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Anusha Chaturvedi Date

Interrupted Time-Series Analysis of the Impact of *Clostridium difficile* Infection Control Interventions at Emory Healthcare.

By

Anusha Chaturvedi

Degree to be awarded: Master of Public Health

Epidemiology

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By

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Doctor of Medicine (MD)
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2016

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ABSTRACT

Interrupted Time-Series Analysis of the Impact of *Clostridium difficile* Infection Control Interventions at Emory Healthcare.
By Anusha Chaturvedi

Background: *Clostridium difficile* Infection (CDI) is one of the leading causes of healthcare associated infections in the USA. Due to the risk factors and colonization associated with this infection, judicious utilization of testing for *C.difficile* is necessary for prevention of both Hospital onset- (HO) and Community onset- (CO) CDI.

Methods: This was an interrupted time-series analysis intended to assess the impact of three *C.difficle* control initiatives on hospital onset *C.difficile* infection at Emory Healthcare. The study included 32 months (January 2016 - August 2018) of data from four healthcare facilities. The population under study consisted on patients who were hospitalized and had suspected *C.difficile* diarrhea. The interventions consisted of laxative alert, *C.diffile* testing algorithm education and cancellation of testing orders at 48 hours. Laxative alert was the primary intervention to be tested as it was rolled out at the same time point across Emory Healthcare.

Results: The cumulative incidence of HO- and CO-CDI at Emory Healthcare was 0.81 per 1,000 patient-days and 0.07 cases per 100 admissions, respectively. The testing rate for *C.difficile* was 6.55 tests per 1,000 patient-days and 0.33 tests per 100 admissions for HO- and CO- CDI, respectively. Over the entire study period, there was a statistically significant downward trend in testing rates and CDI incidence at almost all metrics and facilities. Immediately after the laxative alert intervention was rolled out, there was a statistically significant reduction in the incidence of HO-CDI by -0.44 cases per 1,000 patient-days at Emory University Hospital [rate ratio (RR): 0.64; 95% CI: 0.54, 0.77].

Conclusion: This study shows that there was a reduction in the incidence of HO-CDI following the laxative alert. Testing the impact of multifaceted control interventions is an important step towards the prevention of CDI.

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BACKGROUND AND LITERATURE REVIEW

*Clostridium difficil*e is an anaerobic, spore-forming, toxin-producing, Gram-positive bacilli, and is known to be a leading cause of nosocomial diarrhea. *C.difficile* infection (CDI) has been identified as the most frequent healthcare associated infections (HAI) in the USA. *C.difficile* is a colonic pathogen, and is responsible for antibiotic-associated diarrhea and colitis (1,2). Acquisition of *C.difficile* occurs by ingestion of spores that are transmitted from other patients. These spores are resistant to the acidic environment within the stomach, and germinate into vegetative bacteria in the small intestine.

Within healthcare settings, spread of *C.difficile* occurs as a result of person-to-person transmission via the feco-oral route and through exposure to contaminated surface. The most probable modes of transmission are the contaminated hands of healthcare-workers and inanimate objects (3).

The median incubation period for *C.difficile* enteritis ranges between 2-3 days and patients with clinically significant infection present with diarrhea (3 or more loose stools per day for 1-2 days), crampy abdominal pain and leucocytosis. The spectrum of CDI ranges from diarrhea to systemic toxic effects marked by sepsis and death (4). Mortality rate is approximately 9% among hospitalized patients and rises to about 80% in patients with fulminant disease (5,6). 3-26% of hospitalized adults in acute care facilities are asymptomatically colonized with *C.difficile* (7).

Risk factors associated with the development of CDI consist of recent antimicrobial use, hospitalization, gastrointestinal surgery, older age, immunosuppression, gastric acid suppression and inflammatory bowel disease. Based on studies, over 90% of the patients who develop CDI, have a history of prior antibiotic therapy or in hospital treatment (8).

Increase in the incidence of CDI can be largely attributed to the recent increase in exposure to broad spectrum antibiotics, significantly higher number of population and hospitalization rates among individuals aged ≥65 years, changing molecular epidemiology of *C.difficile* with the emergence of a novel and more virulent BI/NAP1/027 strain, and inadequate preventive measures at healthcare facilities. King et.al., in their study demonstrated the incidence of CDI in the USA to be 107.8 cases per 100,000 population in 2007. These rates have dropped by 10% from 2011 to 2013. In a retrospective cohort study with data from VA hospitals and clinics, the CDI incidence between 2003 and 2013 rose from 1.6 per 10,000 to 5.1 per 10,000, and subsequently decreased to 4.6 per 10,000 in 2014. (9,10,11,5)

There has also been an increase in the number of Community Onset (CO-) CDI patients who present with diarrheal symptoms, and are diagnosed with CDI without any prior risk factors or do not have significant medical co-morbidity. A case of CO-CDI develops symptoms of CDI in the community or within 48 hours of hospitalization, provided that symptoms appear less than 4 weeks after the last discharge from a healthcare facility. It is commonly documented among the younger population who lack the traditional risk factors for CDI. Such community

acquired cases account for approximately 40% of CDI cases (12). A six-center study from the USA reported the prevalence of CO-CDI to be 20% (13,14). In another survey from Canada, a 27% of the cases of CDI were classified as community onset, with the incidence being 32 cases per 100,000 person-days (15).

The average cost for a single inpatient CDI is more that $35,000 with the estimated annual cost burden exceeding $3 billion for the healthcare system (16). In a meta-analysis by Zhang et.al., the total cost attributed to CDI management in the US ranges between $1.9-7.0 billion and the range for CDI-related length of stay is 8.7-13.6 days; with patients with HO-CDI having longer length of stay (9.7 days) than CO-CDI cases (5.7days) (17). The US Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project identified 24,200 hospital stays in 1993 and 110,600 hospital stays in 2009 with CDI as the primary diagnosis (14).

It is recommended that the test for *C.difficile* should only be done for patients experiencing diarrhea, unless ileus is suspected. Asymptomatic patients should not be screened as they may only be colonized. Several studies have shown the colonization rate for *C.difficile* among adults to be between 0-17.5%, and 1-5% for toxigenic strains. (16, 18) Diagnostic testing for CDI consists of enzyme immunoassay (EIA) for *C.difficile* toxins A and B, nucleic acid amplification tests (NAATs) for *C.difficile* genes and Glutamate Dehydrogenase (GDH) antigen testing. These tests are usually performed as a two- or three-step testing algorithm (19).

According to the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) updated

guidelines, preventive strategies for *C.difficile* transmission in hospitalized patients consist of educating healthcare workers, patients and families about CDI, antibiotic restriction and implementation of antimicrobial stewardship program, use of appropriate contact precautions and hand hygiene practices, isolation practices that consist of restricting patients with CDI to private rooms, and environmental decontamination of CDI patient room with 1:10 sodium hypochlorite solution (20).

Various studies have mentioned the use of 'multifaceted approach' consisting of various CDI control interventions. Primary step in this approach consists of early recognition of patients with suspected or diagnosed CDI, thereby preventing the spread of *C.difficile* (21). Accurate diagnosis of CDI is challenging, and with the use of NAAT, patients who have clinically insignificant diarrhea or are on laxatives tend to be overdiagnosed (22,23). This increases the probability of identifying carrier state instead of actual CDI, and in turn leads to unnecessary antibiotic exposure and overestimation of hospital CDI rates. In a quasi-experimental study, restricting testing for *C.difficile* to unformed stools and limiting testing to once per diarrheal episode resulted in the reduction in the testing rates by 0.71 and test positivity rate by 0.14 per 1,000 patient encounters (24).

Patients who are on laxative within the previous 48 hours of diarrhea should be tested with caution. In a study by Dubberke et.al., it was found that 19% of the patients who were tested for CDI were on laxatives and of those 36% did not have clinically significant diarrhea.

Poor patient selection for CDI testing can impact the testing rates well as the incidence of HO-CDI (25).

Another approach for improving test utilization through diagnostic stewardship can be the use of computerized clinical decision support. Madden et.al. in their quasi-experimental quality improvement study observed a 41% reduction in overall rate of *C.difficile* tests and 31% lower incidence of HO-CDI incidence (26).

Starting in 2016, a set of initiatives was introduced at four hospitals under Emory Healthcare to control the testing rates and incidence of CDI. These consisted of testing algorithm & education, laxative alert and order cancellation at 48 hours. These interventions utilized diagnostic stewardship as well as the use of computerized clinical decision support system. In order to assess the impact of these interventions, an interrupted time-series (ITS) analysis was used. ITS analysis is a type of quasi-experimental design at lowest risk of bias and is preferred as a reasonable approach for evaluating interventions within healthcare facilities (2, 27).

This study helps describe the implementation and analyze the impact of CDI control interventions over a period of 32 months (January 2016 to August 2018) in four healthcare facilities.

METHODS

Study Design:

In this study an interrupted time series (ITS) analysis was conducted on 32 months' of data (January 2016 to August 2018) from four healthcare facilities under Emory Healthcare, Atlanta. We looked at three interventions, out of which the impact of one was tested at four facilities. Two of the interventions were rolled out in February 2017 and August 2017, while the third was implemented at varying time points in the three facilities.

Population and Data Sources:

The study population consisted of patients hospitalized between January 2016 and August 2018, and whose stool samples were tested for suspected CDI and were positive for *C. difficile.*

De-identified data from four healthcare facilities [Emory St. Joseph's Hospital (ESJH), Emory John's Creek Hospital (EJCH), Emory University Hospital (EUH), and Emory University Hospital Midtown (EUHM)] was obtained from Emory Healthcare Infection Control Department's Healthcare Associated Infections database. The variables consisted of monthly statistics for the number of stool specimens tested for CDI, number of positive specimens, patient-days and admissions. To distinguish between CO- and HO-CDI; number of tests performed and number of CDI cases were classified into tests performed within 0-3 days of hospitalization and after 3 days of hospitalization.

Interventions:

Starting in 2016, three interventions were introduced with the aim of reducing CDI testing rates and incident cases at Emory Healthcare. The time points at which these were rolled out at different facilities is described in Table1. The interventions consisted of testing algorithm & education initiative, laxative alert and cancellation of orders at 48 hours.

Laxative Alert: Testing for CDI was determined by laxative prescription in within the previous 24-48 hours. Patients with laxative related diarrhea could be colonized with *C.difficile*.

Testing Algorithm & Education: This intervention engaged nursing staff and providers in a diarrheal decision tree, to influence primary decision of testing for CDI requiring presence diarrhea (≥3 unexplained loose stools in 24 hours), no laxative prescription within the last 48 hours and some clinical signs and symptoms suggestive of CDI.

Cancellation of Orders at 48 hours: Among patients with an order for *C. difficile* in the ordering system, but if a stool specimen had not been collected within 48 hours, the order was automatically cancelled by the ordering system.

Definitions:

CDI was defined as any patient with laboratory confirmed positive toxin assay or PCR positive for *C.difficile*, or visualization of pseudomembranes on sigmoidoscopy or colonoscopy, or a histological/ pathological diagnosis for pseudomembranous colitis (2).

Hospital or Healthcare facility Onset (HO-) CDI: LabID Event specimen collected > 3 days after admission to the facility (on or after hospital day 4).

Community Onset (CO-) CDI: LabID Event specimen collected in an outpatient location or in an inpatient location ≤ 3 days after admission to the facility (hospital days 1 (admit date), 2, or 3) (28).

Statistical Analysis:

We examined the rates for tests performed for *C.difficile* and CDI cases for both HO- and CO-CDI. The primary outcome for HO-CDI was facility-wide rates of CDI per 1,000 patient-days for each month between January 2016 and August 2018. Additional outcomes assessed on monthly basis were the number of tests for HO-CDI per 100 patient-days, and rate of CDI per 100 admissions and tests per 100 admissions for 100 admissions.

A simple linear regression model was tested for each facility to look at the distribution of rates of CDI cases and tests over 32 time points. The coefficients for slopes, P-values and percentage reduction in rates over time were also tested.

For preliminary analysis we looked for evidence of autocorrelation using the Durban-Watson statistic and plots of autocorrelation function. Values close to 2.0 indicated no serious correlation, and if the statistic was significant, the model was adjusted by estimating autocorrelation parameter and included in the ITS regression model. To rule out seasonal

variations in the rates, seasonality was assessed using the Dickey-Fuller unit root test (2, 29, 30).

ITS analysis was performed to assess the effect of laxative alert on the incidence of HO-CDI cases. Since this analysis requires at least 8 time points to be present on each side of an intervention, laxative alert, which was rolled out in February 2017 across Emory Healthcare and was the 14^{th} time point, was tested as the primary intervention at all four facilities.

For ITS analysis, a model was developed based on the following general equation:

$$Ln(R)= \beta_0 + \beta_1 T_1 + \beta_2 I_1 + \beta_3 T_2 + e$$

where R is the rate at month T_1, Ln denoted the natural logarithm; β_0 signifies the baseline monthly rate; β_1, β_2 and β_3 give an estimate of linear trend prior to intervention, level change at the time of intervention and monthly trend after the intervention, respectively; T_1 is a continuous variable that indicates the time in months from the start of study period; I_1 is the time point at which the intervention was implemented, and was coded as 0 for pre- and 1 for post- intervention time points; T_2 is a continuous variable and was coded as 0 before the intervention and had the same value as T_1 afterwards (31).

Rate ratios were calculated by taking the exponent of the coefficient estimates and considering pre-intervention estimates as the reference.

An alpha level of 0.05 was considered significant for all analyses. All statistical analyses were performed using SAS v 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

Summary of *Clostridium difficile* Infection:

The cumulative rate for tests performed and incidence for HO-CDI across all facilities was 6.55 tests per 1,000 patient-days and 0.81 cases per 1,000 patient-days, respectively. EUH had the highest testing rate of almost 10 tests per 1,000 patient-days and CDI incidence of 1.07 cases per 1,000 patient days, while ESJH had the lowest testing rates and HO-CDI cases. The number of HO-CDI tests and cases ranged between 570 and 5,477, and between 83 and 594, respectively, with the highest number reported from EUH and lowest from EJCH.

The cumulative testing rate and case rate for CO-CDI was 0.33 tests per 100 admissions and 0.07 cases per 100 admissions, respectively. The lowest numbers of tests were done at EJCH (940) and highest at EUH (3,336). The testing rate was lowest for EUHM (0.18 tests per 100 admissions) and highest for ESJH (0.45 tests per 100 admissions). EUHM and ESJH reported the lowest and highest incidence CO-CDI cases (Table 1).

Of the 2,630 cases of CDI diagnosed, 1,066 (40.5%) were hospital onset and 1,564 (59.5%) were of community onset. A total of 16,283 tests for *C.difficile* were performed over the entire study period, with the positivity rate being 16.2%. 12.4% of tests done for HO-CDI and 20.3% for CO-CDI were positive for infection.

Over the entire study period, there was a statistically significant downward trend in testing rates and CDI incidence for almost all metrics and at all facilities. The exception was with incidence of HO-CDI at EUHM, which reported a 0.2% increase in the monthly rates. The highest percent reduction in the testing rates for HO-CDI was observed at EJCH (22.9%), and the lowest decline in rates was at EUHM (6.8%). There was also a 2-4% reduction in the incidence of HO-CDI at ESJH, EJCH and EUH over the 32-month period (Table 3). Figures 1a-d show facility-wide slopes in the incidence of HO-CDI cases and the time points at which various interventions were rolled out. Here, EUHM has an upward slope for the incidence of HO-CDI (Figure 1d). On visual inspection, ESJH, EJCH and EUH had a downward trend for the incidence of HO-CDI cases and this corresponds with the co-efficient of the respective values for the slopes (Figures 1a, b, c).

Testing algorithm & education was the first intervention to be implemented at ESJH and EJCH but was rolled out after the laxative alert at EUH and was not implemented until after the entire study period at EUHM. Laxative alert and order cancellation at the end of 48 hours were implemented at the same time points at the four facilities (Figures 1a-d).

Interrupted Time-Series Analysis and Impact of Intervention on the Incidence of HO-CDI:

On visual inspection of the pre-intervention trends for laxative alert, there is a decline in HO-CDI rates at ESJH and EJCH; no change over time is seen at EUH and there is an upward trend at EUHM. Post-intervention,

there is a downward trend at ESJH, EJCH and EUH, but not at EUHM (Figures 2a-d).

No seasonality was detected in this study. Since the Durban-Watson statistic value was close to 2.0 for all the four facilities, we could rule out autocorrelation. Figures 2a-d depicts the pre- and post- intervention trends in the incidence of HO-CDI cases across Emory Healthcare.

Immediately after laxative alert was rolled out, there was a statistically significant (P-value= 0.03) reduction in the incidence of HO-CDI by -0.44 cases per 1,000 patient-days at EUH [rate ratio (RR): 0.64; 95% CI: 0.54, 0.77]. Non-significant decreases were observed in the HO-CDI rates at EUHM and EJCH. During the post-intervention period, a downward trend by −0.004 cases per 1,000 patient-days was seen only at EUH (Table 4).

Testing algorithm & education alert was the first intervention that was rolled out at ESJH, EJCH. There were insufficient number time points prior to its implementation at these facilities. This intervention was not rolled out at EUHM and could not be assessed. At EUH it was the second intervention to be rolled out a few months after the laxative alert. We attempted to test for its effect of on HO-CDI at EUH in addition to laxative alert. For this the following model with two interventions was used:

$$Ln(R)= \beta_0 + \beta_1 T_1 + \beta_2 I_1 + \beta_3 T_2 + \beta_4 I_2 + \beta_5 T_3 + e$$

here I_2 is the time point at which the second intervention (testing algorithm and education) was implemented, and was coded as 0 for pre- and 1 for post- intervention time points, and T_3 is a continuous variable

and was coded as 0 before the second intervention and had the same value as T_1 afterwards.

Using the second model, immediately after the testing algorithm & education was rolled out, there was a reduction in the incidence of HO-CDI by −0.33 cases per 1,000 patient-days at EUH [rate ratio (RR): 0.72]. A post-intervention decline by −0.09 cases per 1,000 patient-days was seen following this intervention. Both these changes were not statistically significant (Table 5).

DISCUSSION

In this study, the cumulative testing rate and incidence of HO-CDI was 6.5 tests per 1,000 patient-days and 0.81 cases per 1,000 admissions, respectively. Based on the statistics reported by Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project, CDI was responsible for approximately 1% of all hospital stays in 2009; which was approximately 336,600 hospitalizations. The burden of HO-CDI in the US ranges from 2.8–9.3 cases per 10,000 patient-days (32). Most studies focus on reporting of CDI cases associated with healthcare facilities; we observed the rate of CO-CDI to be 0.07 cases per 100 admissions, which accounted for almost 60% of the total CDI cases. A study from Southern California reported the rates of CO-HCFA (Community Onset- Healthcare Facility Associated) CDI to be to be nearly twice as high as HO-HCFA (Hospital Onset- Healthcare Facility Associated) CDI (11.1 per 10,000 patient-days vs 6.8 per 10,000 patient-days) (33).

Current CDI control interventions for inpatients focus on bundle strategies, which include isolation of infected and colonized patients, and antimicrobial stewardship programs and novel methods for decontamination (34). This study focused on three major interventions that were part of a multifaceted initiative and was rolled out between 2016 and 2018 at Emory Healthcare. These were; laxative alert, testing algorithm & education, and cancellation of orders at the end of 48 hours; with laxative alert being the primary intervention that was tested at all

four facilities. Since the diagnostic results for CDI are unable to distinguish between asymptomatic carriage and disease state, and the asymptomatic colonization rate for *C.difficile* among hospitalized ranges between 4.4-15%, these interventions are an important step towards preventing over diagnosis and inflation of HO-CDI incidence (35, 36, 37).

The rationale behind using laxative alert as the primary intervention was that patients on laxatives tend to be over-diagnosed for CDI due to colonization with *C.difficile*. This intervention forces providers to think critically about *C.difficile* testing in the presence of laxative use or in the absence of undocumented diarrhea. May *et.al.* in their study observed a decrease in testing rates by 30% and HO-CDI incidence by 45% during the first month of implementation of a similar intervention (38).

An interrupted time-series analysis was performed on 32 months of data to examine the effect of CDI control interventions on the incidence of HO-CDI. Laxative alert resulted in an immediate decline in HO-CDI rates at three of the four healthcare facilities. The results show that laxative alert was associated with a significant reduction in the incidence of HO-CDI at EUH, where there was a 36% decline as compared to the pre-intervention trend. The second intervention (testing algorithm and education) also resulted in an immediate drop in HO-CDI incidence, as well as a 9% reduction in the post-intervention trend. Significance of this change cannot be ascertained, as there were not enough (≥ 8 time points) between the two interventions used in the second model at EUH. Also, impact of the two interventions cannot be differentiated at EUH, even

though there was a decline in the rates of HO-CDI after testing algorithm & laxative alert was implemented.

The analysis was performed on data from 32 months, which is a relatively short duration for a pre- post-intervention study. ITS analysis requires at least 8 times points between interventions for it to be statistically significant. All interventions could not be tested, as there were insufficient inter-intervention time points.

This study shows that there was a reduction in the incidence of HO-CDI following the laxative alert. Testing the impact of multifaceted control interventions is an important step towards the prevention of CDI.

PUBLIC HEALTH IMPLICATIONS

Given multiple sources of transmission and diagnostic challenges associated with *C.difficile*, control of CDI is difficult and challenging. With better understanding of the incidence of CDI and its spread within healthcare facilities and community, optimizing interventions like diagnostic test utilization remains an important component of the quality healthcare delivery (39, 40, 26).

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TABLES

Table 1: Timeline of *Clostridium difficile* infection Control Interventions.

	LAXATIVE ALERT	ALGORITHM & EDUCATION	ORDER CANCELLATION AT 48hours
ESJH	Feb-17	May-16	Aug-17
EJCH	Feb-17	Aug-16	Aug-17
EUH	Feb-17	May-17	Aug-17
EUHM	Feb-17	NA	Aug-17

ESJH: Emory St. Joseph's Hospital, EJCH: Emory John's Creek Hospital, EUH: Emory University Hospital, EUHM: Emory University Hospital Midtown

Table 2: Facility-wide Summary of Monthly Counts and Rates for Hospital Onset- (HO) and Community Onset- (CO) *Clostridium difficile* Infections (CDI).

			FACILITY											
			ESJH			EJCH			EUH			EUHM		
VARIABLE	CUMULATIVE RATE PER 1,000 PD	PARAMETER	TOTAL	MONTHLY RATE PER 1,000 PD	MONTHLY COUNTS	TOTAL	MONTHLY RATE PER 1,000 PD	MONTHLY COUNTS	TOTAL	MONTHLY RATE PER 1,000 PD	MONTHLY COUNTS	TOTAL	MONTHLY RATE PER 1,000 PD	MONTHLY COUNTS
HO-SPECIMENS	6.55	Mean ± SD Median, Range	729	3.38	22.78 ± 16.36 17, 7 - 63	570	5.24	17.81 ± 9.51 15.5, 6 - 47	5477	9.86	171.16 ± 25.58 165.5, 124 - 229	1809	4.20	56.53 ± 12.8 55, 37 - 80
HO-POSITIVE	0.81	Mean ± SD Median, Range	107	0.50	3.34 ± 2.52 2.5, 0 - 10	83	0.76	2.59 ± 2.3 2, 0 - 13	594	1.07	18.56 ± 6.22 18, 8 - 35	282	0.65	8.82 ± 3.41 8.5, 2 - 20
PATIENT-DAYS (PD)	–	Mean ± SD Median, Range	215846	–	6745.19 ± 408.84 6717, 6073- 7597	108758	–	3398.69 ± 229.34 3405, 3001 - 3930	555365	–	17355.16 ± 761.54 17254.5, 15553 - 18917	431033	–	13469.78 ± 710.29 13554.5, 12020 - 14691
VARIABLE	**CUMULATIVE RATE PER 100 ADM**	**PARAMETER**	**TOTAL**	**MONTHLY RATE PER 100 ADM**	**MONTHLY COUNTS**	**TOTAL**	**MONTHLY RATE PER 100 ADM**	**MONTHLY COUNTS**	**TOTAL**	**MONTHLY RATE PER 100 ADM**	**MONTHLY COUNTS**	**TOTAL**	**MONTHLY RATE PER 100 ADM**	**MONTHLY COUNTS**
CO-SPECIMENS	0.33	Mean ± SD Median, Range	1836	0.45	57.38 ± 11.84 57, 36 - 90	940	0.38	29.38 ± 7.45 28.5, 18 - 44	3336	0.43	104.25 ± 11.43 105, 86 - 132	1586	0.18	49.56 ± 7.91 49, 34 - 69
CO-POSITIVE	0.07	Mean ± SD Median, Range	425	0.10	13.28 ± 4.81 13, 5 - 25	184	0.08	5.75 ± 2.75 6, 1 - 13	628	0.08	19.63 ± 4.29 20, 10 - 27	327	0.04	10.22 ± 2.62 10, 6 - 17
ADMISSIONS (ADM)	–	Mean ± SD Median, Range	409643	–	12801.34 ± 1047.98 12742, 10728 - 14431	244653	–	7645.4194 ± 798.18 7703, 6076 - 8947	781621	–	24425.66 ± 2532 24478, 21004 - 28277	899959	–	28123.72 ± 2324 28104.5, 23106 - 32051

Table 3: Facility-wide Analysis for Slope and Percent Reduction in HO- and CO-CDI Tests and Rates

FACILITY	PARAMETER	SLOPE	% REDUCTION IN RATE	P - value
ESJH	HO-CDI Tests	-0.170	15.63	<0.0001
	HO-CDI Rates	-0.020	1.98	0.02
	CO-CDI Tests	-0.010	1.00	0.0002
	CO-CDI Rates	-0.002	0.20	0.01
EJCH	HO-CDI Tests	-0.260	22.89	<0.0001
	HO-CDI Rates	-0.040	3.92	0.002
	CO-CDI Tests	-0.010	1.00	0.001
	CO-CDI Rates	-0.002	0.20	0.01
EUH	HO-CDI Tests	-0.120	11.31	<0.0001
	HO-CDI Rates	-0.020	1.98	0.0003
	CO-CDI Tests	-0.006	0.60	<0.0001
	CO-CDI Rates	-0.001	0.10	0.01
EUHM	HO-CDI Tests	-0.070	6.76	<0.0001
	HO-CDI Rates	0.002	-0.20	0.67
	CO-CDI Tests	-0.002	0.20	0.0001
	CO-CDI Rates	-0.001	0.10	0.003

Table 4: Facility-wide Interrupted Time-Series Analysis for Effect of Laxative Alert on HO-CDI Incidence.

	INTERVENTION: LAXATIVE ALERT			
Facility	**HO-CDI Incidence**	**Estimate (SE)**	**RR (95% CI)**	**P-value**
ESJH	Pre-Intervention trend	−0.04 (0.03)	–	0.12
	Change in level between pre- and post-intervention period	0.11 (0.25)	1.162 (1.080, 1.251)	0.66
	Change in trend post-intervention	0.03 (0.03)	1.073 (1.064, 1.077)	0.29
EJCH	Pre-Intervention trend	−0.05 (0.04)	–	0.24
	Change in level between pre- and post-intervention period	−0.14 (0.42)	0.914 (0.849, 0.984)	0.75
	Change in trend post-intervention	0.03 (0.05)	1.083 (1.075, 1.091)	0.52
EUH	Pre-Intervention trend	5.41*10^-6 (0.02)	–	1
	Change in level between pre- and post-intervention period	−0.44 (0.20)	0.644 (0.542, 0.765)	0.03
	Change in trend post-intervention	−0.004 (0.02)	0.996 (0.996, 0.996)	0.86
EUHM	Pre-Intervention trend	0.008 (0.02)	–	0.7
	Change in level between pre- and post-intervention period	−0.18 (0.20)	0.829 (0.770, 0.892)	0.31
	Change in trend post-intervention	0.005 (0.02)	0.997 (0.997, 0.997)	0.21

Table 5: Interrupted Time-Series Analysis for the effect of for Laxative Alert and Algorithm & Education Initiatives HO-CDI Incidence at Emory University Hospital (EUH).

INTERVENTION: LAXATIVE ALERT AND TESTING ALGORITHM & EDUCATION				
Facility	**HO-CDI Incidence**	**Estimate (SE)**	**RR (95% CI)**	**P-value**
EUH	Pre-intervention trend	5.41*10^-6 (0.02)	–	1
	*Change in level between pre- and post-intervention period	−0.52 (0.46)	0.59 (0.367, 0.949)	0.27
	*Change in trend post-intervention	0.10 (0.20)	1.11 (1.066, 1.156)	0.64
	#Change in level between pre- and post-intervention period	−0.33 (0.30)	0.72 (0.594, 0.873)	0.29
	#Change in trend post-intervention	−0.09(0.20)	0.91 (0.877, 0.944)	0.66

* laxative alert, # algorithm & education initiative

FIGURES

Figure 1a. Emory St. Joseph's Hospital (ESJH): Hospital-onset *Clostridium difficile* infection (CDI) incidence (Vertical lines: Implementation of CDI control initiatives; Blue line: CDI testing algorithm and education initiative, Red line: laxative alert, Green line: cancellation of testing orders at 48 hours; Solid line: slope of CDI rates during the study period; Blue dots: monthly incidence per 1,000 patient-days.

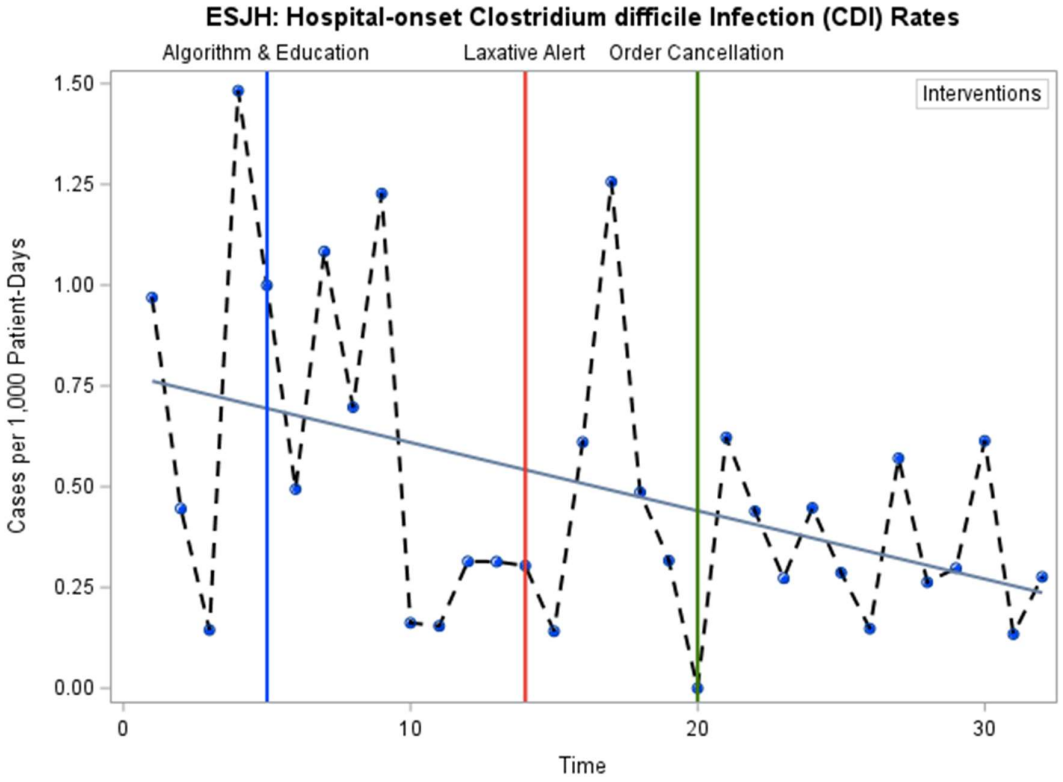

Figure 1b. Emory Johns Creek Hospital (EJCH): Hospital-onset *Clostridium difficile* infection (CDI) incidence (Vertical lines: Implementation of CDI control initiatives; Blue line: CDI testing algorithm and education initiative, Red line: laxative alert, Green line: cancellation of testing orders at 48 hours; Solid line: slope of CDI rates during the study period; Blue dots: monthly incidence per 1,000 patient-days)

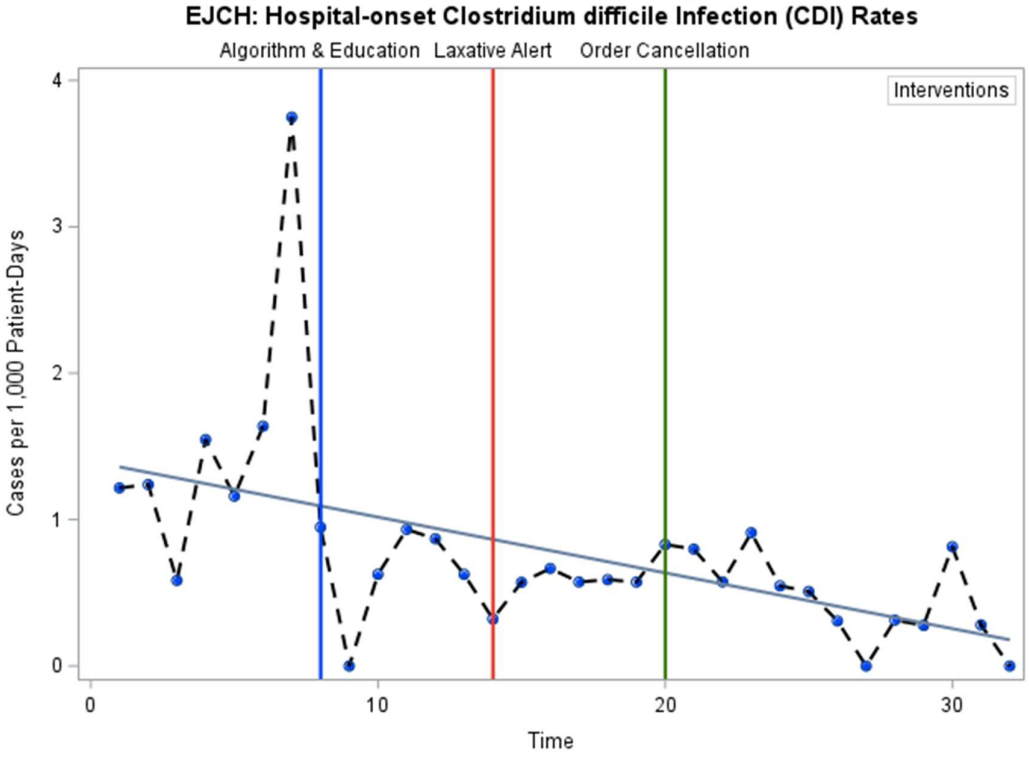

Figure 1c. Emory University Hospital (EUH): Hospital-onset *Clostridium difficile* infection (CDI) incidence (Vertical lines: Implementation of CDI control initiatives; Blue line: CDI testing algorithm and education initiative, Red line: laxative alert, Green line: cancellation of testing orders at 48 hours; Solid line: slope of CDI rates during the study period; Blue dots: monthly incidence per 1,000 patient-days)

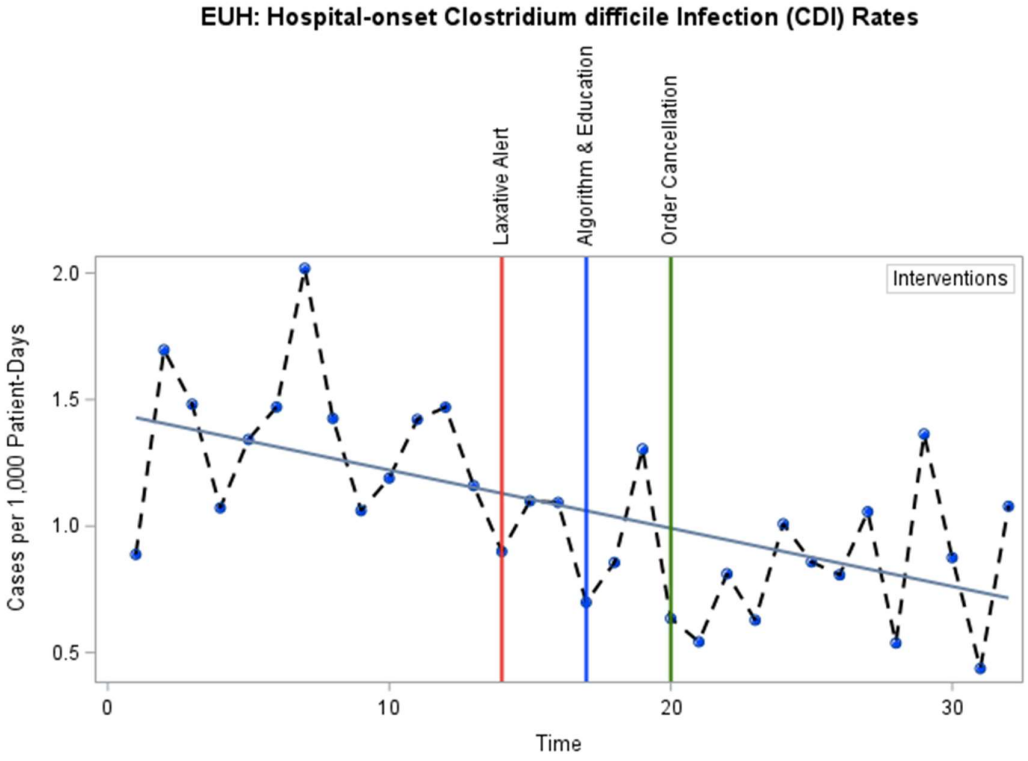

Figure 1d. Emory University Hospital Midtown (EUHM): Hospital-onset *Clostridium difficile* infection (CDI) incidence (Vertical lines: Implementation of CDI control initiatives; Blue line: CDI testing algorithm and education initiative, Red line: laxative alert, Green line: cancellation of testing orders at 48 hours; Solid line: slope of CDI rates during the study period; Blue dots: monthly incidence per 1,000 patient-days)

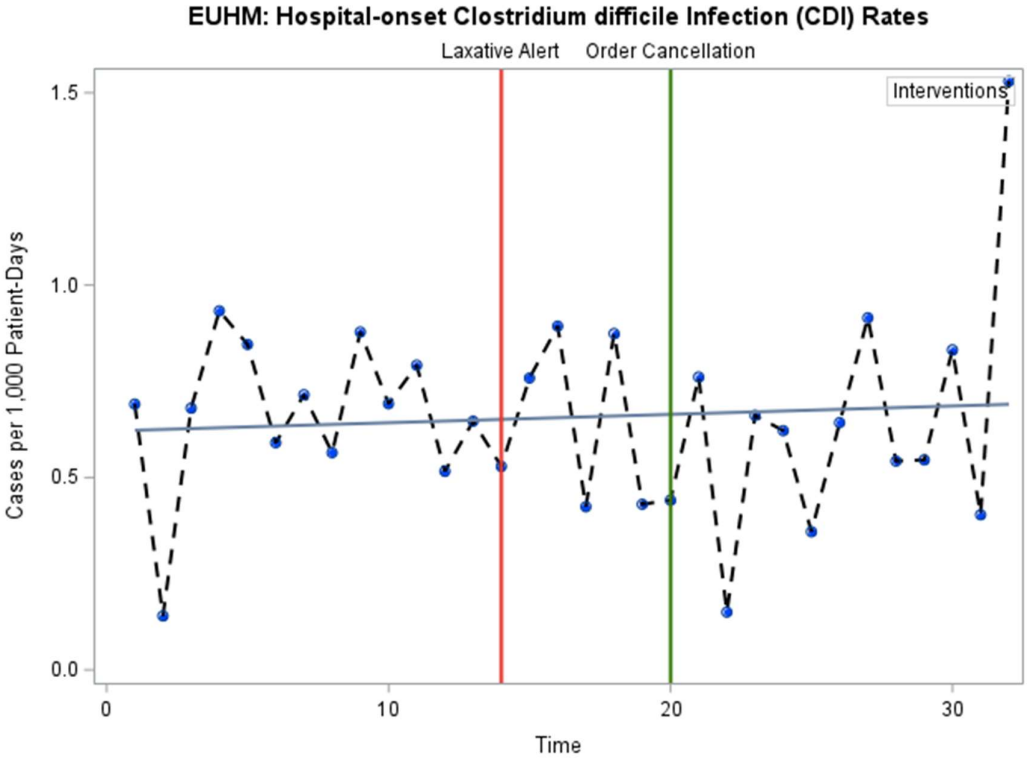

Figure 2a. Emory St. Joseph's Hospital (ESJH): Pre- and Post- intervention trends for Hospital-onset *Clostridium difficile* infection (CDI) incidence (Vertical dashed line: Implementation of laxative alert during 14th time point, i.e., February 2017; Blue dots: monthly CDI incidence per 1,000 patient-days.

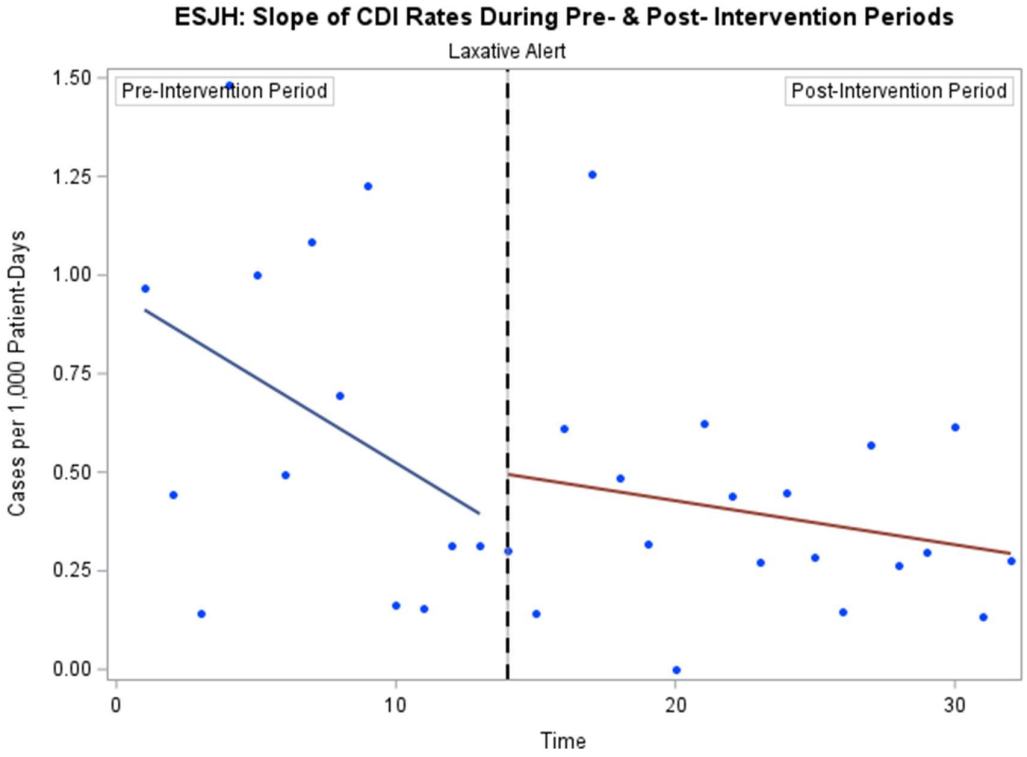

Figure 2b. Emory John's Creek Hospital (EJCH): Pre- and Post- intervention trends for Hospital-onset *Clostridium difficile* infection (CDI) incidence (Vertical dashed line: Implementation of laxative alert during 14th time point, i.e., February 2017; Blue dots: monthly CDI incidence per 1,000 patient-days

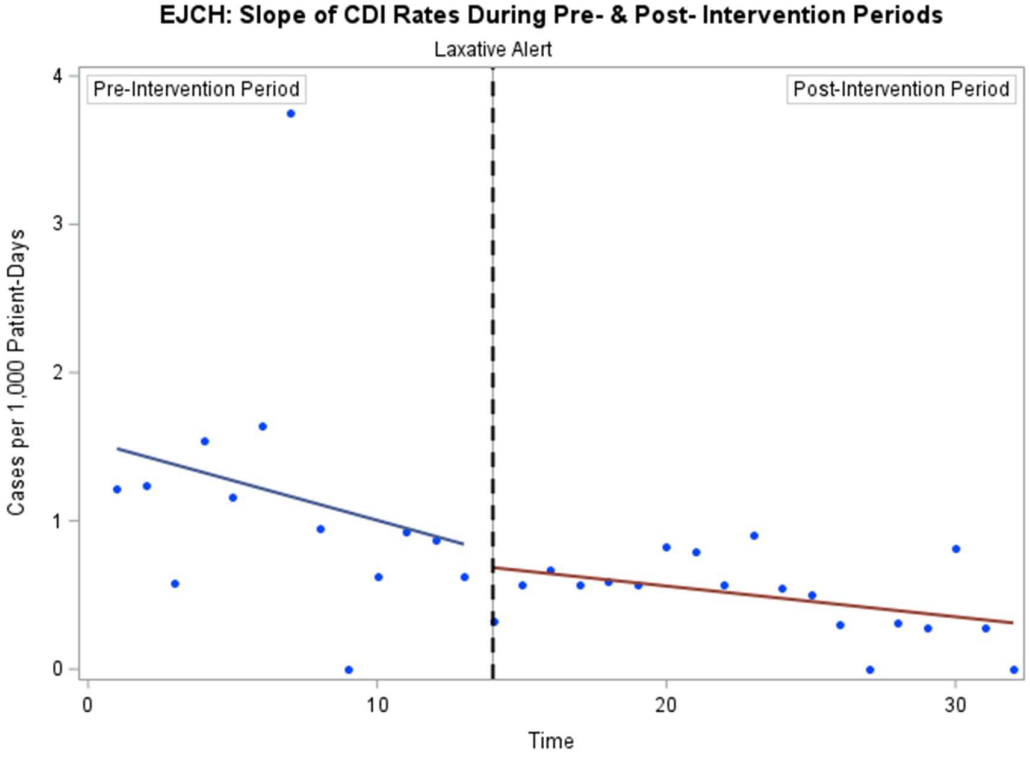

Figure 2c. Emory University Hospital (EUH): Pre- and Post- intervention trends for Hospital-onset *Clostridium difficile* infection (CDI) incidence (Vertical dashed line: Implementation of laxative alert during 14th time point, i.e., February 2017; Blue dots: monthly CDI incidence per 1,000 patient-days.

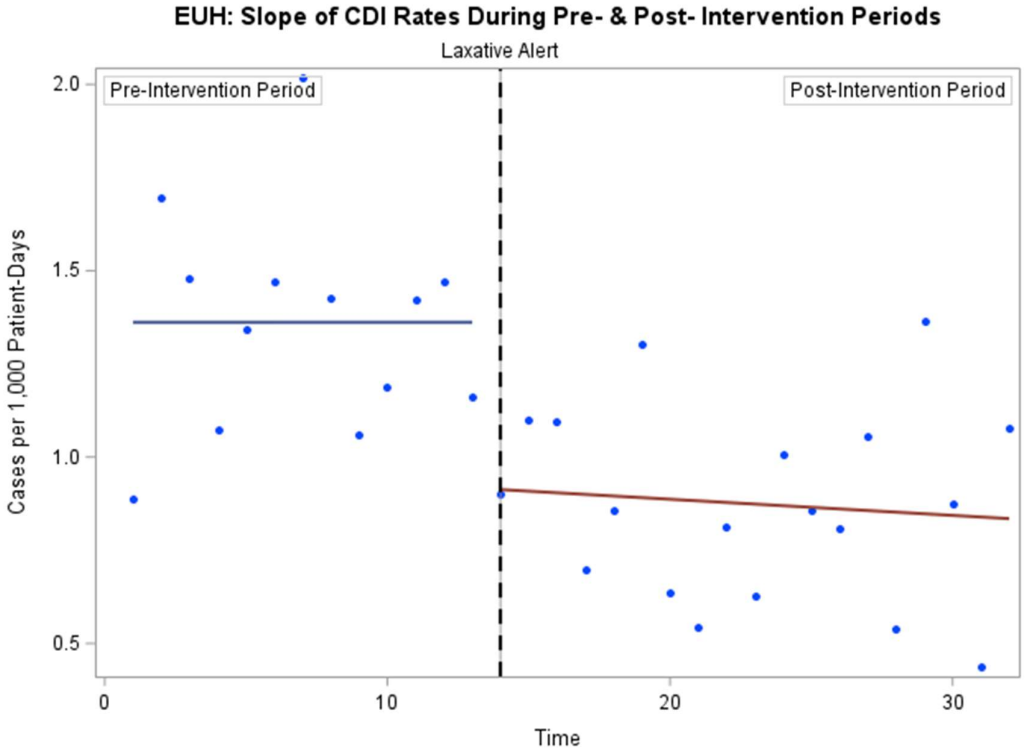

Figure 2d. Emory University Hospital Midtown (EUHM): Pre- and Post-intervention trends for Hospital-onset *Clostridium difficile* infection (CDI) incidence (Vertical dashed line: Implementation of laxative alert during 14th time point, i.e., February 2017; Blue dots: monthly CDI incidence per 1,000 patient-days.