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

Sharon A. McGrath-Morrow, MD, MBA[1], Amit Agarwal, MD[2], Stamatia Alexiou, MD[1], Eric D. Austin, MD, MSCI[3], Julie L. Fierro, MD[1], Lystra P. Hayden, MD, MMSc[4], Khanh Lai, MD[5], Jonathan C. Levin, MD[4], Winston M. Manimtim, MD[6], Paul E. Moore, MD[3], Lawrence M. Rhein, MD, MPH[7], Jessica L. Rice, DO, MHS[1], Catherine A. Sheils, MD[4], Michael C. Tracy, MD[8], Manvi Bansal, MD[9], Christopher D. Baker, MD[10], A. Ioana Cristea, MD, MS[11], Antonia P. Popova, MD[12], Roopa Siddaiah, MD[13], Natalie Villafranco, MD[14], Leif D. Nelin, MD[15], and Joseph M. Collaco, MD, PhD[16]

Objectives To test the hypothesis that daycare attendance among children with bronchopulmonary dysplasia (BPD) is associated with increased chronic respiratory symptoms and/or greater health care use for respiratory illnesses during the first 3 years of life.

Study design Daycare attendance and clinical outcomes were obtained via standardized instruments for 341 subjects recruited from 9 BPD specialty clinics in the US. All subjects were former infants born preterm (<34 weeks) with BPD (71% severe) requiring outpatient follow-up between 0 and 3 years of age. Mixed logistic regression models were used to test for associations.

Results Children with BPD attending daycare were more likely to have emergency department visits and systemic steroid usage. Children in daycare up to 3 years of age also were more likely to report trouble breathing, having activity limitations, and using rescue medications when compared with children not in daycare. More severe manifestations were found in children attending daycare between 6 and 12 months of chronological age.

Conclusions In this study, children born preterm with BPD who attend daycare were more likely to visit the emergency department, use systemic steroids, and have chronic respiratory symptoms compared with 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. *(J Pediatr 2022;249:22-8)*.

Infants born preterm 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 greatest for those with more severe BPD.[6] Community-acquired respiratory illnesses remain an important cause of rehospitalization and morbidity in infants born preterm 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 children born preterm with BPD who have decreased pulmonary reserve. Therefore, minimizing exposures associated with respiratory illnesses during the first 3 years of life may help mitigate the risk of lung function deficits in adult life.

Several previous studies have shown an association between daycare attendance and increased risk of respiratory morbidities in children with very low birth weight (VLBW).[14,15] One prospective study reported that daycare attendance increased the risk for respiratory problems in a statewide cohort of children with VLBW 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

BPD	Bronchopulmonary dysplasia
VLBW	Very low birth weight

From the [1]Division of Pulmonary and Sleep Medicine, Children's Hospital of Philadelphia and University of Pennsylvania, Philadelphia, PA; [2]Division of Pediatric Pulmonary and Sleep Medicine, Arkansas Children's Hospital, University of Arkansas for Medical Sciences, Little Rock, AR; [3]Pulmonary Medicine, Vanderbilt University and Vanderbilt University Medical Center, Nashville, TN; [4]Division of Pulmonary Medicine, Boston Children's Hospital and Harvard Medical School, Boston, MA; [5]Division of Pediatric Pulmonary and Sleep Medicine, University of Utah, Salt Lake City, UT; [6]Neonatal/Perinatal Medicine, Children's Mercy Hospital, Kansas City, MO; [7]Neonatal-Perinatal Medicine/Pediatric Pulmonology, University of Massachusetts, Worcester, MA; [8]Division of Pediatric Pulmonary, Stanford University, Stanford, CA; [9]Pulmonology and Sleep Medicine, Children's Hospital of Los Angeles, Los Angeles, CA; [10]Section of Pulmonary and Sleep Medicine, Department of Pediatrics, University of Colorado School of Medicine, Aurora, CO; [11]Division of Pediatric Pulmonology, Allergy and Sleep Medicine, Riley Children's Hospital and Indiana University, Indianapolis, IN; [12]Pediatric Pulmonology, University of Michigan, Ann Arbor, MI; [13]Pediatric Pulmonology, Penn State Health, Hershey, PA; [14]Pulmonary Medicine, Texas Children's Hospital and Baylor University, Houston, TX; [15]Division of Neonatology, Nationwide Children's Hospital and Ohio State University, Columbus, OH; and [16]Eudowood Division of Pediatric Respiratory Sciences, Johns Hopkins University, Baltimore, MD

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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] In addition, infants born preterm and children with BPD can display inappropriate immune responses to respiratory viruses, such as respiratory syncytial virus and rhinovirus, often resulting in increased respiratory morbidities.[17] In this study, we sought to determine whether daycare attendance in children with BPD is a generalizable risk factor for respiratory morbidities and acute care use following initial hospital discharge, and whether risk for respiratory morbidities from daycare exposure decreases with increasing age. This study included outpatient tertiary care centers from diverse geographic areas across the US. To address the risk of daycare exposure on respiratory illnesses in children with BPD, we collected registry data from 9 tertiary care centers in the US who participate in the BPD Collaborative Outpatient Registry.

Methods

Participants were drawn from the BPD Collaborative Outpatient Registry on the basis of inclusion criteria of a diagnosis of BPD, at least 1 clinical visit before 3 years of age, and documentation of daycare attendance or nonattendance before 3 years of age.[18] The diagnosis of BPD and its severity was determined through chart review based on the 2001 National Heart, Lung, and Blood Institute consensus statement.[19] Contributing BPD clinics included 9 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). Data were collected at the first 8 institutions, and the last institution listed, anonymized data were housed at Nationwide Children's Hospital, and analysis was conducted at Johns Hopkins University. Participating centers obtained approval from their local institutional review board and data use agreements were completed for compiling anonymized data. Informed consent was obtained from caregivers per local institutional review boards.

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 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 neonatal intensive care unit 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 of postmenstrual age.[20] Home respiratory support was defined as any use of supplemental oxygen, tracheostomy, or invasive/noninvasive 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 Analyses

Demographic and inpatient characteristics were compared among those with any reported daycare attendance vs those without using logistic (dichotomous characteristics), ordered logistic (categorical characteristics), and linear (continuous characteristics) regression models clustered by center (**Table I**). 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 II**). To test for associations between exposure to daycare and acute care use/chronic respiratory symptoms, ORs 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 coefficient for age at the time of visit was included as well (**Table III**). To assess for age-related and disease-severity effects, ORs 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 IV**; and **Table V** available at www.jpeds.com). All of the regressions for outcomes (**Tables III** and **IV**; and **Table V** available at www.jpeds.com) 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 of postmenstrual 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

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Table I. Demographics and inpatient characteristics

Characteristics	Entire study population (n = 341)	Any daycare (n = 64)	No daycare (n = 277)	*P* value*
Age at recruitment, y, mean ± SD [range]	0.9 ± 0.7 [0.2, 3]	1.1 ± 0.7 [0.3, 3]	0.9 ± 0.7 [0.2, 3]	.15
Sex (% female)	43.6% (n = 337)	40.6%	44.3% (n = 273)	.50
Race (% non-White)	45.2%	37.5%	46.9%	.12
Ethnicity (% Hispanic)	12.2% (n = 336)	9.7% (n = 62)	12.8% (n = 274)	.46
Gestational age, wk, mean ± SD [range]	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)	.90
Birth weight, g, mean ± SD [range]	906 ± 356 [370, 2250] (n = 333)	924 ± 337 [410, 1920] (n = 62)	902 ± 360 [370, 2250] (n = 271)	.61
Length of initial admission, mo, mean ± SD [range]	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)	.87
BPD severity (%)				.13
Mild	10.1%	17.2%	8.4%	
Moderate	19.3%	18.8%	19.4%	
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)	.15
Pulmonary hypertension after 36 wk (% yes)	21.8% (n = 331)	20.2%	28.1% (n = 267)	.27
Cyanotic heart disease (% yes)	0.9% (n = 334)	1.6%	0.7% (n = 270)	.38
Congenital anomaly or syndrome (% yes)	10.4% (n = 327)	12.7% (n = 63)	9.9% (n = 264)	.49

CSF, cerebrospinal fluid.
**P* values were generated through regression models clustered by center.

(StataCorp) was used for all analyses. *P* values < .05 were considered significant.

Results

There were 341 subjects with BPD who completed 715 clinic visits with respiratory outcome questionnaires before 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* = .23).

Daycare Attendance

A minority of subjects (18.8%) were reported to attend daycare at least on 1 clinic visit, before 3 years of age (**Table I**). Daycare attendance varied across the 9 tertiary care centers from 3.3% to 34.9% of subjects at a given center (χ^2 *P* = .002). Subject characteristics by center are summarized in **Table VI** (available at www.jpeds.com). 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 and 2019 was greater (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: .001), which may be related to the coronavirus disease 2019 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 g). 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 2 groups (**Table II**).

Table II. Outpatient clinical characteristics at time of recruitment

Characteristics	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%	.39
Children in the home, No., mean ± SD [range]	2.0 ± 1.2 [1, 7] (n = 328)	1.9 ± 1.1 [1, 6] (n = 62)	2.0 ± 1.2 [1, 7] (n = 266)	.63
Nasal cannula oxygen (% yes)	37.8%	32.8%	39.0%	.97
Tracheostomy (% yes)	14.7%	9.4%	15.9%	.06
Home (invasive) ventilator (% yes)	11.1%	6.3%	12.3%	.07
Inhaled steroids (% yes)	45.2%	45.3%	45.1%	.44
Pulmonary hypertension medications (% yes)	10.0%	10.9%	9.8%	.92
Feeding tube (% yes)	38.3% (n = 337)	29.0% (n = 62)	40.4% (n = 275)	.24
Any human milk (% yes)	22.6%	18.8%	23.5%	.84
Medicaid (% yes)	52.0% (n = 333)	50.8% (n = 82)	52.2% (n = 251)	.84

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

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Table III. Clinical outcomes with daycare attendance

Outcomes	OR with attending daycare,* OR ± SE (95% CI)	*P* value	aOR with attending daycare,† OR ± SE (95% CI)	*P* value
Acute care				
Sick visits	1.67 ± 0.77 (0.68-4.12) (n = 336 with 705 visits)	.27	1.81 ± 0.83 (0.74-4.43) (n = 321 with 681 visits)	.20
Emergency department visits	2.54 ± 1.05 (1.14-5.71) (n = 332 with 700 visits)	**.023**	2.81 ± 1.16 (1.26-6.31) (n = 318 with 678 visits)	**.012**
Hospital readmissions	1.86 ± 0.81 (0.79-4.35) (n = 332 with 700 visits)	.16	2.15 ± 0.92 (0.93-4.97) (n = 318 with 678 visits)	.07
Antibiotics	2.13 ± 0.90 (0.93-4.89) (n = 330 with 696 visits)	.07	1.71 ± 0.65 (0.82-3.60) (n = 315 with 672 visits)	.16
Systemic steroids	4.66 ± 2.32 (1.76-12.35) (n = 328 with 692 visits)	**.002**	4.23 ± 2.02 (1.66-10.76) (n = 315 with 671 visits)	**.002**
Chronic symptoms and medication use				
Trouble breathing	2.16 ± 0.72 (1.12-4.17) (n = 335 with 687 visits)	**.022**	2.66 ± 0.90 (1.37-5.17) (n = 319 with 663 visits)	**.004**
Night-time symptoms	1.49 ± 0.54 (0.73-3.05) (n = 336 with 688 visits)	.28	1.79 ± 0.66 (0.86-3.70) (n = 319 with 663 visits)	.12
Activity limitations	3.92 ± 1.68 (1.69-9.09) (n = 332 with 681 visits)	**.001**	4.03 ± 1.74 (1.73-9.38) (n = 315 with 656 visits)	**.001**
Rescue medication use	8.96 ± 4.67 (3.22-24.90) (n = 333 with 685 visits)	**<.001**	7.38 ± 3.51 (2.90-18.77) (n = 316 with 660 visits)	**<.001**

P values in bold are significant.
*ORs were generated through univariate nested mixed logistic regression models with clinic visits (before 3 years of age) nested within subjects nested within BPD centers. A random coefficient 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 of corrected age, any respiratory support at the time of clinic visit (ie, supplemental oxygen, tracheostomy, home ventilator, and/or continuous positive airway pressure/bilevel positive airway pressure), and any feeding tube at the time of clinic visit (ie, 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.

Respiratory Morbidities

Using data from 715 clinical encounters, mixed models were used to determine the risk of respiratory morbidities with daycare attendance. Acute care use was greater in children who attended daycare (Table III). Children attending daycare were more likely to have emergency department visits (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 IV). We found that daycare attendance during infancy (6-12 months) was

Table IV. Selected clinical outcomes with daycare attendance by age

Outcomes	6-12 months old: OR with attending daycare,* OR ± SE	*P* value	12-24 months old: OR with attending daycare,* OR ± SE	*P* value	24-36 months old: OR with attending daycare,* OR ± SE	*P* value
Emergency department visits	2.11 ± 0.96 (n = 180 with 278 visits)	.11	2.55 ± 1.33 (n = 110 with 174 visits)	.07	3.99 ± 3.08 (n = 50 with 65 visits)	.07
Hospital readmissions	3.50 ± 1.85 (n = 180 with 278 visits)	**.018**	0.73 ± 0.48 (n = 109 with 173 visits)	.63	5.79 ± 5.08 (n = 51 with 66 visits)	**.045**
Systemic steroids	4.69 ± 2.71 (n = 178 with 276 visits)	**.007**	1.64 ± 0.89 (n = 104 with 169 visits)	.36	2.70 ± 2.42 (n = 50 with 65 visits)	.27
Trouble breathing	1.43 ± 0.59 (n = 178 with 269 visits)	.38	1.52 ± 0.74 (n = 104 with 166 visits)	.39	3.64 ± 3.51 (n = 53 with 67 visits)	.18
Activity limitations	4.24 ± 1.85 (n = 173 with 264 visits)	**.001**	2.36 ± 1.53 (n = 104 with 165 visits)	.19	11.70 ± 11.51 (n = 52 with 66 visits)	**.012**
Rescue medication use	1.83 ± 0.77 (n = 176 with 266 visits)	.15	2.47 ± 1.16 (n = 105 with 167 visits)	.054	1.69 ± 2.18 (n = 52 with 66 visits)	.22

P values in bold are significant.
*ORs were generated through logistic regression models with clinic visits (before 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 of corrected age, any respiratory support at the time of clinic visit (ie, supplemental oxygen, tracheostomy, home ventilator, and/or continuous positive airway pressure/bilevel positive airway pressure), and any feeding tube at the time of clinic visit (ie, 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.

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associated with a greater 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- to 24-month age group, but did observe that daycare attendance during early childhood (24-36 months) was associated with a greater 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 (ie, supplemental oxygen, ventilation, and/or tracheostomy) at the time of the clinic visit influenced associations between daycare and respiratory outcomes through stratified analyses (**Table V** available at www.jpeds.com). 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

In our multicenter cohort of children born preterm with a history of BPD, daycare attendance during the first 3 years of life was associated with a greater likelihood of visits to the emergency department, systemic steroid use, and chronic respiratory symptoms when compared with children who did not attend daycare, despite being less likely to have feeding tubes and tracheostomies. The study examined data collected from 9 tertiary care centers across the US that specialize in the outpatient care of children with BPD. Our findings support previous findings from geographically limited studies that indicated that daycare was a risk factor for acute care usage and respiratory symptoms in children who are VLBW and children with BPD.[14,15] Overall, these findings suggest that daycare attendance within the first 3 years of life associates with increased risk for 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 use in children born preterm 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 vs in-home daycare) was associated with greater risk, there are some measures that may mitigate risk associated with daycare in infants with preterm. Palivizumab prophylaxis has been shown to decrease, although not eliminate, the risk of respiratory syncytial virus admissions,[23] and breastfeeding has been associated with a decreased risk for admission for rhinovirus-associated illness in one study performed in Argentina.[9] 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 use and thus cannot rule out viral infections in the daycare environment as a contributor to greater 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 use. 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 use, 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. Although 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.[24]

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- to 12-month 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. In addition, 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 toward 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. In addition, although our data collection is geographically diverse within the US, 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 counseling practices for daycare attendance by center were not assessed, differences in daycare attendance by

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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. In addition, older subjects attending a pulmonary clinic may have more severe disease. Thus, this group may be biased toward 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 coronavirus disease-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 (eg, 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).

In conclusion, in a diverse multicenter population of infants with BPD, daycare attendance was associated with high risk of acute care use and chronic respiratory symptoms. 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 before 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. ■

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Reprint requests: Sharon A. McGrath-Morrow, MD, MBA, Division of Pulmonary and Sleep, Children's Hospital of Philadelphia, Abramson Research Building, Suite 416H, 3615 Civic Center Blvd, Philadelphia, PA 19104. E-mail: mcgrathmos@chop.edu

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50 Years Ago in *THE JOURNAL OF PEDIATRICS*

Iron Deficiency through the Years

Hunter RE, Smith NJ. Hemoglobin and hematocrit values in iron deficiency in infancy. J Pediatr 1972;81:710-3.

Iron deficiency and iron-deficiency anemia continue to be worldwide concerns, affecting approximately 2 million people across the world, according to the World Health Organization. Low-income countries and certain at-risk populations, such as infants, are more commonly affected.[1]

In 1971, the American Academy of Pediatrics promoted the early use of iron-fortified formulas instead of cow milk within a special program to address iron and other nutritional deficiencies. These initiatives have had a tremendous impact on the health of children. For instance, in one review including children aged 6-60 months, the prevalence of anemia declined from 7.8% in 1975 to 2.9% in 1985.[2]

In 1972, Hunter and Smith recognized the need to make a reliable assessment of the adequacy of iron nutrition in children. They emphasized that a normal hemoglobin and hematocrit level did not rule out iron deficiency, hence the need for a simple method of detecting early iron deficiency. In a prospective study, they concluded that its detection in the infant without anemia required determination of serum iron and transferrin levels.

Now, 50 years later, no single measurement is currently available that will characterize the iron status of a child; a battery of studies is still needed, including measurement of hemoglobin and 1 of the 3 variables that provide discriminatory information about iron status: serum ferritin, TfR1 (serum transferrin receptor 1 concentration), and/or CHr (hemoglobin content of reticulocytes). The latter recently has been declared as the most effective screening test for iron deficiency, showing decreased iron levels before the onset of anemia.[3] We now face a new challenge: to develop a cost-effective screening test to detect iron deficiency to prevent iron-deficiency anemia.

María Guadalupe García-Lima, MD
Paulina Blanco-Murillo, MD
Karen González-Moctezuma, MD
Instituto de Pediatria
Tecnologico de Monterrey
Escuela de Medicina y Ciencias de la Salud
Monterrey, Nuevo León, Mexico

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Table V. Clinical outcomes with daycare attendance

Outcomes	aOR with attending daycare with no respiratory support,* OR ± SE (95% CI)	*P* value	aOR with attending daycare with respiratory support,* OR ± SE (95% CI)	*P* value
Acute care				
Sick visits	1.44 ± 0.58 (0.66-3.17) (n = 204 with 324 visits)	.36	1.07 ± 0.60 (0.36-3.18) (n = 170 with 357 visits)	.90
Emergency department visits	2.10 ± 0.84 (0.96-4.60) (n = 204 with 323 visits)	.06	2.81 ± 1.17 (1.25-6.37) (n = 167 with 355 visits)	**.013**
Hospital readmissions	1.79 ± 1.22 (0.47-6.79) (n = 204 with 323 visits)	.39	2.00 ± 0.89 (0.84-4.78) (n = 167 with 355 visits)	.12
Antibiotics	2.09 ± 0.82 (0.97-4.52) (n = 203 with 323 visits)	.06	1.20 ± 0.56 (0.48-3.01) (n = 165 with 349 visits)	.70
Systemic steroids	2.88 ± 1.24 (1.25-6.68) (n = 203 with 322 visits)	**.013**	3.64 ± 2.26 (1.08-12.27) (n = 164 with 349 visits)	**.037**
Chronic symptoms and medication use				
Trouble breathing	1.50 ± 0.54 (0.74-3.04) (n = 200 with 314 visits)	.27	1.78 ± 0.72 (0.80-3.94) (n = 169 with 349 visits)	.16
Nighttime symptoms	1.00 ± 0.50 (0.38-2.66) (n = 199 with 313 visits)	1.00	3.26 ± 1.45 (1.36-7.82) (n = 170 with 350 visits)	**.008**
Activity limitations	2.41 ± 0.99 (1.08-5.41) (n = 197 with 310 visits)	**.033**	6.57 ± 3.16 (2.56-16.86) (n = 167 with 346 visits)	**<.001**
Rescue medication use	2.53 ± 0.95 (1.22-5.27) (n = 197 with 311 visits)	**.013**	1.84 ± 0.82 (0.77-4.39) (n = 170 with 349 visits)	.17

P values in bold are significant.

*ORs were generated through logistic regression models with clinic visits (before 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 of corrected age, and any feeding tube at the time of clinic visit (ie, nasogastric, gastrostomy, jejunostomy, or gastrojejunostomy tubes). Regressions were stratified by any respiratory support at the time of clinic visit (ie, supplemental oxygen, tracheostomy, home ventilator, and/or continuous positive airway pressure/bilevel positive airway pressure). "n" refers to the number of subjects and their total number of clinic visits in aggregate for each outcome.

Table VI. Selected characteristics by center

Characteristics	Center 1 (n = 29)	Center 2 (n = 43)	Center 3 (n = 19)	Center 4 (n = 113)	Center 5 (n = 38)	Center 6 (n = 7)	Center 7 (n = 30)	Center 8 (n = 14)	Center 9 (n = 48)
Daycare attendance (% yes)	27.6%	34.9%	21.1%	11.5%	34.2%	14.3%	3.3%	7.1%	16.7%
Age at recruitment, y, mean ± SD [range]	1.8 ± 0.6	1.0 ± 0.7	1.3 ± 0.8	1.0 ± 0.7	0.5 ± 0.3	0.8 ± 0.7	0.3 ± 0.3	1.1 ± 0.7	0.7 ± 0.5
Number of visits per subject	1.1 ± 0.3	1.2 ± 0.5	1.0 ± 0.0	1.3 ± 0.7	3.1 ± 1.4	4.6 ± 1.8	5.4 ± 3.5	1.1 ± 0.3	2.8 ± 1.6
Sex (% female)	48.3%	46.5%	36.8%	46.9%	21.6% (n = 37)	28.6%	51.7% (n = 29)	61.5% (n = 13)	42.6% (n = 47)
Race (% non-white)	44.8%	32.6%	52.6%	55.8%	42.1%	57.1%	33.3%	42.9%	37.5%
Ethnicity (% Hispanic)	7.1% (n = 28)	14.0%	31.6%	5.3%	15.8%	42.9%	23.3%	7.7% (n = 13)	8.9% (n = 45)
Gestational age, wk, mean ± SD [range]	27.0 ± 2.3	27.3 ± 2.2	26.6 ± 2.7 (n = 15)	27.0 ± 2.7	26.4 ± 2.5	25.8 ± 1.8	26.9 ± 1.9	27.1 ± 3.3 (n = 13)	26.1 ± 2.3 (n = 47)
Birth weight, g, mean ± SD [range]	914 ± 357 (n = 27)	977 ± 362	717 ± 277 (n = 15)	945 ± 368	942 ± 401	763 ± 153	870 ± 317	873 ± 406 (n = 13)	824 ± 313 (n = 47)
Length of initial admission, mo	8.6 ± 3.6 (n = 26)	3.6 ± 1.0 (n = 42)	8.3 ± 2.9 (n = 15)	4.5 ± 2.2	5.6 ± 3.6	6.3 ± 5.0	3.3 ± 0.7	3.7 ± 1.0 (n = 13)	4.0 ± 1.9 (n = 45)
Severe BPD, (% yes)	78.6% (n = 28)	46.5%	100% (n = 18)	69.9%	100%	71.4%	100%	69.2% (n = 13)	36.2% (n = 47)
Pulmonary hypertension after 36 weeks (% yes)	44.4% (n = 27)	7.0%	53.3% (n = 15)	15.2% (n = 112)	23.7%	57.1%	6.7%	15.4% (n = 13)	32.6% (n = 46)
Tracheostomy (% yes)	69.0%	0.0%	47.4%	8.0%	18.4%	28.6%	0.0%	0.0%	6.3%
Home ventilator (% yes)	48.3%	0.0%	31.6%	7.1%	18.4%	14.3%	0.0%	0.0%	4.2%
Feeding tube (% yes)	77.8% (n = 27)	21.0%	94.1% (n = 17)	33.6%	44.7%	42.9%	10.0%	21.4%	39.6%
Medicaid (% yes)	88.5% (n = 26)	16.3%	68.8% (n = 16)	40.7%	63.2%	28.6%	77.3%	28.6%	71.7% (n = 46)

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