Received: 16 January 2023 | Revised: 24 March 2023 | Accepted: 19 April 2023

DOI: 10.1002/emp2.12966

JACEP OPEN
JOURNAL OF THE AMERICAN COLLEGE OF EMERGENCY PHYSICIANS OPEN
A GLOBAL JOURNAL OF EMERGENCY MEDICINE
WILEY

BRIEF REPORT

Pediatrics

# Factors associated with mild bronchiolitis in young infants

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**Funding and support**: By *JACEP* Open policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist.

## Abstract

**Objective:** Bronchiolitis within the first 3 months of life is a risk factor for more severe illness. We aimed to identify characteristics associated with mild bronchiolitis in infants ≤90 days old presenting to the emergency department (ED).

**Methods:** We conducted a secondary analysis of infants ≤90 days old with clinically diagnosed bronchiolitis using data from the 25th Multicenter Airway Research Collaboration prospective cohort study. We excluded infants with direct intensive care unit admissions. Mild bronchiolitis was defined as (1) sent home after the index ED visit and did not have a return ED visit or had a return ED visit without hospitalization, or (2) were hospitalized from the index ED visit to the inpatient floor for <24 hours. Multivariable logistic regression, adjusting for potential clustering by hospital site, was used to identify factors associated with mild bronchiolitis.

**Results:** Of 373 infants aged ≤90 days, 333 were eligible for analysis. Of these, 155 (47%) infants had mild bronchiolitis, and none required mechanical ventilation. Adjusting for infant characteristics, clinical factors associated with mild bronchiolitis included older age (61–90 days vs 0–60 days) (odds ratio [OR] 2.72, 95% confidence interval [CI] 1.52–4.87), adequate oral intake (OR 4.48, 95% CI 2.08–9.66), and lowest ED oxygen saturation ≥94% (OR 3.12, 95% CI 1.55–6.30).

**Conclusions:** Among infants aged ≤90 days presenting to the ED with bronchiolitis, about half had mild bronchiolitis. Mild illness was associated with older age (61–90 days), adequate oral intake, and oxygen saturation ≥94%. These predictors may help in the development of strategies to limit unnecessary hospitalization in young infants with bronchiolitis.

## 1 | INTRODUCTION

### 1.1 | Background

Bronchiolitis is a leading cause of hospitalization in infants <1 year, with the highest rate of hospitalization among infants <4 months.[1–3] Bronchiolitis within the first 3 months of life is a risk factor for more severe illness, hospitalization, and use of respiratory support.[4–8] As such, clinicians' concern for clinical deterioration is heightened in young infants with bronchiolitis, potentially leading to unnecessary hospitalizations even when presenting with seemingly mild presentations.

Supervising Editor: Sing-Yi Feng, MD

### 1.2 | Importance

The identification of specific characteristics associated with a mild bronchiolitis course among young infants would allow clinicians to safely discharge home a subgroup of infants unlikely to develop worsening. Safe discharges would reduce exposure to nosocomial infections, family burden, and the strain on the health care system, which is currently experiencing a severe respiratory virus surge.[9] Clinical prediction models for bronchiolitis exist, but most were derived from cohorts of children <2 years of age and are not well calibrated for the youngest infants. Within the group of infants ≤90 days old with bronchiolitis, there are sparse data on whether specific clinical factors can help distinguish illness severity. Additionally, although it is generally assumed that the older the age, the lower the risk of severe bronchiolitis, available data suggest that the relationship between age and illness severity may not be linear.[2]

**The Bottom Line**

Bronchiolitis has always been a difficult course of illness to predict in children. This large multicenter study looked at a cohort of young infants in the emergency department to help better define which infants are more likely to have mild bronchiolitis and therefore less likely to have morbidity and mortality. This is important for the ED practitioner because it can facilitate an earlier and safer ED disposition decision.

### 1.3 | Goals of this investigation

Our primary aim was to identify clinical factors associated with mild bronchiolitis among infants ≤90 days old presenting to the emergency department (ED). We hypothesized that variables from patient history and physical exam could help identify a subgroup of infants who are more likely to have mild bronchiolitis and may not need hospitalization.

## 2 | METHODS

### 2.1 | Study design and setting

We conducted a secondary analysis of infants ≤90 days old who participated in a multicenter prospective cohort study, the 25th Multicenter Airway Research Collaboration (MARC-25), a program of the Emergency Medicine Network (www.emnet-usa.org). Chronologic age was used without correction for gestational age. As described previously, participants in the original study were infants <2 years old with clinically diagnosed bronchiolitis presenting to 1 of 30 EDs across 14 US states from December 2004 to March 2006.[8] Written consent was obtained for all participants, and institutional review boards of all participating sites approved the study.

### 2.2 | Measurements

An interview at the index ED visit was conducted to collect participants' demographic information and medical history. Details of presenting illness, ED vital signs and exam findings, and hospitalization data (when applicable) were collected through medical record review. Respiratory rate was collected as a continuous variable and dichotomized as <70 or ≥70 based on prior literature.[4,10] A follow-up telephone call was conducted 2 weeks after the index ED visit to assess for unplanned clinician encounters. Length of stay (LOS) in hours was calculated using the date and time of hospital admission and discharge orders.

### 2.3 | Outcomes

Our primary outcome was mild bronchiolitis, defined as either (1) being sent home after the index ED visit and not returning to the ED or returning but without hospitalization, or (2) being hospitalized from the index ED visit to the general inpatient floor with a LOS <24 hours. We used this short hospital LOS as a surrogate for infants who may have been admitted for observation purposes only and potentially could have been safely discharged home from the ED.

We excluded infants who were directly admitted to the ICU, as there is less of a clinical conundrum regarding the need for hospitalization. Those with missing data for admission or discharge information were also excluded.

Given the subjectivity associated with using hospitalization as a marker of severity, we performed a sensitivity analysis to further differentiate infants with mild versus moderate to severe bronchiolitis. In this sensitivity analysis, we excluded infants with an index LOS < 24 hours, as well as those discharged from index ED visits but returned and were hospitalized for <24 hours.

### 2.4 | Analysis

Data are presented as counts and percentages for categorical variables, and medians with interquartile ranges for continuous variables. We used logistic regression to generate multivariable models of mild bronchiolitis and used a clustered sandwich estimator for SEs in Stata to adjust for potential clustering by site. We chose potential predictors of mild bronchiolitis based on prior studies of bronchiolitis in infants up to 2 years old.[4,6,7] We considered adjusting for at-home apnea but did not include it in the model due to low frequency. We similarly conducted the sensitivity analysis using a multivariable logistic regression model adjusted for the same covariates. All analyses were conducted using Stata 15.1 software (StataCorp, College Station, TX).

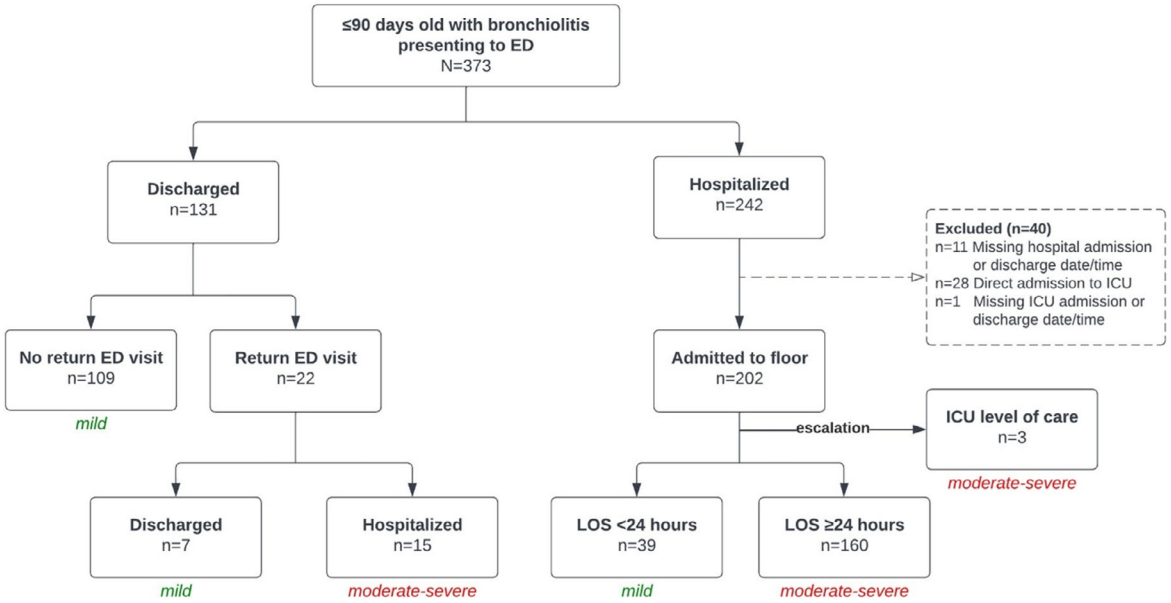


**FIGURE 1** Flow diagram of inclusion criteria and outcome categorization by severity of bronchiolitis. ED, emergency department; LOS, length of stay; ICU, intensive care unit.

## 3 | RESULTS

### 3.1 | Characteristics of study subjects

Of the 1459 participants included in the original MARC-25 study, 373 (26%) were aged ≤90 days at enrollment. We excluded 29 infants who were directly admitted to the ICU and 11 infants missing admission and/or discharge date and/or time.

For the 333 infants included in the final analytic cohort, demographic factors, illness history, and exam findings are summarized in Table 1. Of these, 138 (41%) infants were aged 61–90 days, and 155 (47%) met the definition for mild bronchiolitis (Figure 1). Two-hundred eighty-seven infants (86%) completed 2-week follow-up. Overall, 217 (65%) infants were hospitalized at some point between the index ED visit and 2-week follow-up interview. There were 3 infants initially admitted to the general inpatient floor who subsequently had care escalated to the ICU. None required intubation.

Eight infants (2%) had apnea observed in the ED. Of these, 1 infant was categorized as having mild bronchiolitis based on our main outcome definition (discharged home without a return visit). Of the 7 (2%) infants who had apnea while hospitalized, 2 were born prematurely (gestational age <37 weeks), 5 had parent-observed apnea at home, and 3 had apnea observed in the ED.

### 3.2 | Main results

Adjusting for infant characteristics and potential clustering by hospital site, 3 predictors were independently associated with mild bronchiolitis: older age (61–90 days vs 0–60 days) (odds ratio [OR] 2.72, 95% confidence interval [CI] 1.52–4.87), adequate oral intake by history (OR 4.48, 95% CI 2.08–9.66), and lowest room air oxygen saturation ≥94% (OR 3.12, 95% CI 1.55–6.30) (Table 2). Demographic factors other than age, and exam findings such as tachypnea or retractions, were not associated with bronchiolitis severity. Of 87 infants who met all 3 criteria, 24 (28%) infants were hospitalized from the index ED visit, with 7/24 (29%) having hospital LOS <24 hours.

In the sensitivity analysis, we excluded another 39 infants with an index hospitalization LOS <24 hours and 9 infants with an overnight hospitalization from a return ED visit. The results did not differ significantly from the overall study results, except that absence of retractions was also associated with mild bronchiolitis (OR 2.06, 95% CI 1.02–4.16) (Table 3).

## 4 | LIMITATIONS

We used hospitalization to define our outcomes, understanding that admission criteria and level of care dictated by hospital policy vary both within and across institutions. However, we used the length of hospitalization as an additional measure of illness severity and conducted a sensitivity analysis excluding those infants with brief hospitalizations.

Prior studies including older infants with bronchiolitis have shown a relationship between the caretaker report of apnea and clinician-observed apnea; however, we were not able to assess for this association in our study as few infants (2%) had documentation of apnea while hospitalized.[4,5] One infant with clinician-observed apnea in the ED was categorized as having mild bronchiolitis. Given that infants were considered to have apnea if there was documentation that apnea occurred in the medical records, it is unclear if this infant would have met strict criteria for apnea.

**TABLE 1** Characteristics of infants with mild versus moderate to severe bronchiolitis.

| Characteristics | Total (n = 333, 100%) | Mild bronchiolitis (n = 155, 47%) | Moderate to severe bronchiolitis (n = 178, 53%) |
|---|---|---|---|
| **Demographics** | | | |
| Chronologic age, median (IQR) | 38 (57–71) | 47 (64–78) | 33 (50–65) |
| 0 to 60 days | 195 (59) | 69 (45) | 126 (71) |
| 61 to 90 days | 138 (41) | 86 (55) | 52 (29) |
| Male sex | 189 (57) | 86 (55) | 103 (58) |
| Race or ethnicity | | | |
| Non-White and/or Hispanic | 196 (59) | 82 (54) | 114 (64) |
| Non-Hispanic White | 134 (41) | 71 (46) | 63 (36) |
| Insurance type | | | |
| Private | 104 (31) | 49 (32) | 55 (31) |
| Public or none | 229 (69) | 106 (68) | 123 (69) |
| **Medical history** | | | |
| Gestational age ≥37 weeks | 287 (88) | 129 (86) | 158 (89) |
| Personal history of wheezing | 31 (9) | 18 (12) | 13 (7) |
| Prior hospitalization ≥1 day (excluding immediately after birth) | 36 (11) | 22 (14) | 14 (8) |
| History of ICU, premature nursery, or special care facility hospitalization immediately after birth | 45 (14) | 21 (14) | 24 (13) |
| History of intubation | 7 (2) | 3 (2) | 4 (2) |
| **Presenting illness** | | | |
| <24 hours of symptoms related to current illness | 25 (8) | 11 (7) | 14 (8) |
| Parent-reported apnea at home | 33 (10) | 9 (6) | 24 (13) |
| Oral intake | | | |
| Inadequate | 67 (20) | 15 (10) | 52 (29) |
| Adequate | 245 (74) | 135 (87) | 110 (62) |
| Missing | 21 (6) | 5 (3) | 16 (9) |
| **ED exam** | | | |
| Respiratory rate | | | |
| ≥70 respirations per minute | 43 (13) | 13 (8) | 30 (17) |
| <70 respirations per minute | 289 (87) | 142 (92) | 147 (83) |
| Lowest room air oxygen saturation during ED evaluation | | | |
| <94% | 85 (26) | 18 (12) | 67 (38) |
| ≥94% | 228 (68) | 129 (83) | 99 (56) |
| Not on room air or missing | 20 (6) | 8 (5) | 12 (7) |
| Presence of retractions | | | |
| Yes | 192 (58) | 84 (54) | 108 (61) |
| No | 121 (36) | 68 (44) | 53 (30) |
| Missing | 20 (6) | 3 (2) | 17 (10) |
| Presence of wheezing | 217 (66) | 93 (62) | 124 (70) |
| Apnea | | | |
| Yes | 8 (2) | 1 (1) | 7 (4) |
| No | 320 (98) | 154 (99) | 166 (96) |
| **Inpatient apnea** | | | |
| Yes | 7 (2) | 0 (0) | 7 (4) |
| No | 185 (56) | 36 (23) | 149 (84) |
| Not applicable (not hospitalized) | 116 (35) | 116 (75) | 0 (0) |
| Missing | 25 (8) | 3 (2) | 22 (12) |

*Note*: All results reported as n (%) except where otherwise noted.
Abbreviations: ED, emergency department; IQR, interquartile range; ICU, intensive care unit.

**TABLE 2** Multivariable logistic regression of factors associated with mild bronchiolitis.

| Characteristics | Odds ratio (95% CI) |
|---|---|
| Chronologic age | |
| 0 to 60 days | 1.00 (reference) |
| 61 to 90 days | **2.72 (1.52–4.87)** |
| Male sex | 0.93 (0.56–1.55) |
| Race or ethnicity | |
| Non-White and/or Hispanic | 1.00 (reference) |
| Non-Hispanic White | 1.74 (0.93–3.27) |
| Insurance type | |
| Private | 1.00 (reference) |
| Public or none | 1.24 (0.72–2.15) |
| Gestational age ≥37 weeks | 0.99 (0.45–2.19) |
| <24 hours of symptoms related to current illness | 1.19 (0.43–3.32) |
| Oral intake | |
| Inadequate | 1.00 (reference) |
| Adequate | **4.48 (2.08–9.66)** |
| Missing | 1.33 (0.27–6.66) |
| Respiratory rate | |
| ≥70 respirations per minute | 1.00 (reference) |
| <70 respirations per minute | 1.88 (0.71–4.94) |
| Lowest room air oxygen saturation during ED evaluation | |
| <94% | 1.00 (reference) |
| ≥94% | **3.12 (1.55–6.30)** |
| Not on room air or missing | 1.53 (0.45–5.16) |
| Retractions | |
| Present | 1.00 (reference) |
| Not present | 1.56 (0.88–2.77) |
| Missing | 0.22 (0.07–0.73) |
| Presence of wheezing | 0.65 (0.40–1.06) |

Abbreviations: CI, confidence interval; ED, emergency department.
Bolding denotes statistically significant association (p<0.05).

**TABLE 3** Sensitivity analysis: Multivariable logistic regression of factors associated with mild bronchiolitis (n = 294).[a]

| Characteristics | Odds ratio (95% CI) |
|---|---|
| Chronologic age | |
| 0 to 60 days | 1.00 (reference) |
| 61 to 90 days | **3.98 (2.06–7.72)** |
| Male sex | 1.30 (0.63–2.69) |
| Race or ethnicity | |
| Non-White and/or Hispanic | 1.00 (reference) |
| Non-Hispanic White | 1.64 (0.74–3.64) |
| Insurance type | |
| Private | 1.00 (reference) |
| Public or none | 1.43 (0.67–3.09) |
| Gestational age ≥37 weeks | 0.67 (0.22–2.07) |
| <24 hours of symptoms related to current illness | 2.07 (0.54–7.89) |
| Oral intake | |
| Inadequate | 1.00 (reference) |
| Adequate | **9.60 (3.25–28.30)** |
| Missing | 2.59 (0.29–22.97) |
| Respiratory rate | |
| ≥70 respirations per minute | 1.00 (reference) |
| <70 respirations per minute | 3.05 (0.83–11.14) |
| Lowest room air oxygen saturation during ED evaluation | |
| <94% | 1.00 (reference) |
| ≥94% | **7.15 (2.23–22.99)** |
| Not on room air or missing | 2.56 (0.41–15.93) |
| Retractions | |
| Present | 1.00 (reference) |
| Not present | **2.06 (1.02–4.16)** |
| Missing | 0.16 (0.01–2.01) |
| Presence of wheezing | 0.55 (0.28–1.09) |

Abbreviations: CI, confidence interval; ED, emergency department.
[a]Excludes infants with an index hospitalization length-of-stay <24 hours and infants discharged from the index ED visit but returned and were hospitalized for < 24hours.
Bolding denotes statistically significant association (p<0.05).

Finally, data regarding supportive care, such as the use of supplemental oxygen and intravenous fluids, were not collected. Thus, it is unclear if some of the hospitalizations, particularly for those with the LOS <24 hours, were for observation purposes only. Follow-up was complete for the majority of the patients, but for those whom we could not reach, we cannot be certain that they were not hospitalized elsewhere.

## 5 | DISCUSSION

In this secondary analysis of a multicenter prospective cohort study of infants ≤90 days old with bronchiolitis presenting to the ED, nearly one half of infants were classified as having a mild illness. Three variables, older age (61–90 days), adequate oral intake, and oxygen saturation ≥94%, were associated with mild bronchiolitis in the multivariable model. These variables were also associated with safe ED discharge in a prior study using the full MARC-25 cohort encompassing infants <2 years.[8] No young infant in our analysis required mechanical ventilation.

Low oxygen saturation has been frequently identified as a marker of bronchiolitis severity in prior studies, although each study has had different threshold levels, ranging from 85% to 95%.[4,6–8,11] Based on the American Academy of Pediatrics (AAP) bronchiolitis guidelines, we considered analyzing oxygen saturation as <90% versus ≥90%.[12] However, few infants with mild bronchiolitis had an oxygen saturation of <90% (n = 5) in our cohort. We chose 94% as a cutoff, both based on prior literature and in recognition that clinicians may be uncomfortable with lower thresholds in young infants, particularly in those with a

history of prematurity, who may have different physiologic responses to hypoxemia compared with older infants and children.[8,13,14]

Additionally, despite its association with hospitalization, oxygen saturation has not been strongly associated with respiratory distress.[15] In our study, other clinically used measures of respiratory distress, such as tachypnea and retractions, were not associated with bronchiolitis severity using the main outcome definition. The absence of retractions, however, was associated with mild bronchiolitis in our sensitivity analysis. The use of oxygen saturation and age alone to predict severity, without a clear understanding of how these factors affect respiratory outcomes, may contribute to the practice of over-hospitalization of young infants with bronchiolitis.

Adequate oral intake as a predictor of mild bronchiolitis is helpful but provides less guidance regarding those otherwise well-appearing infants who may have respiratory decompensation after ED evaluation. Symptoms other than breathing difficulties, such as nasal congestion, post-tussive emesis, and increased mucus production, may be the driver of poor feeding and hospitalization in some infants with bronchiolitis.

In addition to concern for respiratory decompensation or dehydration, there are other factors not analyzed in our study that may contribute to a decision to hospitalize a young infant, including family discomfort with discharge or inability to obtain timely follow-up evaluation. Although hospitalization in these settings may be appropriate, for some, accurate anticipatory guidance based on objective data regarding the risk of bronchiolitis progression may provide an opportunity to safely discharge patients home.

Although our study provides insight into how clinicians may safely reduce potentially unnecessary hospitalizations in young infants with bronchiolitis, we used data from 2004 to 2006. Our findings, therefore, should be considered in the context of changing bronchiolitis epidemiology, management, and prognosis over the past 2 decades. The viruses that cause bronchiolitis have remained relatively unchanged during this period.[16,17] The COVID-19 pandemic introduced distinct changes in both the prevalence and seasonality of respiratory virus worldwide, including uncharacteristic peaks in bronchiolitis cases during summer months of 2021.[18–23] In the ongoing respiratory season, surges in respiratory syncytial virus, influenza, and SARS-CoV-2 infections have led to widespread respiratory illnesses.[9,24–27] Whether these epidemiological changes have altered the prognosis of bronchiolitis is unclear. Prior studies have not identified a clear association between viral etiology and apnea, though apnea rates vary considerably in the literature, from <1% to 23.8%.[4,5,28,29] The changing epidemiology and burden, however, have led to discussions about how to best use available resources and decrease unnecessary hospitalizations.[30–32]

Additionally, clinical management of infants with bronchiolitis has changed in the prior 2 decades without clear alteration in prognosis. The AAP guideline on bronchiolitis management, last updated in 2014, advocates for the deimplementation of diagnostic tests and treatments previously used.[12,33] Adoption of these recommendations has been variable and has not resulted in substantial changes in hospital admission rates.[34–37] Since 2004, ICU admissions have increased significantly without appreciable increase in bronchiolitis severity.[36,38] A potential driver of the observed trends may be the widespread availability and use of non-invasive ventilation and high-flow nasal cannula, although insufficient evidence exists regarding their efficacy to decrease the severity of illness and the need for intubation.[39–41]

The 2 most well-powered clinical algorithms used in today's care of infants presenting to the ED with bronchiolitis were developed from the MARC-25 cohort (n = 1459), from which this secondary analysis was conducted, and the Pediatric Emergency Research Network (PERN) cohort (n = 2722).[7,8,42] Although the PERN study used newer patient data—from 2013—it is limited by retrospective design. Still, both clinical algorithms identify similar factors on physical exams, such as desaturations, retractions, young age, and poor feeding, as markers of severity. These data combined with ours suggest that clinical models can be derived to predict outcomes in young infants with bronchiolitis but will require further research using a large, contemporary, and diverse population of infants ≤90 days.

In summary, we identified 3 predictors of mild bronchiolitis, including older age (60–91 days), adequate oral intake, and oxygen saturation ≥94%, in infants ≤90 days presenting to the ED. We encourage future research with a clearly defined outcome based on respiratory progression, as well as prospectively collected data on ED examination, to more clearly delineate which clinical factors may help identify young infants with mild bronchiolitis who are safe for ED discharge.

## AUTHOR CONTRIBUTIONS

Son H. McLaren, Peter S. Dayan, and Carlos A. Camargo conceived the study. Ying (Shelly) Qi and Janice A. Espinola analyzed the data. Son H. McLaren drafted the manuscript, and all authors contributed substantially to its revision. Son H. McLaren takes responsibility for the paper as a whole.

## CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest..

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**How to cite this article:** McLaren SH, Qi YS, Espinola JA, Mansbach JM, Dayan PS, Camargo CA. Factors associated with mild bronchiolitis in young infants. *JACEP Open*. 2023;4:e12966. https://doi.org/10.1002/emp2.12966

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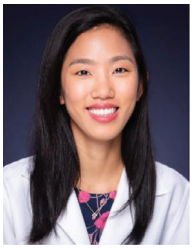

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