Department Chair, and Chief Medical Officer."

We evaluated the following: (1) National Healthcare Safety Network (NHSN) case counts per 10,000 patient days and standardized infection ratios (SIRs), (2) tests ordered in patients receiving laxatives within 24 hours, (3) repeat testing within 7 days, and (4) protocol overrides. We used χ^2 tests to compare changes in CDI testing and rates preintervention versus post intervention; quarterly SIRs were compared using *t* tests.

RESULTS

The baseline CDI testing rate decreased from 284 per 10,000 patient days preintervention to 268 per 10,000 patient days postintervention (P = .02). The CDI testing in the hospitalonset (HO) period decreased 56% postintervention, from 155 per 10,000 patient days preintervention to 84 tests per 10,000 patient days postintervention (P < .001). At baseline, 49% of CDI tests were for patients receiving laxatives within 24 hours, and 18% were ordered despite prior results available within 7 days. Testing while on laxatives decreased by 64%, from 77 per 10,000 patient days preintervention to 24 per 10,000 patient days postintervention (P < .001) (Figure 1B). The number of CDI tests reordered within 7 days also decreased by 64%, from 28 per 10,000 patient days preintervention to 8 per 10,000 patient days postintervention (P < .001). Hospital-onset CDI rates decreased 54%, from 17 per 10,000 patient days preintervention to 7 cases per 10,000 patient days postintervention (P < .001), resulting in a 51% reduction in the average quarterly HO SIR, from 1.62 preintervention to 0.82 postintervention (P < .001) (Figure 1B). Improved testing protocol compliance was tied to monitoring and feedback with a templated CMO response to physicians bypassing the protocol without approval. In the first month of implementation, there were 22 unauthorized overrides, but these incidents decreased to zero by the end of the study period.

DISCUSSION

Proactive approaches to clinically appropriate diagnostic testing can be important for high-sensitivity tests, such as the



FIGURE 1. Hospital-onset *C. difficile* infection (CDI) orders decreased after launch of the automated real-time intervention, while community-onset orders were unchanged. The number of orders placed for patients receiving laxatives decreased sharply after a real-time computer physician order entry (CPOE) system was launched.

C. difficile PCR test, which can identify colonization and can lead to unnecessary treatment and concern.^{1–3} Our real-time CPOE criteria-based testing protocol reduced inappropriate testing by 64% and HO *C. difficile* rates by 50% without changing the CDI testing method.

Electronic health record (EHR) strategies using passive alerts with information alone run the risk of being ignored over time and can be met with variable compliance.^{7,8} Our smart prompt provided clinicians with actionable data and also used a "hard stop" when testing criteria were not met. To address the rare but important possibility of CDI in complicated or high-risk patients not meeting testing criteria (eg, ICU patient on daily laxatives who develops abdominal distention and leukocytosis), physicians could override the protocol with ID or GI physician approval. This strategy encouraged thoughtful testing and provided an opportunity for specialist-level education of frontline physicians.

Electronic algorithms and protocols can often be circumvented; compliance monitoring and timely feedback are needed to achieve meaningful and sustainable changes.⁸ In our case, noncompliant physicians were sent e-mail warnings signed by our CMO, sending a clear message that appropriate testing was an institutional priority while also educating physicians.

An important limitation of this intervention was the inability to capture the number of times a CDI test order was initiated but then cancelled due to the protocol, which limited our ability to describe the learning curve associated with this CPOE strategy. Nevertheless, the sustained decreases in overall testing strongly suggest decreases in order initiation.

Data on the harmful effects antibacterial agents on the gut microbiome are mounting, and treatment of asymptomatic *C. difficile* colonization has been shown to increase future risk of colitis and recurrent disease.^{9,10} In addition, oral vancomycin use increases the carriage rate of vancomycin-resistant enterococci, a drug-resistant organism associated with healthcare-associated infections.¹⁰

As data showing the harms of overtesting and overtreatment for CDI emerge, CPOE strategies can be an effective training tool to improve use and stewardship of diagnostic tests.^{2,3} Our electronic solution to enforce clinically appropriate CDI testing is an example of a strategy that integrates real-time CPOE alerts, specialist review, compliance monitoring and feedback, and leadership-level enforcement.

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SUPPLEMENTARY MATERIAL

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Pneumocystis jirovecii Exhalation in the Course of *Pneumocystis* Pneumonia Treatment

Pneumocystis jirovecii is a transmissible and uncultivable micromycete that causes severe acute pneumonia (ie, *Pneumocystis* pneumonia, PCP) in immunosuppressed patients. *Pneumocystis* spp are host specific, and no exosaprophytic form of *Pneumocystis* sp has been identified so far. Thus, humans may represent the reservoir of *P. jirovecii* and potential infectious sources for susceptible individuals.¹

Pneumocystis jirovecii DNA has been detected and quantified using quantitative polymerase chain reaction (qPCR) in the air surrounding PCP patients, suggesting exhalation and spread of *P. jirovecii* from infected patients within their environment.^{2,3} This finding emphasizes the risk of patient-to-patient transmission of *P. jirovecii* via the airborne route, which was also prompted by investigations of PCP case clusters in hospitals (see the review by Yiannakis et al⁴). Taken together, these data support the maintenance of prevention measures based at least on patient treatment and isolation.⁵ Nonetheless, there are no