Supplemental Information

CONSTRUCTING A HOMOGENOUS SAMPLE BETWEEN NEW YORK AND CONTROL STATES

In our prespecified analysis plan, we identified 4 control states: Florida, Maryland, Massachusetts, and New Jersey. We chose the control states because they have similar demographic characteristics to New York and, except for Florida, they are geographically proximal to New York. Additionally, the use of administrative data and the availability of data elements across states limited our selection. In particular, the marker for ICU use contributed to our selection of these states for the comparison analysis.

To create a more homogenous sample of hospitals across states, we categorized hospitals on the basis of the following characteristics: hospital type (a designated children's hospital based on Children's Hospital Association membership; a non–children's hospital with a high pediatric volume [for which we selected a cutoff of 1200 annual pediatric admissions, which was roughly equivalent to the smallest children's hospital in our sample]; a non–children's hospitals with medium pediatric volume [for which we selected cutoffs of $<$1200 but $>$50 annual pediatric admissions]; or a non–children's hospitals with low pediatric volume [for which we selected a cutoff of $\leq$50 annual pediatric admissions, $<$1 pediatric admission per week on average]); academic status (based on the presence or absence of trainees); and regional population (small = non-MSA or MSA population of $<$100 000; medium = MSA population of 100 000–1 million; large = MSA population of $>$1 million). With 3 characteristics and defined categories for each characteristic, there was a total of $4 \times 2 \times 3 = 24$ possible combinations of group characteristics. We excluded hospitals in groups that appeared only in New York or only in control states or groups that did not appear in both the pre- and the postintervention periods. The intent of this process was to ensure that we could adequately control for hospital characteristics in the multivariable model.

Hospitals in 5 strata were excluded because there were no hospitals in either New York or control states. The strata containing only control state hospitals were (1) nonteaching children's hospitals in large MSAs (4 hospitals before regulation and 6 hospitals after regulation); (2) large, nonteaching non–children's hospitals in large MSAs (3 hospitals before regulation and 1 hospital after regulation); and (3) large, nonteaching non–children's hospitals in medium MSAs (2 hospitals before regulation and 3 hospitals after regulation). The strata containing only New York hospitals were (1) medium, teaching non–children's hospitals in small MSAs (8 hospitals) and (2) small, teaching non–children's hospitals in small MSAs (1 hospital before regulation and 3 hospitals after regulation).

DETAILED MODEL SPECIFICATIONS

To understand the association between the regulation and patient outcomes, we used a comparative interrupted time-series approach. This approach is used to test if outcomes in New York deviated from a preintervention trend by a greater amount than in control states. We considered the preintervention period to be from January 1, 2011, to March 31, 2013 (ie, the period of time before the official filing of the regulations). The base model includes a continuous time variable (allowing for secular changes in outcome over time, independent of any intervention), an interaction term between the continuous time variable and treatment (allowing the preintervention trends to differ between New York and control states), an indicator for the postintervention period, and a term for the interaction between the indicators and treatment (allowing the postintervention estimates to vary across New York and control states). This model allows us to test the direct impact of the regulation as well as the impact of the regulation on the outcome trend. With the models, we also controlled for patient characteristics and hospital characteristics, as described in the Methods, as well as seasonality based on calendar quarter (implemented as a "season" term alone and interacted with the treatment indicator).

This model is specified as follows:

$$Y_{ijt} = \eta_0 + \eta_1 NY_j + \eta_2 Post_t + \eta_3 q_t$$

$$+ \beta_1 (NY_j Post_t) + \beta_2 (NY_j q_t)$$
$$+ \beta_3 (Post_t q_t) + \alpha (NY_j Post_t q_t)$$
$$+ \sum_{s=2}^{4} (\phi_{0s} Season_s$$
$$+ \phi_{1s} (NY_j Season_s))$$
$$+ \sum_{v=1}^{V} \lambda_v X_{vij} + \square_{ijt}$$

in which Y_{ijt} is the outcome of interest (eg, mortality), NY_j is an indicator equal to 1 for hospitals in New York, $Post_t$ is an indicator equal to 1 in the postregulation period, q_t is a continuous time variable centered at the first quarter after the regulation, $Season_s$ is an indicator for season based on calendar quarter, X_{vij} is the patient- and hospital-level covariates to be adjusted for, and $\square_{ijt}$ is a patient-level error term.

Under this specification, the 2 measures of interest are β_1 (the immediate impact of the regulation; differential change in intercept) and α (the impact of the regulation on the outcome trend; differential change in slope). The null hypothesis for our primary test of the regulations is whether these parameters are equal to zero.

A comparative interrupted time-series approach offers several benefits over other identification strategies. First, this approach does not require that the pre-implementation trends be similar between New York and control states. Despite choosing our control states on the basis of their similarities to New York in terms of demographics and policy landscapes, the pre-implementation trends in pediatric mortality were opposite, necessitating a model that allowed for this difference.

Second, the comparative interrupted time-series approach does not require that the association between the regulations and patient outcomes be constant over time or require a phase-in period of an arbitrary length. The model allows the association between an intervention and outcomes to differ over time without excluding any data for a phase-in period. This aspect of the comparative interrupted time-series approach is important because the introduction and implementation of Rory's Regulations was staged, spanning over a year (Supplemental Table 6).

DEVIATIONS FROM THE PRESPECIFIED ANALYSIS PLAN AND THEIR RATIONALE

In an effort to support the rigor and transparency of our results, we prepublished our complete statistical analysis plan on Open Science Framework before receipt of the final data set (https://osf.io/jcwdv/). However, in our prepublished plan, we acknowledged the possibility that we might need to alter our plans because of unforeseen circumstances. Here, we provide the details of such instances along with the rationale for the changes.

Subgroup Analyses Performed Only for Main Outcome of Mortality

In the prepublished statistical analysis plan, we indicated that we would perform subgroup analyses for both our primary outcome variable and our 4 secondary outcome variables. However, on seeing our primary results and given the small sample sizes, we did not think that subgroup analyses on the secondary outcomes would be sufficiently informative to justify the risk of false discovery, considering the adjustments for multiple comparisons. Therefore, we opted not to perform these analyses.

Adjustment to the Regression Model

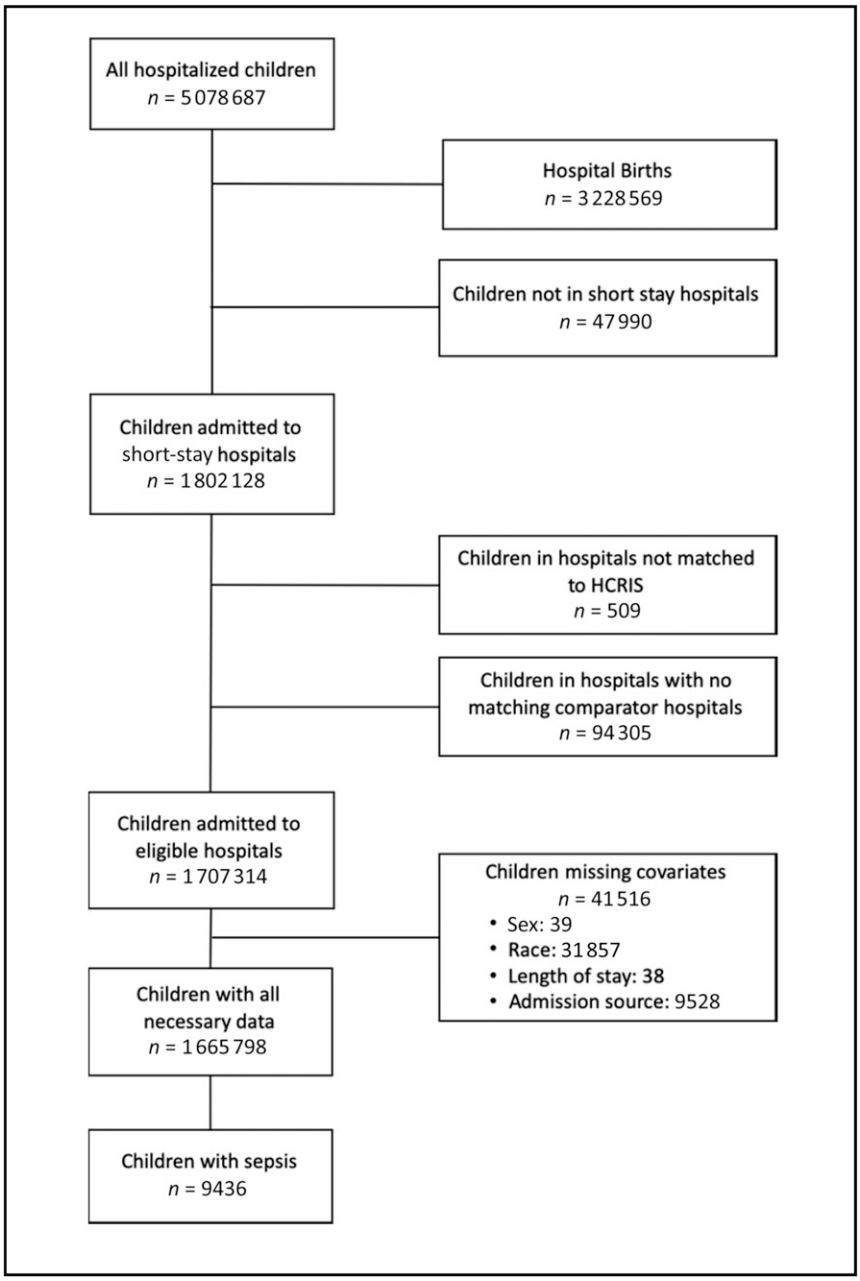
In the prepublished statistical analysis plan, we indicated that we would include a hierarchical infection category as a covariate. However, when we analyzed the cohort of patients with sepsis on the basis of the modified Dombrovskiy criteria, >99% were categorized as having septicemia. Thus, we did not have adequate variation in hierarchical infection categorization, and this covariate was excluded from the final regression model.

Presentation of Level Change

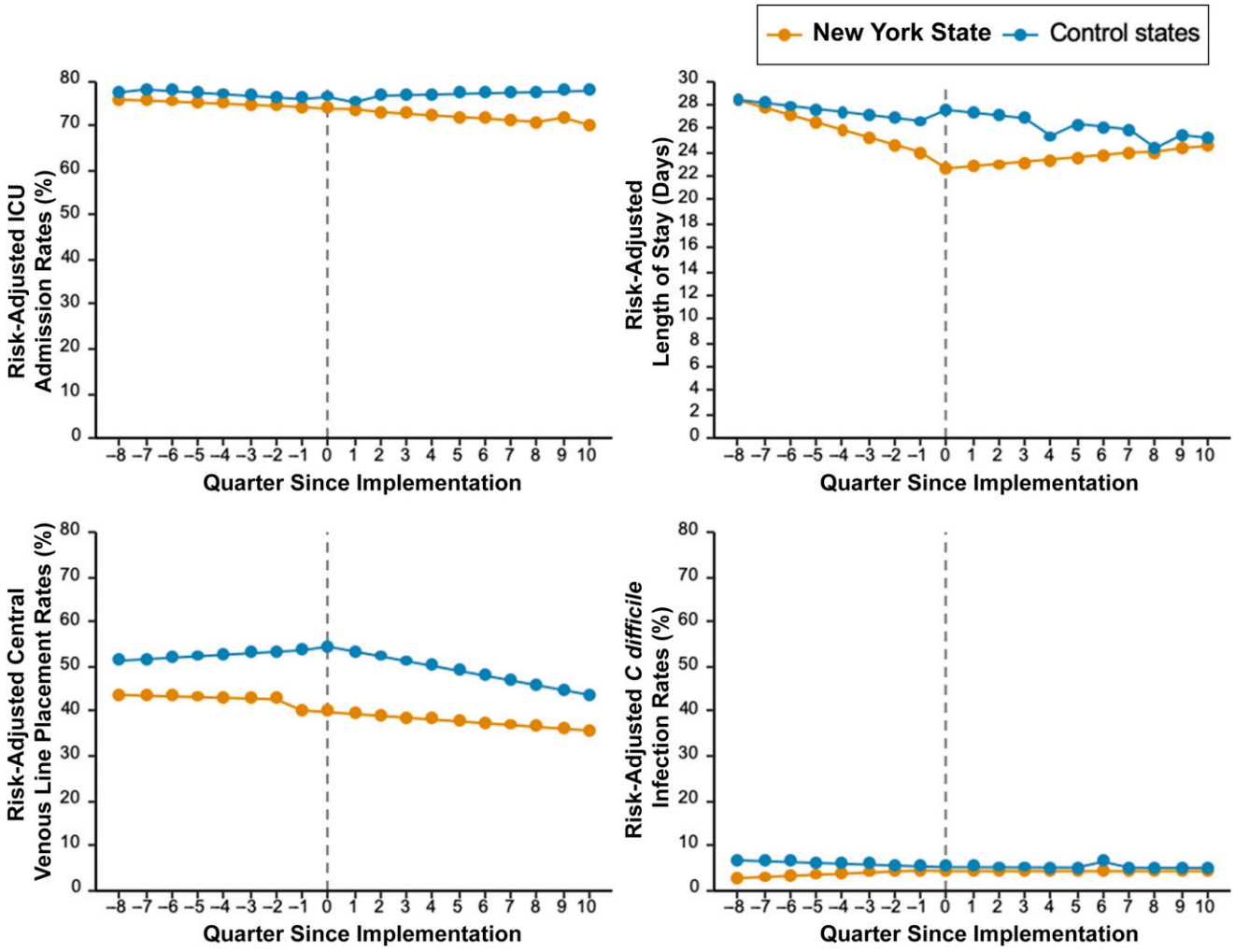
In the prepublished statistical analysis plan, we intended to include 2 measures of effect: (1) a point estimate (the level change at the time of the intervention) and (2) the slope (the differential change in the outcomes over time relative to implementation of the regulations). However, as expected, the first measure (point estimate) did not explain significant differences given the regulations' rolling implementation time line, so we moved those results to Supplemental Table 7. Given that the differential change in the outcomes over time (slope) is more important to assessing the impact of regulation, it is the highlight of the article.

Sepsis Coding Over Time

Sepsis awareness has increased, and we believe that has led to overall increases in the number of pediatric sepsis cases in both New York and control states. We wanted to ensure that there was not a differential change in sepsis coding in New York relative to control states that might have been related to implementation of the regulations. As a post hoc analysis, we examined the rates of sepsis coding over time (Supplemental Table 9) to assess for a differential change in rates of sepsis coding during the study period in New York compared with control states.



SUPPLEMENTAL FIGURE 2
Patient flow diagram.



SUPPLEMENTAL FIGURE 3
Quarter-specific risk-adjusted secondary outcomes over time in New York and control states.

SUPPLEMENTAL TABLE 5 Full List of Variables and Their Definitions

Variable	Definition
Sepsis: main definition (modified Dombrovskiy)[a]	Organ dysfunction by any diagnosis of 2866, 2869, 2874, 2875, 2930, 3481, 3483, 4275, 4580, 4588, 4589, 51881, 51882, 570, 5722, 5734, 584*, 78081, 7855*, 78609, 7963, or 7991; plus infection by any diagnosis of 0031*, 0202*, 0223*, 0362*, 0363*, 0380*, 0381*, 0382*, 0383*, 0384*, 0388*, 0389*, 0545*, 09889, 1125*, 78552, 99591, 99592; or any diagnosis (with or without an organ dysfunction) of 78552 or 99592
Hospital LOS	LOS
In-hospital mortality	DISPUNIFORM = 20 (ie, discharge disposition of "died")
ICU admission	UB-04 revenue codes for intensive care (0200–0209) and/or coronary care (0210–0219); for states other than Florida: U_ICU = 1 and/or U_CCU = 1; for Florida: any nonzero nonmissing charges recorded for CHG5 and/or CHG6
Central-line insertion	Any procedure of 3893, 3897, 36555, or 36556
Peripherally inserted central catheters	Any procedure of 36568 or 36569
C difficile infection	Any diagnosis of 00845
Age	AGE
Sex	FEMALE
Race or ethnicity	RACE as categorized for white, African American, and Hispanic; other = Asian American or Pacific Islander, American Indian, or other. Race and ethnicity were taken from the fixed categories in the HCUP database as ascertained by the reporting hospitals.
Outside hospital transfer	TRAN_IN = 1 or TRAN_IN = 2
Emergency department use	For states other than Florida, U_ED = 1; for Florida, any nonzero nonmissing charges recorded for CHG18
Complex chronic conditions	Per Feudtner et al[38]
Organ failures on admission	Any diagnosis as listed below with correlated present-on-admission indicator (DXPOAn) equal to "Y": respiratory failure: 51881, 51882, 51885, 78609, 7991; cardiovascular failure: 4580, 4588, 4589, 7855, 78551, 78559, 7963; renal failure: 580, 584, 5845, 5846, 5847, 5848, 5849; liver failure (hepatic): 570, 5722, 5733; coagulopathy (hematologic): 2862, 2866, 2869, 2873, 2874, 2875; acidosis (metabolic): 2762; neurologic: 293, 3481, 3483, 78001, 78009
Infection categories, Angus infection codes[a]	Any diagnosis as listed below, with the hierarchy in the order listed: septicemia: 038*, 99591; heart: 420*, 421*; peritoneum: 567*, 56983, 00845; lung: 010*, 011*, 012*, 0310*, 481*, 482*, 485*, 486*; fungal: 1120*, 1124*, 1125*, 114*, 115*, 116*, 117*, 118*; blood: 018*, 7907*, 0312*; CNS: 013*, 036*, 094*, 320*, 322*, 3240*, 3241*, 3249*, 325*; other: 001*, 002*, 004*, 005*, 008* except 00845, 009*, 020*, 021*, 022*, 023*, 024*, 025*, 026*, 027*, 030*, 0318*, 0319*, 032*, 033*, 034*, 037*, 039*, 040*, 041*, 0545*, 090*, 091*, 092*, 093*, 095*, 096*, 097*, 100*, 101*, 102*, 103*, 104*, 1121*, 1122*, 1128*, 1129*, 49121, 494*, 510*, 513*, 730*, 9966*, 9985*, 9993*; GU: 016*, 098*, 590*, 597*, 5990*, 601*, 614*, 615*, 616*; skin: 015*, 017*, 0311*, 035*, 110*, 111*, 1123*, 451*, 681*, 682*, 683*, 686*, 7110*, 730*; GI: 003*, 014*, 540*, 541*, 542*, 56201, 56203, 56211, 56213, 566*, 5695*, 5720*, 5721*, 5750*; throat: 461*, 462*, 463*, 464*, 465*
Sepsis: sensitivity analysis definition (modified Angus)[a]	Any infection as listed above plus organ dysfunction by any diagnosis of 2866*, 2869*, 2874*, 2875*, 293*, 3481*, 3483*, 458*, 570*, 5734*, 584*, and 7855*, but not 78552, or by any procedure of 967*; or any diagnosis (with or without an organ dysfunction) of 78552 or 99592.
Sepsis: sensitivity analysis definition, explicit codes	Any diagnosis of 78552 or 99592
Continuous time variable	Based on DQTR and YEAR
Season variable	Based on DQTR

Variables obtained directly from HCUP data sets are denoted by using the HCUP variable name in all caps in the definition column. Diagnosis and procedure codes are based on the ICD-9-CM. CNS, central nervous system; DXPOAn, diagnosis n, present on admission; DQTR, discharge quarter; GI, gastrointestinal; GU, genitourinary ; HCUP, Healthcare Cost and Utilization Project; LOS, length of stay.

[a] The suffix * indicates that any code beginning with the given value was included, as applicable. For example, 421* includes 421, 4210, 4211, and 4219.

SUPPLEMENTAL TABLE 6 Complete Policy Time Line

Month and Year	Event
April 1, 2012	Rory Staunton died of sepsis, leading to media coverage in the summer of 2012
January 29, 2013	New York Governor Andrew Cuomo announced the development of Rory's Regulations
May 1, 2013	Regulations adopted
September 1, 2013	Hospitals required to submit sepsis protocols for review by the New York State Department of Health
December 31, 2013	Hospitals required to begin protocol implementation
April to June 2014	Hospitals required to begin reporting patient-level data on protocol adherence and outcomes to the state
July to September 2014	Hospitals received their first performance feedback from the New York State Department of Health

SUPPLEMENTAL TABLE 7 Comparative Interrupted Time-Series Analysis Point Estimates at the Time of the Policy Implementation (Intercepts) for the Risk-Adjusted Primary and Secondary Outcomes

Outcome	Study Group	*N*	Point Estimate (Change After the First Quarter of Implementation), % (95% CI)	Difference in Change, % (95% CI)	*P*
Mortality					
	New York	3964	0.82 (−4.88 to 6.51)	0.91 (−5.64 to 7.46)	.79
	Control	5472	−0.09 (−3.58 to 3.40)	—	—
ICU use					
	New York	3964	−0.56 (−4.88 to 3.75)	−1.49 (−6.89 to 3.91)	.59
	Control	5472	0.93 (−2.37 to 4.23)	—	—
Length of stay					
	New York	3964	−0.59 (−4.74 to 3.65)	−1.55 (−6.58 to 3.48)	.54
	Control	5472	0.96 (−1.99 to 3.91)	—	—
Central venous catheter placement					
	New York	3964	−2.97 (−8.71 to 2.77)	−2.37 (−10.10 to 5.35)	.55
	Control	5472	−0.59 (−5.75 to 4.56)	—	—
C difficile infection					
	New York	3964	−0.44 (−3.76 to 2.88)	−0.45 (−4.32 to 3.42)	.82
	Control	5472	0.01 (−2.02 to 2.03)	—	—

—, not applicable.

SUPPLEMENTAL TABLE 8 Comparative Interrupted Time-Series Analysis Slope Estimates of the Risk-Adjusted Secondary Outcomes for the Primary Analysis

Outcome	Study Group	*N*	Preimplementation Quarterly Trend, % (95% CI)	Postimplementation Quarterly Trend, % (95% CI)	Change in Quarterly Trend, % (95% CI)	Differential Change, % (95% CI)	*P*
ICU use	New York	3964	−0.25 (−1.00 to 0.50)	−0.38 (−0.99 to 0.24)	−0.13 (−1.27 to 1.01)	−0.61 (−2.04 to 0.82)	.40
	Control	5472	−0.35 (−1.04 to 0.35)	0.13 (−0.38 to 0.65)	0.48 (−0.41 to 1.38)	—	—
Length of stay	New York	3964	−0.64 (−1.31 to 0.02)	0.19 (−0.24 to 0.62)	0.84 (0.01 to 1.67)	0.82 (−0.38 to 2.02)	.18
	Control	5472	−0.26 (−0.85 to 0.34)	−0.24 (−0.75 to 0.27)	0.02 (−0.84 to 0.88)	—	—
Central venous catheter placement	New York	3964	−0.16 (−1.22 to 0.89)	−0.41 (−1.03 to 0.21)	−0.25 (−1.57 to 1.07)	1.20 (−0.61 to 3.01)	.19
	Control	5472	0.34 (−0.51 to 1.19)	−1.11 (−1.77 to 0.44)	−1.45 (−2.68 to 0.22)	—	—
C difficile infections	New York	3964	0.27 (−0.07 to 0.62)	0.00 (−0.02 to 0.02)	−0.27 (−0.65 to 0.10)	−0.46 (−1.08 to 0.17)	.15
	Control	5472	−0.20 (−0.54 to 0.14)	−0.02 (−0.32 to 0.28)	0.18 (−0.31 to 0.68)	—	—

—, not applicable.

SUPPLEMENTAL TABLE 9 Supplementary Analysis Examining the Association Between the Regulations and Sepsis Coding

Quarter	New York State, % With Sepsis (95% CI)	Control State, % With Sepsis (95% CI)
Q2 2013	0.66 (0.55 to 0.76)	0.43 (0.34 to 0.52)
Q3 2013	0.68 (0.57 to 0.79)	0.44 (0.36 to 0.53)
Q4 2013	0.70 (0.59 to 0.82)	0.46 (0.38 to 0.55)
Q1 2014	0.72 (0.60 to 0.85)	0.48 (0.39 to 0.57)
Q2 2014	0.75 (0.61 to 0.88)	0.50 (0.41 to 0.59)
Q3 2014	0.77 (0.63 to 0.91)	0.52 (0.43 to 0.61)
Q4 2014	0.79 (0.64 to 0.95)	0.54 (0.44 to 0.63)
Q1 2015	0.81 (0.64 to 0.98)	0.55 (0.45 to 0.66)
Q2 2015	0.84 (0.66 to 1.02)	0.57 (0.46 to 0.68)
Q3 2015	0.86 (0.67 to 1.05)	0.59 (0.47 to 0.71)

The goal of this analysis was to understand the potential association between the regulations and sepsis coding. If the regulations were associated with differential increased sepsis coding, it would introduce endogeneity because the regulations could be associated with the size and characteristics of the population under study. For this analysis, the population was all pediatric hospital admissions after implementation of the regulations; the dependent variable was whether the admission was coded for sepsis by using the primary definition, and covariates were patient and hospital characteristics, excluding any present-on-admission diagnosis flags. The *P* value of .42 and the coefficient on the interaction term of −0.01% (95% CI: −0.03 to 0.01) indicate no significant relationship between the regulation and sepsis coding that would indicate a differential sepsis coding pattern in New York after the regulations. The figure reveals the risk-adjusted quarter and group-specific sepsis diagnosis rates. Q1, quarter 1; Q2, quarter 2; Q3, quarter 3; Q4, quarter 4.