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Racial/ethnic Differences In The Presentation And Management Of Severe Bronchiolitis

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Racial/Ethnic Differences in the Presentation and Management of Severe Bronchiolitis

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RACIAL/ETHNIC DIFFERNCES IN THE PRESENTATION AND MANAGEMENT OF SEVERE BRONCHIOLITIS

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We examined if racial/ethnic differences exist in the presentation and management of severe bronchiolitis using a 16-center, prospective cohort study from 2007-2010. Children <2 years hospitalized with a diagnosis of bronchiolitis were included. A structured interview, chart review, and 1-week phone follow-up were completed. Multivariable logistic regression was used to examine the independent association between race/ethnicity and diagnostic imaging, treatment, management, discharge on inhaled corticosteroids, and bronchiolitis relapse. Among 2,130 patients, 818 (38%) were non-Hispanic white (NHW), 511 (24%) were non-Hispanic black (NHB), and 801 (38%) were Hispanic. Compared with all groups, NHB children were most likely to receive albuterol before admission (OR 1.58; 95%CI, 1.20-2.07) and least likely to receive chest x-rays during hospitalization (OR 0.66; 95%CI, 0.49-0.90); Hispanic children were most likely to be discharged on inhaled corticosteroids (OR 1.92; 95%CI, 1.19-3.10). We observed differences between NHW and minority children regarding pre-admission albuterol use, inpatient diagnostic imaging, and prescription of inhaled corticosteroids at discharge; practices that deviate from the American Academy of Pediatrics guidelines. The causes of these differences require further study but they support implementation of clinical care pathways for severe bronchiolitis.

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INTRODUCTION

Bronchiolitis is the leading cause of hospitalization for infants in the U.S., costs more than $500 million annually, and has seen a 30% increase ($1.34 billion to $1.73 billion) in related hospital charges from 2000-2009.[1-3] Almost all children <2 years are infected with respiratory syncytial virus (RSV), the most common cause of bronchiolitis, with 40% developing clinically recognizable bronchiolitis and 2% becoming hospitalized with severe bronchiolitis.[4,5]

Current American Academy of Pediatrics (AAP) guidelines state that routine use of bronchodilators, corticosteroids, and chest x-rays is not recommended and supportive care is strongly encouraged.[6] However, a lack of consensus among clinicians persists regarding bronchiolitis management.[7-10] Although minority children and those with a lower socioeconomic status (SES) in the U.S. are more likely to present with bronchiolitis to the emergency department (ED) and be subsequently admitted when compared to the general population,[11-13] to our knowledge, no study has yet examined if race/ethnicity is independently associated with differences in the presentation and management of severe bronchiolitis (i.e., bronchiolitis causing hospitalization).

Epidemiology & Microbiology

Bronchiolitis secondary to RSV resulted in 34 million episodes of acute lower respiratory infections and 3.4 million hospitalizations in children <5 years globally in 2005.[14] In their landmark study to determine the global burden of RSV, Nair et al. listed RSV as the third leading cause of childhood death secondary to acute lower respiratory

infection (i.e., 66,000-199,000 deaths; 99% of mortality found in developing countries), after pneumococcal pneumonia and Haemophilus influenza type b. The toll of bronchiolitis is much less burdensome in the United States where 132,000-172,000 pediatric hospitalizations are reported annually.[15,16] Although primarily affecting the pediatric population, bronchiolitis can also be a source of significant morbidity and mortality in both the elderly and immunosuppressed patient populations.[17,18] In fact, Thompson et al. suggest that up to a quarter of excess wintertime mortality secondary to acute respiratory tract infections in adults may be attributed to RSV.[19]

Bronchiolitis incidence typically increases during seasonal outbreaks – November to April in the northern hemisphere and May to September in the southern hemisphere.[20] Although RSV is the most common cause of bronchiolitis, multiple viruses – parainfluenza, influenza A/B, adenovirus, human metapneumovirus, and rhinovirus – can causes bronchiolitis. Bacterial causes of bronchiolitis include Mycoplasma pneumonia and Bordetella pertussis. Despite the variety in etiology, identifying the infectious agent has not been shown to provide any clinical utility.[21,22]

Up to a quarter of patients hospitalized with bronchiolitis are found to be co-infected with multiple agents.[23,24] However, the implications of co-infection are unclear. Several studies have shown co-infection to result in higher hospitalization rates and longer hospital length of stay (LOS).[23,25] Other data suggest no differences in severity, duration of illness, or hospital LOS.[26-28]

Clinical Presentation & Management

The AAP defines bronchiolitis as a clinical diagnosis consisting of "rhinitis, tachypnea, wheezing, cough, crackles, use of accessory muscles, and/or nasal flaring."[6] In terms of clinical research, bronchiolitis is defined as the first episode of wheezing in a child younger than 12-24 months who has physical findings of a viral lower respiratory infection and no other explanation for wheezing.[29,30] The natural history of the disease begins with upper respiratory tract symptoms followed by lower respiratory tract symptoms within 24-48 hours. Signs of moderate to severe respiratory distress include nasal flaring, respiratory rate >70/min, dyspnea, cyanosis, retractions, and often result in hospitalization. Disease progression typically peaks within 5-7 days. Average hospital LOS is 2-3 days.[31,32]

Bronchiolitis is usually a self-limited disease. Risk factors for severe disease include prematurity (gestational age <37 weeks), age less than 12 weeks, chronic pulmonary disease (e.g., bronchopulmonary dysplasia), congenital and anatomic airway defects, congenital heart disease, immunodeficiency, and neurologic disease.[33-36] The majority of infants infected with bronchiolitis are managed in the outpatient setting with supportive care. Supportive care includes suctioning, symptom control, and monitoring disease progression. Indications to seek medical care are commonly associated with episodes of apnea, cyanosis, fever, increased respiratory rate, increased work of breathing, and poor feeding.

There are currently no vaccines to prevent the most common causes of bronchiolitis (e.g., RSV, rhinovirus, etc.). Hand washing to limit the transmission of infections agents is the primary mode of prevention. Palivizumab, a humanized monoclonal antibody, provides defense against RSV and has been shown to decrease the risk of hospitalization among infants with comorbidities such as bronchopulmonary dysplasia, premature birth, and hemodynamically significant congenital disease. A multicenter randomized trial comparing palivizumab and placebo use in children with bronchopulmonary dysplasia or prematurity found a decrease in hospitalization rate of approximately 33% in infants taking palivizumab.[37]

Supplemental oxygen is a first line treatment for severe bronchiolitis and should be provided to maintain oxygen saturation above 90%. Bass et al. showed that there carries a significant risk of adverse long-term cognitive and behavioral effects from chronic or intermittent hypoxemia (i.e., oxygen saturation between 90-94%) in cases such as severe bronchiolitis.[38] Oxygen saturation read by pulse oximetry is the standard of care in determining whether an infected infant is hypoxemic. While arterial blood gases have been used to measure oxygen levels, pulse oximetry was found to overestimate arterial blood gases in a multicenter study if the oxygen saturation range was between 76-90%.[39] Conversely, oxygen saturation and arterial oxygen levels were similar if the oxygen saturation range was between 91-97%.

Continuous positive airway pressure (CPAP) has become increasingly utilized to decrease work of breathing and hypercarbia.[40] Many clinicians view CPAP as a safer

alternative to endotracheal intubation and its associated risks. In a randomized control trial comparing nasal CPAP to standard treatment, Thia et al. demonstrated an improvement in ventilation for children with bronchiolitis undergoing CPAP treatment.[41] Similarly, Cambonie et al. demonstrated CPAP's ability to decrease respiratory muscle overload and improve respiratory distress symptoms in children with severe acute viral bronchiolitis.[42] However, despite its increasing use and positive findings, a systematic review found the evidence for CPAP use to be inconclusive due to the low methodological quality found in a majority of CPAP studies.[43]

The AAP guidelines recommend that inhaled bronchodilators (e.g., albuterol, epinephrine) not be used routinely. Multiple systematic reviews and meta-analyses of randomized trials have found use of bronchodilators to increase healthcare costs and adverse effects while not affecting overall outcome.[44,45] For example, Gadomski et al. and Skjerven et al. demonstrated that the use of bronchodilators resulted in no clinical score improvement or decreased LOS for children with severe bronchiolitis.[46,47] However, bronchodilators can potentially provide short-term clinical improvement. Hartling et al. found that while use of bronchodilators did not affect LOS or admission within one week, they were associated with short-term clinical improvements.[44] Despite the evidence, bronchodilators continue to be overprescribed in severe bronchiolitis cases.

Systemic corticosteroids are also not recommended by the AAP. A double-blinded randomized control trial by Panickar et al. demonstrated no difference in clinical outcomes among preschool children with mild-to-moderate virus associated wheezing

when comparing oral prednisolone to placebo use.[48] Furthermore, a meta-analysis conducted by Fernandes et al. in 2013 showed no difference in LOS, clinical score, admission and readmission rates for children taking corticosteroids.[49] Their analysis consisted of 17 trials with 2,596 patients and is one of the largest and most recent reviews arguing against the use of systemic corticosteroids in bronchiolitis cases.

Bronchiolitis infection during the first decade of life has been associated with increased risk for asthma, recurrent wheezing, and reduced pulmonary function.[50-52] One subgroup analysis of a 20-year prospective follow-up study by Piippo-Savolainen et al. concluded that even infants with non-RSV bronchiolitis requiring hospital treatment were up to eight times more likely to be diagnosed with asthma in adulthood.[53] Bronchiolitis' association with asthma may have multiple implications on the part of clinicians attempting to stem the high prevalence of asthma, particularly in communities of color.

Bronchiolitis Clinical and Prediction Rules

Severe bronchiolitis is associated with multiple clinical, environmental, and demographic factors. For example, previous studies have demonstrated gender differences in lung function as male infants are more likely to be hospitalized and die from bronchiolitis when compared to female infants.[54,55] Urban environments and low socioeconomic status also predispose infants to severe bronchiolitis.[56,57] In addition to the comorbidities previously discussed, household factors (e.g., crowding, passive smoke exposure), maternal smoking during pregnancy, and family atopy have been shown to increase the risk of severe bronchiolitis infection.[58-61]

One multicenter study and two single center studies have attempted to compare the relative effect of these variables as it relates to bronchiolitis severity.[33,62-63] Opasvsky et al. examined the ability of prognostic models to predict a composite severity index or intensive care unit (ICU) admission regarding bronchiolitis infection.[64] Despite their original attempts, many of these studies suffer from important limitations. Multiple models did not include important clinical factors (e.g., intubation outcomes) and ED assessments. Furthermore, the cohorts used to develop previous models were published prior to 1998 and the use of palivizumab.

It is well-documented that admission rates for infants with bronchiolitis vary significantly when comparing general and pediatric EDs.[65] Adding to the variability is also the noted difference in admission rates among pediatric ED attendings.[66] Establishing an evidence-based bronchiolitis severity index would be helpful in limiting the variability in clinical care and disposition received by patients. Furthermore, a bronchiolitis severity index can also guide a clinician's decision to intervene in complicated cases involving pediatric endotracheal intubation, a procedure noted for its risks and difficulties.[67,68]

Health Disparities in Respiratory Disease

Racial and ethnic differences in healthcare access and quality have been widely documented in the U.S.[69] Prevalence of childhood asthma vary across race/ethnicity – 8.8% for non-Hispanic white (NHW), 12.7% for non-Hispanic (NHB), 25.7% for Puerto Ricans, and 6.6% for Mexican-Americans.[70] Moreover, studies have found that

racial/ethnic minorities have worse morbidity and mortality indices associated with respiratory diseases such as asthma when compared to NHW children.[71-74] Meurer et al. demonstrated that NHB children were significantly more likely to visit pediatric emergency departments for asthma after controlling for multiple clinical and socioeconomic factors. Jane Miller's research goes one step further by suggesting that lifetime income and sociodemographic characteristics do not explain the excess risks of asthma and ED visits associated with asthma among NHB children.[75] She argues that asthma prevalence, hospitalization, and emergency room use declined with increasing income for all children except for NHB children.

Although bronchiolitis is associated with an increased risk of asthma diagnosis, the role of race and ethnicity in the presentation and management of severe bronchiolitis remains unclear. The few studies that have provided some insight into the role race/ethnicity may play focused primarily on clinical objectives and not race/ethnicity. For example, Mansbach et al. suggested that multiple factors, Hispanic race/ethnicity among others, were associated with longer ED LOS for children with bronchiolitis.[76] Accordingly, he concluded that optimizing translation services may help shorten ED LOS in bronchiolitis cases. Damore et al. demonstrated that bronchiolitic children with public insurance, more often a variable associated with Hispanic and NHB children, were less likely to receive inhaled beta-agonists or antibiotics in the week before the ED visit while children without insurance were less likely to have a PCP or receive laboratory testing in the ED.[77] However, her study found no difference between insurance groups when it came to hospital admission rates, clinical presentation (e.g., respiratory rate, oxygen

saturation, and retractions), and ED treatments (e.g., inhaled beta-agonists, inhaled racemic epinephrine, systemic corticosteroids, and antibiotics). She concludes her analysis suggesting that all children, regardless of insurance status, should receive similar care.

Contrary to the studies previously described, two analyses looking at bronchiolitis associated ICU admissions and unscheduled visits post ED discharge found no differences across race/ethnicity.[78,79] ICU admission secondary to bronchiolitis was found to be associated with four independent factors: age <2 months, an ED visit in the past week, moderate/severe retractions, and inadequate oral intake. Norwood et al. demonstrated that three predictors (e.g., age <2 months, male sex, and previous hospitalization) were associated with unscheduled visits within 2 weeks of ED discharge. In a comparable asthma study of young children, Chandra et al. did not identify any racial/ethnic differences regarding inpatient treatment and outcomes; however, he did note that Hispanic children were less likely to receive an asthma action plan compared to NHW and NHB children, possibly due to language or socioeconomic differences.[80]

STATEMENT OF PURPOSE

This study seeks to address the knowledge gap by examining prospective data from a multicenter study designed to evaluate factors related to bronchiolitis hospitalization. The primary objective is to determine if racial/ethnic differences exist in the presentation and management of severe bronchiolitis. By utilizing race/ethnicity as a primary exposure, this analysis has potential implications from both a health disparities

standpoint (i.e., unequal care based on race/ethnicity) and from a clinical perspective (i.e., the potential of certain practices, such as clinical care pathways, to increase the likelihood of equitable treatment).

HYPOTHESIS AND SPECIFIC AIMS

Hypothesis

Racial/ethnic differences exist in the presentation and management of severe bronchiolitis; Hispanic and NHB children present with a more severe case of bronchiolitis and are less likely to receive standard treatments and care when compared to NHW children.

Specific Aims

1. Calculate a respiratory distress severity score for NHW, Hispanic, and NHB children with severe bronchiolitis.
2. Determine if racial/ethnic differences exist in the use of albuterol, corticosteroids, and chest x-rays during pre-admission visit and hospitalization.
3. Determine if racial/ethnic differences exist in the use of intensive respiratory support (i.e., CPAP, intubation, and/or ICU admission).
4. Determine if racial/ethnic differences exist regarding LOS, discharge on inhaled corticosteroids, and relapse of bronchiolitis.

METHODS

Study Design

We conducted a multicenter prospective cohort for 3 consecutive years (2007-2010) as part of the Multicenter Airway Research Collaboration (MARC), a division of the Emergency Medicine Network (EMNet) (www.emnet-usa.org). Sixteen hospitals in 12 states (see Appendix) participated from November 1st until March 31st in each study year. The number of sites varied by year: 13 sites in year 1, 16 sites in year 2, and 14 sites in year 3. At the beginning of each month, site investigators used a standardized protocol to enroll a target number of patients from the inpatient wards and ICU. Once the site reached their target enrollment for that month, the investigators would stop enrollment until the beginning of the next month.

All patients were treated at the discretion of their physician. Inclusion criteria were hospital admission with physician diagnosis of bronchiolitis, age <2 years, and ability of the child's guardian (e.g., parent) to give informed consent. Patients were enrolled within 18 hours of admission. Physician diagnosis of bronchiolitis followed the AAP definition of a child with an acute respiratory illness with some combination of rhinitis, cough, tachypnea, wheezing, crackles, and/or retractions. The exclusion criteria were previous enrollment and if a patient was transferred to a participating site hospital >48 hours after the initial admission. All consent and data forms were translated into Spanish. The institutional review board at each participating site approved the study.

Data Collection

Site investigators used a standardized protocol to enroll 2,207 patients admitted with bronchiolitis. Investigators conducted a structured interview that assessed patients' demographic characteristics, medical and environmental history, duration of symptoms, and details of the acute illness. Race/ethnicity was assigned by report of the child's guardian to standard U.S. Census groups. For the purpose of this analysis, mutually exclusive race/ethnicity categories were determined: NHW, NHB, or Hispanic. Non-Hispanic patients who identified as being both white and black were categorized as NHB. Patients were excluded from analysis if neither white or black race nor Hispanic ethnicity were reported (e.g., if only Asian race was reported) because of small numbers (n=67), as were patients missing all race/ethnicity data (n=10). This resulted in a total of 2,130 (97%) patients in our analytical dataset. SES was assessed with two variables: insurance status (public, private, none) and family income, estimated by matching patients' home ZIP codes and year of enrollment to ZIP code-based median household annual incomes obtained from Esri Business Analyst Desktop.[81]

ED and daily clinical data, including laboratory tests (e.g., complete blood count, basic metabolic panel, urine analysis, blood culture, etc.), respiratory rates, oxygen saturation, medical management, and disposition were obtained by medical chart review. Additionally, in an attempt to evaluate bronchiolitis severity at presentation, a modified Respiratory Distress Severity Score (RDSS) was calculated based on four assessments made during the pre-admission visit (i.e., ED or office visit before hospital admission): respiratory rate by age, presence of wheezing (yes or no), air entry (normal, mild

difficulty, or moderate/severe), and retractions (none, mild, or moderate/severe).[82] Each component was assigned a score of 0, 1 or, 2, with the exception of wheeze which was assigned either a 0 (no wheeze) or a 2 (wheeze), and then summed for a possible total score of 0 to 8.

Lastly, a follow-up telephone interview was conducted one week after hospital discharge for each enrolled patient. Interviews assessed acute relapse, recent symptoms, and provided additional endpoints for longitudinal analysis of specific symptoms. All data were manually reviewed at the EMNet Coordinating Center and site investigators were queried about missing data and discrepancies identified.

Outcome Measures

The major outcomes of this analysis were: albuterol and corticosteroid (inhaled or systemic) use during pre-admission visit and hospitalization, chest x-rays performed at pre-admission visit and hospitalization, need for intensive respiratory support (i.e., receiving continuous positive airway pressure (CPAP), intubation, or ICU admission), hospital LOS $\geq$3 days, discharge on inhaled corticosteroids, and relapse of bronchiolitis requiring medical attention and a change of medication within one week of discharge.

Statistical Analysis

Stata 11.2 (Stata Corp, College Station, TX) was used for all analyses. We examined unadjusted differences between racial/ethnic groups and clinical presentation, patient management, and outcomes using χ^2, Fisher's Exact, or Kruskal-Wallis test, as

appropriate, with results reported as proportions with 95% confidence intervals (CI) or medians with interquartile ranges (IQR). Imputed values, calculated with the Stata impute command, were used to calculate the RDSS when one of the four components was missing; patients missing more than one component were not assigned an RDSS value. Multivariable logistic regression was conducted to evaluate the adjusted association between race/ethnicity and the outcomes listed above. Besides race/ethnicity, all multivariable models included the demographic variables of age, sex, insurance, and median household income. Other factors were considered for inclusion if they were associated with the outcome in unadjusted analyses ($P<0.20$) or deemed clinically relevant. All models were adjusted for the possibility of clustering by site. Results are reported for the race/ethnicity factor as odds ratios (OR) with 95% CI.

RESULTS

Of the 2,130 subjects included in this analysis, 818 (38%) were NHW, 511 (24%) were NHB, and 801 (38%) were Hispanic. The median age for children was 4.0 months (IQR 1.8-8.5 months) and 60% were male. Most children were publicly insured (65%), 31% had private insurance, and approximately 4% had no insurance. The median household income defined by patient ZIP code was $51,810 (IQR $39,916-$66,272) and nearly all children (97%) had a primary care provider (PCP). Approximately 21% of all children had relevant comorbidities and 17% of children were enrolled from the ICU. Overall, the median LOS was 2 days (IQR 1-4 days).

The unadjusted associations between race/ethnicity and other demographic and historical characteristics are shown in **Table 1**. NHB and Hispanic children were more likely to have public insurance, live in a ZIP code with a lower median household income, and less likely to have relevant major comorbidities when compared to NHW children. NHB children were more likely to experience second-hand smoke exposure, have been previously intubated, and received palivizumab. With regard to care received the week before hospitalization, NHW children were more likely to have visited their PCP, taken corticosteroids and/or antibiotics, and least likely to have visited an ED when compared to NHB and Hispanic children.

TABLE 1: Demographic and Clinical Characteristics of Subjects Before the Pre-admission Visit*, by Race/Ethnicity

	White (non-Hispanic) n=818	**Black (non-Hispanic) n=511**	**Hispanic n=801**	
		column %		P
Demographic characteristics				
Age (months), median (IQR)	3.2 (1.5-7.4)	5.0 (1.9-9.2)	4.4 (2.0-9.1)	<0.001
Female	39.7	40.9	40.4	0.91
Insurance				<0.001
Private	56.7	17.0	13.1	
Medicaid	32.8	70.9	77.5	
Other public	6.8	7.6	4.2	
None	3.7	4.6	5.3	
Median household income by zip code (US $), median (IQR)	$60,406 ($48,086-$75,077)	$44,191 ($32,922-$55,640)	$50,394 ($39,242-$62,148)	<0.001
Has primary care provider	98.5	97.3	95.4	0.001
History				
Gestational age at birth				0.002
<32 weeks	4.5	9.2	6.6	
32 - 35 weeks	5.7	8.8	6.0	
35 - 37 weeks	13.3	10.0	9.7	

	White (non-Hispanic) n=818	**Black (non-Hispanic) n=511**	**Hispanic n=801**	
		column %		P
≥37 weeks	76.0	71.4	76.9	
Missing	0.4	0.6	0.7	
Weight when born				<0.001
<3 pounds	3.3	6.9	5.8	
3-4.9 pounds	6.8	11.9	6.2	
5-6.9 pounds	33.4	39.7	33.2	
≥ 7 pounds	55.8	40.3	53.6	
Missing	0.7	1.4	1.4	
Kept in an ICU, premature nursery, or any type of special care facility when born	24.5	29.7	24.9	0.07
Breast fed	62.3	49.1	65.5	<0.001
Attends daycare	20.7	25.2	13.3	<0.001
Number of other children (<18 old) living in home				<0.001
1	24.2	25.6	17.0	
2	42.7	29.2	28.3	
≥3	33.1	45.2	54.7	
Neither parent has asthma	66.1	56.6	77.7	<0.001
Maternal smoking during pregnancy	21.8	21.3	6.0	<0.001

	White (non-Hispanic) n=818	**Black (non-Hispanic) n=511**	**Hispanic n=801**	
		column %		P
Second-hand smoke exposure	12.9	20.2	8.7	<0.001
History of wheezing	21.1	25.9	21.8	0.12
Ever intubated	9.5	13.2	9.2	0.05
Major relevant comorbidities**	23.6	21.1	18.2	0.03
Received palivizumab (respiratory syncvtial virus vaccine)	8.7	12.7	8.9	0.04
Received influenza vaccine this year	20.2	24.7	21.2	0.15
In past 12 months, admitted overnight to hospital for bronchiolitis/wheezing/reactive airway disease	45.0	57.9	55.9	0.06
In past 12 months, admitted overnight to hospital for pneumonia	16.1	14.9	25.0	0.049
<u>Current illness</u> (before index visit)				
Any primary care provider or clinic visits during past week	75.0	44.1	58.3	<0.001

	White (non-Hispanic) n=818	**Black (non-Hispanic) n=511**	**Hispanic n=801**	
		column %		P
Any ED visits during past week	29.1	30.3	34.6	0.049
Over the past week, used inhaled bronchodilator	40.6	36.2	37.0	0.18
Over the past week, used inhaled/nebulized corticosteroids	8.7	8.1	7.7	0.76
Over the past week, taken any steroid liquids or pills or shots for bronchiolitis	12.8	11.7	8.3	0.012
Over the past week, taken antibiotics	21.9	17.0	17.9	0.045
Onset of difficulty breathing				0.03
None	2.0	2.2	2.4	
<24 hours	28.8	27.2	25.1	
1-3 days	41.1	41.6	45.9	
4-7 days	22.1	19.1	21.2	
> 7days	6.0	9.9	5.3	
Over the past 24 hours, the level of discomfort or distress felt by child because of symptoms				<0.001
Mild	15.5	21.3	18.5	

	White (non-Hispanic) n=818	**Black (non-Hispanic) n=511**	**Hispanic n=801**	
		column %		P
Moderate	47.8	39.3	37.2	
Severe	36.1	37.6	42.6	

Abbreviations: IQR, interquartile range; ED, emergency department
* Pre-admission visit is the emergency department or office visit preceding hospital admission.
** Major relevant comorbid disorders included reactive airway disease or asthma, spastic di/quadriplegia, chronic lung disease, seizure disorder, immunodeficiency, congenital heart disease, gastroesophageal reflux, and other major medical disorders.

The unadjusted associations between race/ethnicity and clinical characteristics at pre-admission visit and hospital admission are shown in **Table 2**. Significant differences across race/ethnicity were found regarding why guardians brought their child to the hospital. Febrile Hispanic children and NHW children not drinking well were two reasons for seeking care that showed the strongest association. RDSS values were calculated for 2,130 children; 1,752 (82%) RDSS values contained all four components. Of those requiring imputed values, 234 (11%) were missing one component and 139 (7%) were missing more than one component. Per RDSS scores, NHB children presented with a more severe case of bronchiolitis when compared to NHW and Hispanic children. During admission, minority children were more likely to receive nebulized albuterol and less likely to visit the ICU. NHB children received the least inpatient laboratory testing and were least likely to receive chest x-rays during hospital admission among all groups.

TABLE 2: Clinical Characteristics at Pre-admission Visit and During Admission, by Race/Ethnicity

	White (non-Hispanic) n=818	**Black (non-Hispanic) n=511**	**Hispanic n=801**	
		column %		P
Pre-admission clinical findings and treatments				
Reason Brought To Hospital:				
Fever	29.7	30.2	40.7	<0.001
Fussy	32.6	31.6	28.4	0.18
Ear Infection	6.0	4.3	4.4	0.23
Not drinking well	35.0	27.5	27.2	0.001
Cough	54.1	55.5	61.3	0.009
Other reasons	29.0	27.6	23.5	0.04
Apnea	8.5	6.2	6.1	0.11
Respiratory rate (breaths/minute)				0.001
<40	23.8	18.2	28.1	
40-49	30.8	30.7	29.3	
50-59	17.6	15.5	16.0	
≥60	27.8	35.6	26.6	
Presence of cough	83.0	88.0	87.0	0.045
Presence of wheezing	63.0	69.0	63.0	0.42

	White (non-Hispanic) n=818	**Black (non-Hispanic) n=511**	**Hispanic n=801**	
		column %		P
Fever (Temperature ≥100.4°F)	22.7	28.5	35.4	<0.001
Retractions				0.002
None	22.9	19.0	23.0	
Mild	39.4	41.7	44.4	
Moderate/severe	28.4	31.1	28.1	
Missing	9.4	8.2	4.5	
Air entry on auscultation				0.01
Normal	39.6	31.7	33.6	
Mild difficulty	31.4	33.5	36.3	
Moderate difficulty	11.0	14.3	14.1	
Severe difficulty	2.0	2.3	2.6	
Missing	16.0	18.2	13.4	
Oxygen saturation on room air <90	12.2	9.8	11.8	0.37
Given nebulized albuterol	53.0	65.0	63.0	<0.001
Given nebulized epinephrine	15.4	20.4	18.4	0.06
Given steroids, inhaled or systemic	16.0	20.5	19.4	0.08
Given antibiotics	25.5	22.6	27.8	0.12

	White (non-Hispanic) n=818	**Black (non-Hispanic) n=511**	**Hispanic n=801**	
		column %		P
Oral Intake				<0.001
Adequate	41.3	50.7	40.8	
Inadequate	43.5	32.5	47.7	
Missing	15.2	16.8	11.5	
IV placed	56.9	51.5	61.9	0.001
Any laboratory tests	86.3	91.3	88.0	0.02
Chest x-ray	59.0	64.0	65.0	0.03
RDSS, tertiles				<0.001
1 (≤3.00)	36.0	24.0	34.0	
2 (3.011-5.00)	30.0	33.0	34.0	
3 (>5)	25.0	36.0	27.0	
Not Calculated	9.0	6.0	4.0	
Virology Results				
Respiratory syncytial virus	75.9	67.5	71.0	0.003
Human rhinovirus	23.8	30.1	25.0	0.03
Human metapneumovirus	6.1	6.8	8.4	0.20

	White (non-Hispanic) n=818	**Black (non-Hispanic) n=511**	**Hispanic n=801**	
		column %		P
Inpatient clinical findings and treatments				
Length of stay ≥3 days	46.5	39.3	45.4	0.03
Ever in observation unit	8.6	7.8	4.0	0.001
Ever in regular ward	89.4	93.0	94.5	0.001
Ever in step-down unit	5.0	3.2	7.8	0.002
Ever in ICU	20.3	15.0	15.9	0.02
Required CPAP or intubation	7.7	4.6	8.8	0.02
Given nebulized albuterol	37.6	48.0	46.7	<0.001
Given nebulized epinephrine	10.7	14.9	13.0	0.07
Given steroids, inhaled or systemic	21.3	27.3	23.5	0.047
Given antibiotics	38.9	34.3	38.6	0.19
Received IV fluids	53.1	45.6	57.1	<0.001
Any laboratory tests	52.2	41.6	51.7	<0.001
Chest x-ray	27.1	18.6	22.9	0.002

Abbreviations: RDSS, Respiratory Distress Severity Score; ICU, intensive care unit; CPAP, continuous positive airway pressure.

Discharge treatment and outcomes at one week follow-up are shown in **Table 3.** A total of 1,771 patients (83%) were reached by telephone. No statistically significant differences between racial/ethnic groups were found regarding two primary outcomes, hospital discharge on corticosteroids and likelihood of bronchiolitis-related relapse.

TABLE 3: Discharge Treatment and Outcome Measures at 1-Week Follow-Up, by Race/Ethnicity

	White (non-Hispanic) n=818	**Black (non-Hispanic) n=511**	**Hispanic n=801**	
		column %		P
Discharged on inhaled corticosteroids	9.5	11.1	13.3	0.08
Discharged on oral corticosteroids	9.8	12.4	8.5	0.11
Child's condition at 1 week follow-up compared to on discharge				0.001
Much worse/worse	1.8	0.7	0.4	
About the same	3.4	6.4	2.5	
Better	38.2	39.1	34.2	
All better	56.6	53.7	62.9	
Child's cough at 1 week follow-up compared to on discharge				0.10
Much worse/worse	2.1	1.2	1.0	
About the same	5.0	8.4	5.2	
Better	29.4	31.2	28.6	
All better	63.5	59.2	65.2	
Bronchiolitis relapse	10.7	11.9	10.3	0.81

Given the large potential for confounding regarding our initial findings, we examined multivariable-adjusted associations of race/ethnicity and bronchiolitis management **(Table 4**). Receiving albuterol during the pre-admission visit and chest x-rays during hospitalization remained significantly associated with race/ethnicity in adjusted analyses, as NHB children were most likely to receive albuterol during the pre-admission visit but least likely to receive chest x-rays during hospitalization. Several outcomes with statistically significant differences found during unadjusted analyses (e.g., chest x-rays at pre-admission visit, albuterol during hospitalization, CPAP/intubation use, ICU admission, and LOS) were not independently associated with race/ethnicity in multivariable models. By contrast, adjusted analyses revealed Hispanic children as significantly more likely to be discharged on inhaled corticosteroids when compared to NHW and NHB children; this association had borderline statistical significance (P=0.08) in the unadjusted analysis. Lastly, we observed no significant racial/ethnic differences with respect to corticosteroids given at pre-admission visit or hospitalization as well as no differences regarding bronchiolitis-related relapse in either unadjusted or adjusted analyses.

TABLE 4: Multivariable Results of Clinical Decisions and Outcomes among Children Admitted for Bronchiolitis, by Race/Ethnicity

	White (Non-Hispanic)		**Black (Non-Hispanic)**		**Hispanic**	
	OR	95%CI	OR	95%CI	OR	95%CI
Preadmission visit						
Chest x-ray*	1.00	(Reference)	1.06	(0.83-1.36)	1.09	(0.74-1.60)
Albuterol use[Ѧ]	1.00	(Reference)	**1.58**	**(1.20-2.07)**	1.42	(0.89-2.26)
Steroid use, inhaled or systemic[§]	1.00	(Reference)	1.05	(0.72-1.54)	1.11	(0.75-1.65)
During hospitalization						
Chest x-ray[†]	1.00	(Reference)	**0.66**	**(0.49-0.90)**	0.95	(0.60-1.50)
Albuterol use[₪]	1.00	(Reference)	1.21	(0.82-1.79)	1.23	(0.63-2.38)
Steroid use, inhaled or systemic[#]	1.00	(Reference)	1.13	(0.72-1.80)	1.19	(0.79-1.79)
ICU care[∩]	1.00	(Reference)	0.74	(0.42-1.29)	0.87	(0.63-1.21)
Required CPAP/intubation[¶]	1.00	(Reference)	0.72	(0.36-1.41)	1.84	(0.93-3.64)
Length of stay ≥3 days[€]	1.00	(Reference)	0.77	(0.58-1.03)	1.05	(0.76-1.47)
Discharge						
Discharged on inhaled steroids[$]	1.00	(Reference)	1.31	(0.86-2.00)	**1.92**	**(1.19-3.10)**
Bronchiolitis relapse[¥]	1.00	(Reference)	1.08	(0.62-1.87)	0.96	(0.55-1.65)

Abbreviations: OR, odds ratio; CI, confidence interval; ICU, intensive care unit; CPAP, continuous positive airway pressure.

All models control for age, sex, median household income by zip code, and insurance status.

*Also control for gestational age, parental asthma, past pneumonia or bronchiolitis admission, discomfort and dyspnea at home, chief complaint, virology.
[A]Also control for birth weight, medications and dyspnea before preadmission, virology.
[§]Also control for birth weight, NICU, children at home, parental asthma, comorbidity, flu shot, medications at home, virology.
†Also control for gestational age, birth weight, prenatal smoking, palivizumab, past pneumonia admission, steroids before preadmission, preadmission oral intake, O_2 saturation, RDSS, apnea, virology, antibiotics, and labs.
[≈]Also control for gestational age, wheezing history, flu shot, discomfort at home, chief complaint, preadmission medications, labs and virology, RDSS.
[#]Also control for breast feeding, parental asthma, wheezing history, comorbidities, flu shot, past pneumonia admission, medications before preadmission, preadmission fever, O_2 saturation, RDSS, apnea, virology, medications, and labs.
[∩]Also control for family history, birth weight, breast feeding, prenatal smoking, antibiotics and discomfort before preadmission, chief complaint, preadmission apnea, O_2 saturation, RDSS, antibiotics, intravenous line, and labs.
[¶]Also control for birth weight, prenatal smoking, past bronchiolitis admission, steroids before preadmission, preadmission O_2 saturation, RDSS, apnea, intravenous line, and antibiotics.
[€]Also control for birth weight, NICU, other children at home, prenatal smoking, palivizumab, discomfort and dyspnea before preadmission, chief complaint, preadmission oral intake, O2 saturation, RDSS, virology, and epinephrine.
[$]Also control for prenatal smoking, wheezing history, palivizumab, medications before preadmission, chief complaint, oral intake, step down, ICU, inpatient steroids, and labs.
[¥]Also control for parental asthma, intubation history, past bronchiolitis admission, virology, and LOS.

Values in bold are considered statistically significant with $P<0.05$.

DISCUSSION

It is unclear if management and treatment differences found in children with severe bronchiolitis are associated with race/ethnicity. We sought to determine if such differences exist by analyzing data from a prospective multicenter cohort study. Differences in management and treatment are discussed in the context of AAP guidelines as they are widely used in clinical practice.

The RDSS was used to help assess severity of illness across race/ethnicity. NHB children had the highest RDSS score (i.e., most severe bronchiolitis presentation) compared to NHW and Hispanic children. The reason for this difference in severity is unclear but one potential explanation may be that minority communities lack access to care and as a result delay care and treatment for respiratory disease until care seems absolutely necessary. Drawing on the Institute of Medicine's Report on Access to Care, Rand et al. argues that excess respiratory disease morbidity may be attributed to personal barriers (e.g., lack of parental knowledge about respiratory disease management, folk illness beliefs, and behaviors), structural barriers (e.g., lack of primary caretaker, organizational impediments), and financial barriers (e.g., trouble paying for primary care visits or prescriptions).[83] Indeed, in our sample, minority children were less likely to visit their PCP and take corticosteroids the week before hospitalization when compared with NHW children. Our finding runs counter to a similar study by Boudreaux et al. that found no association between race/ethnicity and the clinical presentation of children with acute asthma during the pre-admission setting.[84] The more severe bronchiolitis presentation among NHB children may have suggested that these children would require a longer

hospital LOS (≥3 days). However, our multivariable analysis found no difference in LOS across racial/ethnic groups. This LOS finding is intriguing given previous studies suggesting that minorities, of diverse ages and with diverse diagnoses, were more likely to have a shorter LOS (as well as less likely to be admitted to the ICU with a similar diagnosis) when compared to non-minorities.[85,86] Additionally, because our study sampled 16 sites, variation in clinical judgment and pediatric ICU protocol may have also played a role.[87]

Our findings also shed light on how differences in bronchiolitis management relate to AAP guidelines. According to the AAP, corticosteroid medications should not be used routinely in the management of bronchiolitis. Despite this recommendation, previous reports indicate that up to 60% of infants with severe bronchiolitis receive corticosteroid therapy.[88,89] Our finding that Hispanic children with severe bronchiolitis were most likely to be discharged on inhaled corticosteroids is potentially concerning as it exposes a subset of children to treatment that is not recommended. On the other hand, given the increased risk of future asthma in Hispanic communities, a higher use of inhaled corticosteroids might be seen as appropriate. Either way, our findings are inconsistent with related studies concluding that racial minority pediatric patients with asthma were less likely to receive inhaled corticosteroids.[90-93] Similarly, NHB children were most likely to receive albuterol during the pre-admission visit on multivariable analysis. Although a trial dose of albuterol may be common practice in treating severe bronchiolitis, AAP recommendations do not support its routine application. Increased albuterol during pre-admission may have been related to an elevated bronchiolitis

severity at presentation among NHB children (as indicated by the RDSS). Potential reasons for these two differences in treatment remain unclear. They may represent medical management efforts by discharging physicians to prescribe: (1) corticosteroids to racial/ethnic communities with a higher risk of childhood asthma; (2) albuterol to children presenting with a more severe case of bronchiolitis. These possibilities merit further study.

The AAP also recommends diagnosis of bronchiolitis on the basis of history and physical examination; laboratory and radiologic studies should not be routinely used for diagnostic purposes. Although it is possible for chest radiograph abnormalities to be consistent with bronchiolitis, there is little evidence that an abnormal finding is associated with disease severity.[94] The clinical value of diagnostic testing in children with bronchiolitis is not well supported by evidence and limiting exposure to radiation should be a priority.[95] Our analysis found that NHW and Hispanic children were more likely to receive chest x-rays while hospitalized when compared with NHB children. Unnecessary and increased radiation exposure in children is potentially harmful and warrants intervention to minimize risk.

Establishing systematic clinical care pathways in bronchiolitis management may address the practice variation found nationwide and across race/ethnicity in this study. While clinical guidelines provide general recommendations, clinical care pathways are defined treatment protocols aiming to standardize and optimize patient outcomes and clinical efficiency. The incorporation of these algorithmic pathways into healthcare

systems has increased recently as a result of their favorable associations. In a large systematic review consisting of 27 studies involving 11,398 patients, Rotter et al. found that clinical care pathways helped reduce in-hospital medical complications and improve documentation without negatively impacting LOS and hospital costs.[96] With respect to bronchiolitis, such treatment protocols have proven to be successful. Wilson et al. found that the implementation of clinical care pathways in bronchiolitis cases reduced inappropriate antibiotic use from 27% to 9% in addition to reducing healthcare costs and LOS.[97] Similarly, Cheney et al. proved that their adoption could reduce readmission rates.[98] The inclusion of clinical pathways in her study not only reduced readmission rates within 2 weeks from 7.2% to <1%, but also decreased the number of children receiving supplemental fluids and steroids. Ralston et al. went one step further by analyzing the results of a voluntary quality improvement collaborative of pediatric hospitals from 17 centers. The goal of the collaborative, Value in Inpatient Pediatrics, was to link academic and community-based hospitalist groups to disseminate evidence-based management strategies for bronchiolitis. In his landmark study observing 11,568 bronchiolitis hospitalizations post intervention, he demonstrated a 46% reduction in overall volume of bronchodilators prescribed (overall exposure to any bronchodilators decreased by 12%).[99]

Notwithstanding the differences found in this study, management of children with bronchiolitis was, in many respects, comparable across racial/ethnic groups. For example, our multivariable analysis found no significant differences across racial/ethnic groups with respect to chest x-rays and corticosteroid use during the pre-admission visit, administration of albuterol or corticosteroids during hospitalization, use of

CPAP/intubation, ICU admission, hospital LOS, or likelihood of a bronchiolitis-related relapse. The general lack of race/ethnic differences is consistent with similar research on pediatric inpatient management of acute asthma.[80]

This study has potential limitations. The hospitals participating in the study are predominantly urban, academically-affiliated hospitals. This may result in findings that are less generalizable to rural and community hospitals. Second, the race/ethnicity classification used does not take into consideration the diversity and complexity of defining race/ethnicity in the U.S. Third, bronchiolitis is defined as a clinical diagnosis that can encapsulate multiple lower respiratory infection diagnoses. As a result, there may have been variability in clinical and institutional practice. An additional limitation was utilizing RDSS to assess bronchiolitis severity. While there is currently no validated, universally-accepted score to assess bronchiolitis severity, several scores are available in the literature with varying performance. Lastly, the ZIP code-based median household incomes used to assess SES are higher than federal data in similar geographic locations, potentially resulting in findings that are less generalizable.

CONCLUSION

This multicenter prospective cohort study found several differences in bronchiolitis presentation and management among children stratified by race/ethnicity in 16 geographically-dispersed sites after controlling for multiple factors including SES. Our analysis showed that, when compared to NHW children, NHB children were more likely to be given albuterol during the pre-admission visit and less likely to receive chest

x-rays as inpatients; Hispanic children were more likely to be discharged on inhaled corticosteroids. These differences are concerning for two reasons: (1) based on current evidence, race/ethnicity should not affect care in children with severe bronchiolitis; and (2) the observed differences in diagnostic testing and treatment are not recommended by the evidence-based AAP guidelines. It is also important to note that these differences do not demonstrate that a specific race/ethnicity received better or worse clinical care. The goal of this analysis was not to determine the effectiveness of certain management tendencies in children with severe bronchiolitis, but rather to examine differences in the presentation and management of children from different racial/ethnic groups. The causes for the observed findings require further study. In the meantime, we suggest increasing the number of hospitals that incorporate clinical care pathways for severe bronchiolitis to control variation in practice and limit the impact that race/ethnicity may have in the provision of services.

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APPENDIX 1

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Eugene Mowad, MD	Akron Children's Hospital, Akron, OH
Brian Pate, MD	Children's Mercy Hospital& Clinics, Kansas City, MO
M. Jason Sanders, MD	Children's Memorial Hermann Hospital, Houston, TX
Alan Schroeder, MD	Santa Clara Valley Medical Center; San Jose, CA
Michelle Stevenson, MD, MS	Kosair Children's Hospital, Louisville, KY
Erin Stucky Fisher, MD	Rady Children's Hospital, San Diego, CA
Stephen Teach, MD, MPH	Children's National Medical Center, Washington, DC
Lisa Zaoutis, MD	Children's Hospital of Philadelphia, Philadelphia, PA

APPENDIX 2

Abbreviations:
AAP – American Academy of Pediatrics
CI – confidence interval
CPAP – continuous positive air pressure
ED – emergency department
EMNet – Emergency Medicine Network
ICU – intensive care unit
IQR – interquartile range
LOS – length of stay
MARC – Multicenter Airway Research Collaboration
NHW – non-Hispanic white
NHB – non-Hispanic black
OR – odds ratio
PCP – primary care provider
RDSS – Respiratory Distress Severity Score
RSV – respiratory syncytial virus
SES – socioeconomic status