

## RESEARCH ARTICLE

# High-Flow Nasal Cannula in Bronchiolitis at a Pediatric Emergency Department: Trends and Outcomes

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## ABSTRACT

**OBJECTIVES:** Use of high-flow nasal cannula (HFNC) for bronchiolitis has increased, but data describing the current use and impact of this therapy are limited. Our objective with this study was to describe the use of HFNC for bronchiolitis in a pediatric emergency department (ED) from 2013 to 2019 and to explore associations with clinical outcomes.

**METHODS:** This was a retrospective cohort study of children aged 2 to 24 months with the diagnosis of bronchiolitis. The primary outcome was HFNC initiation in the ED. Secondary outcomes included admission rate, ICU (PICU) admission, transfer to PICU from floor, and endotracheal intubation. An adjusted interrupted times series analysis was performed to analyze changes in rates of primary and secondary outcomes over time.

**RESULTS:** In total 11 149 children met inclusion criteria; 902 (8.1%) were initiated on HFNC. The rate of HFNC initiation increased from 1.3% in 2012–2013 to 17.0% in 2018–2019 ( $P_{\text{trend}} \leq .001$ ). Less than 30% of children initiated on HFNC were hypoxic. There were no significant changes over time in rates of hospital admission, PICU admission, or PICU transfer, adjusting for clinical severity, seasonality, and provider variation. Intubation rate increased over the study period.

**CONCLUSIONS:** We found a 13-fold increase in HFNC use over a 6-year period with no evidence of improvement in clinically meaningful outcomes. Clinical benefit should be clearly defined before further expansion of the use of HFNC for bronchiolitis in the ED.

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Bronchiolitis is one of the most common causes of pediatric emergency department (ED) use and hospitalization for children <2 years of age in the United States.<sup>1</sup> There is no therapy recommended in the United States to change the course of illness of children with bronchiolitis and no high-quality evidence for interventions other than supportive care.<sup>2</sup> In the past decade, heated, humidified high-flow nasal cannula (HFNC), a noninvasive respiratory therapy, has been widely adopted in hospitals and EDs.<sup>3</sup> Although there have been small retrospective studies suggesting a decrease in endotracheal intubation rates in critical care settings, or improvement in measures such as heart or respiratory rate after the introduction of HFNC, larger studies and randomized trials have not shown an improvement in patient-centered outcomes such as length of stay or endotracheal intubation rates associated with the use of HFNC.<sup>2,4-8</sup> Additionally, the large randomized studies of HFNC have been performed in children with hypoxia (with varying definitions of hypoxia).<sup>4,5</sup> The prevalence of hypoxia among children placed on HFNC in the United States is unknown, but in practice, it is often used for respiratory support in children without hypoxia.<sup>9</sup>

Despite the low risk of clinical complications due to the use of HFNC, there are potential downsides of increased HFNC use, including increased costs and interrupted oral feeding.<sup>10,11</sup> The clinical criteria for use of HFNC in bronchiolitis in the United States have not been defined, and it is unclear whether the increased use of HFNC has led to improved clinical outcomes in children with bronchiolitis.

Our objectives with this study were to (1) determine the clinical factors associated with the use of HFNC in the ED for young children with bronchiolitis and (2) describe the trends in HFNC use and associated clinically important outcomes over 6 consecutive years.

## METHODS

### Study Design and Setting

We performed a single-center retrospective cohort study of all children presenting to a large tertiary care children's hospital ED in

the midwestern United States with a diagnosis consistent with bronchiolitis between January 1, 2013, and June 30, 2019. At the beginning of our study period in 2013, HFNC use was restricted to the ED and PICU. A protocol allowing HFNC use at flow rates up to 6 L/minute on the general pediatric inpatient unit was implemented on January 1, 2016, and this limit was increased to 2 L per patient kilogram per minute on January 24, 2018. There were no clinical guidelines for ED HFNC initiation for bronchiolitis at our institution during the study period. Our institutional review board approved this study.

### Selection of Participants

We identified all children aged 2 to 24 months evaluated in the ED with an assigned ED provider discharge diagnosis or billing diagnosis of bronchiolitis (*International Classification of Diseases, 10th Revision, Clinical Modification* [ICD-10-CM] code of J21). When ICD-10-CM codes replaced *International Classification of Diseases, 9th Revision* codes in 2015, our electronic medical record (EMR) converted all *International Classification of Diseases, 9th Revision* codes to ICD-10-CM retroactively. We excluded children <2 months of age to avoid including children initiated on HFNC for apnea. To avoid potential diagnostic misclassification, we excluded children with an ICD-10-CM code consistent with a chronic complex condition at the time of the ED visit.<sup>12</sup> Children could be enrolled multiple times over the study period.

### Measurements

Patient demographics and clinical characteristics were extracted from the EMR. Clinical variables extracted from the ED encounter included age, sex, encounter date and time, medical history, evaluation in the resuscitation bay, Emergency Severity Index (ESI) triage score, initial vital signs (temperature, heart rate, respiratory rate, systolic and diastolic blood pressures, and pulse oxygen saturation [SpO<sub>2</sub>]), lowest ED oxygen saturation, medication administered, initiation of HFNC in the ED, presence of tracheal intubation, and disposition (admission to PICU, admission to general floor, discharge). We defined hypoxia as

<90% oxygen saturation at any time during the visit, which is consistent with American Academy of Pediatrics recommendations.<sup>2,13</sup> For admitted patients, outcomes extracted from the EMR included transfer to the PICU from the general floor after admission and tracheal intubation after admission.

### Outcomes

The primary outcome was the initiation of HFNC in the ED. HFNC was defined as flow rates >4 L/minute and administered with an HFNC device.<sup>14</sup> To ensure proper classification of the primary outcome (the initiation of HFNC in the ED), we manually reviewed the ED charts of 50 randomly selected admitted patients per year (300 total). Secondary outcomes included the rate of admission to the general inpatient unit, rate of admission to the PICU, rate of transfer from the inpatient general unit to the PICU, and endotracheal intubation in the ED or after admission.

### Analysis

We examined the factors associated with the initiation of HFNC using the  $\chi^2$  test for categorical variables, the *t* test for normally distributed continuous variables, and the Wilcoxon rank test for nonnormally distributed continuous variables.

We assessed for unadjusted temporal trends in the rates of the primary and secondary outcomes using the Cochran-Armitage test.<sup>15</sup> The primary outcome was modeled by using generalized linear mixed models with providers as a random effect to account for between-provider variation and the patients' age, ESI level, initial oxygen saturation, lowest ED oxygen saturation, and academic year of visit as covariates.

We performed an interrupted time series (ITS) analysis of the primary and secondary outcomes to determine (1) if there was an increase in rates of the outcomes associated with changes in floor policy adjusting for baseline temporal trends and (2) if rates of the primary and secondary outcomes were increasing or decreasing over the study period adjusting for seasonality and clinical covariates. To determine if increases in the rates of the primary and secondary outcomes were associated with changes in hospital policy

in January 2016 and January 2018, we performed a robust ITS analysis with segmented regression, separated into 3 segments: before 2016, during 2016–2017, and 2018 and after. We used a generalized linear mixed model with random effects to account for autocorrelation by seasonality and provider-to-provider variations. An adjusted model was built to evaluate the effects of covariates, including the patient's age, triage ESI level, triage oxygen saturation, and the minimum ED oxygen saturation. Odds ratios (ORs) of rates of outcomes in posthospital policy change periods over prechange periods were estimated and tested for significance. To determine if rates of the primary and secondary outcomes were increasing or decreasing overall over the study period in the adjusted models, we determined the slopes of the adjusted ITS models and tested them for significance. Statistical analyses were conducted by using the R statistical software (version 3.5.0) and SAS 9.4 (SAS Institute, Inc, Cary, NC).

## RESULTS

### Characteristics of Study Subjects

Over the 6-year study period, 87 357 eligible encounters were identified on the basis of age. Of the 11 660 encounters (13.3%) with an ICD-10-CM diagnosis code for bronchiolitis, 511 (0.5%) were excluded because of complex chronic conditions. Of the 11 149 analyzed encounters, 4719 (42.3%) were admitted and 902 (8.1%) were initiated on HFNC in the ED (Fig 1). The median age of study subjects was 8.4 months, and 59.5% were male. We found the extracted EMR classification of the initiation of HFNC to have excellent agreement with manual review ( $\kappa$  statistic of 0.99; 95% confidence interval [CI]: 0.97–1.0).

### Main Results

Children initiated on HFNC were older, more likely to be evaluated in the resuscitation bay, had a lower triage ESI level, and had significant differences in vital signs, including oxygen saturation on arrival, compared with children not initiated on HFNC (Table 1). A total of 249 (27.6%) children initiated on HFNC during their ED encounter were hypoxic (<90%) at any time

**TABLE 1** Clinical Characteristics of Children Initiated on HFNC in the ED

|                                                | No ED HFNC Initiation<br>(n = 10 247) | ED HFNC Initiation<br>(n = 902) | P    |
|------------------------------------------------|---------------------------------------|---------------------------------|------|
| Age, median (IQR), d                           | 233 (141–384)                         | 262 (136–432)                   | .01  |
| Male, %                                        | 6089 (59.4)                           | 545 (60.4)                      | .98  |
| Wt, mean (SD), kg                              | 8.58 (2.45)                           | 8.61 (2.42)                     | .69  |
| Resuscitation bay activation, %                | 591 (5.8)                             | 388 (43.0)                      | <.01 |
| ESI level, %                                   |                                       |                                 | <.01 |
| 1                                              | 13 (0.1)                              | 16 (1.8)                        | —    |
| 2                                              | 2936 (28.7)                           | 712 (79.5)                      | —    |
| 3                                              | 4939 (48.3)                           | 150 (16.7)                      | —    |
| 4                                              | 2132 (20.8)                           | 18 (2.0)                        | —    |
| 5                                              | 209 (2.0)                             | 0 (0.0)                         | —    |
| Temperature, mean (SD), °F                     | 99.7 (1.6)                            | 99.8 (1.5)                      | .40  |
| Fever, %                                       | 2924 (28.6)                           | 269 (29.8)                      | .46  |
| Respiratory rate, mean (SD)                    | 48.7 (12.6)                           | 54.7 (14.8)                     | <.01 |
| Pulse rate, mean (SD)                          | 153.0 (19.6)                          | 166.8 (20.0)                    | <.01 |
| Triage MAP, mean (SD)                          | 81.1 (12.6)                           | 83.7 (13.9)                     | <.01 |
| Triage O <sub>2</sub> saturation, median (IQR) | 97 (95–99)                            | 95 (92–97)                      | <.01 |
| Triage hypoxia (O <sub>2</sub> <90%), %        | 207 (2.1)                             | 123 (13.6)                      | <.01 |
| Lowest ED O <sub>2</sub> saturation, %         |                                       |                                 | <.01 |
| <90                                            | 747 (7.4)                             | 249 (27.6)                      | —    |
| 90–92                                          | 809 (8.0)                             | 201 (22.2)                      | —    |
| 93–94                                          | 1397 (13.9)                           | 205 (22.7)                      | —    |
| >95                                            | 7131 (70.7)                           | 247 (27.4)                      | —    |

IQR, interquartile range; MAP, mean arterial pressure; O<sub>2</sub>, oxygen.

in the ED. A total of 655 (72.6%) children initiated on HFNC in the ED had oxygen saturations <95%.

According to the generalized linear mixed model, we found lower ESI level (ESI 1 or 2: OR 21.9 [95% CI: 12.5–38.5]; ESI 3: OR 3.42 [95% CI: 2.0–5.8]), lower triage oxygen saturation (OR 0.96; 95% CI: 0.93–0.99), and lower minimum ED oxygen saturation (OR 0.92; 95% CI: 0.90–0.95) to be associated with the initiation of HFNC in the ED. Age was not significantly associated with ED HFNC initiation (OR 0.99; 95% CI: 0.98–1.0).

### Changes in the Use of HFNC and Associated Outcomes by Academic Year

The rate of ED HFNC initiation among all eligible encounters rose from 1.3% in the 2012–2013 academic year to 17.0% in the 2018–2019 academic year ( $P_{\text{trend}} \leq 0.01$ ). Among admitted patients, the rates of initiation rose from 3.3% in 2012–2013 to 35.6% in 2018–2019 ( $P_{\text{trend}} \leq 0.01$ ).

The total admission rate increased from 39.1% to 47.7% ( $P_{\text{trend}} \leq 0.01$ ). Among admitted patients, the rate of patients admitted to the PICU increased from 9.8% to 23.2% ( $P_{\text{trend}} \leq 0.01$ ) and the rate of transfer to the PICU increased from 3.1% to 5.1% ( $P_{\text{trend}} = 0.01$ ). Outcome rates by year are presented in Table 2.

### Adjusted ITS Analysis

In the adjusted ITS analysis, rates of ED HFNC initiation increased significantly in January 2016 when HFNC was allowed on the general inpatient floor (OR 1.67; 95% CI: 1.12–2.49) and when maximum floor HFNC rates were liberalized to 2 L/kg in January 2018 (OR 2.55; 95% CI: 1.39–4.68) (Fig 2). Adjusted and unadjusted ORs for the primary and secondary outcomes in the 3 time periods are shown in Table 3. No secondary outcomes revealed significant changes in the 3 periods of interest except for intubation rates from 2016 to 2017 to after 2017 (OR 4.93; 95% CI: 1.36–17.85). The

**TABLE 2** Rates of HFNC and Outcomes by Year

|                                               | Academic Year (July–June) |            |            |            |            |            |            | P <sup>a</sup> |
|-----------------------------------------------|---------------------------|------------|------------|------------|------------|------------|------------|----------------|
|                                               | 2012–2013                 | 2013–2014  | 2014–2015  | 2015–2016  | 2016–2017  | 2017–2018  | 2018–2019  |                |
| ED HFNC initiation, <i>n</i> (%) <sup>b</sup> | 15 (3.3)                  | 38 (7.1)   | 71 (9.8)   | 95 (15.5)  | 133 (20.6) | 203 (26.1) | 345 (35.6) | <.01           |
| Admission, <i>n</i> (%)                       | 458 (39.1)                | 535 (36.1) | 722 (40.6) | 613 (41.3) | 645 (41.3) | 777 (45.9) | 969 (47.7) | <.01           |
| PICU admission, <i>n</i> (%) <sup>b</sup>     | 45 (9.8)                  | 132 (24.7) | 128 (17.7) | 106 (17.3) | 146 (22.6) | 131 (16.9) | 225 (23.2) | <.01           |
| Transfer to PICU, <i>n</i> (%) <sup>b</sup>   | 14 (3.1)                  | 14 (2.6)   | 29 (4.0)   | 27 (4.4)   | 23 (3.6)   | 40 (5.1)   | 49 (5.1)   | .01            |
| Intubation, <i>n</i> (%) <sup>b</sup>         | 5 (1.1)                   | 15 (2.8)   | 23 (3.2)   | 19 (3.1)   | 15 (2.3)   | 26 (3.3)   | 28 (2.9)   | .2             |

<sup>a</sup> Cochran-Armitage test for trend.

<sup>b</sup> Percentage among admitted patients.

ITS models for secondary outcomes are presented in the Supplemental Information.

The significance testing of the slopes of the primary and secondary outcomes over the entire period of study are presented in Table 4. Rates of ED HFNC increased over the study period in the unadjusted and adjusted ITS models. There was no significant change over the study period in rates of admission, PICU admission, or PICU transfer in either the adjusted or unadjusted ITS models. There was an increased rate of endotracheal intubation in the adjusted ITS

model, which was not present in the unadjusted model.

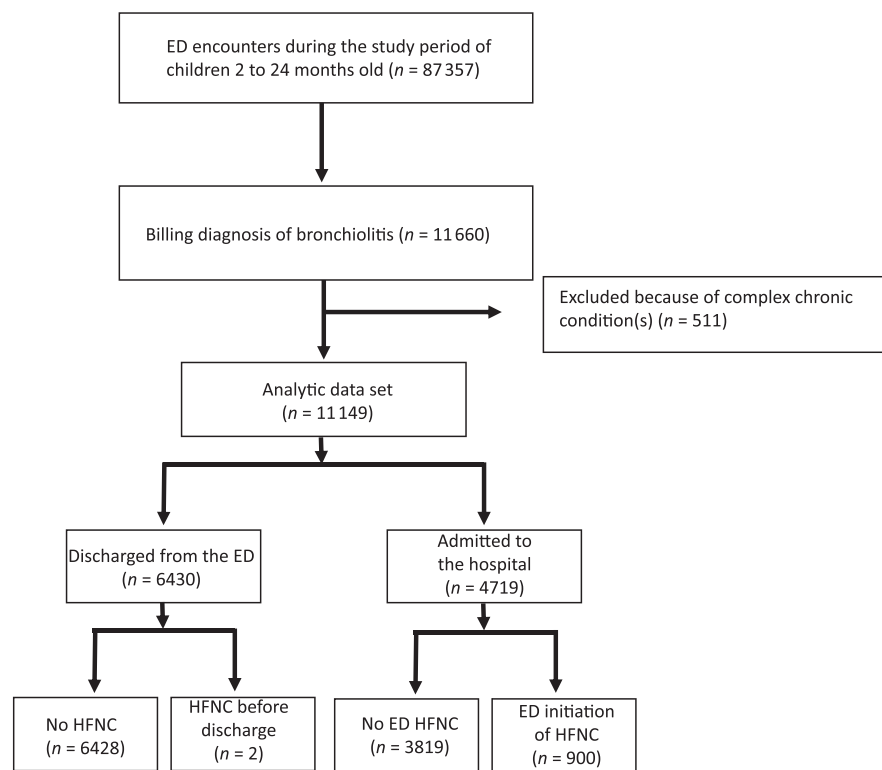
## DISCUSSION

Over the study period, we observed a 13-fold increase in the use of HFNC, with a clear temporal association between the institution and liberalization of hospital general inpatient floor-based HFNC protocols on ED HFNC use. In the ITS models, which adjusted for provider variation and seasonality in addition to clinical factors, we found no overall change in rates of hospital admission, PICU admission, or PICU transfer.

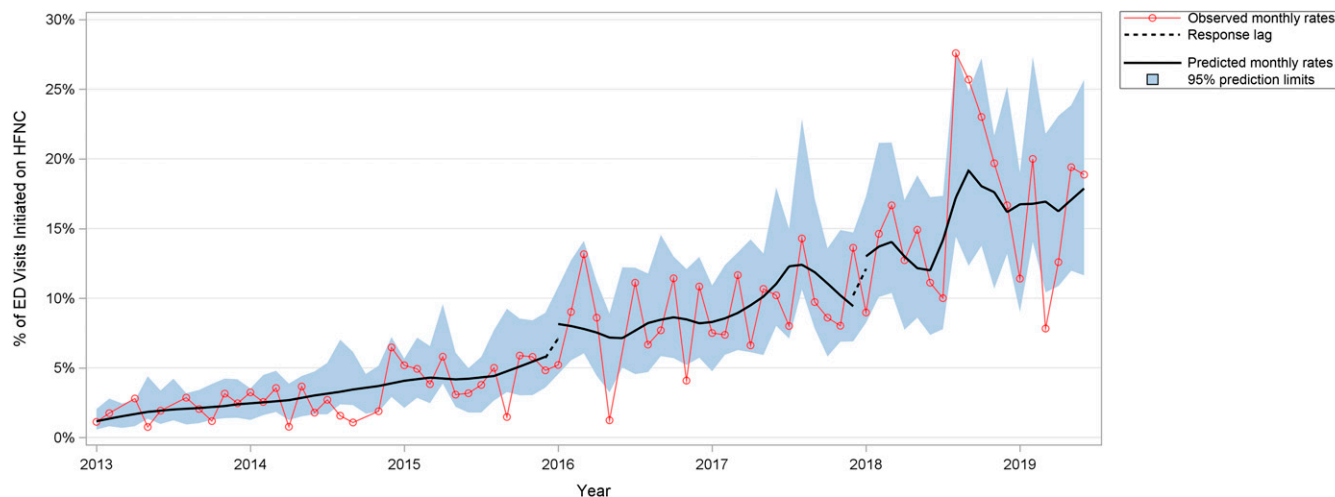
There was an increase in rates of intubation over the study period after adjusting for age, ESI level, and triage and ED lowest oxygen saturation.

Although HFNC has been shown to improve physiologic measures of work of breathing such as respiratory rate, its effect on clinical end points is less certain.<sup>16</sup> The most robust evidence for the efficacy of HFNC in bronchiolitis is found in the results of 3 randomized clinical trials (RCTs) of children defined as having hypoxia (<94%), none of which revealed strong clinically relevant effects.<sup>4,5,17</sup> Franklin et al<sup>4</sup> found a decreased incidence of treatment failure, the definition of which included crossover from nasal cannula to HFNC. In a similar study but with crossover eliminated, Durand et al<sup>17</sup> was unable to detect such an effect. Kepreotes et al<sup>5</sup> did not find a decrease in the total time of oxygen supplementation in children initiated on HFNC. Similar to our study, none of the RCTs found an improvement in rates of intubation or ICU transfer associated with HFNC.

Riese et al<sup>18</sup> demonstrated that the initiation of a floor-based HFNC protocol increased inpatient HFNC rates. Similarly, our study suggests that increases in ED HFNC initiation rates in our institution were associated with changes in floor-based HFNC policies. The availability of continuance of therapy on the floor, rather than the PICU, may have lowered the ED provider threshold to initiate HFNC. The change in ED HFNC use after a change in inpatient protocols also reveals the lack of clear ED-based HFNC protocols or guidelines for indications other than refractory hypoxia.



**FIGURE 1** Study flow diagram.



**FIGURE 2** Adjusted ITS analysis of ED HFNC initiation by year.

Over the course of our study period, we witnessed an increase in rates of hospital admission, PICU admission, and transfer to the PICU. These increases were not statistically significant after adjusting for seasonality, age, ESI level, and ED oxygen saturation in our ITS models. One explanation for the lack of evidence of improvement in outcomes despite increased HFNC use would be increased severity of illness over time. The lack of improvement in these clinical outcomes after adjusting for clinical severity suggests that this was not the case.

With this study, we are the first to examine the association of HFNC initiation in the ED with PICU admission rates. Although we were able to detect a significant linear trend of increased PICU admission rates during the study period, this was not significant in our adjusted ITS model. There have been several reports of HFNC leading to increased PICU use.<sup>7,19</sup> Garland et al<sup>7</sup>

found an increase in rates of PICU admission after the introduction of HFNC across Canada using an ITS analysis. Coon et al<sup>19</sup> found that initiation of inpatient floor protocols were associated with increased, rather than decreased, PICU use rates in US hospitals. Their analyses differed from ours in several respects. First, these were unadjusted analyses and did not control for individual patient-level variables as in our study. The time point used in the Garland et al<sup>7</sup> study (introduction of HFNC in Canada) predates the time period in our analysis because HFNC was available but uncommon in the ED at the beginning of our study period. Similar to our segmented regression ITS analysis, Coon et al<sup>19</sup> examined the impact of inpatient HFNC protocols; however, our analysis did not reveal an increase in PICU use associated with floor HFNC protocol change. Although there was a linear increase in rates of transfer to the PICU from the general floor

during our study period, this trend was not significant in our ITS analysis adjusting for age and several variables associated with severity (ESI and oxygen saturation). Similar to our findings, Riese et al<sup>18</sup> found no difference in rates of PICU transfer after the implementation of a floor-based HFNC protocol.

The effect of HFNC use on endotracheal intubation rates has varied across studies. Two small single-center studies revealed a decrease in intubation rate after the initiation of HFNC.<sup>6,20</sup> This decrease was not demonstrated in either of the RCTs comparing HFNC to standard oxygen therapy.<sup>4,5</sup> Garland et al<sup>7</sup> did not find any differences in intubation rates across Canada after the introduction of HFNC using an ITS model. Some of the incongruity of previous results may have been from the indications for HFNC expanding over time to include fewer critically ill infants. The statistically significant increase in the rate

**TABLE 3** Results of ITS Analysis

| Outcome, OR (95% CI) | Period    |                  |                        |                    |                        |
|----------------------|-----------|------------------|------------------------|--------------------|------------------------|
|                      | Pre-2016  | 2016–2017        | 2016–2017 <sup>a</sup> | Post-2017          | Post-2017 <sup>a</sup> |
| ED HFNC initiation   | Reference | 1.30 (0.91–1.88) | 1.67 (1.12–2.49)*      | 1.97 (1.14–3.43)*  | 2.55 (1.39–4.68)*      |
| Admission            | Reference | 0.95 (0.79–1.14) | 1.16 (0.95–1.43)       | 1.06 (0.77–1.45)   | 1.18 (0.82–1.71)       |
| PICU admission       | Reference | 1.33 (0.95–1.86) | 1.53 (0.95–3.20)       | 1.51 (0.84–2.69)   | 1.74 (0.95–3.20)       |
| Transfer to PICU     | Reference | 1.46 (0.76–2.80) | 1.53 (0.80–2.94)       | 2.28 (0.80–6.49)   | 2.32 (0.81–6.66)       |
| Intubation           | Reference | 1.15 (0.57–2.33) | 1.37 (0.65–2.88)       | 3.75 (1.08–12.95)* | 4.93 (1.36–17.85)*     |

<sup>a</sup> Adjusted for age, ESI level, triage SpO<sub>2</sub>, and lowest ED SpO<sub>2</sub>.

\* *P* < .05.

**TABLE 4** ITS Overall Slope Significance by Outcome

| Outcome            | Unadjusted ITS |            | Adjusted ITS <sup>a</sup> |            |
|--------------------|----------------|------------|---------------------------|------------|
|                    | P              | Trend      | P                         | Trend      |
| ED HFNC initiation | <.001          | Increasing | <.001                     | Increasing |
| Admission          | .059           | —          | .052                      | —          |
| PICU admission     | .658           | —          | .67                       | —          |
| Transfer to PICU   | .937           | —          | .753                      | —          |
| Intubation         | .083           | —          | .04                       | Increasing |

—, not applicable.

<sup>a</sup> Adjusted for age, ESI level, triage SpO<sub>2</sub>, and lowest ED SpO<sub>2</sub>.

of endotracheal intubation over the course of our study revealed by the adjusted ITS model is difficult to interpret but highlights the unlikelihood that HFNC is having a beneficial effect on intubation rates because rates of HFNC among admitted patients rose from <5% to >30% during our period of study. Of note, our analysis did not adjust for multiple comparisons of secondary outcomes, and this outcome (with its *P* value of .04) would likely have not been considered significant after adjustment.

Increasing linear trends of several secondary outcomes in the year-to-year analysis were not significant in the ITS analysis, which adjusted for seasonality and provider, which suggests that these factors played a role in the linear trends.

Our study has several limitations. First, it was based at a single center and therefore may not be fully generalizable. In addition, our study population was defined by ICD-10-CM codes, which are known to have variable accuracy for outcomes research.<sup>21</sup> In addition, the retrospective nature of our study may have led to sampling bias for some outcomes (eg, a child in respiratory distress receiving more vital sign checks and therefore being found to be hypoxic). Although we did use a multilevel regression model to control for confounding on the basis of clinical variables, our study was retrospective and nonrandomized; therefore, residual confounding may exist. In our study, we excluded children <2 months of age in an attempt to limit diagnostic misclassification, but this may have biased the results of our study if this group was more likely to show a benefit from HFNC. Over the same time period as our study, 170 infants <2 months old were

placed on HFNC (15% of total HFNC use), most of whom were <1 month. Our study cannot rule out clinical benefit in this younger population, but it is unlikely that their inclusion would change the overall results given the majority of HFNC use was in older children. In addition, our study relied on data extracted from the EMR. Although we were able to ensure the reliability of our primary outcome, the initiation of HFNC in the ED, it is possible that there was inadvertent misclassification of secondary outcomes during the data pull from the EMR.

## CONCLUSIONS

We found an increased rate of ED HFNC use corresponding to liberalization of inpatient HFNC policies without significantly impacting clinically important outcomes. A population of patients more likely to receive clinical benefit, with clearly defined HFNC initiation criteria, should be identified before further expansion of the use of HFNC for bronchiolitis.

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