Consumer Price Index), the official Brazilian inflation index, is the main variable (Decree no. 4,937, December 29, 2003). The accumulated CMED escalation amounted to 11.93% in the studied period, while the purchase prices of cefazolin and ceftriaxone (the antibiotics of choice for surgical prophylaxis and for treatment of pneumonia, urinary tract infections, meningitis, and intra-abdominal infections) increased 617% and 292%, respectively. On the other hand, amikacin and gentamicin, old drugs that are discouraged due to adverse reactions, suffered a 0.9% reduction and a 3% increase in the purchase price. Despite the disproportionate increase, the purchase prices did not exceed the maximum prices allowed by CMED. However, the annual trend suggests that the prices charged by laboratories and distributors will be very close to the maximum price allowed for widely marketed hospital antibiotics.

Recently, a small Missouri-based drug maker more than quadrupled the price of nitrofurantoin.[5] In an interview, the chief executive said he had priced the product according to market dynamics and that it is a moral requirement to make money when you can. Furthermore, he said that this is a capitalist economy, and if you cannot make money, you cannot stay in business.

Clearly, antibiotic prices in Brazil are uncontrolled and antibiotics are in demand from suppliers. Antibiotics are considered the most important drugs in the treatment of serious infections. Many hospitals have avoided the most expensive antibiotics, but this may compromise the treatment of patients. Cost should be part of the ASP, but it should not be the main engine of an amazing model of therapeutic rationalization.

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Achieving and maintaining low rates of hospital-onset *Clostridioides difficile*

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To the Editor—The Cambridge Health Alliance (CHA) is a safety-net organization consisting of 277 beds spread between 2 community teaching hospitals and 3 emergency departments. We adopted polymerase chain reaction testing (PCR, Cepheid, Sunnyvale, CA) for *Clostridioides difficile* infection (CDI) in 2011 and, similar to other hospitals, we noted an increase in our hospital-onset (HO) CDI rate after adopting the more sensitive molecular assay. This increase occurred despite excellent hand hygiene practices, private rooms with contact precautions, daily bleach disinfection of high-touch surfaces, ultraviolet disinfection after terminal cleaning, and an antimicrobial stewardship program. A performance improvement project initiated in 2015 led our organization to successfully reduce the HO-CD standardized infection ratio (SIR) to <1 at 2 hospitals.[1] We have been able to sustain a low HO-CD rate over the past 3.5 years despite changes in the National Healthcare Safety Network's (NHSN's) risk stratification methodology[2] and without imposing additional testing restrictions on providers. In fact, our SIR has been maintained at <1 and has continued to decline.

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Methods

The initiation of an incentive program in 2015 led our institution to successfully implement a plan in February 2016 to drive the HO-CDI SIR to <1 via an automated nurse testing protocol (NTP). The goal of the NTP was to optimize identification of patients with community onset (CO) CDI to avoid inaccurate attribution of HO-CDI and inflation of the SIR due to a delay in stool specimen acquisition. In the NTP, which was embedded in Epic healthcare software (Verona, WI), documentation of diarrhea on the flowsheet during hospital days 1–3 led to a nurse best-practice alert that, when accepted, automatically led to stool collection and PCR testing of the specimen as well as initiation of contact precautions. We were careful to educate nurses and providers that a positive PCR test did not necessarily require antibiotic therapy because PCR detects *C. difficile* bacteria with the gene for toxin production but does not detect the toxin itself. Patients with recent risk factors for CDI or clinical characteristics of disease (eg, fever, severe diarrhea, or leukocytosis) were started on treatment, whereas those who had other reasons for diarrhea (eg, medications, diet, or laxatives) were advised to continue with watchful waiting.

In July 2016, a combined glutamate dehydrogenase (GDH) antigen and toxin assay for toxins A and B (Abbott Diagnostics,

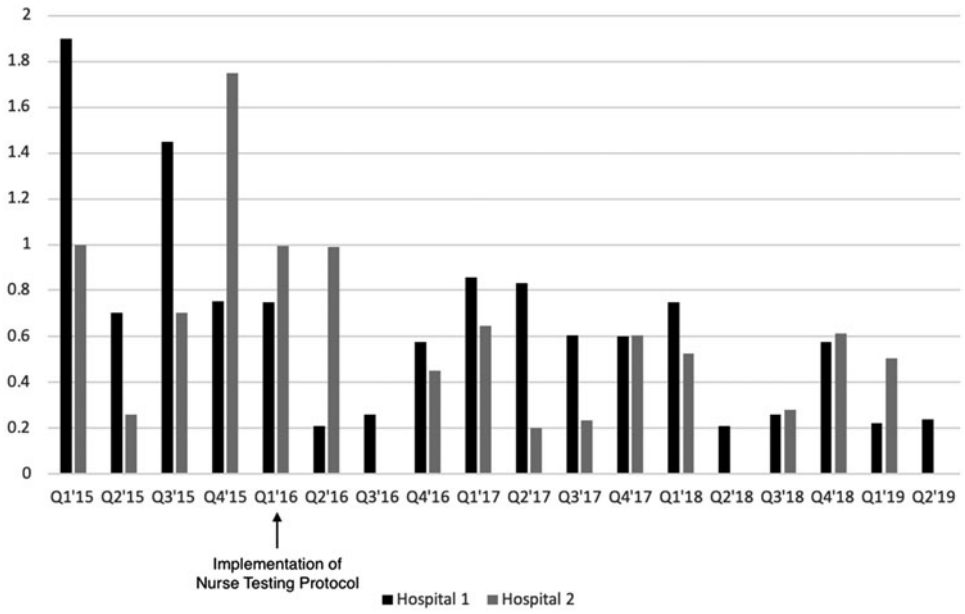

Fig. 1. *Clostridioides difficile* standardized infection ratio (SIR) over time.

Chicago, IL) was implemented for patients experiencing diarrhea beyond hospital day 3 due to its increased specificity. Diagnostic stewardship measures included limitations of *C. difficile* testing to stool samples taking the shape of the container and 1 test per patient per week.

In January 2018, the NHSN changed its risk stratification according to the last *C. difficile* test performed.[3] This change had the potential to negatively impact our healthcare-associated CDI metrics. Hence, we report an update on our performance since our prior publication.

Results

Immediately after implementation of the NTP in February 2016, both CHA sites observed fewer HO-CDI cases than would be predicted according to bed size, hospital affiliation, number of CO-CDI cases, and laboratory test used (Fig. 1). Upon adoption of the GDH/toxin assay in July 2016 and the change in the NHSN risk stratification in January 2018, this improvement was sustained.

Discussion

Our implementation of an automated process for identifying CO-CDI via the NTP, a process with minimal burden to staff and providers, has driven our CDI SIR to <1, and this change has been maintained for nearly 4 years.

Notably, indeterminate GDH and toxin results are reflexed to PCR testing. Although this methodology has the potential to increase our SIR due to the fact that the PCR test is of higher sensitivity, we have maintained this testing strategy (ie, not requiring approval from the infectious disease team to obtain this test) because our excellent performance has been maintained. We argue that delaying PCR testing could lead to delayed diagnosis and treatment of true CDI and therefore pose a danger to patient care.

We also posit that restrictions or hard stops that prevent providers from ordering *C. difficile* testing in the setting of recent laxative use have the potential to delay identification and treatment of CDI. A recent publication supported this argument,[4] reporting that, despite 2017 IDSA-SHEA guidelines[5] that recommend against testing for CDI if a patient has received a laxative within the preceding 48 hours, patients who recently received laxatives had no difference in CDI or symptom severity. Had we followed the IDSA-SHEA guidelines, a diagnosis of CDI would have been missed in nearly one-third of the laxative-treated cohort.

Controversy persists regarding the optimal testing strategy for diagnosing CDI. Our approach has been effective in maintaining a low SIR without imposing the need for approval from the infectious disease team or the laboratory, without a hard stop for laxative use in the preceding 48 hours, and without imposing PCR testing restrictions for patients with indeterminate GDH and toxin results. Empowering nurses in both diagnostic and antimicrobial stewardship efforts for CDI continues to be an effective strategy for reducing HO-CDI.

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First report of IMP-1 in a clinical isolate of *Escherichia coli* in Latin America

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To the Editor—The emergence of carbapenem-resistant *Enterobacterales* (CRE) is a matter of public health concern that seriously compromises antibiotic treatment for severe infections. Since the first report of acquired IMP-1 in *Pseudomonas aeruginosa* in Japan in 1988,[1] genes encoding IMP enzymes have spread rapidly among *Acinetobacter* spp and *Enterobacterales*.[2] Here, we describe the characteristics of a clinical isolate of *E. coli* harboring $bla_{\text{IMP-1}}$ gene in Latin America.

An *Escherichia coli* (termed *E. coli* 7469F) was recovered from the blood of a patient at Hospital de Clínicas de Porto Alegre in Southern Brazil in May 2019. The *E. coli* 7469F was not susceptible in vitro to meropenem and ertapenem by the disk-diffusion method. The presence of carbapenemase genes ($bla_{\text{NDM-1}}$, $bla_{\text{KPC-2}}$, $bla_{\text{VIM-type}}$, $bla_{\text{GES-type}}$, $bla_{\text{OXA-48-like}}$, and $bla_{\text{IMP-type}}$) was evaluated using multiplex high-resolution melting (HRM) real-time polymerase chain reaction (PCR),[3] which yielded a positive result only for the $bla_{\text{IMP-type}}$ gene. The clinical isolate was submitted to conjugation experiment using *E. coli* J53 as a receptor, and 1 transconjugant (T7469F) was selected for further analysis. The minimal inhibitory concentrations (MICs) of antibiotics representative of β-lactams, aminoglycosides, glycilcycline, and chloramphenicol were evaluated by broth microdilution for the *E. coli* 7469F and its transconjugant (T7469F). The transconjugant T7469F presented significant increase in MICs of the carbapenems and ceftazidime compared with *E. coli* J53 (Table 1). T7469F did not present an increased MIC for aminoglycosides, chloramphenicol, or tigecycline. This whole-genome shotgun project has been deposited at DDBJ/ENA/GenBank under the accession WTVT00000000. The version described here is version WTVT01000000.

The whole genomes of the clinical isolate and its transconjugant were sequenced using the MiSeq platform (Illumina, San Diego, CA), and the data were analyzed using the following tools from the Centre for Genomic Epidemiology website (http://www.genomicepidemiology.org): MLST to characterize sequence typing (ST), ResFinder to characterize antibiotic resistance mechanisms, and PlasmidFinder to characterize plasmid types. Analyses of the whole-genome sequencing (WGS) data confirmed the presence of the $bla_{\text{IMP-1}}$ gene in isolate 7469F and its transconjugant. Other genes related to resistance to β-lactam ($bla_{\text{CTX-M-15}}$ and $bla_{\text{OXA-1}}$) were found in the clinical isolate using in silico data analyses. *E. coli* 7469F presented 4 plasmids, and the $bla_{\text{IMP-1}}$ gene was identified in the plasmid IncA/C_2. In silico data confirmed that the IncA/C_2 was the only plasmid identified in the transconjugant T7469F. Plasmids belonging to the IncA/C incompatibility group are broad host–range vehicles commonly identified among animal and clinical bacterial isolates of *Enterobacterales* worldwide. This plasmid usually harbors different resistance genes, including bla_{CMY}, bla_{NDM}, bla_{VIM}, and bla_{IMP}.[4] The WGS analyses also indicated that the *E. coli* 7469F belonged to the ST648. ST648 is a predominant multidrug-resistant ST observed worldwide; it is increasingly reported in multiple regions.[5-8] In addition, several publications have reported the frequent occurrence of ST648 strains with various β-lactamases (extended-spectrum β-lactamases [ESBLs], New Delhi metallo-β-lactamases [NDMs], and *Klebsiella pneumoniae* carbapenemase [KPCs]),[9,10] as well as the *mcr*-1 gene.[8]

To the best of our knowledge, this is the first report of a clinical isolate of *E. coli* ST648 carrying an IncA/C_2 plasmid with the $bla_{\text{IMP-1}}$ gene in Latin America. Notably, the broad host range

Table 1. Minimal Inhibitory Concentrations (MICs) of Several Antibiotics Used to Treat *Escherichia coli* 7469F, Transconjugant 7469F, and *E. coli* J53

	MIC (mg/L)		
Antibiotics	*E. coli* 7469F	Transconjugant T7469F	*E. coli* J53
Ertapenem	128	8	≤0.03
Imipenem	16	4	0.5
Meropenem	64	8	0.06
Ceftazidime	512	512	0.5
Gentamicin	2	2	2
Tigecycline	0.25	0.5	0.5
Amicacin	8	8	4
Chloranphenicol	8	8	8

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