RESEARCH ARTICLE

Clinical Outcomes of Bronchiolitis After Implementation of a General Ward High Flow Nasal Cannula Guideline

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ABSTRACT

OBJECTIVE: The goal of this study was to assess the association of the introduction of a ward's high-flow nasal cannula (HFNC) guideline with clinical outcomes of infants with bronchiolitis.

METHODS: We conducted a retrospective, pre–post intervention study with an interrupted time series analysis of infants admitted with bronchiolitis between 2010 and 2014 at an urban, tertiary care children's hospital. Patients admitted in the 24 months before and after initiation of a guideline for HFNC use on the general wards were compared. The primary outcome was length of hospital stay. Secondary outcomes were PICU transfer rate and length of stay, intubation rate, and 30-day readmission, adjusted for season.

RESULTS: A total of 1937 patients met inclusion criteria; 936 were admitted before and 1001 admitted after the introduction of HFNC use on the general wards. Comparing the 2 groups, the hospital-wide rate of HFNC use in bronchiolitis treatment increased after HFNC became available on the wards (23.9% vs 35.2%; $P < .001$). The ward's HFNC guideline was not associated with a change in preintervention trajectory of total hospital length of stay ($P = .48$), PICU length of stay ($P = .06$), or rate of PICU transfer ($P = .97$). There was also no difference in intubation rate or 30-day readmission between the 2 groups.

CONCLUSIONS: Initiating a guideline for HFNC use on the general pediatric wards was associated with an increase in the use of the intervention with no significant change in total hospital length of stay, PICU length of stay and transfer rate, intubation rate, or 30-day readmission for patients with bronchiolitis.

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Bronchiolitis is the most common cause of hospitalization of infants aged <1 year in the United States and has a high associated health care cost.[1] The mainstay of treatment is supportive, including oxygen therapy for hypoxia, maintenance of hydration, and respiratory support.[2] High-flow nasal cannula (HFNC) therapy has been increasingly used for infants with bronchiolitis. Explanations for its mechanism of efficacy vary in the literature, with multiple proposed mechanisms.[3–5] HFNC is reserved in some hospitals for patients in the ICU. Studies of infants in the ICU setting noted increases in end-expiratory lung volume and slower respiratory rates among infants receiving HFNC.[6,7] There is evidence that HFNC is effective at reducing intubation in both the ICU and emergency department (ED) setting.[6,8,9] In addition, safety for this therapy when used on the general wards has been suggested in several small studies.[10–14]

Little has been published on clinical outcomes and resource utilization of patients with bronchiolitis receiving HFNC, and even less has been published regarding its use on the general wards. Most notably, there have been no randomized controlled trials published regarding HFNC. Two large reviews found insufficient data to enable a summary statement on the efficacy of this therapy.[15,16] In addition, the American Academy of Pediatrics' Bronchiolitis Guidelines from 2014 called for more research on the efficacy of HFNC in pediatric bronchiolitis.[2]

We recently studied an institutional change in practice that allowed for the use of HFNC on our general ward in patients initially admitted to the PICU and found an associated decreased hospital length of stay (LOS).[14] The objective of the present study was to assess the association between introduction of HFNC therapy on the general wards with clinical outcomes of any child admitted with bronchiolitis; an interrupted time series analysis was used to better control for secular trends. Our primary outcome measure was total LOS. In addition, we sought to measure the association of PICU transfer rate, PICU LOS, intubation rates, and 30-day readmission with the introduction of this guideline for infants with bronchiolitis.

METHODS

Study Design and Participants

We conducted a retrospective, pre–post intervention study of infants aged <24 months admitted with a diagnosis of bronchiolitis to Hasbro Children's Hospital between April 1, 2010, and March 31, 2014. Hasbro Children's Hospital is a tertiary care facility located in Providence, Rhode Island; this site admits ∼600 patients for bronchiolitis annually. It is the principal tertiary pediatric care center for the state of Rhode Island and bordering communities and serves a predominantly urban and suburban population.

HFNC Guideline

Hasbro Children's Hospital initiated an institutional guideline for HFNC use on the general wards in March 2012. The guideline stated that a patient could be initially admitted to the wards on HFNC, the therapy could be initiated for an established patient on the wards, or a patient in the ICU receiving HFNC could be transferred to the general wards while continuing this therapy. It includes guidelines for indications, initiation, and weaning of HFNC.[17] During the years of study, maximum flow for patients <6 months old was 8 liters per minute (LPM); for those aged 6 to 18 months, it was 12 LPM; and for patients aged ≥18 to 24 months, the maximum flow was 15 LPM. Flow rates above these parameters warrant attending and respiratory therapy discussion. The ability to wean off HFNC is based on patient work of breathing, respiratory rate, and improvements in other clinical factors.

Data Collection

For the present study, we compared patients in the 24 months before and the 24 months after introduction of the HFNC guideline. The hospital billing database was used to identify patients who were admitted with bronchiolitis during the 2 study time periods, and data contained within the database were extracted electronically. In addition, chart review was conducted by the primary researcher and 1 research assistant, each of whom was unblinded to the nature of the study.

Inclusion/Exclusion Criteria

All charts with any discharge diagnosis with International Classification of Diseases, Ninth Edition, codes 466.19 (non–respiratory syncytial virus [RSV] bronchiolitis), 466.11 (RSV bronchiolitis), 786.03 (apnea), 465.9 (acute upper respiratory infection), and V73.99 (unspecified viral illness) were screened for inclusion by reviewers. High flow was defined as >2 LPM for patients <18 months old, and >4 LPM for patients >18 months old, while utilizing a heated, humidification device, which is consistent with other studies.[4,6] Patients aged >24 months were excluded to reduce the inclusion of non-bronchiolitis acute respiratory tract infections; also excluded were children hospitalized for >21 days to reduce the inclusion of patients with a more complex course. We excluded infants <37 weeks' gestation and patients with specific diagnoses of chronic lung diseases, asthma, chromosomal abnormalities, heart disease, and neurologic diseases.

This study was approved by the hospital's institutional review board.

Outcome Measures

The primary outcome assessed was hospital LOS (in integer days) after initiation of the general ward HFNC guideline. Secondary clinical outcomes, including PICU transfer from the wards (yes/no), PICU LOS (in days), and potential adverse outcomes (intubation and 30-day readmission [yes/no]), were recorded by chart reviewers from documentation within the medical record.

Other Covariates

Demographic data (including age, sex, and race/ethnicity) were extracted electronically by using the hospital billing database. Severity levels (1 = minor to 4 = extreme) for each patient encounter were obtained from All Patient Refined Diagnosis Related Group (APR-DRG) documentation provided by the billing department. The research team recorded insurance status (private, public, or uninsured) from the patient demographic sheet (completed by registration at the time of admission). Reviewers examined patients' charted

admission history and recorded secondhand smoke exposure (yes/no) if it was noted in the record. PICU LOS data were provided by Hasbro Children's Hospital's virtual PICU database. Chart reviewers also collected information on diagnostic testing in any clinical area (RSV [positive, negative, or not tested] and chest radiograph [yes/no]) and therapeutic interventions of total number of days of HFNC.

Inter-rater Reliability

Ten percent of charts were randomly selected and reviewed by the 2 abstractors, each with 9 indicators per chart. Charts were considered discrepant if any indicator differed between abstractors. The Cohen's κ score for overall inter-rater reliability was 0.94 (95% confidence interval, 0.89–0.99), with a chart review agreement of 96%. Conflicting data were re-reviewed by both reviewers for final resolution.

Data Analysis

Using Stata version 12.1 (StataCorp, College Station, TX), descriptive statistics were calculated to characterize the overall study population. We reported counts and proportions for categorical variables, means and 95% confidence intervals for normally distributed continuous variables, and medians and interquartile ranges (IQRs) for skewed variables. Two groups of patients were created to compare those admitted during the 24 months before the introduction of the HFNC guideline and those admitted during the 24 months after the start of the guideline. We then conducted a bivariate analysis using χ^2 tests for categorical variables and Student's *t* test or Wilcoxon rank sum test for continuous variables. Results were considered significant if a 2-sided *P* value was $< .05$.

Changes in outcomes before and after guideline implementation were assessed by using an interrupted time series analysis applied to a Generalized Linear Model framework assuming an underlying binomial distribution for proportions and an underlying exponential distribution for maximum HFNC rate and time variables (LOS, ICU LOS, and days' HFNC). Covariates in the model included a preimplementation slope effect, a postimplementation slope effect, and an effect to capture any change in model intercept between the preimplementation and postimplementation periods. Model fit statistics were assessed to ensure a lack of evidence for overdispersion.

All interrupted time series analyses were conducted by using SAS version 9.4 (SAS Institute, Inc, Cary, NC). Tests with a *P* value $\leq .05$ were considered statistically significant.

RESULTS

A total of 936 patients were admitted in the 24 months before introduction of HFNC on the general wards ("before group"), and 1001 were admitted in the 24 months after introduction of HFNC ("after group") (Fig 1). The baseline characteristics of the 2 groups are presented in Table 1. Patients in the before group were younger, and there was a significant difference in patients' race between the 2 cohorts. However, there was no significant difference in sex, ethnicity, insurance status, or secondhand smoke exposure.

Table 2 summarizes unadjusted analyses, including diagnostic testing, illness severity, therapeutic interventions occurring in any clinical area during hospitalization, and clinical outcomes. Comparing the 2 groups of patients with bronchiolitis, fewer patients were tested for RSV in the after group. However, of those tested for RSV, there was no difference in RSV positivity. Fewer patients had a chest radiograph in the group after HFNC was introduced on the wards. More patients with bronchiolitis received HFNC therapy in the 24 months after HFNC introduction on the wards (23.9% [224 of 936] vs 35.2% [352 of 1001]; $P < .001$).

Figures 2 and 3 detail interrupted time series adjusted outcome rates and trajectories. In the unadjusted comparison of the 2 groups before and after introduction of HFNC on the general wards, the mean number of days of HFNC was significantly less (2.5 vs 2.0 days; $P < .001$). However, in the adjusted interrupted time series model, the introduction of HFNC on the general wards was not associated with a change in the length of HFNC trajectory or a difference in the number of days of HFNC relative to the before group trend (Table 2, Fig 3).

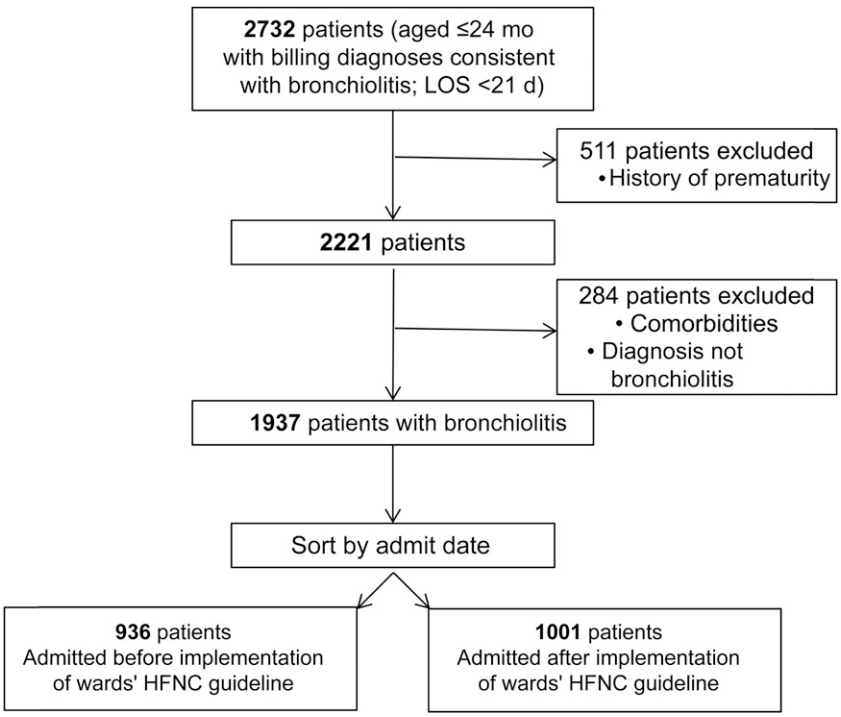

FIGURE 1 Patient flow diagram.

TABLE 1 Baseline Characteristics of Patients With Bronchiolitis Before and After Implementation of HFNC on the General Pediatric Wards ($N = 1937$)

Characteristic	Before ($n = 936$)	After ($n = 1001$)	P
Age, median (IQR), mo	4 (1.75–10)	5 (2–11)	.001
Male	526/936 (56.2%)	592/1001 (59.1%)	.19
Race			.004
White	529/913 (57.9%)	624/973 (64.1%)	—
African American	125/913 (13.7%)	91/973 (9.4%)	—
Other	259/913 (28.4%)	258/973 (26.5%)	—
Hispanic/Latino	288/907 (31.8%)	286/973 (29.4%)	.27
Public insurance	716/936 (76.5%)	756/1001 (75.5%)	.63
Secondhand smoke exposure	273/844 (32.3%)	273/884 (30.9%)	.53

Data are presented as *n/N* (%) unless otherwise indicated. —, not applicable.

Based on APR-DRG severity levels, the after group had a significantly higher mean severity level (1.41 vs 1.86; $P < .001$). Using an adjusted interrupted time series model, the after group also had an increased percentage of bronchiolitis discharges classified with greater severity (levels 3 and 4) ($P = .035$ for the preimplementation vs postintervention slope difference).

Total Hospital LOS

In the unadjusted comparison of the 2 groups before and after introduction of HFNC on the general wards, both the median and mean total LOS for patients with bronchiolitis were significantly reduced (2 days [IQR, 1–3 days] vs 1 day [IQR, 1–3 days], $P = .001$, and 2.4 ± 2.0 days vs 2.2 ± 1.9 days, $P = .02$). However, in the adjusted interrupted time series model, the introduction of HFNC on the general wards was not associated with a change in the LOS trajectory or a difference in the LOS relative to the before group trend. When separating the groups into those who did not receive HFNC and patients requiring HFNC, and adjusting using an interrupted time series model, the introduction of HFNC on the general wards was again not associated with a change in the LOS trajectory for either group (Table 2, Fig 2).

TABLE 2 Unadjusted Interventions Performed and Clinical Outcomes of Bronchiolitis Before and After Implementation of HFNC on the General Pediatric Wards ($N = 1937$)

Characteristic	Before ($n = 936$)	After ($n = 1001$)	P
Diagnostic testing/severity			
RSV tested	583/936 (62.3)	464/1001 (46.4)	<.001
RSV positive (of tested)	387/583 (66.4)	292/464 (62.9)	.27
Chest radiograph performed	562/936 (60.0)	476/1001 (47.6)	<.001
APR-DRG severity level, mean ± SD (95% CI)[a]	1.41 ± 0.02 (1.36–1.45)	1.86 ± 0.02 (1.81–1.91)	<.001
Therapeutic interventions			
Received any HFNC therapy	224/936 (23.9)	352/1001 (35.2)	<.001
Days of HFNC, mean ± SD (95% CI)	2.5 ± 1.5 (2.3–2.7)	2.0 ± 1.4 (1.9–2.2)	<.001
Hospital LOS, median (IQR), d			
All patients with bronchiolitis	2 (1–3)	1 (1–3)	.001
HFNC patients	4 (3–6)	3 (2–4)	<.001
Clinical outcomes			
PICU LOS, median (IQR), d	2.3 (1.5–3.4)	1.7 (1.0–2.6)	<.001
Transfer back to PICU (after leaving PICU)	6/239 (2.5)	5/273 (1.8)	.76
Intubation	12/936 (1.3)	15/1001 (1.5)	.70
30-d readmission	73/936 (7.8)	90/1001 (9.0)	.37

Data are presented as *n/N* (%) unless otherwise indicated. CI, confidence interval.
[a] APR-DRG severity levels were rated as 1 = minor to 4 = extreme.

PICU Outcomes

In the unadjusted comparison of the 2 groups before and after introduction of HFNC on the general wards, the median PICU LOS for patients with bronchiolitis was significantly reduced (2.3 days [IQR, 1.5–3.4] vs 1.7 days [IQR, 1.0–2.6]; $P < .001$). However, in the adjusted interrupted time series model, the introduction of HFNC on the general wards was not associated with a change in the PICU LOS trajectory or a difference in the PICU LOS relative to the before group trend. Similarly, there was no significant difference in the rate of PICU admission ($P = .38$ for the preimplementation vs postintervention slope difference) or in the PICU transfer rate ($P = .97$ for the preimplementation vs postintervention slope difference) in the adjusted interrupted time series model (Fig 3). There was no difference in the proportion of patients returning to the PICU once they were transferred out of the PICU to the general wards (2.5% vs 1.8%; $P = .76$).

Other Secondary Outcomes

In both the unadjusted analysis and the adjusted interrupted time series model, the introduction of HFNC on the general wards was not associated with a difference in intubation rate ($P = .70$ and $P = .06$, respectively, for the preimplementation vs postintervention slope difference) or 30-day readmission rate ($P = .37$ and $P = .8$ for the preimplementation vs postintervention slope difference). There were no cases of pneumothorax or other complications from HFNC in either group, and there were no deaths in either group.

Overall, we found that the availability of high flow demonstrated an increased use of the intervention with no significant impact on important outcomes such as LOS, PICU LOS, and PICU transfer rate.

DISCUSSION

We found that initiating a guideline for HFNC use on the general pediatric wards was

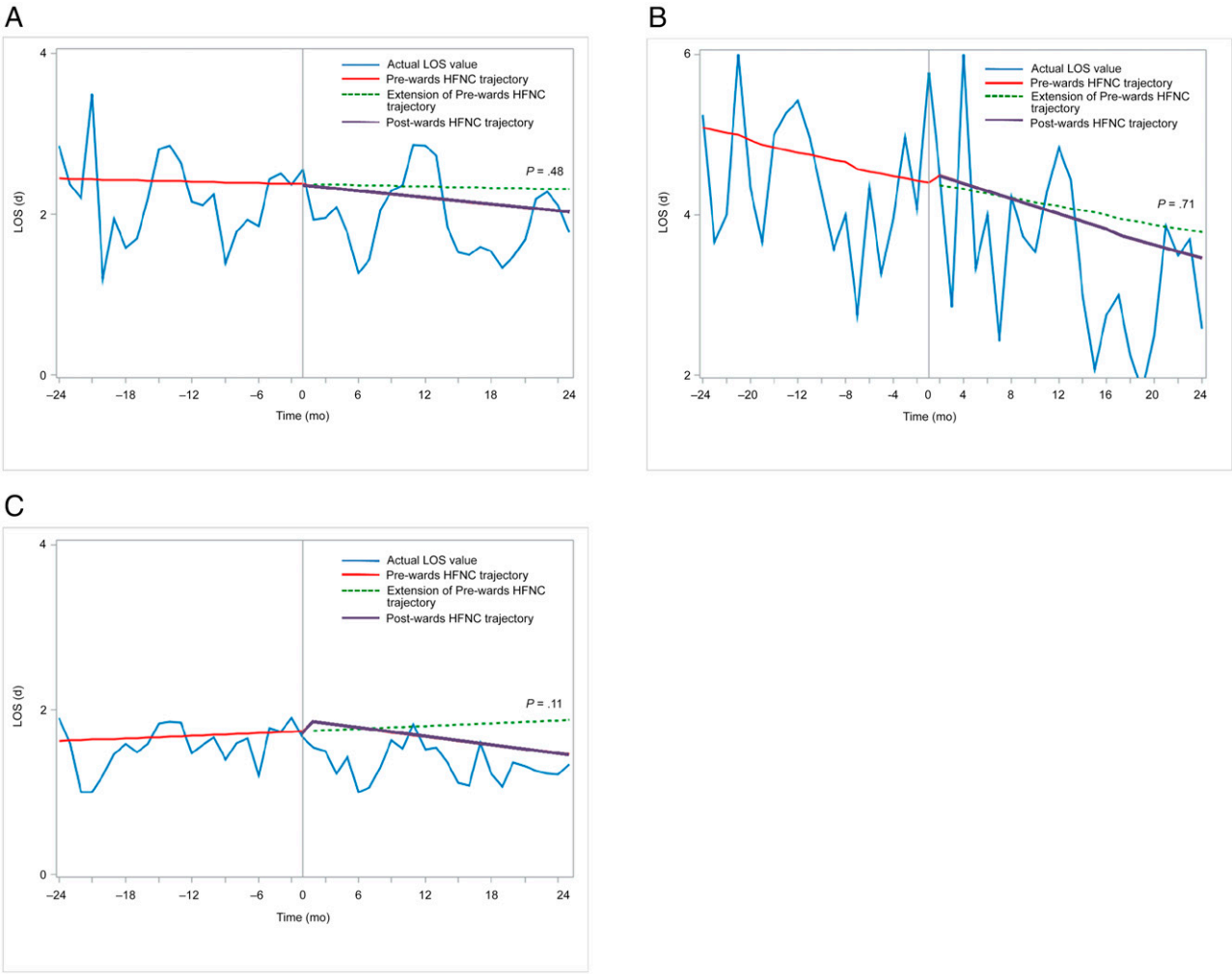

FIGURE 2 Length of stay (LOS) and pre- and post-guideline trajectories. A, Hospital LOS for all patients with bronchiolitis. B, LOS for patients with bronchiolitis who received HFNC. C, LOS for patients with bronchiolitis who did not receive HFNC. The vertical line at time 0 (March 2012) indicates the month of the ward's HFNC guideline implementation. *P* value represents difference in preimplementation versus postintervention slope.

associated with an increase in the use of the intervention with no significant change and any measured clinical outcome of bronchiolitis. There is limited evidence for clinical outcomes of HFNC use in bronchiolitis outside of the ED and PICU. Our study examined the largest cohort to date of patients with bronchiolitis on HFNC (N = 576), including its use on the general wards and the impact on PICU transfer rate and PICU LOS. Our previous study found a reduced hospital LOS in those patients with bronchiolitis initially admitted on HFNC to the PICU.[14] However, our present study corrects potential misconceptions generated in this previous research by controlling for secular trends and addressing whether outcomes could be explained by trends already in place before the HFNC guideline was implemented.

Overall, more patients with bronchiolitis received HFNC therapy in the 24 months after introduction of the guideline. One explanation for the increased use is that this group had more severe bronchiolitis, based on APR-DRG severity levels, thus necessitating more HFNC use. However, it is more likely that, because of the elements that contribute to a severity level assignment, the use of HFNC itself could explain the increase in APR-DRG rather than any other patient characteristics. Some patients in the after group were likely started on HFNC earlier in their hospital course because before implementation of the guidelines, its use would obligate the patient to be transferred to the PICU. There is a paucity of evidence to support earlier HFNC initiation on the general wards, but earlier use has been shown to reduce intubation rates in the ED and PICU.[6,8,9] However, because we found no difference in our measured outcomes, we postulate that the increased HFNC use may be due, in part, to its increased availability across clinical areas, subsequently resulting in overuse of this intervention.

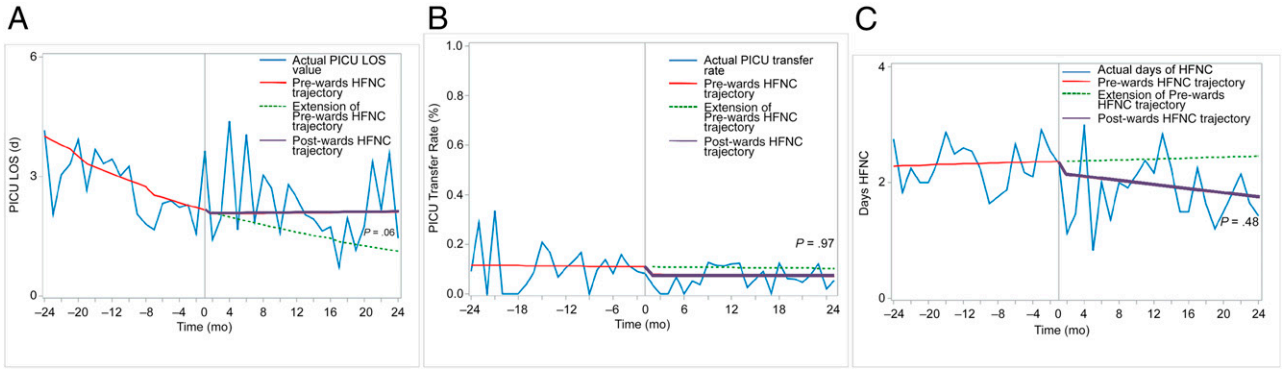

FIGURE 3 Outcome rates and pre- and post-guideline trajectories. A, PICU LOS. B, Transfer rate to the PICU. C, Number of days of HFNC therapy. The vertical line at time 0 (March 2012) indicates the month of the ward's HFNC guideline implementation. *P* value represents difference in preimplementation versus postintervention slope.

Nationally, the overall hospital LOS for bronchiolitis has been steadily decreasing.[18] Although it may be tempting to evaluate interventions, including HFNC, and attribute these to explain this trend, we found implementing the wards' HFNC guideline was not associated with a reduction in total hospital LOS, PICU LOS, PICU admission, or transfer rate. In fact, it is possible that use of HFNC and the time associated with weaning this therapy may actually lead to an increase in LOS. This information may be helpful to institutions debating the barriers, costs, and challenges of developing and implementing a ward HFNC guideline.

There are limitations to our study. A significant limitation of a single-site, nonrandomized, pre–post intervention study design is difficulty in controlling for confounding variables. Although we compared some baseline patient demographic characteristics, there is the possibility that the outcome differences could be explained by some other patient-level factors or unmeasured variables.

APR-DRG severity levels were used to measure severity rather than patients' respiratory distress scores, which have been used in previous studies of both ICU and ER bronchiolitis management,[19–21] due to the inconsistent documentation of respiratory scores in our charts. The reasons for intubation (ie, hypercapnia, respiratory fatigue, persistent apneas) were neither consistently nor objectively recorded, and thus we are unable to comment on its indication. Once again, it is possible that the use of HFNC itself could explain the increase in APR-DRG severity level rather than any other patient characteristic.

Total hospital LOS was measured in whole integer number of days. This method is most likely the biggest limitation of our study. The electronic medical record at the time of study was not sophisticated enough to measure LOS in actual time between admission and discharge, which may have resulted in the difference in LOS being understated. Because hospitalization cost has been shown to be closely related to LOS in bronchiolitis,[22,23] and our LOS data were imprecise, we did not analyze cost data.

Limitations of an interrupted time series analysis include difficulty in analyzing the independent impact of separate components between groups that were initiated close together in time, and the lack of a suitable control population. The estimates of the overall effect on LOS and other outcomes involve extrapolation, which is inevitably associated with uncertainty.

HFNC has been increasingly used in bronchiolitis treatment because of its tolerance and ease of use, but it is restricted to the ICU setting in many pediatric hospitals. Our findings are generalizable only to hospitals that perform HFNC on the general wards, but our study may be relevant to institutions debating considering establishing HFNC use on the general wards. Although we found no reduction in total LOS for patients with bronchiolitis with the availability of HFNC on the general wards, more research using longitudinal observational designs and randomized controlled trials are required to determine the relationship between a general ward's HFNC guideline and clinical outcomes in bronchiolitis.

CONCLUSIONS

Using interrupted time series analysis, we found no difference in total hospital LOS, PICU LOS, transfer to the PICU, intubation rate, or 30-day readmission after initiating a guideline for HFNC use for bronchiolitis on general pediatric wards.

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