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Characteristics of Infants/Children Presenting to Outpatient Bronchopulmonary Dysplasia Clinics in the United States

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Data were collected at institutions 1-5 and 7-8, anonymized data were housed at Nationwide Children's Hospital, and analysis was conducted at Johns Hopkins University.

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Abstract

Introduction: Bronchopulmonary dysplasia (BPD) is a common respiratory sequelae of preterm birth, for which longitudinal outpatient data are limited. Our objective was to describe a geographically diverse outpatient cohort of former preterm infants followed in BPD-disease specific clinics.

Methods: Seven BPD specialty clinics contributed data using standardized instruments to this retrospective cohort study. Inclusion criteria included preterm birth (<37 weeks) and respiratory symptoms or needs requiring outpatient follow-up.

Results: A total of 413 preterm infants and children were recruited (mean age: 2.4±2.7 years) with a mean gestational age of 27.0±2.8 weeks and a mean birthweight of 951±429 grams of whom 63.7% had severe BPD. 51.1% of subjects were non-white. Severe BPD was not associated with greater utilization of acute care/therapies compared to non-severe counterparts. Of children with severe BPD, differences in percentage of those on any home respiratory support (p=0.001), home positive pressure ventilation (p=0.003), diuretics (p<0.001), inhaled corticosteroids (p<0.001), and pulmonary vasodilators (p<0.001) were found between centers, however no differences in acute care use were observed.

Discussion: This examination of a multicenter collaborative registry of children born prematurely with respiratory disease demonstrates a diversity of management strategies among geographically distinct tertiary care BPD centers in the United States. This study reveals that the majority of children followed in these clinics were non-white and that neither variation in management nor severity of BPD at 36 weeks influenced outpatient acute care utilization. These findings suggest that post-NICU factors and follow-up may modify respiratory outcomes in BPD, possibly independently of severity.

Keywords

Bronchopulmonary dysplasia; prematurity; chronic lung disease; outpatient

INTRODUCTION

Bronchopulmonary dysplasia (BPD) is a disorder of lung development resulting from premature birth that affects almost 50,000 infants born in the United States annually, including over 10,000 with severe disease.[1] Although a substantial portion of lung catch-up growth and injury recovery may occur by 2 years of age,[2] the course of BPD and other manifestations of post prematurity respiratory disease can be highly variable with some patients having pulmonary consequences throughout childhood, and others with symptoms into adulthood.[1,3] Overall, the longitudinal natural history of post prematurity respiratory disease is not well defined.

While there has been some effort to begin outlining the elements needed for following these patients long-term,[4] care of these infants/children is notable for an absence of evidence-

based guidelines for management and follow-up after NICU discharge. In contrast to the well established guidelines for treating childhood asthma and cystic fibrosis, the paucity of standardized recommendations in BPD may lead to significant variation in management strategies and outcomes.[5] The absence of guidelines may be partially due to the lack of standardized respiratory phenotypes after 36 weeks corrected gestational age. Although the commonly used 2001 NHLBI definition of BPD[6] correlates with respiratory outcomes within the first several years of life,[7] it has been criticized both for being limited by being assessed at a single timepoint and also being based on respiratory therapy delivered rather than other measures based on pathology or symptomatology.[8,9]

With this in mind our goal was to develop a longitudinal outpatient cohort of former preterm infants who were seen in BPD-disease specific clinics for respiratory symptoms or disease and to describe their epidemiology. To achieve this objective, seven outpatient BPD clinics from different geographic regions throughout the United States recruited participants and collected standardized demographic, clinical, and environmental data through caregiver-completed questionnaires and chart review within the structure of a multicenter BPD collaborative.[4] This study represents the initial report from a new multicenter collaborative outpatient database designed to provide data on long-term outcomes for infants and children with BPD.

METHODS

Study Population:

The BPD Collaborative includes 21 academic institutions with multidisciplinary teams in the United States and Sweden dedicated to optimizing outcomes of infants and children with established severe BPD through filling in gaps in knowledge. Within the structure of this collaborative we created a registry of participants recruited from outpatient BPD clinics. Inclusion criteria included preterm birth (<37 weeks gestational age) and ongoing respiratory symptoms or needs requiring outpatient follow-up in a BPD clinic. Seven tertiary care centers within the United States but from diverse geographical areas recruited a total of 413 participants between May 2019 and July 2020 from pulmonary and neonatology outpatient clinics for this outpatient registry. Participating centers obtained local IRB approval and data use agreements for compiling anonymized data.

Data Collection:

Data collection instruments (unvalidated) were generated through an iterative process involving eleven members of the BPD Collaborative (See Supplement for instrument). Data were collected by caregiver questionnaires in the clinic or extracted from the electronic medical record. At the time of recruitment, a demographic form was completed that collated data on participant demographics, birth history, and NICU history. At the time of recruitment and subsequent encounters in clinic, a clinic visit form was completed that collated data on the home environment, respiratory and nutritional support, medications, insurance coverage, and self-reported acute care use (since NICU discharge or the last clinic visit). All ages reported in this study are chronological ages. BPD severity was defined using the 2001 NHLBI workshop definitions.[6] Pulmonary hypertension was defined as its presence on

echocardiography or cardiac catheterization after 36 weeks corrected gestational age.[10] Home respiratory support was defined by any use of supplemental oxygen or invasive/non-invasive positive pressure ventilation within the home setting. Pulmonary vasodilator medications included any use of phosphodiesterase-5 inhibitors, endothelin receptor antagonists, or prostanoids. Feeding tubes included nasogastric, gastrostomy, gastrojejunostomy, and jejunostomy tubes.

Data analysis:

Descriptive frequencies and means for demographic data (from the demographics form) were compared using chi-square tests and t-tests (Tables 1 and 3). Variation in outpatient features (from the clinic visit form) between those with and without severe BPD was compared using logistic regression clustered by center and adjusted for age that the time of form completion, with the outpatient outcome as the dependent variable and the presence of severe BPD as the independent variable (Table 2). Variation in outpatient features for only subjects with severe BPD between centers was compared using analysis of covariance (ANCOVA) adjusted for age at the time of form completion with center treated as a dummy categorical variable (Table 4). Data presented in Tables 2 and 4 are limited to the clinic visit form completed at the time of recruitment (one form per participant) provided the recruitment visit occurred at ≤2 years of age. STATA IC 14 (StataCorp LP, College Station, TX) was used for all statistical analyses. *P* values <0.05 were considered statistically significant.

RESULTS

Study Population:

A total of 413 infants and children were recruited from seven tertiary care centers' BPD clinics (Table 1). A majority of participants were male (56.2%), and a total of 51.1% reported either non-white racial ancestry and/or Hispanic ethnic ancestry. Of note, 35.0% of participants were over 2 years of age at the time of recruitment. The mean gestational age at birth was 27.0±2.8 weeks [Range: 22.3, 36.0; however, only 27 individuals were born ≥32 weeks gestation]. The mean birthweight was 951±429 grams [Range: 370, 3125], The mean age at recruitment was 2.4±2.7 years [Range: 0.2, 12.5; median: 1.0]. Using the NHLBI definition of BPD severity the population enrolled included: mild BPD: 10.7%; moderate BPD: 20.1%; severe BPD: 63.7%. Severity of BPD was not documented in 2.2%; and 3.4% did not meet NHLBI BPD criteria, but were born preterm with ongoing respiratory symptoms.[6] A subgroup of participants (20.6%) had pulmonary hypertension that persisted beyond 36 weeks corrected age. Not unexpectedly, multiple gestations (18.3%), *in vitro* fertilization pregnancies (9.7%), and Caesarean section deliveries (66.0%) were common. While cyanotic heart disease was rare (1.0%), the presence of congenital anomalies or syndromes was more common (11.7%).

Features associated with Severe BPD:

Within the study population, 263 participants met the criteria for severe BPD (Table 1). Compared to their 150 counterparts without severe BPD, they were born 1.2 weeks earlier ($p<0.001$) and weighed 205 grams less at birth ($p<0.001$). Those with severe BPD were

more likely to receive pharmaceutical or procedural interventions for patent ductus arteriosus than their non-severe counterparts (p=0.012). Oligohydramnios was less common among those with severe BPD compared to their counterparts (p=0.040). Those with severe BPD were 3.8 times more likely to have pulmonary hypertension than their non-severe counterparts (OR clustered by center p<0.001). However, 9.0% of children without severe BPD also had pulmonary hypertension. Those with severe BPD also spent an additional 2.8 months in the hospital after birth compared to those without severe BPD (p<0.001). We did not observe any differences by sex, race, ethnicity, congenital anomalies/syndrome, or other features between those with and without severe BPD.

We also examined outpatient features of participants with the first completed questionnaire prior to 2 years of age to determine if differences existed by BPD severity (severe versus non-severe) (Table 2). Using logistic regression adjusted for age at the time of form completion and clustered by center, we observed that participants with severe BPD were more likely to be on home positive pressure ventilation (adjusted OR: 16.94; p=0.001), diuretics (adjusted OR: 5.01; p<0.001), inhaled corticosteroids (adjusted OR: 3.32; p=0.010), and pulmonary vasodilator medications (adjusted OR: 12.59; p=0.028) as well as have a feeding tube (adjusted OR: 4.20; p<0.001) compared to those without severe BPD. There were no differences in terms of secondhand smoke exposure or daycare attendance. Notably, those with severe BPD who were 2 years of age or less, were not more likely to utilize acute care (sick office visits, urgent care visits, emergency department visits, or hospital admissions) or receive systemic steroids for respiratory exacerbations than their non-severe counterparts (p values=0.27-0.89). As a secondary analysis we analyzed infants and young children with severe BPD by gestational age (arbitrary cut-off of 28 weeks gestation) to assess whether prematurity contributed to outcomes in severe BPD (Supplemental Table 1). We observed that children with severe BPD less than 2 years of age were more likely to reported an ED visit (23.3%; n=116) if they were born ≤28 weeks gestation than if they were born >28 weeks gestation (9.3%; n=43; p<0.049). No other differences in therapies or acute care use were observed.

Variation in Severe BPD Demographics by Center:

Intercenter differences in severe BPD populations among the seven pediatric tertiary care centers were examined (Table 3). When comparing the centers, there were differences in racial and ethnic compositions with the percentage of those identifying as African-American ranging between 0%-47.6% between centers (intercenter p=0.002) and those identifying as Hispanic ranging between 0%-40.0% (p=0.011). While there were no intercenter differences observed with gestational age or birthweight, the mean age of discharge for patients differed between centers ranged from 4.1 months to 7.6 months (p<0.001). Additionally, we observed differences in the management of patent ductus arteriosus (p<0.001), prevalence of pulmonary hypertension after 36 weeks corrected gestational age (center range: 11.6%-80.0%; p<0.001), and the presence of congenital anomalies or syndromes (center range: 0.0%-25.0%; p=0.023), which may reflect differences among centers in both inpatient and outpatient demographics and follow-up care.

Variation in Severe BPD Outpatient Features by Center:

Intercenter differences in outpatient exposures, management, and outcomes for infants/children with severe BPD who were less than 2 years of age (Table 4) were also examined; of note, the mean age for subjects included in this analysis did not differ between centers (ANOVA p=0.10). Over 10% of participants lived with a smoker, although this did not differ by center (ANCOVA p=0.14 adjusted for age at the time of form completion), and over 20% attended daycare, which did differ by center (p<0.001). Almost 50% of participants were covered by public insurance, but the percentage varied between centers from 14.3%-77.8% (p<0.001). There were differences in most measures of management between centers including the percentage of those on any home respiratory support (p=0.001), any home positive pressure ventilation (p=0.003), diuretics (p<0.001), inhaled corticosteroids (p<0.001), and pulmonary vasodilator medications (p<0.001). The presence of feeding tubes trended towards being different between centers as well (p=0.06). No differences were observed between centers in terms of emergency department visits (p=0.16), hospital admissions (p=0.52), or outpatient courses of systemic steroids (p=0.68), but the percentage of participants reporting a sick office or urgent care visit did differ by center (p=0.012).

DISCUSSION

This study examines population and care practice variations across seven US BPD outpatient tertiary care centers following former preterm infants with respiratory disease. While the majority of preterm infants and children who presented to the BPD outpatient clinics had severe BPD (63.7%), a significant minority had either mild or no history of BPD as defined by the 2001 NHLBI definition. Also, those receiving outpatient BPD management in these centers were more likely to report racial or ethnic minority ancestry (51.1%) than the general population. Additionally, we noted that over a third of patients were over 2 years of age at recruitment, indicating that a substantial population of preterm children had ongoing respiratory disease or symptoms requiring subspecialty care after 2 years of age.

We observed that more severe BPD was associated with earlier gestational ages and lower birth weight at all centers, as would be expected given that these are two primary risk factors for developing BPD.[11] Pulmonary hypertension (after 36 weeks corrected gestational age) was also common (27.1%) in those with severe BPD, and approached a prevalence of almost 10% in those without severe BPD, stressing the need to maintain high clinical suspicion for this diagnosis in any preterm infant with respiratory disease. Alternatively, the prevalence of pulmonary hypertension may also reflect referral patterns at tertiary care centers. Length of NICU stay for infants with severe BPD was 6.0 months on average, and 2.4 months longer than those without severe BPD even after adjusting for gestational age and birthweight (clustered regression p=0.003). Given that NICU costs can reach $100,000 monthly,[12] this highlights the healthcare resources needed to care for severe BPD. There was a significant difference in length of NICU hospitalization between centers for patients with severe BPD, suggesting that inpatient practice model and/or outpatient resource availability may impact length of NICU stay.

Overall, hospital admission rates for BPD patients across all centers were low (15.8%) and there was not significant variability in admission rates between centers. This differs from the

previously reported high rates of readmission for preterm infants with BPD, which has been reported to be up to 50% within the first 2 years of life,[13] and may reflect a shorter period of data capture, a more heterogeneous population in this study or attendance at a BPD disease-specific clinic. Infants with severe BPD did require a higher degree of respiratory support and medications within the first two years of life in the outpatient setting, but notably they did not experience a higher likelihood of acute care use when compared to those with non-severe BPD. It is unclear why this may be the case. It may be that infants with severe BPD managed under the guidance of outpatient BPD programs benefit from this subspecialty care and are able to develop sick plans and home management strategies that prevent admission, especially considering that they are most likely to have access to respiratory monitoring and support in the home given their disease severity.[14] Additionally, there could be elements of recruitment bias present, where the non-severe BPD patients referred to outpatient subspeciality programs are those who have ongoing symptoms or have required admission – meaning those who are not symptomatic are not being captured. Furthermore, those with non-severe BPD seen in clinic may have higher rates of pulmonary hypoplasia (as suggested by a higher prevalence of oligohydramnios) that could lead to them being seen in BPD clinics. Type of insurance did not seem to influence rate of readmission in this cohort as rates of public insurance coverage were similar between those with and without severe BPD. Additionally, this lack of difference in acute care use post-NICU discharge between non-severe BPD and severe BPD may also reflect problems with the current definitions/classifications of BPD, which are all based on respiratory support in the NICU, and thus may not capture important differences in disease progression after NICU discharge.[15,16] Finally, we did observe at least an increase in emergency department visits associated with earlier gestational age in severe BPD; further studies are needed to determine the effects of gestational age on long-term outcomes with severe BPD to see if this is respiratory-related or associated with other comorbidities of earlier gestational age.

In terms of intercenter variation, differences were observed in racial/ethnic composition of participants by center, likely reflecting local demographics. It should be noted that caregivers of participants were more likely to report racial or ethnic minority ancestry (51.1%) relative to the general population, which may reflect referral patterns to urban care centers or the higher rates of preterm birth among minorities.[17] For those with severe BPD, there was also significant variation in the age of discharge, prevalence of pulmonary hypertension at 36 weeks corrected gestational age, and prevalence of congenital anomalies/syndromes. This may reflect local referral patterns, including the variability in birthing hospitals versus referral centers. Furthermore, it may reflect the local criteria for BPD clinic referral after NICU discharge given the known gradation of severity even within the group with severe BPD.[4] We found differences in PDA management between centers for participants with severe BPD, which also may reflect local practices. Despite this being a population of infants with severe BPD, there were substantial differences in outpatient management in terms of respiratory support and related medications. This could partially reflect referring NICU practices, given that the BPD Collaborative previously observed substantial differences in the use of chronic medications for established severe BPD within the NICU setting prior to discharge between centers.[5] However, despite these observed management differences, we did not observe substantial differences in acute care outcomes

between centers in terms of emergency department visits, hospital admissions, or systemic steroid use. There was a difference in sick office/urgent care visits, which again may reflect center referral patterns and resource availability for ill outpatients. Although, it is not possible to determine in this data-set the exact causes of these center differences, it would be interesting in future studies to apply comparative effectiveness approaches to determine if differences in clinical approach may be associated with them.

Limitations of our study include an outpatient study population that may be biased towards more severe disease as those with mild respiratory disease or symptoms may not present to outpatient subspecialty clinics for respiratory care or may cease care after a certain age. While our centers are geographically diverse, they are all located in urban areas and may not provide a full representation of all pulmonary disease among preterm infants and children. Strict screening criteria for certain concurrent conditions were not mandated in this observational study so that diagnostic and management strategies, such as to identify and treat PH, were not standardized across centers. Given the variability in management strategies among outpatient centers, we may not have captured the breadth of management, or this could reflect the underlying variability in focus among the BPD centers, with some led by pulmonologists and others by neonatologists, and some focused on sub-subspecialty aspects of BPD care including tracheostomy patients or those with pulmonary hypertension. Lastly, although we adjusted for age and restricted certain analyses to participants less than 2 years of age, our analyses may be subject to biases from the natural history of disease and differing lengths of follow-up for different participants. There may also be selection biases within the group of subjects less than 2 years of age as younger infants may have more use of therapies or acute care; our study population size did not permit further stratification. Parental recall bias is also possible, particularly for inpatient data for older patients, although chart review was undertaken to verify data when possible. It should be kept in mind though that part of the rationale for this study was to begin to understand the natural history of BPD post-NICU discharge. Although this study is descriptive, its strengths include describing a “real world” population from a geographically diverse group of outpatient centers using a standardized instrument.

This description of a multicenter collaborative registry of infants and children born prematurely with respiratory disease demonstrates a diversity of outpatient management strategies among pediatric tertiary care BPD centers. The variability in referral populations and management strategies did not result in significant differences in ED visits, admissions, or courses of corticosteroid for acute care. The similarities in acute care use between milder and more severe disease may suggest that either some individuals with milder disease have more significant longer term consequences than commonly realized and/or that close subspecialty outpatient management of severe BPD can mitigate some outcomes and/or outpatient factors post NICU can modify respiratory outcomes. The observation that approximately 35% of children receiving care in BPD clinic are over the age of 2 years highlights the potential long-term needs of this population. Finally, minorities were disproportionately represented in the outpatient BPD clinics, paralleling the higher incidence of premature birth in these populations.[18] This study represents the initial report from a geographically diverse multicenter collaborative outpatient database. We would anticipate that future longitudinal data from this expanding cohort will provide information on the

respiratory outcomes of these children as they age and variability in long-term outcomes among centers; information needed to ultimately improve outcomes and reduce health care costs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Collaborative Clinic Population

Mean ± S.D. Median [Range]		**Entire Population (n =413)**	**Severe BPD (n = 263)**	**Not Severe BPD (n = 150)**	***P* Value***
Sex (% female; n=411)		43.8%	43.0%	45.3%	0.52
Race (%)	White	54.0%	53.2%	55.3%	0.68
	Black or African-American	34.9%	36.1%	32.7%	0.48
	Asian	6.3%	4.9%	8.7%	0.13
	Native Hawaiian/Pacific Islander	0.7%	1.1%	0.0%	0.19
	Native American/Alaska Native	0.5%	0.0%	1.3%	0.06
	Other	6.3%	6.8%	5.3%	0.54
Ethnicity (% Hispanic; n=408)		10.3%	8.8%	12.9%	0.19
Age at recruitment (years; n=397)		2.4 ± 2.7 Median: 1.0 [0.2, 12.5]	2.5 ± 2.8 Median: 1.2 [0.2, 12.5]	2.1 ± 2.6 Median: 0.19 [0.2, 11.7]	0.19
Gestational Age (weeks; n=411)		27.0 ± 2.8 Median: 26.4 [22.3, 36.0]	26.6 ± 2.5 Median: 26.0 [22.3, 35.0]	27.7 ± 3.1 Median: 27.2 [22.3, 36.0]	**<0.001**
Birth Weight (grams; n=409)		951 ±429 Median: 840 [370, 3125]	877 ± 383 Median: 770 [370, 3125]	1083 ± 475 Median: 975 [450, 2869]	**<0.001**
Multiple Gestation (% yes; n=409)		18.3%	19.5%	16.3%	0.43
Oligohydramnios (% yes; n=371)		11.6%	9.0%	16.1%	**0.040**
***In Vitro* Fertilization** (% yes; n=381)		9.7%	10.5%	8.2%	0.47
Delivery (% Caesarean; n=403)		66.0%	67.1%	64.1%	0.55
Age at Initial Hospital Discharge (months; n=401)		5.0 ± 3.3 Median: 4.0 [0.1, 24.5]	6.0 ± 3.5 Median: 4.6 [1.4, 24.5]	3.2 ± 1.7 Median: 3.0 [0.1, 15.0]	**<0.001**
BPD Severity (%)	None	3.4%	-	9.3%	-
	Mild	10.7%	-	29.3%	
	Moderate	20.1%	-	55.3%	
	Severe	63.7%	100.0%	-	
	Unknown severity	2.2%	-	6.0%	
CSF Shunt (% yes; n=401)		6.7%	8.6%	3.5%	0.051
PDA (% yes; n=369)	Not closed	4.9%	3.6%	7.6%	**0.012**
	Closed spontaneously	58.3%	54.4%	66.4%	
	Closed with medication	18.4%	20.0%	15.1%	
	Closed with procedure	18.4%	22.0%	10.9%	
Pulmonary Hypertension (% yes after 36 weeks; n=403)		20.6%	27.1%	9.0%	**<0.001**
Cyanotic Heart Disease (% yes; n=408)		1.0%	0.8%	1.4%	0.55
Congenital anomaly or syndrome (% yes; n=401)		11.7%	12.1%	11.0%	0.75

* *P* values were generated comparing subjects in the Severe and Not Severe BPD categories.

Table 2.

Variation Infants/Children with Severe BPD versus Non-Severe BPD

(Mean ± S.D. or % yes) [Range]	**Severe BPD ≤2 years of age (n = 162)**	**Non-Severe BPD ≤2 years of age (n = 84)**	***P* Value***
Age at ascertainment (years)	0.8 ± 0.5 [0.2, 2.0]	0.7 ± 0.5 [0.2, 2.0]	0.13
Living with Smokers	10.5%	10.7%	0.92
Public Insurance	45.8% (n = 155)	42.1% (n = 76)	0.81
Attends Daycare	22.8%	19.2% (n = 78)	0.74
Any Home Respiratory Support	54.3%	40.5%	0.40
Any Home Positive Pressure Ventilation (Ventilator or CPAP/BiPAP)	16.1%	1.2%	**0.001**
Any Diuretics	44.4%	16.7%	**<0.001**
Any Inhaled Steroids	56.2%	27.4%	**0.010**
Any Pulmonary Vasodilator Medications	13.6%	1.2%	**0.028**
Any Feeding Tube	46.3%	16.7%	**<0.001**
Sick Office or Urgent Care Visits**	19.4% (n = 160)	18.4% (n = 76)	0.88
Emergency Department Visits**	19.5% (n = 159)	19.5% (n = 77)	0.74
Hospital Admissions**	15.8% (n = 158)	12.8% (n = 78)	0.69
Courses of Systemic Steroids**	15.7% (n = 153)	9.2% (n = 76)	0.27

* *P* values were generated through logistic regression clustered by center and adjusted for age at which clinical features were ascertained. The *p* value for age of ascertainment was generated via t test.

** Since NICU discharge or last clinic visit.

Table 3.

Demographic and Inpatient Variation among Centers in Infants/Children with Severe BPD

Mean ± S.D. **Median [Range of mean values between centers]**		**Severe BPD (n = 263)**	**Differences between Centers *P* Value**
Sex (% female; n=261)		43.0% [20.0-66.7%]	0.06
Race (%)	White	53.2% [40.0-66.7%]	0.16
	Black or African-American	36.1% [0.0-47.6%]	**0.002**
	Asian	4.9% [0.0-20.0%]	0.11
	Native Hawaiian/Pacific Islander	1.1% [0.0-5.3%]	0.11
	Native American/Alaska Native	0.0%	-
	Other	6.8% [2.3-40.0%]	**0.011**
Ethnicity (% Hispanic; n=261)		8.8% [0.0, 40.0%]	**0.043**
Gestational Age (weeks)		26.6 ± 2.5 Median: 26.0 [25.9, 27.2]	0.96
Birth Weight (grams; n=262)		877 ± 383 Median: 770 [722, 942]	0.75
Multiple Gestation (% yes; n=262)		19.5% [11.5, 44.4%]	0.27
Oligohydramnios (% yes; n=234)		9.0% [0.0-25.0%]	0.15
***In Vitro* Fertilization** (% yes; n=247)		10.5% [0.0, 33.3%]	0.16
Delivery (% Caesarean; n=258)		67.1% [60.5-88.9%]	0.39
Age at Initial Hospital Discharge (months; n=260)		6.0 ± 3.5 Median: 4.6 [4.1, 7.6]	**<0.001**
CSF Shunt (% yes; n=257)		8.6% [0.0-13.6%]	0.19
PDA (% yes; n=250)	Not closed	3.6% [0.0, 10.5%]	**<0.001**
	Closed spontaneously	54.4% [13.5-88.9%]	
	Closed with medication	20.0% [0.0-43.2%]>	
	Closed with procedure	22.0% [0.0-50.0%]	
Pulmonary Hypertension (% yes after 36 weeks; n=258)		27.1% [11.6, 80.0%]	**<0.001**
Cyanotic Heart Disease (% yes; n=262)		0.8% [0.0, 3.9%]	0.21
Congenital anomaly or syndrome (% yes; n=256)		12.1% [0.0-25.0%]	**0.023**

Table 4.

Outpatient Variation among Centers in Infants/Children with Severe BPD

(% yes) [Range of percentages between centers]	Severe BPD ≤2 years of age (n = 162)	Differences between Centers *P* Value*
Living with Smokers	10.5% [0.0, 27.3]	0.14
Public Insurance (n=155)	45.8% [14.3, 77.8]	**<0.001**
Attends Daycare	22.8% [0.0, 100.0]	**<0.001**
Any Home Respiratory Support	54.3% [29.4, 100.0]	**0.001**
Any Home Positive Pressure Ventilation (Ventilator or CPAP/BiPAP)	16.1% [0.0, 57.1]	**0.003**
Any Diuretics	44.4% [11.8, 100.0]	**<0.001**
Any Inhaled Steroids	56.2% [0.0, 82.6]	**<0.001**
Any Pulmonary Vasodilator Medications	13.6% [0.0, 80.0]	**<0.001**
Any Feeding Tube	46.3% [12.5, 85.7]	0.06
Sick Office or Urgent Care Visits (n=160) **	19.4% [0.0, 53.9]	**0.012**
Emergency Department Visits (n=159) **	19.5% [0.0, 37.5]	0.16
Hospital Admissions (n =158) **	15.8% [10.5, 41.7]	0.52
Courses of Systemic Steroids (n=153) **	15.7% [0.0, 25.0]	0.68

* *P* values were generated through analysis of covariance (ANCOVA) adjusted for age (continuous variable) at which clinical features were ascertained. Center was treated as a categorical dummy variable.

** Since NICU discharge or last clinic visit.