



Published in final edited form as:

*J Pediatr.* 2020 April ; 219: 152–159.e5. doi:10.1016/j.jpeds.2019.12.028.

## Behavior Profiles at 2 Years for Children Born Extremely Preterm with Bronchopulmonary Dysplasia

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### Abstract

**Objective:** To characterize behavior of 2-year-old children based on the severity of bronchopulmonary dysplasia (BPD).

**Study design:** We studied children born at 22–26 weeks' gestation and assessed at 22–26 months' corrected age with the Child Behavior Checklist (CBCL). BPD was classified by level of respiratory support at 36 weeks' postmenstrual age. CBCL syndrome scales were the primary outcomes. The relationship between BPD grade and behavior was evaluated, adjusting for

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Data Sharing: Data reported in this paper may be requested through a data use agreement. Further details are available at <https://neonatal.rti.org/index.cfm?fuseaction=DataRequest.Home>.

perinatal confounders. Mediation analysis was performed to evaluate whether cognitive, language, or motor skills mediated the effect of BPD grade on behavior.

**Results:** Of 2310 children, 1208 (52%) had no BPD, 806 (35%) had grade 1 BPD, 177 (8%) had grade 2 BPD, and 119 (5%) had grade 3 BPD. Withdrawn behavior ( $P<.001$ ) and pervasive developmental problems ( $P<.001$ ) increased with worsening BPD grade. Sleep problems ( $P=.008$ ) and aggressive behavior ( $P=.023$ ) decreased with worsening BPD grade. Children with grade 3 BPD scored 2 points worse for withdrawn behavior and pervasive developmental problems and 2 points better for externalizing problems, sleep problems, and aggressive behavior than children without BPD. Cognitive, language, and motor skills mediated the effect of BPD grade on the attention problems, emotionally reactive, somatic complaints, and withdrawn CBCL syndrome scales ( $P<.05$ ).

**Conclusions:** BPD grade was associated with increased risk of withdrawn behavior and pervasive developmental problems but with decreased risk of sleep problems and aggressive behavior. The relationship between BPD and behavior is complex. Cognitive, language, and motor skills mediate the effects of BPD grade on some problem behaviors.

### Keywords

BPD; premature infants; Child Behavior Checklist; Bayley Scales of Infant and Toddler Development; cognitive; language; motor

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Behavioral challenges are among the developmental sequelae of extremely preterm birth. Early childhood behavioral outcomes may be determinants of functional attainment, independence, and mental health later in life. Extremely preterm children have more difficulties with internalizing behaviors (i.e., anxiety and affective disorders) and attention problems than full term peers.<sup>1,2</sup> Inattention, anxiety, and social problems occur in more than 20% of extremely babies and were recently characterized as a ‘preterm behavioral phenotype’.<sup>3,4</sup>

Bronchopulmonary dysplasia (BPD) is a major pulmonary morbidity affecting nearly half of extremely preterm infants.<sup>5</sup> The diagnosis of BPD is associated with adverse neurodevelopmental outcomes above and beyond those anticipated with extreme prematurity.<sup>6–9</sup> Yet we do not fully understand how BPD severity impacts behavioral outcomes. Prolonged duration of mechanical ventilation is associated with increased risk of neurodevelopmental impairment.<sup>10</sup> Short et al demonstrated that children with severe BPD performed more poorly on mental and psychomotor developmental indices as well as language measures at 3 years compared with children with mild BPD.<sup>11</sup> In the Extremely Low Gestational Age Newborns (ELGAN) study, children with the most severe BPD performed the worst on cognitive and executive function assessments at 10 years.<sup>12</sup>

Our purpose was to better understand how BPD, across the severity spectrum, is related to behavior. We used a recent classification of BPD severity more predictive of late death or serious respiratory morbidity<sup>13</sup> than the NIH Consensus definition.<sup>14</sup> We aimed to describe how BPD grade relates to behavior at 2 years’ corrected age and to evaluate whether language, motor, or cognitive skills mediate the effect of BPD grade on problem behaviors.

## Methods

We performed a secondary analysis of a prospective cohort from the NICHD Neonatal Research Network (NRN) premature infant registry and follow-up database. The sample includes children born before 27 weeks' gestation and cared for at NRN centers between July 2012 and February 2016 for whom a primary caregiver completed the Child Behavior Checklist (CBCL)<sup>15</sup> at 22–26 months' corrected age. Children with major congenital anomalies or syndromes known to affect development were excluded. Children with birth weight less than the 10th centile for gestational age were considered small for gestational age (SGA).<sup>16</sup> Intracranial hemorrhage (ICH) was determined for children who had cranial sonography performed within 28 days of birth, with findings classified by Papile criteria.<sup>17</sup> Severe retinopathy of prematurity (ROP) was defined as having undergone ophthalmologic intervention for ROP or having retinal detachment. BPD status was categorized according to level of respiratory support at 36 weeks' postmenstrual age (PMA), irrespective of oxygen therapy: no BPD (no respiratory support including supplemental oxygen), grade 1 (nasal cannula  $\leq 2$  L/min), grade 2 (nasal cannula  $>2$  L/min or noninvasive positive airway pressure), and grade 3 (invasive mechanical ventilation).<sup>13</sup> Children participated in a comprehensive follow-up evaluation at 22–26 months' corrected age, which included administration of the Bayley Scales of Infant and Toddler Development, 3rd Edition (Bayley-III)<sup>18</sup> and the CBCL. The CBCL consists of 100 behavior-related questions for which the primary caregiver rates each problem behavior on a three-point scale that produces a T-score as its standard score. It is broken down into seven syndrome scales. The CBCL produces an internalizing problems score (composed of four syndrome scales: emotionally reactive, anxious/depressed, somatic complaints, withdrawn behavior), an externalizing problems score (composed of two syndrome scales: attention problems, aggressive behavior), a total problems score, and five DSM-oriented scales (scales oriented to the classifications of the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association). The CBCL syndrome scales were the primary outcomes of interest; the CBCL problem scores, DSM-oriented scales, and Bayley-III composite scores were among the secondary outcomes.

## Statistical Analyses

To characterize the study sample, bivariate comparisons were made by BPD status for maternal and neonatal characteristics, neonatal therapies and morbidities, and 2-year neurosensory outcomes, including the Bayley-III composite scores (cognitive, language, and motor). Comparisons were made using chi-square tests for categorical variables and ANOVA for continuous variables. To control for type 1 error, an overall effect across all BPD grades was first tested, and if significant, pairwise comparisons between individual BPD grades were conducted after adjusting for multiple comparisons using the Holm correction for categorical variables and the Tukey method for continuous variables.

To evaluate whether children with more severe BPD have more behavioral difficulties, bivariate analyses using ANOVA tests were first conducted to compare mean scores on the CBCL syndrome scales and other CBCL scores by BPD grade, followed by pairwise comparisons among individual BPD grades using Tukey adjustment for multiple

comparisons. To determine if BPD grade differences remained after controlling for other factors, linear mixed effect regression models were fit using SAS PROC MIXED to compare CBCL scores by BPD grade, including center as random factor to account for clustering of participants by center and controlling for sex, gestational age, SGA, race, Hispanic ethnicity, maternal education, insurance type, grade III/IV ICH, severe ROP, and postnatal steroids.

The mediation analyses investigated whether a child's cognitive, language, or motor skills mediate the relationship between BPD grade and problem behaviors (Figure 1; available at [www.jpeds.com](http://www.jpeds.com)). Because BPD grade is a multi-category nominal variable, we used the mediation analysis approach for multi-categorical independent variables presented by Hayes and Preacher.<sup>19</sup> For these analyses, BPD status was classified as each grade compared with no BPD. The mediation analyses were conducted in the structural equation modeling framework with Mplus software version 8.3, using bootstrapping to determine confidence intervals. The mediation models controlled for the same potential confounders identified above. Each possible mediator (cognitive, language, or motor skills) was first analyzed separately. To enhance usability of the results, after identifying the significant mediators for each CBCL scale, we then combined the results into one overall path model, including the significant paths for the mediators of the relationship between BPD grades and the CBCL syndrome scales and controlling for potential confounding factors. Due to high correlations between the Bayley cognitive, language, and motor scales and to improve model parsimony, we removed paths between Bayley scores and CBCL scores that were no longer significant and did not affect overall model fit when all three Bayley scores were combined into the same model. Model fit was based on several indices, including the comparative fit index (CFI), Tucker-Lewis index (TLI), and root mean square error of approximation (RMSEA).

## Results

Between July 2012 and February 2016, 4211 extremely preterm infants were cared for in NRN centers with 2710 surviving to discharge (Figure 2; available at [www.jpeds.com](http://www.jpeds.com)). At 22–26 months' corrected age, 2439/2710 children were seen (90% follow-up rate), of which 2310 had the CBCL completed during their comprehensive follow-up assessment. History of BPD was present in 1102 (47.7%) children and 1208 (52.3%) children had no history of BPD. Among those with a history of BPD, 806 children (73.1%) had grade 1 BPD, 177 (16.1%) had grade 2 BPD, and 119 (10.8%) had grade 3 BPD.

Mothers of children with BPD were more likely to have private insurance (37.6% vs. 35.2%,  $P=.005$ ) and be of non-black race (59.8% vs. 51.1%,  $P<.001$ ) than mothers of children without BPD (Table I). Children with BPD were more likely to be outborn (5.2% vs. 3.3%,  $P=.026$ ), male (54.1% vs. 47.5%,  $P=0.002$ ), and SGA (8.4% vs. 3.2%,  $P<.001$ ) than children without BPD. Mothers of children for whom CBCL data were not available, including those who died or were lost to follow-up, were younger ( $P<.001$ ) and were less likely to have received antenatal corticosteroids ( $P<.001$ ) than mothers of children for whom the CBCL was completed. The children for whom the CBCL was not completed (including those who died or were lost to follow-up) had a younger gestational age ( $P<.001$ ) and lower birth weight ( $P<.001$ ), were less likely to be exposed to antenatal steroids ( $P<.001$ ), and

were more likely to be SGA ( $P<.001$ ) and to be male ( $P=.012$ ) than children for whom the CBCL was completed.

Children with BPD had higher rates of patent ductus arteriosus (63.5% vs. 47.2%,  $P<.001$ ), late-onset sepsis (29.7% vs. 21.2%,  $P<.001$ ), surfactant use (95.8% vs. 85.7%,  $P<.001$ ), and postnatal corticosteroid use for BPD (39.9% vs. 11.0%,  $P<.001$ ) than children without BPD (Table I). With regard to neurosensory morbidities, children with BPD experienced higher rates of severe ICH (16.7% vs. 12.8%,  $P=.008$ ) and severe ROP (16.5% vs. 7.8%,  $P<.001$ ) compared with those without BPD.

At 2 years' corrected age, the majority of children were within normal limits by parent report for all domains assessed by the CBCL (Table II; available at [www.jpeds.com](http://www.jpeds.com)). Children with grade 3 BPD were more likely to score in the borderline or clinically significant range for withdrawn behavior ( $P=.007$ ) and pervasive developmental problems ( $P=.007$ ) compared with children without BPD.

For the unadjusted bivariate comparisons on the CBCL scores, children with BPD scored higher (worse) for somatic complaints (mean  $54.2 \pm SD 6.3$  vs.  $53.6 \pm 5.7$ ,  $P=.025$ ), withdrawn behavior ( $56.9 \pm 8.4$  vs.  $55.8 \pm 7.5$ ,  $P<.001$ ), and pervasive developmental problems ( $57.5 \pm 8.5$  vs.  $56.2 \pm 7.9$ ,  $P<.001$ ) compared with those without BPD (Table III). The sleep problems scale revealed statistically lower (better) scores among children with BPD compared with those without BPD ( $54.1 \pm 7.5$  vs.  $54.8 \pm 7.8$ ,  $P=.025$ ) as did the aggressive behavior scale ( $54.4 \pm 7.3$  vs.  $55.1 \pm 8.1$ ,  $P=.0496$ ). When examined by BPD grade, withdrawn behavior and pervasive developmental problems increased with worsening BPD grade ( $P<.001$  for both), whereas sleep problems and aggressive behavior decreased with worsening BPD ( $P=.008$  and  $P=.023$ , respectively).

After controlling for potential confounding factors, children with grade 3 BPD scored 2.4 points higher (worse) on pervasive developmental problems (95% CI 0.76, 3.98) and 2.2 points higher (worse) on withdrawn behavior (95% CI 0.67, 3.78) than those with no BPD (Figure 3). In contrast, children with grade 3 BPD scored 2.4 points lower (better) on externalizing problems (95% CI  $-4.66$ ,  $-0.14$ ), 2.1 points lower (better) on sleep problems (95% CI  $-3.58$ ,  $-0.53$ ), and 1.8 points lower (better) on aggressive behavior (95% CI  $-3.27$ ,  $-0.27$ ) than children with no BPD. The adjusted  $R^2$  values were small (0.023–0.067), suggesting that although statistically significant, BPD grade and other variables in the model did not explain a large portion of the variability observed in problem behaviors.

Mediation analysis revealed that cognitive skills assessed by the Bayley-III were significant mediators for all of the CBCL scales except for aggressive behavior, sleep problems, and oppositional defiant problems (Table IV; available at [www.jpeds.com](http://www.jpeds.com)). In addition, both language and motor skills were significant mediators for attention problems, emotionally reactive, somatic complaints, withdrawn, affective problems, pervasive developmental problems, internalizing problems, and total problems. In some cases, motor skills also were a significant mediator for anxious/depressed behavior. The size of the mediation effect increased with BPD severity. For example, there was a 0.14 standard deviation (SD) difference in mean CBCL attention problems scores due to cognitive skills among those with

BPD grade 1 versus no BPD; however, this value increased to 0.46 SD for grade 2 and 0.85 SD for grade 3 versus no BPD.

Figure 4 shows the path diagram integrating the mediation results into an overall model for the CBCL syndrome scales. The model fit very well (CFI=1.000, TLI=0.998, RMSEA=0.005). This model indicates that higher BPD grades are associated with poorer cognitive, language, and motor skills, which are in turn associated with worse problem behaviors. Cognitive skills were significant mediators of BPD grade on anxious/depressed, attention problems, emotionally reactive, and withdrawn scales. When combining all 3 Bayley scores into a single model, language skills remained a significant mediator only for the withdrawn scale and motor skills remained a significant mediator of both the withdrawn and somatic complaints scales.

## Discussion

Although children with BPD had some increased behavioral difficulties (withdrawn behavior and pervasive developmental problems) compared with those without BPD, children with BPD had decreased problems in other behavior domains (sleep problems and aggressive behavior). The magnitude of the effects of BPD on behavior was small. Although statistically significant, these differences may not be clinically significant at less than half a standard deviation (ie, <5 points with standard deviation of 10 for the CBCL).<sup>20</sup> What is a clinically important difference may vary for pediatric populations and may vary between children. In the current sample, difficulties on the withdrawn and pervasive developmental problems scales were more common in children with BPD and increased with increasing BPD grade. This may signal a role for screening children with BPD for autism spectrum disorder and for monitoring children with BPD for anxiety, because higher scores on withdrawn and pervasive developmental problems scales may correlate with autism spectrum disorder or anxiety diagnoses in childhood.<sup>21,22</sup>

Behavioral outcomes are complex given the endogenous and exogenous factors at play. Cognitive, language, and motor skills, markers of neurodevelopment, all mediated the effect of BPD grade on attention problems, emotional reactivity, somatic complaints, withdrawn, affective problems, pervasive developmental problems, internalizing problems, and total problems. None of the Bayley-III measures of neurodevelopment mediated the effect of BPD grade on aggressive behavior, oppositional defiant problems, or sleep problems. In an earlier NICHD NRN cohort, both language and cognitive skills mediated the relationship between sociodemographic risk factors and problem behaviors.<sup>23</sup> To address the home environment, we included maternal education and insurance type as confounders. Other work by the NRN found language and cognitive skills to be associated with problem behaviors.<sup>24</sup> In contrast, in a previous single center cohort, there was no independent association of BPD severity with cognition.<sup>25</sup>

Significant differences in problem behaviors were most commonly found between those without BPD and those with the most severe grade of BPD. Mechanisms by which BPD may have an effect on behavior include chronic hypercarbia,<sup>26</sup> hypoxemia,<sup>27</sup> and postnatal steroid exposure.<sup>28</sup> The impact of BPD alone on CBCL scores was small, changing the

CBCL scores by at most three points. In an Australian cohort, preterm children with BPD displayed more internalizing behaviors (derived from withdrawn behavior, somatic complaints, and anxious behavior) than children without BPD at 8 years; again, the magnitude of difference was small.<sup>2</sup> This is not to minimize the importance of understanding behavioral outcomes of children born prematurely. The EXPRESS investigators found the incidence of clinical range internalizing and externalizing behaviors on the CBCL to be 20.9% and 19.5% in extremely preterm children at 2 years, which was higher than our cohort (Table II).<sup>29</sup> Although behavioral challenges are not included in definitions of neurodevelopmental impairment, they have functional significance for children, their families, and society, particularly as children grow older. The ELGAN investigators evaluated behavioral outcomes at 10 years for children whose BPD status was known; autism spectrum disorder and communication impairment were more common among children with more severe BPD relative to children with milder or no BPD.<sup>6</sup>

The preterm behavioral phenotype is not a temporary problem limited to toddlerhood. As more extremely preterm children survive to adulthood, we are beginning to better characterize the enduring effects of prematurity. The preterm behavioral phenotype is unusual in the co-occurrence of externalizing behaviors, such as attention difficulties, and internalizing behaviors, such as anxiety. Deficits in executive function, which includes higher order cognitive processes engaged in behavioral control, are more common in adults born preterm with histories of BPD relative to adults born preterm without BPD.<sup>30</sup> In a systematic review and meta-analysis, parents of extremely low birth weight adolescents reported more ADHD symptoms and internalizing behaviors than normal birth weight peers.<sup>31</sup> In adulthood, those born preterm reported more internalizing problems and fewer externalizing problems than adults born at term.<sup>32</sup> Because the effect of prematurity on neurobehavioral outcome measures may not depend on the age of assessment,<sup>10</sup> behavioral difficulties in toddlerhood may hint at adult mental health outcomes. If behavioral difficulties do not improve with age, characterization of risk factors for problem behaviors and identification of behavioral difficulties in toddlerhood raise the potential for early intervention.

Strengths of this study include the application of a novel classification system for BPD that reflects current respiratory support modalities.<sup>13</sup> A second strength is the large size of the cohort (n=2310), which allowed for analyses based on BPD by grade rather than as a binary outcome, and low attrition. Another strength of the study is its nuanced assessment of neurodevelopmental indicators as possible mediators of the relationship between medical illness, specifically BPD grade, and behavior.

This work also has limitations. Prematurity and sociodemographic risk factors are intertwined. Although our analyses adjusted for multiple potential confounders including baseline maternal sociodemographic characteristics, there may be additional confounding factors pertaining to the home environment or neonatal morbidities that we did not consider. Although the analyses were adjusted for multiple comparisons across BPD grades, given the large number of CBCL scales, it is possible that up to 5% of the tests could be significant by chance. The CBCL is a parent report measure, and no standardized direct child assessment of behavior was performed. An additional limitation is the age at follow-up. Two-year

follow-up hinders the ability to evaluate behavior in multiple environments by different caretakers. Children may be identified as having behavioral problems beyond toddlerhood, with new challenges identified after immersion into the classroom setting.

This research informs postnatal counseling for families of children with BPD and comprehensive follow-up for children with BPD. It also contributes to our understanding of the complex relationship between BPD, behavior, and cognitive, language, and motor skills. The effects of BPD grade on behavior were subtle, and the directionality varied for different problem behaviors with some of the differences in behavioral outcomes mediated by cognitive, language, and motor development. Behavioral and mental health services may be a valued addition to the medical home for children born extremely preterm, including those affected by BPD. Given the high demands for pediatric behavioral health services, risk stratification based on neonatal morbidities and disease severity for comprehensive behavioral health screening may be one approach to optimize resource utilization for the highest risk population of children born prematurely, including those with grade 3 BPD.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgements

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

Funded by awards to the participating institutions from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development. Detailed funding information is available in the Appendix (available at [www.jpeds.com](http://www.jpeds.com)). The authors declare no conflicts of interest.

## Appendix

List of additional investigators and participating hospitals of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Neonatal Research Network.

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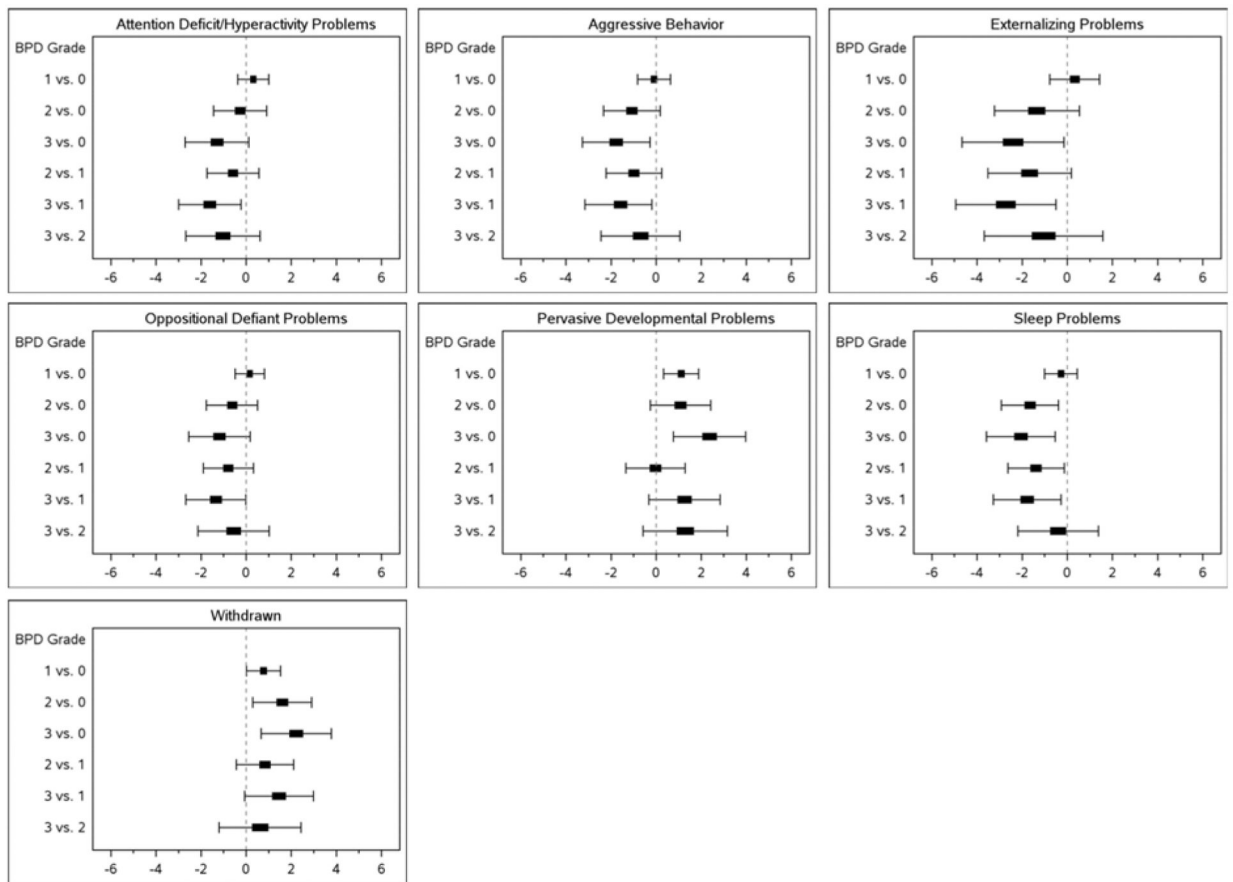
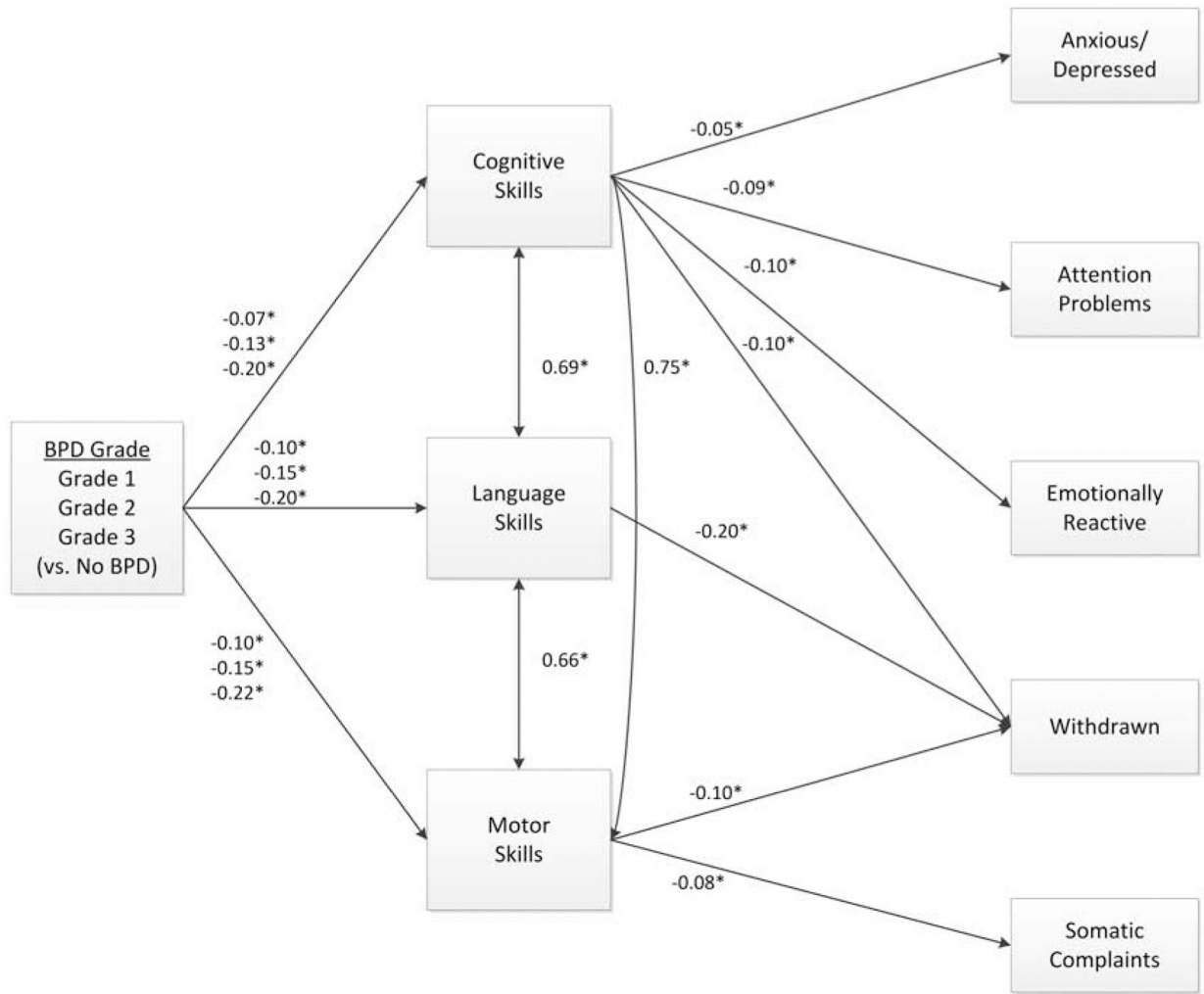
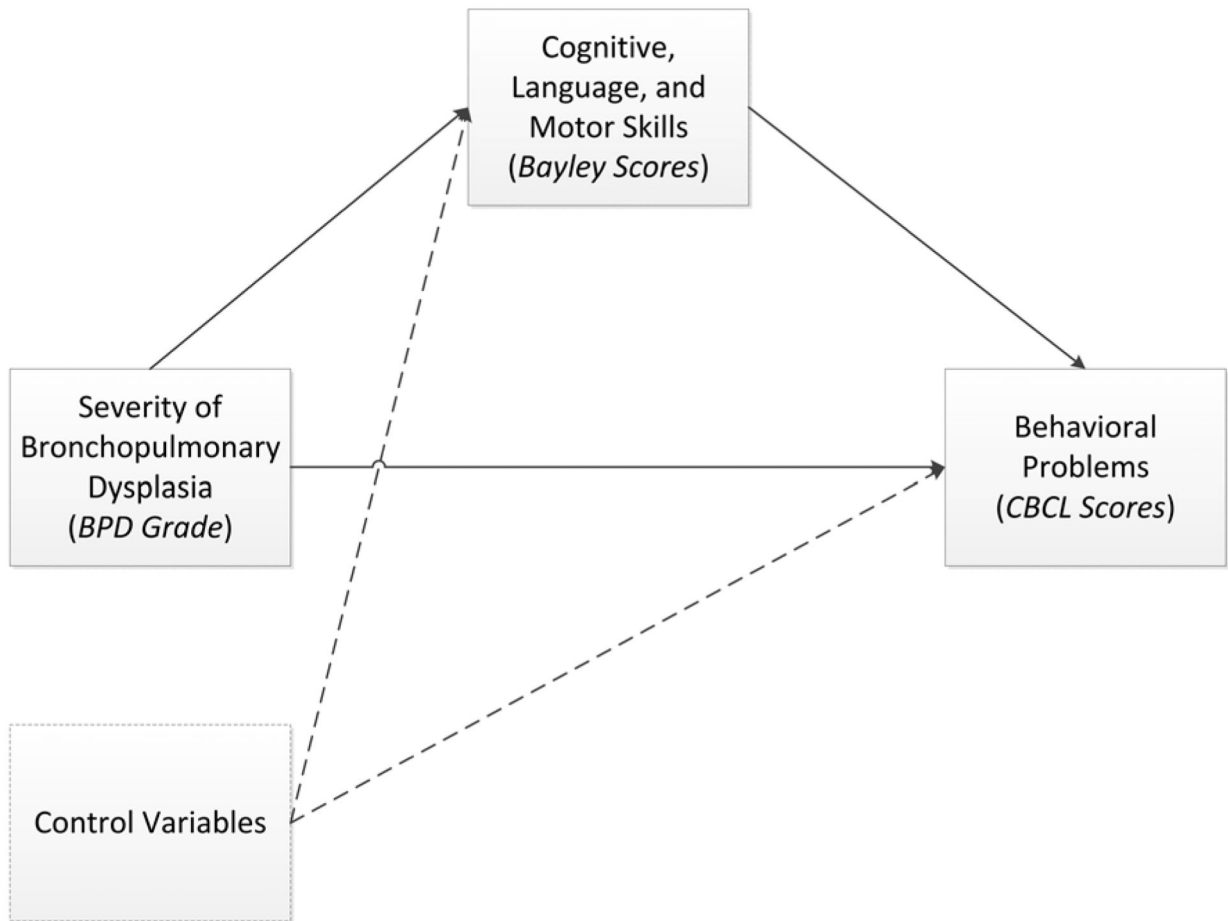


Figure 1. Mediation model.

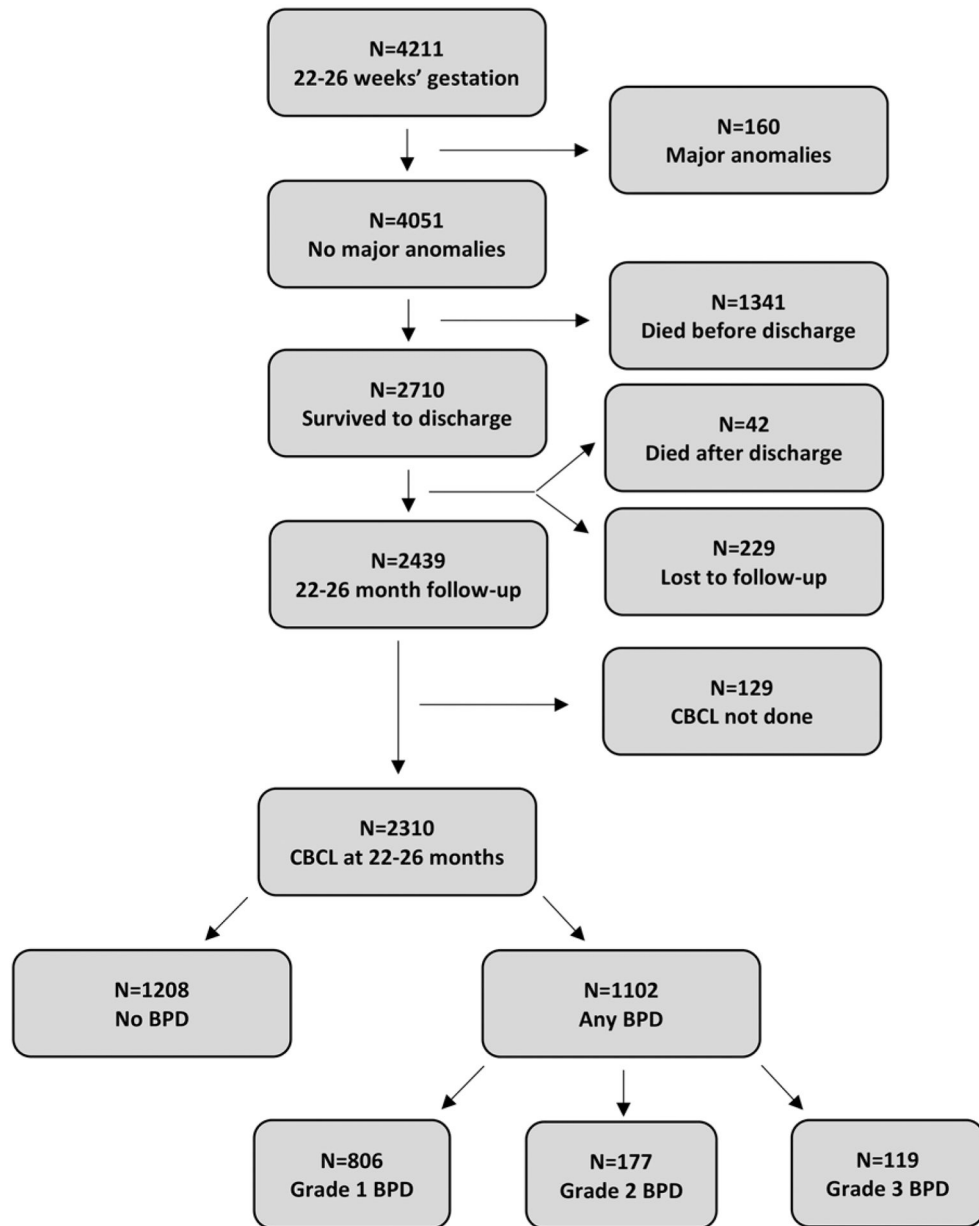


**Figure 2.**  
Flow chart of children.



**Figure 3.** Adjusted mean differences in CBCL scores by bronchopulmonary dysplasia grade. Mean differences are adjusted for sex, gestational age, SGA, race, Hispanic ethnicity, maternal education, insurance type, center, grade III/IV ICH, severe ROP, and postnatal steroids.





**Figure 4.** Path diagram of Bayley cognitive, language, and motor scores as mediators of bronchopulmonary dysplasia grade’s effect on CBCL syndrome scales. \*p <0.05. Values shown are standardized path coefficients. Path coefficients are adjusted for sex, gestational age, SGA, race, Hispanic ethnicity, maternal education, insurance type, center, grade III/IV ICH, severe ROP, and postnatal steroids.

**Table I.**

Characteristics, morbidities, and therapies by BPD grade.

Variable, mean (SD) or N (%)	BPD Grade				P-value
	No BPD	Grade 1	Grade 2	Grade 3	
<b>Maternal</b>					
Age (years)	28.3 (6.3)	28.3 (6.2)	28.6 (6.6)	28.3 (6.0)	.977
Marital status					
Married	435/1075 (40.5)	333/728 (45.7)	80/165 (48.5)	37/106 (34.9)	.020
Education					.898
Less than high school	175/884 (19.8)	112/575 (19.5)	25/132 (18.9)	14/73 (19.2)	
High school diploma	289/884 (32.7)	170/575 (29.6)	36/132 (27.3)	26/73 (35.6)	
Partial college or trade school	218/884 (24.7)	154/575 (26.8)	38/132 (28.8)	16/73 (21.9)	
College degree or higher	202/884 (22.9)	139/575 (24.2)	33/132 (25.0)	17/73 (23.3)	
Medical insurance					.021
Public	632/1075 (58.8)	412/728 (56.6)	91/165 (55.2)	67/106 (63.2)	
Private	378/1075 (35.2)	271/728 (37.2)	68/165 (41.2)	37/106 (34.9)	
Self-pay/uninsured	56/1075 (5.2)	28/728 (3.9)	2/165 (1.2)	1/106 (0.9)	
Other	9/1075 (0.8)	17/728 (2.3)	4/165 (2.4)	1/106 (0.9)	
Race					<.001 <sup>***</sup>
Black	508/1038 (48.9)	275/706 (39.0)	55/162 (34.0)	61/105 (58.1)	
White	479/1038 (46.2)	381/706 (54.0)	98/162 (60.5)	42/105 (40.0)	
Other	51/1038 (4.9)	50/706 (7.1)	9/162 (5.6)	2/105 (1.9)	
Hispanic ethnicity	174/1063 (16.4)	105/719 (14.6)	24/163 (14.7)	11/106 (10.4)	.358
Multiple birth	185/1075 (17.2)	132/728 (18.1)	26/165 (15.8)	11/106 (10.4)	.246
Chorioamnionitis (clinical)	182/1071 (17.0)	120/723 (16.6)	24/164 (14.6)	23/106 (21.7)	.496
Chorioamnionitis (histological)	618/992 (62.3)	378/654 (57.8)	82/150 (54.7)	54/93 (58.1)	.144
Antenatal steroids	959/1074 (89.3)	655/726 (90.2)	153/165 (92.7)	95/106 (89.6)	.576
<b>Infant</b>					
Gestational age (weeks)	25.1 (0.9)	24.7 (1.1)	24.4 (1.2)	24.4 (1.1)	<.001 <sup>***</sup>
Birth weight (grams)	796.7 (157.5)	724.3 (153.7)	688.6 (166.1)	657.5 (136.8)	<.001 <sup>***</sup>
Small for gestational age	39/1208 (3.2)	56/806 (6.9)	20/177 (11.3)	16/119 (13.4)	<.001 <sup>**</sup>
Outborn	40/1208 (3.3)	36/806 (4.5)	10/177 (5.6)	11/119 (9.2)	.012 <sup>†</sup>
Female sex	634/1208 (52.5)	375/806 (46.5)	79/177 (44.6)	52/119 (43.7)	.015 <sup>*</sup>
PDA	570/1208 (47.2)	513/806 (63.6)	112/177 (63.3)	75/119 (63.0)	<.001 <sup>**</sup>
Grade III/IV ICH	154/1203 (12.8)	130/801 (16.2)	27/174 (15.5)	26/119 (21.8)	.019 <sup>†</sup>
Early-onset sepsis	29/1208 (2.4)	14/806 (1.7)	4/176 (2.3)	1/119 (0.8)	.571
Late-onset sepsis	256/1208 (21.2)	208/806 (25.8)	60/176 (34.1)	57/119 (47.9)	<.001 <sup>†</sup>
Meningitis	19/1208 (1.6)	8/806 (1.0)	3/176 (1.7)	2/119 (1.7)	.699
Severe ROP	91/1173 (7.8)	119/783 (15.2)	35/163 (21.5)	21/115 (18.3)	<.001 <sup>**</sup>
Surgeries	215/1208 (17.8)	167/806 (20.7)	29/177 (16.4)	68/119 (57.1)	<.001 <sup>†</sup>

Variable, mean (SD) or N (%)	BPD Grade				P-value
	No BPD	Grade 1	Grade 2	Grade 3	
Surfactant use	1035/1208 (85.7)	772/806 (95.8)	167/176 (94.9)	116/119 (97.5)	<.001 <sup>*†‡</sup>
Invasive ventilation (days)	15.6 (34.9)	34.9 (21.7)	56.9 (32.1)	87.0 (31.7)	<.001 <sup>*†§¶#</sup>
Postnatal steroids for BPD	125/1136 (11.0)	224/695 (32.2)	81/152 (53.3)	75/105 (71.4)	<.001 <sup>*†‡§¶#</sup>

Statistically significant differences at p<0.05 after adjustment for multiple comparisons:

\* No BPD vs. Grade 1;

† No BPD vs. Grade 2;

‡ No BPD vs. Grade 3;

§ Grade 1 vs. Grade 2;

¶ Grade 1 vs. Grade 3;

# Grade 2 vs. Grade 3.

PDA: patent ductus arteriosus. ICH: intracranial hemorrhage. ROP: retinopathy of prematurity. BPD: bronchopulmonary dysplasia.

**Table II.**

CBCL score classification by BPD grade.

CBCL Score Classification <sup>A</sup>	BPD Grade			P-value <sup>B</sup>
	No BDP	Grade 1	Grade 2	
<b>Syndrome Scales</b>				
Emotionally Reactive				.939
Within normal limits	1079/1208 (89.2%)	716/805 (88.9%)	158/177 (89.3%)	105/119 (88.2%)
Borderline	92/1208 (7.6%)	58/805 (7.2%)	14/177 (7.9%)	11/119 (9.2%)
Clinically significant	38/1208 (3.1%)	31/805 (3.9%)	5/177 (2.8%)	3/119 (2.5%)
Anxious/Depressed				.535
Within normal limits	1129/1208 (93.4%)	755/807 (93.6%)	165/177 (93.2%)	114/119 (95.8%)
Borderline	54/1208 (4.5%)	33/807 (4.1%)	11/177 (6.2%)	4/119 (3.4%)
Clinically significant	26/1208 (2.2%)	19/807 (2.4%)	1/177 (0.6%)	1/119 (0.8%)
Somatic Complaints				.456
Within normal limits	1110/1207 (92.0%)	722/806 (89.6%)	159/177 (89.8%)	105/119 (88.2%)
Borderline	64/1207 (5.3%)	59/806 (7.3%)	14/177 (7.9%)	10/119 (8.4%)
Clinically significant	33/1207 (2.7%)	25/806 (3.1%)	4/177 (2.3%)	4/119 (3.4%)
Attention Problems				.450
Within normal limits	966/1206 (80.1%)	629/803 (78.3%)	145/177 (81.9%)	93/118 (78.8%)
Borderline	91/1206 (7.5%)	63/803 (7.8%)	14/177 (7.9%)	14/118 (11.9%)
Clinically significant	149/1206 (12.4%)	111/803 (13.8%)	18/177 (10.2%)	11/118 (9.3%)
Aggressive Behavior				.302
Within normal limits	1072/1208 (88.7%)	722/807 (89.5%)	166/177 (93.8%)	109/119 (91.6%)
Borderline	61/1208 (5.0%)	47/807 (5.8%)	5/177 (2.8%)	5/119 (4.2%)
Clinically significant	76/1208 (6.3%)	38/807 (4.7%)	6/177 (3.4%)	5/119 (4.2%)
Sleep Problems				.134
Within normal limits	1104/1204 (91.7%)	737/805 (91.6%)	169/176 (96%)	110/118 (93.2%)
Borderline	28/1204 (2.3%)	30/805 (3.7%)	2/176 (1.1%)	2/118 (1.7%)
Clinically significant	72/1204 (6.0%)	38/805 (4.7%)	5/176 (2.8%)	6/118 (5.1%)
Withdrawn				.007 <sup>‡</sup>
Within normal limits	1058/1207 (87.7%)	681/806 (84.5%)	145/177 (81.9%)	91/119 (76.5%)

CBCCL Score Classification <sup>A</sup>	BPD Grade			P-value <sup>B</sup>
	No BDP	Grade 1	Grade 2	
Borderline	48/1207 (4.0%)	43/806 (5.3%)	15/177 (8.5%)	10/119 (8.4%)
Clinically significant	101/1207 (8.4%)	82/806 (10.2%)	17/177 (9.6%)	18/119 (15.1%)
<b>Problem Scores</b>				
Externalizing Problems				.524
Within normal limits	1061/1208 (87.8%)	708/807 (87.7%)	161/177 (91.0%)	110/119 (92.4%)
Borderline	69/1208 (5.7%)	51/807 (6.3%)	10/177 (5.6%)	4/119 (3.4%)
Clinically significant	79/1208 (6.5%)	48/807 (5.9%)	6/177 (3.4%)	5/119 (4.2%)
Internalizing Problems				.397
Within normal limits	1102/1208 (91.1%)	717/807 (88.8%)	165/177 (93.2%)	111/119 (93.3%)
Borderline	68/1208 (5.6%)	58/807 (7.2%)	7/177 (4.0%)	6/119 (5.0%)
Clinically significant	39/1208 (3.2%)	32/807 (4.0%)	5/177 (2.8%)	2/119 (1.7%)
Total Problems				
Within normal limits	1047/1208 (86.7%)	700/806 (86.9%)	157/177 (88.7%)	110/119 (92.4%)
Borderline	87/1208 (7.2%)	51/806 (6.3%)	15/177 (8.5%)	4/119 (3.4%)
Clinically significant	74/1208 (6.1%)	55/806 (6.8%)	5/177 (2.8%)	5/119 (4.2%)
<b>DSM-Oriented Scales</b>				
Oppositional Defiant Problems				.669
Within normal limits	1069/1208 (88.4%)	723/807 (89.6%)	162/177 (91.5%)	110/119 (92.4%)
Borderline	49/1208 (4.1%)	29/807 (3.6%)	7/177 (4.0%)	3/119 (2.5%)
Clinically significant	91/1208 (7.5%)	55/807 (6.8%)	8/177 (4.5%)	6/119 (5.1%)
Anxiety Problems				.570
Within normal limits	1120/1208 (92.7%)	745/807 (92.3%)	167/177 (94.4%)	112/119 (94.1%)
Borderline	26/1208 (2.2%)	24/807 (3.0%)	5/177 (2.8%)	4/119 (3.4%)
Clinically significant	62/1208 (5.1%)	38/807 (4.7%)	5/177 (2.8%)	3/119 (2.5%)
Affective Problems				.561
Within normal limits	1098/1208 (90.9%)	727/806 (90.2%)	163/177 (92.1%)	114/119 (95.8%)
Borderline	42/1208 (3.5%)	26/806 (3.2%)	5/177 (2.8%)	2/119 (1.7%)
Clinically significant	68/1208 (5.6%)	53/806 (6.6%)	9/177 (5.1%)	3/119 (2.5%)
AD/Hyperactivity Problems				.117
Within normal limits	1031/1208 (85.3%)	688/806 (85.4%)	160/177 (90.4%)	111/119 (93.3%)

CBCL Score Classification <sup>A</sup>	BPD Grade			P-value <sup>B</sup>
	No BDP	Grade 1	Grade 2	
Borderline	83/1208 (6.9%)	48/806 (6.0%)	7/177 (4.0%)	4/119 (3.4%)
Clinically significant	95/1208 (7.9%)	70/806 (8.7%)	10/177 (5.6%)	4/119 (3.4%)
Pervasive Developmental Problems				
Within normal limits	1007/1208 (83.4%)	634/806 (78.7%)	148/177 (83.6%)	84/118 (71.2%)
Borderline	91/1208 (7.5%)	65/806 (8.1%)	12/177 (6.8%)	15/118 (12.7%)
Clinically significant	110/1208 (9.1%)	107/806 (13.3%)	17/177 (9.6%)	19/118 (16.1%)

<sup>A</sup> CBCL standard scores are scaled with a mean of 50 and standard deviation of 10. Scores <65 are within normal limits. Scores 65–69 are borderline, and scores 70 (i.e. 2 standard deviations or more above the mean) are considered clinically significant.

<sup>B</sup> Statistically significant differences at p<0.05 after adjustment for multiple comparisons:

- \* No BPD vs. Grade 1;
- <sup>†</sup> No BPD vs. Grade 2;
- <sup>‡</sup> No BPD vs. Grade 3;
- <sup>§</sup> Grade 1 vs. Grade 2;
- <sup>¶</sup> Grade 1 vs. Grade 3;
- <sup>#</sup> Grade 2 vs. Grade 3.

Table III.

Outcomes at 22–26 months' corrected age by BPD grade.

Variable	No BPD (N=1,208)	Any BPD (N=1,102)	P-value <sup>A</sup>	Grade 1 (N=806)	Grade 2 (N=177)	Grade 3 (N=119)	P-value <sup>A</sup>
Corrected age (months), mean (SD)	24.4 (2.8)	24.6 (2.7)	0.128	24.5 (2.6)	24.8 (3.3)	24.4 (2.2)	.176
<b>Bayley-III composite, mean (SD)<sup>B</sup></b>							
Cognitive	89.1 (14.2)	83.0 (16.2)	<0.001 <sup>A</sup>	85.5 (15.4)	79.5 (16.3)	71.0 (15.5)	<0.001 <sup>***§##</sup>
Language	85.5 (16.4)	78.7 (17.5)	<0.001 <sup>A</sup>	81.2 (17.0)	74.6 (17.1)	67.1 (16.6)	<0.001 <sup>***§##</sup>
Motor	89.4 (15.1)	80.8 (17.2)	<0.001 <sup>A</sup>	83.6 (15.6)	76.9 (18.2)	68.0 (19.0)	<0.001 <sup>***§##</sup>
<b>CBCL syndrome scales, mean (SD)</b>							
Aggressive Behavior	55.1 (8.1)	54.4 (7.3)	0.050 <sup>A</sup>	54.8 (7.6)	53.6 (5.8)	53.5 (7.2)	.023
Anxious/Depressed	53.5 (5.6)	53.5 (5.5)	0.896	53.7 (5.7)	53.1 (5.1)	52.8 (4.7)	.332
Attention Problems	56.9 (8.0)	57.5 (8.1)	0.067	57.6 (8.3)	56.8 (7.7)	57.3 (7.1)	.189
Emotionally Reactive	54.1 (6.5)	54.2 (6.7)	0.747	54.4 (6.9)	53.7 (5.9)	53.7 (6.5)	.454
Sleep Problems	54.8 (7.8)	54.1 (7.5)	0.024 <sup>A</sup>	54.5 (7.6)	53.1 (6.4)	52.9 (6.9)	.008 <sup>†</sup>
Somatic Complaints	53.6 (5.7)	54.2 (6.3)	0.025 <sup>A</sup>	54.0 (6.4)	54.3 (5.8)	55.0 (6.0)	.055
Withdrawn	55.8 (7.5)	56.9 (8.4)	<0.001 <sup>A</sup>	56.6 (8.4)	57.5 (8.4)	58.5 (8.8)	<0.001 <sup>††</sup>
<b>CBCL DSM-oriented scales, mean (SD)</b>							
Affective Problems	54.6 (6.4)	54.7 (6.4)	0.619	54.8 (6.7)	54.7 (5.8)	54.1 (5.2)	.656
Anxiety Problems	54.1 (6.4)	53.9 (6.5)	0.583	54.2 (6.7)	53.4 (6.1)	53.3 (5.5)	.320
Attention Deficit/Hyperactivity Problems	56.2 (7.3)	56.1 (7.2)	0.752	56.4 (7.4)	55.5 (6.8)	55.4 (5.8)	.289
Oppositional Defiant Problems	54.7 (7.1)	54.4 (6.8)	0.374	54.7 (6.9)	53.7 (6.2)	53.7 (6.2)	.150
Pervasive Developmental Problems	56.2 (7.9)	57.5 (8.5)	<0.001 <sup>A</sup>	57.3 (8.7)	57.4 (7.9)	59.0 (8.2)	<0.001 <sup>††</sup>
<b>CBCL problem scores, mean (SD)</b>							
Externalizing Problems	51.1 (11.9)	50.6 (11.5)	0.247	51.1 (11.7)	49.1 (10.8)	49.1 (10.7)	.051
Internalizing Problems	49.2 (11.0)	49.9 (11.3)	0.094	49.8 (11.5)	49.9 (10.8)	51.3 (9.8)	.179
Total Problems	51.0 (11.7)	51.1 (11.5)	0.882	51.4 (11.9)	50.1 (10.9)	50.8 (10.0)	.598
<b>Neurosensory outcomes, N (%)</b>							
Cerebral palsy	149 (12.4)	232 (21.2)	<0.001 <sup>A</sup>	139 (17.3)	43 (24.9)	50 (42.0)	<0.001 <sup>***§##</sup>

Variable	No BPD (N=1,208)	Any BPD (N=1,102)	P-value <sup>A</sup>	Grade 1 (N=806)	Grade 2 (N=177)	Grade 3 (N=119)	P-value <sup>A</sup>
Hearing impairment	24 (2.0)	38 (3.5)	0.028 <sup>^</sup>	24 (3.0)	8 (4.7)	6 (5.1)	.059
Bilateral blindness	9 (0.7)	21 (1.9)	0.014 <sup>^</sup>	9 (1.1)	5 (2.9)	7 (5.9)	<.001 <sup>^†‡§¶</sup>
<b>Pulmonary outcomes, N (%)</b>							
Current supplemental oxygen use	12 (1.0)	115 (10.5)	<.0001 <sup>^</sup>	41 (5.1)	36 (20.5)	38 (31.9)	<.001 <sup>^†‡§¶</sup>
Current ventilator or CPAP use	4 (0.3)	34 (3.1)	<.0001 <sup>^</sup>	6 (0.7)	8 (4.6)	20 (16.8)	<.001 <sup>^†‡§¶</sup>
Current tracheostomy	1 (0.1)	75 (7)	<.0001 <sup>^</sup>	7 (0.9)	15 (8.5)	53 (44.5)	<.001 <sup>^†‡§¶</sup>

<sup>A</sup> Statistically significant differences at p<0.05 after adjustment for multiple comparisons:

<sup>^</sup> No BPD vs. Any BPD;

<sup>\*</sup> No BPD vs. Grade 1;

<sup>†</sup> No BPD vs. Grade 2;

<sup>‡</sup> No BPD vs. Grade 3;

<sup>§</sup> Grade 1 vs. Grade 2;

<sup>¶</sup> Grade 1 vs. Grade 3;

<sup>#</sup> Grade 2 vs. Grade 3.

<sup>B</sup> Bayley-III composite scores were available for a subset of children for whom the CBCL was completed: N=1151 children with no BPD, N=773 children with grade 1 BPD, N=169 children with grade 2 BPD, and N=110 children with grade 3 BPD.



**Table IV.**

Cognitive, language, and motor skills as mediators of the relationship between BPD grade and problem behaviors.

Problem Behavior	Indirect Effect of BPD Grade on Problem Behavior through a Mediator		
	Cognitive Skills Adj. SMD (95% CI)	Language Skills Adj. SMD (95% CI)	Motor Skills Adj. SMD (95% CI)
<b>CBCL Syndrome Scales</b>			
Aggressive Behavior			
BPD Grade 1 (vs. 0)	0.03 (-0.01, 0.10)	0.00 (-0.08, 0.08)	-0.04 (-0.13, 0.02)
BPD Grade 2 (vs. 0)	0.10 (-0.05, 0.29)	0.00 (-0.21, 0.20)	-0.12 (-0.33, 0.06)
BPD Grade 3 (vs. 0)	0.19 (-0.09, 0.52)	-0.01 (-0.32, 0.31)	-0.21 (-0.57, 0.12)
Anxious/Depressed			
BPD Grade 1 (vs. 0)	0.05 (0.01, 0.11) <sup>A</sup>	0.05 (0.00, 0.13)	0.05 (0.00, 0.13) <sup>A</sup>
BPD Grade 2 (vs. 0)	0.17 (0.05, 0.33) <sup>A</sup>	0.14 (-0.01, 0.31)	0.15 (0.00, 0.33) <sup>A</sup>
BPD Grade 3 (vs. 0)	0.32 (0.09, 0.59) <sup>A</sup>	0.21 (-0.02, 0.47)	0.26 (-0.01, 0.57)
Attention Problems			
BPD Grade 1 (vs. 0)	0.12 (0.04, 0.23) <sup>A</sup>	0.14 (0.05, 0.27) <sup>A</sup>	0.09 (0.02, 0.20) <sup>A</sup>
BPD Grade 2 (vs. 0)	0.41 (0.22, 0.67) <sup>A</sup>	0.37 (0.15, 0.65) <sup>A</sup>	0.24 (0.04, 0.49) <sup>A</sup>
BPD Grade 3 (vs. 0)	0.77 (0.42, 1.20) <sup>A</sup>	0.57 (0.24, 0.98) <sup>A</sup>	0.44 (0.06, 0.86) <sup>A</sup>
Emotionally Reactive			
BPD Grade 1 (vs. 0)	0.11 (0.04, 0.21) <sup>A</sup>	0.14 (0.06, 0.26) <sup>A</sup>	0.13 (0.06, 0.25) <sup>A</sup>
BPD Grade 2 (vs. 0)	0.37 (0.20, 0.61) <sup>A</sup>	0.38 (0.19, 0.62) <sup>A</sup>	0.36 (0.18, 0.61) <sup>A</sup>
BPD Grade 3 (vs. 0)	0.69 (0.38, 1.08) <sup>A</sup>	0.58 (0.29, 0.95) <sup>A</sup>	0.65 (0.32, 1.07) <sup>A</sup>
Sleep Problems			
BPD Grade 1 (vs. 0)	0.00 (-0.05, 0.07)	-0.03 (-0.12, 0.05)	0.01 (-0.07, 0.08)
BPD Grade 2 (vs. 0)	0.01 (-0.18, 0.21)	-0.07 (-0.30, 0.15)	0.02 (-0.19, 0.22)
BPD Grade 3 (vs. 0)	0.02 (-0.32, 0.39)	-0.11 (-0.45, 0.23)	0.04 (-0.34, 0.40)
Somatic Complaints			
BPD Grade 1 (vs. 0)	0.06 (0.02, 0.13) <sup>A</sup>	0.09 (0.03, 0.17) <sup>A</sup>	0.10 (0.04, 0.20) <sup>A</sup>
BPD Grade 2 (vs. 0)	0.19 (0.06, 0.37) <sup>A</sup>	0.23 (0.08, 0.42) <sup>A</sup>	0.27 (0.11, 0.49) <sup>A</sup>
BPD Grade 3 (vs. 0)	0.36 (0.11, 0.66) <sup>A</sup>	0.36 (0.11, 0.64) <sup>A</sup>	0.49 (0.19, 0.83) <sup>A</sup>
Withdrawn			
BPD Grade 1 (vs. 0)	0.35 (0.12, 0.59) <sup>A</sup>	0.58 (0.33, 0.87) <sup>A</sup>	0.49 (0.26, 0.75) <sup>A</sup>
BPD Grade 2 (vs. 0)	1.22 (0.81, 1.70) <sup>A</sup>	1.57 (1.11, 2.06) <sup>A</sup>	1.33 (0.90, 1.83) <sup>A</sup>
BPD Grade 3 (vs. 0)	2.30 (1.72, 2.98) <sup>A</sup>	2.37 (1.73, 3.07) <sup>A</sup>	2.43 (1.82, 3.17) <sup>A</sup>
<b>DSM-Oriented Scales</b>			
Affective Problems			

Problem Behavior	Indirect Effect of BPD Grade on Problem Behavior through a Mediator		
	Cognitive Skills	Language Skills	Motor Skills
	Adj. SMD (95% CI)	Adj. SMD (95% CI)	Adj. SMD (95% CI)
BPD Grade 1 (vs. 0)	0.13 (0.05, 0.24) <sup>A</sup>	0.20 (0.11, 0.33) <sup>A</sup>	0.19 (0.10, 0.31) <sup>A</sup>
BPD Grade 2 (vs. 0)	0.45 (0.27, 0.68) <sup>A</sup>	0.55 (0.34, 0.80) <sup>A</sup>	0.50 (0.31, 0.77) <sup>A</sup>
BPD Grade 3 (vs. 0)	0.84 (0.53, 1.22) <sup>A</sup>	0.83 (0.53, 1.22) <sup>A</sup>	0.91 (0.57, 1.32) <sup>A</sup>
Anxiety Problems			
BPD Grade 1 (vs. 0)	0.04 (0.00, 0.11) <sup>A</sup>	-0.01 (-0.08, 0.06)	0.03 (-0.04, 0.10)
BPD Grade 2 (vs. 0)	0.14 (0.00, 0.32)	-0.03 (-0.21, 0.15)	0.07 (-0.10, 0.26)
BPD Grade 3 (vs. 0)	0.26 (-0.02, 0.57)	-0.04 (-0.32, 0.24)	0.12 (-0.17, 0.46)
Attention Deficit/Hyperactivity			
BPD Grade 1 (vs. 0)	0.05 (0.01, 0.13) <sup>A</sup>	0.04 (-0.03, 0.13)	-0.01 (-0.08, 0.06)
BPD Grade 2 (vs. 0)	0.18 (0.02, 0.37) <sup>A</sup>	0.11 (-0.09, 0.31)	-0.02 (-0.20, 0.16)
BPD Grade 3 (vs. 0)	0.33 (0.04, 0.66) <sup>A</sup>	0.16 (-0.13, 0.48)	-0.04 (-0.37, 0.29)
Oppositional Defiant Problems			
BPD Grade 1 (vs. 0)	0.03 (-0.01, 0.10)	0.03 (-0.04, 0.11)	-0.03 (-0.10, 0.03)
BPD Grade 2 (vs. 0)	0.10 (-0.04, 0.28)	0.08 (-0.11, 0.27)	-0.08 (-0.27, 0.09)
BPD Grade 3 (vs. 0)	0.19 (-0.09, 0.49)	0.12 (-0.17, 0.42)	-0.14 (-0.47, 0.17)
Pervasive Developmental Problems			
BPD Grade 1 (vs. 0)	0.30 (0.10, 0.51) <sup>A</sup>	0.53 (0.29, 0.80) <sup>A</sup>	0.41 (0.22, 0.64) <sup>A</sup>
BPD Grade 2 (vs. 0)	1.04 (0.68, 1.46) <sup>A</sup>	1.43 (1.02, 1.90) <sup>A</sup>	1.11 (0.74, 1.55) <sup>A</sup>
BPD Grade 3 (vs. 0)	1.97 (1.44, 2.58) <sup>A</sup>	2.19 (1.63, 2.86) <sup>A</sup>	2.01 (1.47, 2.66) <sup>A</sup>
<b>Problem Scores</b>			
Externalizing Problems			
BPD Grade 1 (vs. 0)	0.07 (0.00, 0.19) <sup>A</sup>	0.09 (-0.02, 0.25)	-0.02 (-0.14, 0.10)
BPD Grade 2 (vs. 0)	0.24 (-0.02, 0.54)	0.25 (-0.07, 0.61)	-0.05 (-0.37, 0.25)
BPD Grade 3 (vs. 0)	0.44 (-0.04, 0.98)	0.39 (-0.10, 0.94)	-0.09 (-0.66, 0.46)
Internalizing Problems			
BPD Grade 1 (vs. 0)	0.33 (0.12, 0.57) <sup>A</sup>	0.54 (0.31, 0.83) <sup>A</sup>	0.44 (0.24, 0.71) <sup>A</sup>
BPD Grade 2 (vs. 0)	1.14 (0.74, 1.63) <sup>A</sup>	1.45 (1.00, 1.98) <sup>A</sup>	1.19 (0.79, 1.71) <sup>A</sup>
BPD Grade 3 (vs. 0)	2.14 (1.52, 2.86) <sup>A</sup>	2.20 (1.55, 2.96) <sup>A</sup>	2.16 (1.52, 2.93) <sup>A</sup>
Total Problems			
BPD Grade 1 (vs. 0)	0.21 (0.07, 0.39) <sup>A</sup>	0.35 (0.19, 0.59) <sup>A</sup>	0.24 (0.11, 0.44) <sup>A</sup>
BPD Grade 2 (vs. 0)	0.72 (0.42, 1.12) <sup>A</sup>	0.95 (0.59, 1.40) <sup>A</sup>	0.65 (0.33, 1.05) <sup>A</sup>
BPD Grade 3 (vs. 0)	1.35 (0.82, 1.98) <sup>A</sup>	1.46 (0.91, 2.14) <sup>A</sup>	1.18 (0.61, 1.85) <sup>A</sup>

<sup>A</sup>  
p<0.05.

Note: Adj. SMD: adjusted standardized mean difference

Values shown are the indirect effect of BPD grade on CBCL scores through the mediator and are expressed as the standardized mean difference in CBCL scores for each BPD grade versus no BPD. Analyses were adjusted for sex, gestational age, small-for-gestational age, race, Hispanic ethnicity, maternal education, insurance type, center, grade III/IV ICH, severe ROP, and postnatal steroids.

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