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Daycare Attendance is linked to Increased Risk of Respiratory Morbidities in Preterm Children with Bronchopulmonary Dysplasia

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Abstract

Introduction: Postnatal lung growth during the first few years of life is critical for infants with bronchopulmonary dysplasia (BPD) who have altered alveolar, airway, and vascular development in the setting of premature birth. Acute respiratory illnesses may further disrupt postnatal lung growth and development during this crucial period. Identifying modifiable factors that mitigate risk of respiratory illnesses may help improve respiratory outcomes in these children. We hypothesized that children with BPD in daycare would have greater healthcare utilization for respiratory illnesses during the first three years of life.

Methods: This was a retrospective cohort study (n=341) using data collected from nine BPD specialty clinics from diverse geographic areas, using standardized instruments. Subjects were former preterm infants (<34 weeks) with bronchopulmonary dysplasia (71% severe) requiring outpatient follow-up between 0–3 years of age.

Results: Children with BPD attending daycare were more likely to have emergency department visits and systemic steroid usage. Children in daycare up to three years of age were also more likely to report trouble breathing, having activity limitations, and using rescue medications when compared to children not in daycare. More severe manifestations were found in children attending daycare between 6–12 months chronological age.

Conclusion: In this study, preterm children with BPD who attend daycare were more likely to visit the emergency department, use systemic steroids and have chronic respiratory symptoms compared to children not in daycare indicating that daycare may be a potential modifiable risk factor to minimize respiratory morbidities in children with BPD during the preschool years.

Keywords

Daycare; Bronchopulmonary dysplasia; Respiratory morbidities; rehospitalizations

INTRODUCTION

Preterm infants with chronic lung disease (bronchopulmonary dysplasia: BPD) are at increased risk for recurrent wheezing, asthma medication use, and respiratory-related hospitalizations especially during the first few years of life.(1–5) These risks are highest for those with more severe BPD.(6) Community acquired respiratory illnesses remain an important cause of re-hospitalization and morbidity in preterm infants worldwide.(7–10) Lower respiratory tract infections and pneumonias during early childhood in the general population have been associated with long-term adverse effects on lung function in adult life, including airflow obstruction.(11–13) More specifically, these respiratory illnesses may impair much needed alveolar growth in preterm children with BPD who have decreased pulmonary reserve. Therefore, minimizing exposures associated with respiratory illnesses

during the first three years of life may help mitigate the risk of lung function deficits in adult life.

Several prior studies have shown an association between daycare attendance and increased risk of respiratory morbidities in very low birth weight (VLBW) children.(14, 15) One prospective study reported that daycare attendance increased the risk respiratory problems in a statewide cohort of VLBW children followed up to age 2–3 years. Another single center study found that daycare attendance in children with BPD was associated with emergency department visits, systemic corticosteroid use, antibiotic use and days with trouble breathing. These studies suggest that daycare attendance during early life may be a risk factor for short-term respiratory morbidities, with a potential impact on long-term respiratory outcomes.

Exposure to daycare is a leading cause of recurrent respiratory tract infections in young children worldwide. (16) Additionally, preterm infants and children with BPD can display inappropriate immune responses to respiratory viruses, such as RSV and rhinovirus, often resulting in increased respiratory morbidities. (17) In this study we sought to determine if daycare attendance in children with bronchopulmonary dysplasia, is a generalizable risk factor for respiratory morbidities and acute care usage following initial hospital discharge, and if risk for respiratory morbidities from daycare exposure decreases with increasing age. This study included outpatient tertiary care centers from diverse geographic areas across the United States. To address the risk of daycare exposure on respiratory illnesses in children with BPD, we collected registry data from nine tertiary care centers in the United States who participate in the BPD Collaborative Outpatient Registry.

METHODS

Study Population:

Participants were drawn from the BPD Collaborative Outpatient Registry on the basis of inclusion criteria of (1) a diagnosis of BPD, (2) at least one clinical visit prior to 3 years of age, and (3) documentation of daycare attendance or non-attendance prior to 3 years of age.(18) The diagnosis of BPD and its severity was determined through chart review based on the 2001 NHLBI consensus statement.(19) Contributing BPD clinics included nine tertiary care centers (Johns Hopkins Children’s Center, Children’s Hospital of Philadelphia, Monroe Carell Jr. Children’s Hospital at Vanderbilt, Boston Children’s Hospital, Children’s Mercy Hospital Kansas City, Arkansas Children’s Hospital, Lucille Packard Children’s Hospital Stanford, University of Massachusetts Memorial Children’s Medical Center, and Intermountain Primary Children’s Hospital-University of Utah). Participating centers obtained approval from their local institutional review board (IRB) and data use agreements were completed for compiling anonymized data. Informed consent was obtained from caregivers per local IRBs.

Data Collection:

Data collection instruments were generated by the BPD Collaborative as previously described.(18) At the time of recruitment (September 2018 to February 2021), participant

demographics, birth history, and neonatal intensive care unit (NICU) history were collected via questionnaire/chart review. At the time of recruitment and at subsequent encounters in clinic, data on daycare attendance, clinical characteristics, acute care use (since NICU discharge or the last clinic visit), and chronic respiratory symptoms (in the past 4 weeks) were collected via the same questionnaire at each site. Pulmonary hypertension was defined as its presence on echocardiography or cardiac catheterization after 36 weeks post menstrual age.(20) Home respiratory support was defined as any use of supplemental oxygen, tracheostomy, 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:

Demographic and inpatient characteristics were compared among those with any reported daycare attendance versus those without using logistic (dichotomous characteristics), ordered logistic (categorical characteristics), and linear (continuous characteristics) regression models clustered by center (Table 1). For comparing outpatient characteristics assessed at the time of recruitment, *P* values were generated through logistic (dichotomous characteristics) and linear (continuous characteristics) regression models adjusted for recruitment age and clustered by center (Table 2). To test for associations between exposure to daycare and acute care use/chronic respiratory symptoms, odds ratios were generated through univariate and multivariate mixed logistic regression models with clinic visits nested within subjects nested within BPD centers to account for longitudinal data obtained at follow-up clinic visits and to account for any center-specific variation; daycare attendance was coded as time-varying and a random co-efficient for age at the time of visit was included as well (Table 3). To assess for age-related and disease-severity effects, odds ratios for acute care use and chronic respiratory symptoms were generated through multivariate clustered logistic regression models with clinic visits (stratified by age categories or respiratory support) clustered by subject (Table 4 and Supplemental Table 2). All of the regressions for outcomes (Tables 3 and 4 and Supplemental Table 2) were adjusted for covariates chosen *a priori* that may affect the ability to attend daycare: age at the time of clinic visit, age at initial hospital discharge, presence of pulmonary hypertension on or after 36 weeks post menstrual age based on a previous study from the Children's Hospital Neonatal Consortium,(21) any respiratory support at the time of clinic visit, and any feeding tube at the time of clinic visit. STATA IC 15.0 (StataCorp, College Station, TX) was used for all analyses. *P* values < 0.05 were considered significant.

RESULTS

Study Population:

There were 341 subjects with BPD who completed 715 clinic visits with respiratory outcome questionnaires prior to 3 years of age (2.1 ± 1.9 visits per subject; range: 1–15). Caregivers who did report daycare attendance had a similar number of visits with questionnaires (1.8 ± 1.3) as those who did not (2.2 ± 2.0; p=0.23).

Daycare Attendance:

A minority of subjects (18.8%) were reported to attend daycare at least on one clinic visit, prior to 3 years of age (Table 1). Daycare attendance varied across the nine tertiary care centers from 3.3% to 34.9% of subjects at a given center (chi square p=0.002). Subject characteristics by center are summarized in Supplemental Table 1. Of the 64 participants who attended daycare, 41 (64.0%) attended only in-home daycare, 22 (34.4%) attended only center daycare, and 1 (1.6%) attended both locations at different time points. Of note, daycare attendance at the time of recruitment among those recruited between 2018–19 was higher (21.4%; n=206) compared those recruited between 2020–2021 (6.7%; n=135) even after adjusting for recruitment age (adjusted logistic regression p value: 0.001), which may be related to the COVID-19 pandemic.

There were no significant differences in age of recruitment, gestational age or birth weight between either group (mean age of recruitment, 0.9 ± 0.7 years; mean gestational age, 26.8 ± 2.4 weeks; mean birth weight, 906 ± 356 grams). There also were no differences in public insurance coverage, supplemental oxygen use, tracheostomy presence, ventilator use, feeding tube presence, human milk intake, or number of children living in the home between the two groups (Table 2).

Respiratory Morbidities:

Using data from 715 clinical encounters, mixed models were used to determine the risk of respiratory morbidities with daycare attendance. Acute care utilization was higher in children who attended daycare (Table 3). Children attending daycare were more likely to have emergency department visits (adjusted odds ratio (aOR) of 2.81 ± 1.16) and systemic steroid use (aOR of 4.23 ± 2.02). Regarding chronic respiratory symptoms and medication use, children who attended daycare were more likely to report activity limitation (aOR of 4.03 ± 1.74), trouble breathing (aOR of 2.66 ± 0.90), and rescue (beta-agonist) medication use (aOR of 7.38 ± 3.51) than those who did not attend daycare.

Age-Related Effects:

We examined chronological age as a risk factor for respiratory morbidities in children attending daycare by generating age-stratified (6–12 months, 12–24 months, and 24–36 months) adjusted regression models for the five outcomes that were associated with daycare attendance across the entire study population as well as hospital admission, which approached significance (Table 4). We found that daycare attendance during infancy (6–12 months) was associated with a higher likelihood of hospital admissions (aOR 3.50 ± 1.85), systemic steroid use (aOR 4.69 ± 2.71), and activity limitations (aOR 4.24 ± 1.85). We did not observe any specific associations in the 12–24 month age group, but did observe that daycare attendance during early childhood (24–36 months) was associated with a higher likelihood of hospital admission (aOR 5.79 ± 5.08) and activity limitations (aOR 11.70 ± 11.51).

Disease Severity-Related Effects:

We also attempted to assess whether the presence of respiratory support (i.e., supplemental oxygen, ventilation, and/or tracheostomy) at the time of the clinic visit influenced

associations between daycare and respiratory outcomes through stratified analyses (Supplemental Table 2). Associations between daycare and some outcomes (emergency department visits and nighttime symptoms) were only seen in the group on respiratory support, one association (rescue medication use) was only seen in the group off of respiratory support, and some associations were seen in both groups (systemic steroid use and activity limitations).

DISCUSSION

This multicenter study found that daycare attendance in preterm children with a history of BPD during the first three years of life was associated with a higher likelihood of ED visits, systemic steroid use, and chronic respiratory symptoms when compared to children who did not attend daycare, despite being less likely to have feeding tubes and tracheostomies. The study examined data collected from nine tertiary care centers across the United States that specialize in the outpatient care of children with BPD. Our findings support previous findings from geographically limited studies which indicated that daycare was a risk factor for acute care usage and respiratory symptoms in VLBW children and children with BPD.(14, 15) Overall, these findings suggest that daycare attendance within the first 3 years of life associates with a relatively high risk of acute care need (~3-fold for emergency department visits and ~4-fold for systemic steroid use).

It is reasonable to suggest that exposure to daycare may be a proxy for increased exposure to respiratory viruses and other pathogens. Respiratory illnesses are associated with increased healthcare utilization in preterm children with BPD and respiratory diagnoses are the most common reason for readmission among infants with BPD.(22) Although we could not determine whether the type of daycare (center versus in-home daycare) was associated with higher risk, there are some measures that may mitigate risk associated with daycare in preterm infants. Palivizumab prophylaxis has been shown to decrease, although not eliminate, the risk of RSV admissions(23) and breastfeeding has been associated with a decreased risk for admission for rhinovirus-associated illness in one study performed in Argentina.(24) However, in our study we found no difference in daycare status between children who received any human milk at the time of recruitment and those who did not.

Our study did not collect data to elucidate the relationship between respiratory viruses and the need for acute care usage and thus cannot rule out viral infections in the daycare environment as a contributor to higher respiratory morbidities in children with BPD. In addition, it is possible that other factors such as the number of children living at home or exposure to secondhand smoke increase the likelihood of acute care usage. However, with regard to these exposures, we did not find significant differences between children in daycare and those not attending daycare, suggesting that daycare attendance contributes to higher respiratory morbidities in this population.

In addition to increased acute care usage, we also observed a greater risk of chronic respiratory symptoms in children who attended daycare. These respiratory symptoms included trouble breathing (coughing or wheezing), activity limitation, and rescue medication use. While these increased symptoms may be provoked by acute illnesses, their

frequency and severity may be representative of underlying chronic small airway disease. In either case, these symptoms increase the burden of disease and have been shown to decrease caregiver quality of life.(25)

Because these findings may impact provider recommendations to families, we attempted to stratify our data by chronological age (6–12 months, 12–24 months, and 24–36 months). We found that risk of acute care use associated with daycare attendance was highest in the 6–12 months age group, but may persist until 36 months of age. We would speculate that additional associations in early childhood may not have been observed as a result of there being fewer subjects in later age groups. The age limitations of this dataset do not permit us to speculate whether the subjects who attended daycare are at higher risk for the development of asthma-like phenotypes during childhood or long-term lung function decrements. Additionally, we did see associations between daycare and respiratory outcomes in both groups on respiratory support and those off at the time of clinic visit suggesting that those with milder disease are not entirely without risk when attending daycare.

There are limitations to this study. As a retrospective questionnaire-based study, recall bias may exist. The population followed in our BPD clinics is biased towards subjects with more severe respiratory disease and it is possible that individuals with mild or moderate BPD may not have the same risk for respiratory morbidities associated with attending daycare. Additionally, while our data collection is geographically diverse within the United States, most care was provided in urban centers, which may not be generalizable to all settings. Also, there is known to be some variation in center practices for outpatient clinical management owing to an absence of guidelines for standardized management,(18) and although counselling practices for daycare attendance by center were not assessed; differences in daycare attendance by center were noted (Range: 3.3%–34.9%; median: 16.7%). For our age-stratified analysis, we were underpowered to detect associations in older subjects owing to the fewer clinic visits recorded in the age category of 2–3 years. Additionally, older subjects attending a pulmonary clinic may have more severe disease. Thus, this group may be biased towards detecting associations as subjects with more severe disease (and thus at greater risk of morbidities) may be more likely to present in that age category. Of note, although we did not observe any differences in the social determinants of health that we captured (insurance status, race/ethnicity) with daycare attendance, it is possible that daycare may be a proxy for some other marker of socioeconomic status that was not measured. Our data use agreements prohibit recording exact dates in the registry, thus we were unable to accurately assess for COVID-19 pandemic-related effects (including, but not limited to, mask-wearing, fewer children in daycare, reduced in-person clinic visits, reduction in viral infections for fall-winter 2020–2021) as well as accounting for duration of specific therapies (e.g., respiratory support). Lastly, we acknowledge that we did not assess any of the potential benefits of daycare attendance (such as the ability for caregivers to work and the social skills gained by the child).

Conclusions:

Our study highlights, in a diverse multicenter population of infants with BPD, the high risk of acute care use and chronic respiratory symptoms associated with daycare attendance. This

is most likely due to the acquisition of respiratory infections while in daycare. Recognizing that families may choose to seek child care outside the home for a variety of reasons (caregiver employment, cognitive and language development, social interactions and skills), providers should advise families with infants and young children with BPD about the potential risks of daycare attendance, particularly prior to 1 year of age. Although we did not assess for these measures in our study, this population may benefit from anticipatory guidance for managing respiratory infections, including prescriptions for an “as needed” short acting bronchodilator for acute exacerbations in select patients and judicious use of palivizumab, etc. Further studies are needed to define best practices for mitigating the risk associated with daycare attendance.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Kuint J, Lerner-Geva L, Chodick G, Boyko V, Shalev V, Reichman B. Rehospitalization Through Childhood and Adolescence: Association with Neonatal Morbidities in Infants of Very Low Birth Weight. The Journal of pediatrics. 2017;188:135–41.e2. [PubMed: 28662947]
2. Been JV, Lugtenberg MJ, Smets E, van Schayck CP, Kramer BW, Mommers M, et al. Preterm birth and childhood wheezing disorders: a systematic review and meta-analysis. PLoS Med. 2014;11(1):e1001596. [PubMed: 24492409]
3. Jaakkola JJ, Ahmed P, Ieromnimon A, Goepfert P, Laiou E, Quansah R, et al. Preterm delivery and asthma: a systematic review and meta-analysis. J Allergy Clin Immunol. 2006;118(4):823–30. [PubMed: 17030233]
4. Damgaard AL, Hansen BM, Mathiasen R, Buchvald F, Lange T, Greisen G. Prematurity and prescription asthma medication from childhood to young adulthood: a Danish national cohort study. PloS one. 2015;10(2):e0117253. [PubMed: 25651521]
5. Fawke J, Lum S, Kirkby J, Hennessy E, Marlow N, Rowell V, et al. Lung function and respiratory symptoms at 11 years in children born extremely preterm: the EPICure study. American journal of respiratory and critical care medicine. 2010;182(2):237–45. [PubMed: 20378729]
6. Ehrenkranz RA, Walsh MC, Vohr BR, Jobe AH, Wright LL, Fanaroff AA, et al. Validation of the National Institutes of Health consensus definition of bronchopulmonary dysplasia. Pediatrics. 2005;116(6):1353–60. [PubMed: 16322158]
7. Cunningham CK, McMillan JA, Gross SJ. Rehospitalization for respiratory illness in infants of less than 32 weeks’ gestation. Pediatrics. 1991;88(3):527–32. [PubMed: 1881733]
8. Stein RT, Bont LJ, Zar H, Polack FP, Park C, Claxton A, et al. Respiratory syncytial virus hospitalization and mortality: Systematic review and meta-analysis. Pediatr Pulmonol. 2017;52(4):556–69. [PubMed: 27740723]
9. Miller EK, Bugna J, Libster R, Shepherd BE, Scalzo PM, Acosta PL, et al. Human rhinoviruses in severe respiratory disease in very low birth weight infants. Pediatrics. 2012;129(1):e60–7. [PubMed: 22201153]

10. Costa LF, Queiroz DA, Lopes da Silveira H, Bernardino Neto M, de Paula NT, Oliveira TF, et al. Human rhinovirus and disease severity in children. Pediatrics. 2014;133(2):e312–21. [PubMed: 24420808]
11. Martinez FD. Early-Life Origins of Chronic Obstructive Pulmonary Disease. N Engl J Med. 2016;375(9):871–8. [PubMed: 27579637]
12. Chan JY, Stern DA, Guerra S, Wright AL, Morgan WJ, Martinez FD. Pneumonia in childhood and impaired lung function in adults: a longitudinal study. Pediatrics. 2015;135(4):607–16. [PubMed: 25733757]
13. Hayden LP, Hobbs BD, Cohen RT, Wise RA, Checkley W, Crapo JD, et al. Childhood pneumonia increases risk for chronic obstructive pulmonary disease: the COPDGene study. Respiratory research. 2015;16:115. [PubMed: 26392057]
14. Hagen EW, Sadek-Badawi M, Palta M. Daycare attendance and risk for respiratory morbidity among young very low birth weight children. Pediatric pulmonology. 2009;44(11):1093–9. [PubMed: 19824048]
15. McGrath-Morrow SA, Lee G, Stewart BH, McGinley BM, Lefton-Greif MA, Okelo SO, et al. Day care increases the risk of respiratory morbidity in chronic lung disease of prematurity. Pediatrics. 2010;126(4):632–7. [PubMed: 20876173]
16. Bellanti JA. Recurrent respiratory tract infections in paediatric patients. Drugs. 1997;54 Suppl 1:1–4.
17. Moschino L, Carraro S, Baraldi E. Early-life origin and prevention of chronic obstructive pulmonary diseases. Pediatr Allergy Immunol. 2020;31 Suppl 24:16–8. [PubMed: 32017219]
18. Collaco JM, Agarwal A, Austin ED, Hayden LP, Lai K, Levin J, et al. Characteristics of infants or children presenting to outpatient bronchopulmonary dysplasia clinics in the United States. Pediatric pulmonology. 2021.
19. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. American journal of respiratory and critical care medicine. 2001;163(7):1723–9. [PubMed: 11401896]
20. Abman SH, Hansmann G, Archer SL, Ivy DD, Adatia I, Chung WK, et al. Pediatric Pulmonary Hypertension: Guidelines From the American Heart Association and American Thoracic Society. Circulation. 2015;132(21):2037–99. [PubMed: 26534956]
21. Lagatta JM, Hysinger EB, Zaniletti I, Wymore EM, Vyas-Read S, Yallapragada S, et al. The Impact of Pulmonary Hypertension in Preterm Infants with Severe Bronchopulmonary Dysplasia through 1 Year. The Journal of pediatrics. 2018;203:218–24 e3. [PubMed: 30172426]
22. Smith VC, Zupancic JA, McCormick MC, Croen LA, Greene J, Escobar GJ, et al. Rehospitalization in the first year of life among infants with bronchopulmonary dysplasia. J Pediatr. 2004;144(6):799–803. [PubMed: 15192629]
23. Chida-Nagai A, Sato H, Sato I, Shiraishi M, Sasaki D, Izumi G, et al. Risk factors for hospitalisation due to respiratory syncytial virus infection in children receiving prophylactic palivizumab. European journal of pediatrics. 2021.
24. Miller EK, Bugna J, Libster R, Shepherd BE, Scalzo PM, Acosta PL, et al. Human rhinoviruses in severe respiratory disease in very low birth weight infants. Pediatrics. 2012;129(1):e60–e7. [PubMed: 22201153]
25. McGrath-Morrow SA, Ryan T, Riekert K, Lefton-Greif MA, Eakin M, Collaco JM. The impact of bronchopulmonary dysplasia on caregiver health related quality of life during the first 2 years of life. Pediatric pulmonology. 2013;48(6):579–86. [PubMed: 23129398]

Table 1.

Demographics and Inpatient Characteristics

Mean ± SD [Range]	Entire Study Population (n = 341)	Any Daycare (n = 64)	No Daycare (n = 277)	*P* value *
Age at Recruitment (years)	0.9 ± 0.7 [0.2, 3]	1.1 ± 0.7 [0.3, 3]	0.9 ± 0.7 [0.2, 3]	0.15
Sex (% female)	43.6% (n = 337)	40.6%	44.3% (n = 273)	0.50
Race (% non-white)	45.2%	37.5%	46.9%	0.12
Ethnicity (% Hispanic)	12.2% (n = 336)	9.7% (n = 62)	12.8% (n = 274)	0.46
Gestational age (weeks)	26.8 ± 2.4 [22.3, 33.9] (n = 335)	26.8 ± 2.1 [22.3, 31.4]	26.8 ± 2.5 [22.3, 33.9] (n = 271)	0.90
Birth weight (grams)	906 ± 356 [370, 2250] (n = 333)	924 ± 337 [410, 1920] (n = 62)	902 ± 360 [370, 2250] (n = 271)	0.61
Length of initial admission (months)	4.9 ± 2.8 [1.0, 18.0] (n = 329)	4.8 ± 2.8 [1.9, 14.0] (n = 62)	4.9 ± 2.9 [1.0, 18.0] (n = 267)	0.87
BPD severity (%)				
Mild	10.1%	17.2%	8.4%	
Moderate	19.3%	18.8%	19.4%	0.13
Severe	70.6% (n = 337)	64.1%	72.2% (n = 273)	
CSF Shunt (% yes)	6.4% (n = 327)	8.1% (n = 62)	6.0% (n = 265)	0.15
Pulmonary hypertension after 36 weeks (% yes)	21.8% (n = 331)	20.2%	28.1% (n = 267)	0.27
Cyanotic heart disease (% yes)	0.9% (n = 334)	1.6%	0.7% (n = 270)	0.38
Congenital anomaly or syndrome (% yes)	10.4% (n = 327)	12.7% (n = 63)	9.9% (n = 264)	0.49

* *P* values were generated through regression models clustered by center.

Table 2.

Outpatient Clinical Characteristics at Time of Recruitment

Mean ± SD [Range]	**Entire Study Population (n = 341)**	**Any Daycare (n = 64)**	**No Daycare (n = 277)**	***P* value**
Smokers in the home (% yes)	11.7%	14.1%	11.2%	0.39
Children in the home (#)	2.0 ± 1.2 [1, 7] (n = 328)	1.9 ± 1.1 [1, 6] (n = 62)	2.0 ± 1.2 [1, 7] (n = 266)	0.63
Nasal cannula oxygen (% yes)	37.8%	32.8%	39.0%	0.97
Tracheostomy (% yes)	14.7%	9.4%	15.9%	0.06
Home (invasive) ventilator (% yes)	11.1%	6.3%	12.3%	0.07
Inhaled steroids (% yes)	45.2%	45.3%	45.1%	0.44
Pulmonary hypertension medications (% yes)	10.0%	10.9%	9.8%	0.92
Feeding tube (% yes)	38.3% (n = 337)	29.0% (n = 62)	40.4% (n = 275)	0.24
Any human milk (% yes)	22.6%	18.8%	23.5%	0.84
Medicaid (% yes)	52.0% (n = 333)	50.8% (n = 82)	52.2% (n = 251)	0.84

** P* values were generated through regression models adjusted for recruitment age (years) and clustered by center.

Table 3.

Clinical Outcomes with Daycare Attendance

OR ± SE [95% C.I.]		Odds ratio with attending daycare*	*P* value	Adjusted odds ratio with attending daycare**	*P* value
Acute care	**Sick visits**	1.67 ± 0.77 [0.68, 4.12] (n=336 with 705 visits)	0.27	1.81 ± 0.83 [0.74, 4.43] (n=321 with 681 visits)	0.20
	Emergency department visits	2.54 ± 1.05 [1.14, 5.71] (n=332 with 700 visits)	**0.023**	2.81 ± 1.16 [1.26, 6.31] (n=318 with 678 visits)	**0.012**
	Hospital readmissions	1.86 ± 0.81 [0.79, 4.35] (n=332 with 700 visits)	0.16	2.15 ± 0.92 [0.93, 4.97] (n=318 with 678 visits)	0.07
	Antibiotics	2.13 ± 0.90 [0.93, 4.89] (n=330 with 696 visits)	0.07	1.71 ± 0.65 [0.82, 3.60] (n=315 with 672 visits)	0.16
	Systemic steroids	4.66 ± 2.32 [1.76, 12.35] (n=328 with 692 visits)	**0.002**	4.23 ± 2.02 [1.66, 10.76] (n=315 with 671 visits)	**0.002**
Chronic symptoms and medication use	**Trouble breathing**	2.16 ± 0.72 [1.12, 4.17] (n=335 with 687 visits)	**0.022**	2.66 ± 0.90 [1.37, 5.17] (n=319 with 663 visits)	**0.004**
	Nighttime symptoms	1.49 ± 0.54 [0.73, 3.05] (n=336 with 688 visits)	0.28	1.79 ± 0.66 [0.86, 3.70] (n=319 with 663 visits)	0.12
	Activity limitations	3.92 ± 1.68 [1.69, 9.09] (n=332 with 681 visits)	**0.001**	4.03 ± 1.74 [1.73, 9.38] (n=315 with 656 visits)	**0.001**
	Rescue medication use	8.96 ± 4.67 [3.22, 24.90] (n=333 with 685 visits)	**<0.001**	7.38 ± 3.51 [2.90, 18.77] (n=316 with 660 visits)	**<0.001**

*Odds ratios were generated through univariate nested mixed logistic regression models with clinic visits (prior to 3 years of age) nested within subjects nested within BPD centers. A random co-efficient was included for age at the time of visit. Daycare attendance was coded as time-varying. Outcomes were coded as no=0 and yes=1.

**Regressions were adjusted for age at the time of clinic visit, age at initial hospital discharge, presence of pulmonary hypertension on or after 36 weeks corrected age, any respiratory support at the time of clinic visit (i.e., supplemental oxygen, tracheostomy, home ventilator, and/or CPAP/BiPAP), and any feeding tube at the time of clinic visit (i.e., nasogastric, gastrostomy, jejunostomy, or gastrojejunostomy tubes). N refers to the number of subjects and their total number of clinic visits in aggregate for each outcome.

Table 4.

Selected Clinical Outcomes with Daycare Attendance by Age

	6 – 12 months old		12 – 24 months old		24 – 36 months old	
OR ± SE	**Odds ratio with attending daycare***	***P* value**	**Odds ratio with attending daycare***	***P* value**	**Odds ratio with attending daycare***	***P* value**
Emergency department visits	2.11 ± 0.96 (n=180 with 278 visits)	0.11	2.55 ± 1.33 (n=110 with 174 visits)	0.07	3.99 ± 3.08 (n = 50 with 65 visits)	0.07
Hospital readmissions	3.50 ± 1.85 (n=180 with 278 visits)	**0.018**	0.73 ± 0.48 (n=109 with 173 visits)	0.63	5.79 ± 5.08 (n = 51 with 66 visits)	**0.045**
Systemic steroids	4.69 ± 2.71 (n=178 with 276 visits)	**0.007**	1.64 ± 0.89 (n=104 with 169 visits)	0.36	2.70 ± 2.42 (n = 50 with 65 visits)	0.27
Trouble breathing	1.43 ± 0.59 (n=178 with 269 visits)	0.38	1.52 ± 0.74 (n=104 with 166 visits)	0.39	3.64 ± 3.51 (n = 53 with 67 visits)	0.18
Activity limitations	4.24 ± 1.85 (n=173 with 264 visits)	**0.001**	2.36 ± 1.53 (n=104 with 165 visits)	0.19	11.70 ± 11.51 (n = 52 with 66 visits)	**0.012**
Rescue medication use	1.83 ± 0.77 (n=176 with 266 visits)	0.15	2.47 ± 1.16 (n=105 with 167 visits)	0.054	1.69 ± 2.18 (n = 52 with 66 visits)	0.22

*Odds ratios were generated through logistic regression models with clinic visits (prior to 3 years of age) clustered by subject. Outcomes were coded as no=0 and yes=1. Regressions were adjusted for age at the time of clinic visit, age at initial hospital discharge, presence of pulmonary hypertension on or after 36 weeks corrected age, any respiratory support at the time of clinic visit (i.e., supplemental oxygen, tracheostomy, home ventilator, and/or CPAP/BiPAP), and any feeding tube at the time of clinic visit (i.e., nasogastric, gastrostomy, jejunostomy, or gastrojejunostomy tubes). N refers to the number of subjects and their total number of clinic visits in aggregate for each outcome.