Severity of Bronchopulmonary Dysplasia Among Very Preterm Infants in the United States

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abstract

BACKGROUND AND OBJECTIVES: The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Neonatal Research Network recently proposed new, severity-based diagnostic criteria for bronchopulmonary dysplasia (BPD). This study provides the first benchmark epidemiological data applying this definition.

METHODS: Retrospective cohort study of infants born from 22 to 29 weeks' gestation in 2018 at 715 US hospitals in the Vermont Oxford Network. Rates of BPD, major neonatal morbidities, and common respiratory therapies, stratified by BPD severity, were determined.

RESULTS: Among 24 896 infants, 2574 (10.3%) died before 36 weeks' postmenstrual age (PMA), 12 198 (49.0%) did not develop BPD, 9192 (36.9%) developed grade 1 or 2 BPD, and 932 (3.7%) developed grade 3 BPD. Rates of mortality before 36 weeks' PMA and grade 3 BPD decreased from 52.7% and 9.9%, respectively, among infants born at 22 weeks' gestation to 17.3% and 0.8% among infants born at 29 weeks' gestation. Grade 1 or 2 BPD peaked in incidence (51.8%) among infants born at 25 weeks' gestation. The frequency of severe intraventricular hemorrhage or cystic periventricular leukomalacia increased from 4.8% among survivors without BPD to 23.4% among survivors with grade 3 BPD. Similar ranges were observed for late onset sepsis (4.8%–31.4%), surgically treated necrotizing enterocolitis (1.4%–17.1%), severe retinopathy of prematurity (1.2%–23.0%), and home oxygen therapy (2.0%–67.5%).

CONCLUSIONS: More than one-half of very preterm infants born in the United States died before 36 weeks' PMA or developed BPD. Greater BPD severity was associated with more frequent development of major neonatal morbidities, in-hospital mortality, and use of supplemental respiratory support at discharge.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-030007

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DOI: https://doi.org/10.1542/peds.2020-030007

Accepted for publication Mar 19, 2021

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WHAT THIS STUDY ADDS: Among 24 896 very preterm infants, 10.3% died before 36 weeks postmenstrual age, 36.9% developed grade 1 to 2 BPD, and 3.7% developed grade 3 BPD. The rates of late in-hospital death, neonatal morbidity, and supplemental respiratory support at discharge increased with BPD severity.

WHAT'S KNOWN ON THIS SUBJECT: Bronchopulmonary dysplasia (BPD) is among the most consequential morbidities associated with prematurity. The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Neonatal Research Network recently proposed new, severity-graded diagnostic criteria for BPD; benchmark epidemiological data applying this definition are needed.

To cite: Jensen E A, Edwards E M, Greenberg L T, et al. Severity of Bronchopulmonary Dysplasia Among Very Preterm Infants in the United States. *Pediatrics.* 2021;148(1):e2020030007

Bronchopulmonary dysplasia (BPD) is among the most common and consequential complications of very preterm birth.[1–6] Unlike most major neonatal morbidities, however, the diagnostic criteria used to define BPD continue to evolve.[7–11] These changes have largely been driven by interval advances in newborn medicine, improved survival among very preterm infants, and changes in the pathophysiology and epidemiology of neonatal respiratory disease.[9,12–14] Owing to several limitations of the diagnostic criteria for BPD, investigators from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Neonatal Research Network proposed a new, evidence-based definition of BPD in 2019.[2] Unlike previous definitions, these criteria categorized BPD severity according to the mode of respiratory support administered to very preterm infants at 36 weeks' postmenstrual age (PMA), irrespective of the use or level of oxygen therapy.[2] This new definition, relative to other common diagnostic criteria, was shown to better discriminate between infants who did, compared with did not, develop poor respiratory and neurodevelopmental outcomes in early childhood.[2] As of yet, the epidemiology of BPD as defined by these criteria has not been examined at a population level. Such data may further inform the utility and application of these diagnostic criteria.

In this study, we applied the 2019 Neonatal Research Network definition of BPD to a recent cohort of very preterm infants cared for at hospitals in the United States that participate in the Vermont Oxford Network (VON). The VON database encompasses 85% of all very preterm infants born in the United States. Using this large data set, we described the frequency of BPD as well as associated clinical characteristics and in-hospital outcomes among US-born very preterm infants, stratified by BPD severity level. Our goal was to generate a resource for contemporary, benchmark data on the epidemiology of BPD defined according to these new diagnostic criteria.

METHODS

Population

The VON is a voluntary, worldwide community of practice dedicated to improving the quality, safety, and value of care through a coordinated program of data-driven quality improvement, education, and research. In this retrospective analysis, we used data collected prospectively on infants of 22 + 0/7 to 29 + 6/7 weeks' gestation who were either delivered at a VON member hospital or transferred there within 28 days after birth. All study infants were born in the United States between January 1 and December 31, 2018. Those with a known severe congenital anomaly or genetic syndrome, those who died in the delivery room or within 12 hours of admission to the NICU, and those with missing or implausible values for key study covariates were excluded.

Local staff at each member institution submitted data using uniform definitions for each infant until death, discharge from the reporting hospital, or transfer to another center.[15] All data underwent automated checks for quality and completeness at the time of submission. The University of Vermont Committee on Human Research determined that the use of the VON database for this analysis was not human subjects research. All study data were deidentified.

Measures

Infants were categorized by BPD severity according to the highest mode of respiratory support administered at a PMA of 36 + 0/7 weeks by using the diagnostic criteria proposed in 2019 by the NICHD Neonatal Research Network.[2] Infants receiving no supplemental respiratory support were classified as no BPD, those treated with nasal cannula (any flow rate) or noninvasive positive airway pressure as grade 1 or 2 BPD, and those treated with invasive mechanical ventilation as grade 3 BPD.[2] Grades 1 and 2 BPD were combined into a single severity level because the study data source did not include information on nasal cannula flow rates administered at 36 weeks' PMA. For infants discharged from the hospital before 36 weeks' PMA, BPD severity was categorized on the basis of the respiratory support administered at discharge.[2]

Small for gestational age was calculated as a birth weight <10% for gestational age and sex based on the Fenton growth curves.[16] Endotracheal tube ventilation performed during the initial resuscitation immediately after birth only included infants who received assisted ventilation and excluded those for whom the endotracheal tube was placed solely for suctioning. Invasive ventilation after initial resuscitation included conventional or high frequency modes administered by endotracheal tube at any time after leaving the delivery room or initial resuscitation area. Medications and surfactant therapy were reported if administered at least once. Vitamin A only included intramuscular administration. Systemic corticosteroid therapy was only counted if used after birth to prevent or treat BPD or chronic lung disease. Infections required

identification using blood or a cerebral spinal fluid culture. Early onset bacterial infection occurred on or before day 3 after birth. Late onset bacterial or fungal infection occurred after day 3. Cultures obtained after day 3 that were positive for coagulase-negative *Staphylococcus* were counted if accompanied by at least 1 sign of generalized infection and treatment with at least 5 days of intravenous antibiotics. Severe brain injury was defined as the presence of a grade 3 or 4 intraventricular or periventricular hemorrhage and/or cystic periventricular leukomalacia diagnosed on cranial imaging.[17] Reported treatments for retinopathy of prematurity (ROP) were retinal cryosurgery, laser surgery, or antivascular endothelial growth factor drug therapy (eg, bevacizumab) to one or both eyes. Monitor use at discharge included an apnea or cardiorespiratory monitor (eg, pulse oximeter). Length of stay was measured as the number of days from the date of admission until the date of hospital discharge.

Analyses

Means with SDs or medians with interquartile ranges were used to summarize continuous study data. The numbers of infants and proportions were used to summarize categorical data. The initial demographic data and BPD rates were summarized for all eligible infants. Values describing clinical therapies, comorbidities, and in-hospital outcomes were reported for infants who survived to discharge from the hospital or remained hospitalized at 1 year of age. All analyses were conducted by using R statistical software version 3.5.3 (R Core Team, Vienna, Austria).

RESULTS

After exclusion of ineligible infants, the study cohort consisted of 24 896 very preterm infants born at 715 US hospitals (Supplemental Fig 2). Of these infants, 2574 (10.3%) died before 36 weeks' PMA, 12 198 (49.0%) were classified as no BPD, 9192 (36.9%) developed grade 1 or 2 BPD, and 932 (3.7%) developed grade 3 BPD. Table 1 shows the demographic and antenatal characteristics of the study cohort, stratified by BPD severity. On average, the infants who developed a higher severity of BPD were born less mature, at lower birth weights, and more often small for gestational age. When analyzed by completed weeks' gestation, rates of mortality before 36 weeks' PMA and of grade 3 BPD were inversely related to the gestational age at birth (Table 1, Fig 1). The proportion of infants who survived to 36 weeks' PMA and did not develop BPD of any severity increased with gestational age from 4.5% among infants born at 22 weeks' gestation to 77.8% among those born at 29 weeks' gestation.

Of the 22 321 infants who survived to 36 weeks' PMA and were classified according to BPD severity, 191 (0.9%) died before hospital discharge. Among these late deaths, 119 (62.3%) were diagnosed with grade 3 BPD, 66 (34.6%) with grade 1 or 2 BPD, and 6 (3.1%) with no BPD. In the cohort restricted to infants who survived to discharge, rates of endotracheal tube placement for ventilation during initial resuscitation and treatment with invasive mechanical ventilation at any point after stabilization increased in an incremental, stepwise manner with greater BPD severity (Table 2). A similar trend was observed for the evaluated drug therapies, with the exception of caffeine. Most infants (96.1%) received caffeine at some point during their hospitalization, with minimal variation in the rates of use by BPD severity level (Table 2).

The frequency of all evaluated major neonatal morbidities increased in a stepwise manner as BPD severity increased (Table 3). In most cases, these adverse outcomes were more than twice as common among those who developed grade 3 BPD as those who developed grade 1 or 2 BPD and >4 times more common among those with grade 3 BPD as those with no BPD (Table 3). Hospital lengths of stay and use of durable medical equipment at discharge varied by BPD severity level (Table 4). Few infants (2.0%) without BPD were treated with supplemental oxygen at discharge, whereas 43.3% of those with grade 1 or 2 BPD and 67.5% of those with grade 3 BPD received oxygen therapy at the time of discharge from a VON hospital. Although only 1% of all infants in the study cohort underwent tracheostomy, 18.3% of those who developed grade 3 BPD received this intervention.

DISCUSSION

Using a cohort that represents 85% of all very preterm infants born in the United States, we provide the first benchmark data on the epidemiology of BPD defined according to the severity-based diagnostic criteria proposed in 2019 by the NICHD Neonatal Research Network.[2] In total, 10% of infants born with gestational ages of 22 to 29 weeks died before 36 weeks' PMA, and approximately one-half developed BPD. The majority of infants with BPD were classified with a disease severity of grade 1 or 2; 3.7% developed grade 3 BPD. Rates of survival without BPD increased with greater gestational age, whereas rates of death before 36 weeks' PMA and rates of grade 3 BPD occurred at the highest frequencies among infants born the least mature.

The frequencies of most evaluated outcome measures were reassuring among infants who survived without BPD. However, the rates of major

TABLE 1 Demographic and Antenatal Characteristics

Characteristic	All Infants (N = 24 896)	No BPD (n = 12 198)	Grade 1–2 BPD (n = 9192)	Grade 3 BPD (n = 932)	Died Before 36 wk PMA (n = 2574)
Gestational age, wk					
Mean ± SD	27.1 ± 2	28 ± 1.5	26.5 ± 1.8	25.7 ± 1.8	25 ± 1.8
22 + 0/7 to 22 + 6/7, *n* (%)	313	14 (4.5)	103 (32.9)	31 (9.9)	165 (52.7)
23 + 0/7 to 23 + 6/7, *n* (%)	1580	100 (6.3)	713 (45.1)	118 (7.5)	649 (41.1)
24 + 0/7 to 24 + 6/7, *n* (%)	2474	365 (14.8)	1273 (51.5)	195 (7.9)	641 (25.9)
25 + 0/7 to 25 + 6/7, *n* (%)	2967	802 (27.0)	1538 (51.8)	210 (7.1)	417 (14.1)
26 + 0/7 to 26 + 6/7, *n* (%)	3292	1274 (38.7)	1596 (48.5)	136 (4.1)	286 (8.7)
27 + 0/7 to 27 + 6/7, *n* (%)	3940	2127 (54.0)	1503 (38.1)	110 (2.8)	200 (5.1)
28 + 0/7 to 28 + 6/7, *n* (%)	4853	3256 (67.1)	1387 (28.6)	89 (1.8)	121 (2.5)
29 + 0/7 to 29 + 6/7, *n* (%)	5477	4260 (77.8)	1079 (19.7)	43 (0.8)	95 (1.7)
Birth wt, mean ± SD, g	964 ± 304	1112 ± 269	866 ± 263	738 ± 229	691 ± 226
Small for gestational age,[a] *n* (%)	2294 (9.2)	482 (4.0)	1102 (12.0)	199 (21.5)	511 (20.3)
Male sex, *n* (%)	12 965 (52.1)	5953 (48.8)	4988 (54.3)	539 (57.8)	1485 (57.7)
Multiple gestation, *n* (%)	5660 (22.7)	2859 (23.4)	1984 (21.6)	203 (21.8)	614 (23.9)
Maternal race and/or ethnicity, *n* (%)					
Black non-Hispanic	7966 (32.0)	4046 (33.5)	2692 (29.5)	366 (39.6)	862 (33.9)
White non-Hispanic	9860 (39.6)	4639 (38.4)	3836 (42.1)	364 (39.4)	1021 (40.2)
Hispanic	4913 (19.7)	2435 (20.1)	1889 (20.7)	131 (14.2)	458 (18)
Other	1399 (5.6)	691 (5.7)	521 (5.7)	36 (3.9)	151 (5.9)
Antenatal steroids, *n* (%)	21 848 (88.8)	10 787 (88.8)	8171 (89.3)	823 (89.0)	2067 (80.8)
Vaginal delivery, *n* (%)	7260 (29.2)	3726 (30.6)	2518 (27.4)	235 (25.2)	781 (30.4)

All percentage values were calculated among infants with complete data for the described variable. Data shown in the table were missing in <1% of study infants.

[a] Small for gestational age was defined as a birth wt for gestational age and sex <10% per the Fenton growth curves.[16]

neonatal morbidities and mortality, in-hospital treatment with respiratory drug therapies, and use of supplemental oxygen at hospital discharge all rose in an incremental, stepwise manner among infants with greater BPD severity. It is uncertain whether BPD played a causal role in these observed associations or is simply a marker of illness acuity. Regardless of the etiology of these findings, they agree with several previous studies showing that BPD occurs along a spectrum of disease severity that strongly correlates with the risk of developing multiple, prognostically important adverse outcomes.[2,18–20] Our study adds to this growing body of literature and supports routine severity-based classification of BPD when reporting outcomes in very preterm infants.

The rates of BPD observed in the VON database are lower than those reported by the NICHD Neonatal Research Network.[2] In that previous cohort, 71% of survivors to 36 weeks' PMA developed BPD, with a 9% rate of grade 3 BPD.[2] Among infants in the current study who survived to 36 weeks' PMA, 45.3% developed BPD and 4.2% grade 3 BPD. These differences might be explained by the lower average gestational ages among infants evaluated by the Neonatal Research Network. In total, 89% of infants in the Neonatal Research Network study were born with gestational ages of <27 weeks, compared with 59% of infants in the present cohort.[2] Restricting our data set to infants who were born at <27 weeks' gestation and survived to 36 weeks' PMA revealed similar BPD rates between the two studies. In this subset of infants in the VON database, 69.8% developed BPD of any severity level, and 8.1% developed grade 3 BPD.

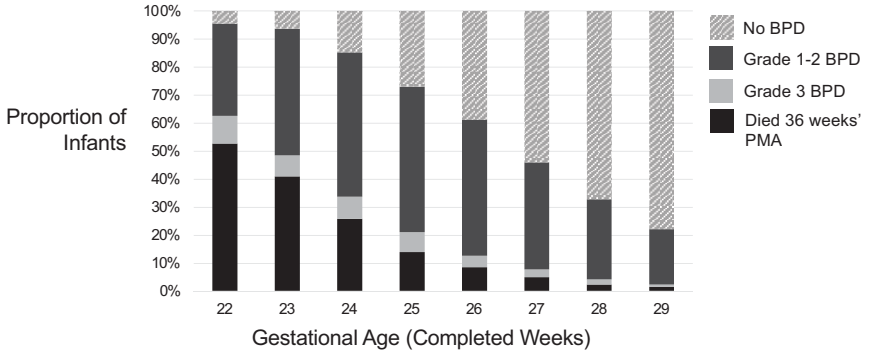

FIGURE 1
Rates of death before 36 weeks' PMA and of BPD, stratified by BPD severity and completed weeks' gestation.

Several of our findings may have implications for future efforts aimed at preventing lung injury and ameliorating BPD severity in very preterm infants. Although there is general consensus that avoidance of invasive ventilation is an evidence-based strategy to reduce the risk of BPD, one-half of the study infants who survived to hospital discharge received mechanical ventilation in the delivery room, and more than two-thirds were treated with invasive respiratory support and surfactant during their hospitalization.[21,22] These numbers are similar to the rates of mechanical ventilation observed among infants randomly assigned to nasal continuous positive airway pressure (nCPAP) in the large clinical trials of prophylactic nCPAP conducted more than a decade ago.[23–25] Together, these results highlight the ongoing need to develop novel therapies that will enable sustained avoidance of invasive ventilation in high-risk infants. Notably, however, more than one-half of the infants

TABLE 2 Delivery Room and Respiratory Focused Therapies Among Survivors to Discharge

Therapy	All Infants (N = 22 131)	No BPD (n = 12 192)	Grade 1–2 BPD (n = 9126)	Grade 3 BPD (n = 813)
Endotracheal tube ventilation during initial resuscitation	11 124 (50.3)	4544 (37.3)	5923 (65.0)	657 (81.0)
Epinephrine or cardiac compressions during initial resuscitation	316 (1.4)	104 (0.9)	183 (2.0)	29 (3.6)
Invasive ventilation after initial resuscitation	15 255 (68.9)	6550 (53.7)	7892 (86.5)	813 (100)
Surfactant	15 930 (72.0)	7321 (60.1)	7850 (86.1)	759 (93.5)
Inhaled nitric oxide	1087 (4.9)	145 (1.2)	708 (7.8)	234 (28.9)
Systemic corticosteroids for chronic lung disease	4009 (18.1)	456 (3.7)	3033 (33.2)	520 (64.0)
Caffeine	21 246 (96.1)	11 502 (94.4)	8952 (98.2)	792 (97.4)
Intramuscular Vitamin A	1772 (8.0)	663 (5.4)	1013 (11.1)	96 (11.8)

Data shown in the table are number of infants (%). All percentage values were calculated among infants with complete data for the described variable. Data shown in the table were missing in <1% of study infants.

who were breathing in room air at 36 weeks' PMA were exposed to invasive mechanical ventilation for some duration. Understanding how the characteristics of these infants differ from those who were ventilated and developed BPD may inform the design of new, lung-protective interventions.

We noted differences in the use of caffeine, intramuscular vitamin A, and systemic corticosteroids, 3 drug therapies shown in randomized controlled trials to lower the risk of developing BPD.[26–29] In particular, there were stark discrepancies in the rates of caffeine and vitamin A use, 2 drugs that are typically administered beginning in the early postnatal period. The overwhelming majority of infants received caffeine with minimal variability in the rates of use between BPD severity levels. In contrast, only 8.0% of infants received vitamin A, including a low treatment rate of 5.4% among those who did not develop BPD. It is uncertain why clinicians have largely abandoned the use of vitamin A in very preterm infants, particularly because there are few evidence-based drug therapies shown to prevent BPD.[30,31] There was a national shortage of the injectable form of vitamin A from 2010 to 2014, but the drug is now widely available, albeit at a much higher purchase price.[32,33] It is possible that the elevated cost, coupled with the need to inject the drug intramuscularly, and questions about the effectiveness of vitamin A to prevent BPD among contemporary very preterm infants contribute to the low treatment rates.[32,33] Nonetheless, it is noteworthy that this medication is used so infrequently, particularly because the trial data indicate that vitamin A may be as or even more effective than prophylactic nCPAP at reducing BPD risk.[22,26] The most recent Cochrane systematic reviews on the prevention of BPD with these 2 therapies report a relative risk of 0.85 (95% confidence interval: 0.74–0.98) with intramuscular vitamin A and 0.89 (0.79–0.99) with prophylactic nCPAP versus invasive assisted ventilation.[22,26]

TABLE 3 Major Nonrespiratory Morbidities Among Survivors to Discharge

Outcome	All Infants (N = 22 131)	No BPD (n = 12 192)	Grade 1–2 BPD (n = 9126)	Grade 3 BPD (n = 813)
Early onset bacterial sepsis or meningitis[a]	279 (1.3)	134 (1.1)	125 (1.4)	20 (2.5)
Late onset bacterial or fungal sepsis or meningitis[a]	2209 (10.0)	582 (4.8)	1372 (15.0)	255 (31.4)
Severe brain injury on cranial imaging[b]	1934 (8.9)	569 (4.8)	1177 (13.1)	188 (23.4)
Surgical or interventional closure of a PDA	1122 (5.1)	96 (0.8)	859 (9.4)	167 (20.6)
Surgery for confirmed or suspected NEC or bowel perforation	786 (3.6)	175 (1.4)	472 (5.2)	139 (17.1)
Surgery or anti-VEGF therapy for ROP	1210 (5.5)	141 (1.2)	882 (9.7)	187 (23.0)

Data shown in the table are number of infants (%). All percentage values were calculated among infants with complete data for the described variable. Data shown in the table were missing in <1% of study infants, except for severe brain injury on cranial imaging, which was missing for 2.1% of the cohort. NEC, necrotizing enterocolitis; PDA, patent ductus arteriosus; VEGF, vascular endothelial growth factor.

[a]Early onset infection occurred on or before day 3 after birth; late onset infection occurred after day 3. All infections were identified by using a culture of blood or cerebral spinal fluid.

[b]Defined as a grade 3 or 4 intraventricular or periventricular hemorrhage and/or cystic periventricular leukomalacia.

Of the 3 evaluated drug therapies shown to prevent BPD, the use of systemic postnatal corticosteroids varied the greatest between BPD severity levels. Use increased from 3.7% among infants who did not develop BPD to 64.0% of those who developed grade 3 BPD. Approximately one-third of infants who developed grade 1 or 2 BPD received systemic corticosteroid therapy. Although the data from randomized controlled trials raise concern for possible long-term neurologic harm with certain corticosteroid regimens, they also suggest the possibility of net benefit among infants at high risk of developing BPD.[27,28,34,35] The relatively large proportion (64%) of infants in this cohort who developed BPD but did not receive

TABLE 4 In-Hospital Outcomes Among Survivors to Discharge

Outcome	All Infants (N = 22 131)	No BPD (n = 12 192)	Grade 1–2 BPD (n = 9126)	Grade 3 BPD (n = 813)
Supplemental oxygen at discharge, n (%)	4238 (20.4)	236 (2.0)	3613 (43.3)	389 (67.5)
Tracheostomy, n (%)	224 (1.0)	2 (0.0)	73 (0.8)	149 (18.3)
Cardiorespiratory monitor at discharge, n (%)	4421 (21.3)	854 (7.2)	3226 (38.7)	341 (59.1)
Length of stay, median (IQR), d	80 (62–106)	66 (53–80)	103 (84–127)	163 (122–233)
PMA at discharge, median (IQR), wk	39 (37–41.6)	37.4 (36.3–39)	41 (39.1–43.9)	48.9 (43.1–58.4)

All percentage values shown in the table were calculated among infants with complete data for the described variable. Data for supplemental oxygen and cardiorespiratory monitor use at discharge were missing for 6.1% of infants. Data for the length of stay and PMA at discharge were missing for 1.1% infants. Data for tracheostomy were missing for <0.1% of infants. IQR, interquartile range.

corticosteroids calls into question whether some of these infants represent a missed opportunity to reduce lung disease severity and improve long-term outcomes with the use of corticosteroid therapy.

The available data indicate that infants who develop grade 3 BPD are at high risk for poor outcomes throughout early childhood.[2,19] Data from the NICHD Neonatal Research Network showed that more than three-quarters of very preterm infants with grade 3 BPD died in the first years of life or developed significant neurocognitive delay.[2] Our findings confirm that infants with grade 3 BPD experience a high burden of prognostically important neonatal comorbidities, which may represent important antecedent events that contribute to poor developmental outcomes. In the present cohort, nearly one-third of those who developed grade 3 BPD were diagnosed with a culture-confirmed bacterial or fungal infection, and almost one-quarter were diagnosed with severe brain injury or ROP.[3,36] Nearly 20% underwent surgery for necrotizing enterocolitis or bowel perforation.[37] In most cases, these event rates are an order of magnitude higher than those observed among the survivors without BPD. More than two-thirds of study infants with grade 3 BPD continued to receive supplemental oxygen at hospital discharge, and the median lengths of hospital stay were almost 100 days longer among those with grade 3 BPD, compared with those without BPD. The frequent presence of multiple complications of prematurity observed among infants with grade 3 BPD underscores the difficult task of improving respiratory and developmental outcomes in this high-risk population.

The key strength of this study is the use of a large and diverse population of very preterm infants with data collected prospectively according to standardized definitions. Our primary limitation is the inability to differentiate between and report stratified outcome rates for infants who developed grade 1 versus grade 2 BPD. Existing data suggest that grade 1 BPD is the most common severity level and infants with grade 2 BPD, on average, experience worse in-hospital outcomes than those with grade 1 BPD.[2] The VON database also does not include information on the timing of most interventions and onset of the evaluated morbidities, preventing assessment of whether these occurred before or after the diagnosis of BPD. Information on interventions and outcomes, other than mortality, may be undercounted in some infants who were transferred from a VON center to one that does not participate in the data repository. Finally, this descriptive analysis does not establish causation between BPD and the evaluated patient characteristics or outcomes.

CONCLUSIONS

This study provides the first benchmark epidemiological data using the diagnostic criteria for BPD proposed in 2019 by the NICHD Neonatal Research Network.[2] Our study data confirm that despite ongoing advances in neonatal care, BPD remains one of the most common and significant complications of premature birth. We found that more than one-half of infants born with gestational ages of 22 to 29 weeks in the United States died before 36 weeks' PMA or met criteria for BPD according to this new definition. Moreover, greater BPD severity was associated with stepwise increases in the rates of multiple major neonatal morbidities and mortality and more frequent use of respiratory drug therapies and supplemental respiratory support, including at the time of hospital discharge. These data emphasize the ongoing need to develop new strategies to prevent and treat BPD in very preterm infants. Furthermore, the stark differences in outcomes and rates of health care use observed across BPD severity levels strongly suggest that future studies should report rates of BPD stratified by severity level rather than by the presence or absence of BPD alone.

ACKNOWLEDGMENTS

We are indebted to our colleagues who submit data to VON on behalf of infants and their families. The list of centers contributing data to this study are shown in Supplemental Table 5.

ABBREVIATIONS

BPD: bronchopulmonary dysplasia
nCPAP: nasal continuous positive airway pressure
NICHD: *Eunice Kennedy Shriver* National Institute of Child Health and Human Development
PMA: postmenstrual age
ROP: retinopathy of prematurity
VON: Vermont Oxford Network

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-030007

FINANCIAL DISCLOSURE: Drs Horbar and Soll and Ms Greenberg are employees of the Vermont Oxford Network. Drs Edwards and Ehret receive salary support from the Vermont Oxford Network; and Dr Jensen has indicated he has no financial relationships relevant to this article to disclose.

FUNDING: Dr Jensen received grant support from the National Heart, Lung, and Blood Institute (grant K23HL136843) and the American Lung Association (Clinical Patient Care Research grant 512247). Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

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