

# Final Comprehensive Report on Grant #MC00334, Psychosocial Sequelae of BPD and VLBW: Phase 3 Primary Investigator, Lynn T. Singer, Ph.D.

## I. Introduction

A. Nature of the research problem: The research study, an extension of Psychosocial Sequelae of BPD and VLBW – Phases 1 and 2, (MCJ 390592 and 390715/R40-MC00127 (1989-2001)), investigated the early adolescent outcomes associated with bronchopulmonary dysplasia (BPD), the leading chronic pulmonary disease of prematurity,<sup>1</sup> with a particular focus on the influence of BPD relative to other medical, neurologic and sociodemographic risk factors, on pulmonary, cognitive, language, neuropsychological and behavioral outcomes. Family stressors associated with BPD and very low birth weight (VLBW) birth will also be investigated as predictors and correlates of outcomes. In particular, our current and prior studies examined the impact of minority (African-American) race and low socioeconomic status on child outcomes, including incidence of mental retardation, as well as maternal coping and stress. The study used a cohort of 3 groups of children (110 BPD, 80 very low birth weight without BPD, 112 healthy, term) who were prospectively, longitudinally followed from birth to 8 years. Since cohort recruitment, the incidence of BPD has continued to increase, rising from 7,000 cases annually in 1989 to >11,000 per year.<sup>2</sup> Yet, there are no comprehensive, controlled studies of the health, psychosocial and long term outcomes of children with a history of BPD and VLBW and their families.

This cohort is also unique in that there is broad representation of racial and socioeconomic groups to allow assessment of the effects of those factors on outcomes. Prior studies of this cohort to 8 years of age indicate that children with a history of BPD have higher rates of mental/motor retardation, varying by race and SES, and perform significantly more poorly than very low birth weight children without BPD on cognitive outcomes. Very low birth weight infants without BPD also performed more poorly than term infants. Gross motor outcomes were uniquely deficient for BPD children at 3 and 8 years, and at 8 years, speech articulation, oral-motor, receptive language, visual-spatial and applied mathematical skills were also differentially affected. Maternal coping mechanisms were related to child outcomes, and parenting stress and coping strategies differed based on race and socioeconomic status.

B. Purpose, scope, and methods of the investigation: The purpose of this study was to test the following hypotheses: **Hypothesis 1**: At 14 years of age, children with history of BPD and VLBW will continue to exhibit impaired functioning in comparison to cohorts of VLBW children without BPD and term, healthy children of similar age, race, sex, and socioeconomic status, when assessed on standard measures of physical health and growth, lung function, cognition, school achievement, language, behavior and specific neuropsychological abilities. **Hypothesis 2**: Parents of children with BPD will experience more symptoms of psychological distress, more parenting stress, and more overall life stress than parents of non-BPD, VLBW and term children at 14 years, controlling for race, sex, socio-economic status (SES), and multiple births. More adaptive coping mechanisms and positive social supports will moderate distress symptoms for mothers of BPD and non-BPD, VLBW children. **Hypothesis 3**: BPD, after consideration of other neurologic, medical, and socioeconomic risk factors, will account for independent variance in gross and fine motor, visual-motor, and phonologic outcomes at 14 years whereas neurologic, sociodemographic, and parenting factors will predict overall verbal IQ, general language skills, and emotional and behavioral functioning. This last hypothesis will be fully explored with support from grant R40MC08966, which supplied funds to explore longitudinal models.

Parents of children from the original cohort were contacted first by mail, then with a follow-up telephone call and asked if they would like to participate in the 14-year follow-up. This study was approved by the Institutional Review Board, University Hospitals Cleveland. Informed consent/assent was obtained from parents and children, and families who participated received a total of \$150 as compensation for their time. Families were interviewed and tested at the study offices for parental interviews and developmental testing. Pulmonary testing and physicals were conducted at University Hospitals. If families wished to participate, but were otherwise unable to come to our offices, testing was done in the family's home, and parental interviews were conducted at home or by telephone.

C. Nature of the findings: Preliminary findings from this 14-year study indicate children with a history of BPD continue to have significant developmental problems when compared to their VLBW and Term peers into adolescence, and that their families continue to experience a greater family and social burden than those of term adolescents.

## II. Review of the Literature:

Considerable research has shown that children born of very low birth weight (VLBW) are at increased risk of developmental problems including neurosensory abnormalities,<sup>3-5</sup> and poorer growth, cognitive abilities, specific neuropsychological functions, and behavioral competence<sup>6-11</sup> than full-term cohorts. Studies indicate that these risks persist into adolescence, even when sociodemographic and medical risk factors are controlled, putting premature, VLBW children at risk for poorer cognition, language, achievement, social and motor abilities, and greater psychological problems,<sup>9, 12-16</sup> as well as greater risk for grade repetition, special education placement and use of school-based services.<sup>14, 15, 17-22</sup> Decreasing birth weight and gestational age increases risk for lower IQ,<sup>7, 9, 11, 14, 23</sup> neuropsychological outcomes, such as attention, memory, visual-motor skills and processing speed<sup>7, 11, 24-28</sup> occurs. Other factors implicated in developmental studies have included neurologic complications such as IVH and PVL,<sup>29-31</sup> necrotizing enterocolitis, steroid use to reduce inflammation, and infant gender;<sup>32</sup> postnatal transport to NICU, maternal race and marital status;<sup>19</sup> lower socioeconomic status;<sup>10, 19</sup> maternal-child interactions,<sup>33-35</sup> and maternal psychological distress.<sup>33-36</sup> In addition, severe chronic lung disease, i.e., bronchopulmonary dysplasia (BPD) or length of time on oxygen has been noted to be a prominent factor leading to increased morbidity among VLBW cohorts.<sup>36-45</sup>

The incidence of BPD climbs with decreasing birth weight and approximates 22% of infants weighing 1,000 – 1,500 g. and 71% of all infants weighing <1,000 g.<sup>46, 47</sup> As first described in 1967 by Northway, diagnostic criteria for BPD included the neonate's sustained need for oxygen supplementation >28 days and radiologic evidence of lung abnormalities related to premature birth, respiratory failure, oxygen toxicity, and barotrauma associated with prolonged mechanical ventilation.<sup>47</sup> Research has since implicated a variety of risk factors for development of BPD, including patent ductus arteriosus (PDA), prenatal intrauterine infection or postnatal nosocomial respiratory infection, sepsis, fluid overload, and deficiencies in antioxidant vitamins.<sup>48-54</sup> Guidelines have been developed<sup>55</sup> that delineate more specific criteria allowing for classification of BPD into mild, moderate and severe, which has proven useful for determining risk for developmental problems.<sup>56, 57</sup>

A number of investigations of sequelae of BPD found significant developmental delays relative to other VLBW and full-term children, or found extended length of oxygen exposure a predictor in outcomes of VLBW children.<sup>42, 58, 59</sup> In the preschool years, studies showed children with BPD to be at higher risk for lower mental, motor and language outcomes,<sup>37, 42, 43, 60</sup> as well as at higher risk for cerebral palsy and other neurological impairment.<sup>61</sup> Further follow-up studies documented increased risk into school-age year for children with BPD, including lower cognitive, motor, visual-motor, and language abilities, lower achievement and higher rates of neurological impairment and learning disabilities and behavior problems.<sup>7, 20, 38, 40, 41, 44, 62-64</sup> Studies following VLBW children with BPD into adolescence are limited, but have found that children of VLBW experience greater rates of cognitive, academic and behavioral difficulties, as well as increased risk of morbidity through young adulthood, especially in ELBW (<1000g).<sup>16, 65-69</sup> Limitations of these studies included small sample size, limited control groups, and design issues, such as not controlling for factors such as drug exposure and medical risk.

Several conceptual models have implicated child risk/illness status as a stressor affecting psychological distress, family functioning, and child developmental outcomes.<sup>33, 70, 71</sup> Maternal-child interactions are particularly relevant to the development of child language, attentional and behavioral capacities, and a number of studies have documented poorer functioning in these areas in children of depressed mothers.<sup>72, 73</sup> VLBW populations may be more vulnerable to the negative impact of early maternal depressive symptoms from several perspectives. First, the birth and parenting of a VLBW child has been related to a higher incidence of maternal psychological distress postpartum.<sup>74, 75</sup> Second, dependent on medical risk, VLBW infants may be differentially affected by differences in maternal caregiving<sup>35, 76</sup> associated with VLBW birth and/or maternal depression. Third, transactional models of development also suggest that infant characteristics and behaviors, which may be negatively affected by preterm birth and medical complications, also affect caregiver psychological distress and interactions, with each reciprocally modifying the other over time.<sup>77</sup>

The relationships among infant VLBW birth, medical risk, maternal psychological distress, and child outcomes are particularly complex, and also are dependent on a host of other factors, including the number of other life stressors, social class, racial characteristics, coping strategies, and social supports. Social supports have been found to have significant impact, either as mediating or independent variables, on maternal distress, maternal-child interactions, and child outcomes<sup>78, 79</sup> in healthy samples, as well as in preterm populations. Maternal positive perception of intimate supports postpartum was associated with better mother-child interactions in preterm dyads at 1 and 4 months,<sup>34</sup> while more general social supports moderated psychological distress postpartum for mothers of VLBW infants. Few studies have examined these relationships into school

age and adolescence, but those that have continued to see fading maternal symptoms of maternal psychological symptoms, but continued impact of long-term health issues on the family and parental stress.<sup>80, 81</sup>

### III. Study Design and Methods

A. Study design. This study employs a prospective, longitudinal quasi-experimental design with prior longitudinal measures administered from birth to 8 years, and currently at 14 years of age. Measures can be summarized as sets of independent, dependent, and control variables. The major independent variables of the study are lung disease status, prematurity, i.e. the presence of BPD and/or very low birth weight (group) and time (repeated measures). Dependent variables include the sets of health, cognitive, school achievement, neuropsychological, language, behavioral and parental outcomes outlined below. Control variables include race, socioeconomic status, multiple birth status, and child age, as those factors could contribute independently to differences in the dependent variables under study. Within group variance among the combined very low birth weight cohorts is also of interest in this study, using multiple birth status, length of hospitalization, severity of BPD (total days of oxygen supplementation), presence of medical problems, neurologic risk score, severity of IVH, and parental stress/coping variables as either independent or control variables within the very low birth weight combined cohorts.

B. Population studied. The study used a cohort of 321 children originally recruited at birth, 302 (110 BPD, 80 very low birth weight without BPD (VLBW), 112 healthy, term) of whom were prospectively, longitudinally followed at six previous points in time from birth, (i.e. 1, 8, and 12 months and 2, 3, and 8 years of age) and were initially recruited from three independent Cleveland hospital sites whose NICUs treated all infants with BPD in the greater Cleveland, Ohio region. The eligibility criteria for BPD infants included birth weight < 1,500 grams, oxygen dependence > 28 days, and radiologic evidence of chronic lung disease. The comparison group of VLBW without BPD were born preterm, weighed < 1,500 grams birth weight, and required oxygen supplementation < 25 days. Term infants had no diagnosed medical illnesses or abnormalities at birth, were > 36 weeks gestational age, and > 2,500 grams birth weight for singleton infants. Detailed description of recruitment can be found in manuscripts already published.<sup>42, 82</sup>

C. Sample selection. All surviving children originally enrolled in the study who could be contacted were actively recruited. Two children (both from the BPD group) had died between the 8 year visit and this 14-year follow-up. The final sample seen for this 14-year follow-up was 268 (101 BPD, 69 VLBW and 98 term), with an overall 84% retention rate of surviving children achieved. A delay in funding and recruitment meant the children were closer to 15 than 14 years old when seen. For the purpose of these analyses, 2 of the BPD group were excluded due to diagnosed genetic disorders. In reporting child cognitive and achievement data, one child with brain cancer was excluded from the data.

D. Instruments used. The tables below indicates the measures used for each outcome area.

DOMAIN: Child Outcomes	MEASURES	SCORE
<b>Medical</b>	Physical	% Abnormal in given areas
Pulmonary	Spirometry	FEV <sub>1</sub> , FEV <sub>75</sub> , FEV <sub>25-75</sub> , FVC, FEV <sub>75</sub> /FVC
	Methacholine Challenge	PC <sub>20</sub>
Growth	Wt/Ht/HC	Percentile for Age
<b>General Cognitive</b>	Wechsler Intelligence Scale for Children – 4 <sup>th</sup> ed. (WISC-IV) <sup>83</sup>	IQ/Standard Scores
Motor Skills	Purdue Pegboard <sup>84</sup>	Z-scores
Speech-Language	Clinical Evaluation of Language Fundamentals – 3 <sup>rd</sup> ed. (CELF-3) <sup>85</sup>	Standard Scores
	Comprehensive Assessment of Spoken Language (CASL) <sup>86</sup> , Ambiguous Sentences subscale	Standard Scores
	Comprehensive Test of Phonological Processing (CTOPP) <sup>87</sup>	Standard Scores
	Speech Repetition Tasks	% Correct, # of distortions
	Diadochokinetic Rates	Rate for age
<b>Neuropsychological</b>		
Motor/Visual Motor	Cambridge Neuropsychological Test Automated Battery (CANTAB) <sup>88</sup> (Motor screening)	Mean latency
	WISC-IV <sup>83</sup> Performance	Standard and Scaled Scores
Memory	CANTAB <sup>88</sup> (Spatial memory span, Spatial working memory)	Maximum span length, number of errors
Attention	CANTAB <sup>88</sup> (Intra-extradimensional shift task, Rapid visual processing)	Total errors adjusted for stages completed; hit rate
	Brown ADD Scale <sup>89</sup>	Scaled Scores
	Connors Rating Scale (parent and teacher versions) <sup>90</sup>	T-scores
Learning ability	CANTAB <sup>88</sup> (Stockings of Cambridge)	Number of problems solved in minimum moves
<b>Achievement</b>	Woodcock Johnson Tests of Achievement-3 <sup>rd</sup> ed. (WJTA-III) <sup>91</sup>	Standard Scores
	Grade Level/Learning Disability	% At grade level, % LD
<b>Socioemotional</b>	Child Behavior Checklist parent (CBCL) <sup>92</sup> , teacher (TRF) <sup>93</sup> and Youth Self Report (YSR) <sup>94</sup>	T-scores
<b>DOMAIN: Parental Outcomes</b>	<b>MEASURE</b>	<b>SCORE</b>
<b>Psychological Status</b>	Brief Symptom Inventory (BSI) <sup>95</sup>	GSI, PST, Depression Score

E. Statistical techniques employed. Group differences were assessed using multivariate analysis of covariance (MANCOVA), analysis of variance (ANOVA), and Kruskal-Wallis tests for continuous data, and Pearson Chi-square tests for categorical data. In the event of a significant group effect, Tukey multiple comparison technique assessed pairwise differences, controlling for the number of comparisons.

#### IV. Detailed Finding

A. Child outcomes. Findings from previous phases of this study indicated that, at three years of age, children with a history of BPD were performing more poorly on mental and motor development than their VLBW and term peers, and that, after controlling for other demographic and medical risk factors, the presence of BPD independently predicted lower motor functioning.<sup>42</sup> In addition, BPD put children at higher risk for language delays.<sup>43</sup> By eight years of age, children with a history of BPD continued to struggle more than their VLBW and term peers in cognitive, receptive language and motor skills.<sup>82, 100</sup> In addition, children with a history of BPD had significantly higher rates of special education placement, including speech-language, occupational and psychological therapies.<sup>82, 100</sup> Analyses of pulmonary function indicated lower pulmonary function of children with a history of BPD than their VLBW and term peers.<sup>101</sup> Furthermore, growth trajectories at eight years indicated that, although children with a history of VLBW and BPD reached normal reference values for height and weight, they remained significantly smaller than their term peers.<sup>102</sup> Findings to date at fourteen years of age indicate the following:

*Demographic and Neonatal Characteristics:* The sample at 14 years did not differ by group on SES, race, gender, or age at testing. The sample was 47% African-American, 48% males, and had a mean age of 15.0 when seen. All groups differed in the rate of multiple birth ( $p < .0001$ ) with the VLBW children without BPD having a 48% rate of multiples, while the group of children with BPD had 24% and term children 10%. Table 1 shows the neonatal characteristics of those children seen for the 14-year follow-up.

Table 1: Child Neonatal Characteristics

	BPD (n=99) M (SD)	VLBW (n=68) M (SD)	Term (n=98) M (SD)	F/ $\chi^2$	p
Birth weight	959 (248)	1264 (181)	3455 (538)	1291.38	<.0001 <sup>a,b,c</sup>
Gestational age	27.3 (2.1)	30.4 (2.2)	39.8 (1.3)	1131.73	<.0001 <sup>a,b,c</sup>
Head circumference at birth	25.1 (2.1)	27.4 (1.8)	34.9 (1.3)	492.39	<.0001 <sup>a,b,c</sup>
Total days on Oxygen	101.7 (150)	4.6 (4)	0 (0)	-----	-----
	n (%)	n (%)	n (%)		
Steroids	27 (30)	0 (0)	-----	22.99	<.0001 <sup>b</sup>
Surfactant	45 (50)	9 (14)	-----	21.22	<.0001 <sup>b</sup>
IVH					
grade 1	19 (19)	5 (7)	-----	18.02	<.002 <sup>b</sup>
grade 2	10 (10)	2 (3)	-----		
grade 3	10 (10)	1 (1)	-----		
grade 4	4 (4)	1 (1)	-----		
none	56 (57)	60 (87)	-----		

<sup>a</sup>BPD differs from Term; <sup>b</sup>BPD differs from VLBW; <sup>c</sup>VLBW differs from Term

*Cognitive findings:* Preliminary analyses indicate that children with BPD performed significantly below term peers on all areas of cognition, as measured by the WISC-IV, including Verbal Comprehension (91 vs. 100  $p < .003$ ), Perceptual Reasoning (85 vs. 98,  $p < .0001$ ), Working Memory (92 vs. 99,  $p < .04$ ) and Processing Speed (84 vs. 94,  $p < .0001$ ) and Full Scale IQ (85 vs. 98,  $p < .0001$ ). Children with BPD performed poorer than their VLBW peers in Processing Speed (84 vs. 90,  $p < .0001$ ), Perceptual Reasoning (85 vs. 92,  $p < .0001$ ) and Full Scale IQ (85 vs. 93,  $p < .0001$ ) on the WISC-IV ( $p$ 's <.0001). VLBW children without BPD did not differ significantly from their term peers. Another measure of memory, Spatial span length of the CANTAB, which measures the longest sequence of items successfully recalled, indicated significant differences between both VLBW groups and their term peers (BPD-5.9, VLBW-6.2, Term-6.7,  $p < .002$ ). A measure of learning ability as measured by the number of special planning problems solved in the minimum moves on the Stockings of Cambridge task of the CANTAB indicated significant differences between VLBW adolescents with a history of BPD and the term peers (BPD-7.6 vs. Term-8.5,  $p < .05$ ).

*Achievement and school outcomes:* Scores were obtained based on normative data based on the grade the child was in at the time of testing. Children of VLBW without BPD performed comparably to their term peers on the WJTA-III. However, VLBW children with BPD performed significantly worse than both their VLBW and Term peers on Passage Comprehension (BPD, 90 vs. VLBW, 97 and Term, 99,  $p < .004$ ), Applied Problems (BPD, 86 vs. VLBW, 96 and Term, 99,  $p < .0001$ ), and Math Fluency (BPD, 86 vs. VLBW, 95 and Term, 98,  $p < .0003$ ), subscales of the WJTA-III. In terms of school placement and services, more adolescents

with a history of BPD were placed in special education classrooms than their term peers (BPD-25% vs. Term-9% $p<.02$ ). In addition, more adolescents with a history of BPD had Individual Education Plans (IEP) (BPD-39%, VLBW-25%, Term-12%,  $p<.0003$ ), and more received services for math (BPD-28%, VLBW-13%, Term-7%,  $p<.0004$ ) and cognitive abilities (BPD-21%, VLBW-7%, Term-4%,  $p<.0006$ ) than either their term and VLBW peers. More children with a history of BPD were receiving physical (BPD-18%, VLBW-7%, Term-5%,  $p<.01$ ), occupational (BPD-16%, VLBW-4%, Term-3%,  $p<.003$ ) and speech-language (BPD-23%, VLBW-10%, Term-5%,  $p<.002$ ) therapies than either their VLBW or Term peers; however, more adolescents who were born full-term were receiving psychological therapy or counseling than adolescents born VLBW with or without BPD ( $p<.04$ ). More adolescents of VLBW without BPD had IEPs than their term peers (25% vs. 12%,  $p<.0003$ ).

*Motor skills:* Fine motor skills were analyzed using the Purdue Pegboard. Adolescents with a history of BPD performed significantly worse than both their VLBW and term peers ( $p$ 's  $<.0001$ ) on all measures of the Purdue Pegboard, where they are timed on their ability to place pegs into holes and assemble items with pegs and washers. No differences were found between VLBW adolescents without BPD and their term peers.

*Behavioral and Attention abilities:* Term adolescents rated themselves higher in externalizing behaviors than their VLBW peers with a history of BPD (BPD= 47.6, VLBW=48.4, Term=51.4,  $p<.03$ ) on the Youth Self Report. Parents of VLBW adolescents reported lower internalizing behaviors than parents of either VLBW with BPD or term parents (BPD=49.6, VLBW=44.7, Term 49.3,  $p<.02$ ) on the CBCL. In addition, parents of VLBW adolescents with a history of BPD rated their children as more anxious than parents of VLBW adolescents without BPD (BPD=49.1, VLBW=45.3, Term 47.3,  $p<.03$ ). No significant group differences were found in attentional abilities on the parent or self report forms. However, results of the intra-extradimensional shift task of the CANTAB indicated that adolescents with a history of BPD made significantly more errors than their term peers (51 vs.38,  $p<.02$ ) and were slightly worse (non-significant trend) at responding to target signals in the Rapid Visual Processing task of the CANTAB (.91 vs. .93,  $p<.06$ ).

*Language outcomes:* Children with BPD differed significantly from their term peers in most areas of language abilities measured, including the Receptive Language (86 vs. 97,  $p<.0004$ ), Expressive Language (88 vs.96,  $p<.02$ ) and Total Language (86 vs.96,  $p<.002$ ) composites of the CELF-3. On a measure of phonological abilities, children with BPD performed worse than their term peers on a measure of their ability to break words into parts (Elision on the CTOPP) ( $p<.03$ ), but did not differ in their ability to repeat nonsense words, or on the Phonological Awareness composite score of the CTOPP. On the Ambiguous Sentences of the CASL, children with BPD performed more poorly on a measure of their ability to explain dual meanings in ambiguous sentences (90 vs. 96,  $p<.02$ ). Children with BPD differed from their VLBW peers on Receptive Language of the CELF-3 (86 vs. 94,  $p<.0004$ ). Children of VLBW without BPD performed comparably to their term peers in all aspects of language measured.

*Pulmonary Outcomes:* Adolescents with a history of BPD were significantly more likely to have poorer lung function than their VLBW and term peers. All groups differed on the percentage of children who had a ratio of forced expiratory volume in the one second ( $FEV_1$ ) to forced vital capacity (FVC) of less than 80 (BPD-50%, VLBW-36%, Term-16%,  $p<.0001$ ) and adolescents with a history of BPD differed from their VLBW and term peers in both the percentage of children having an  $FEV_1 <80$  (BPD-18%, VLBW-5%, Term-1%,  $p<.0003$ ) and forced midexpiratory flow rate ( $FEF_{25-75}$ ) less than 60 (BPD-31%, VLBW-9%, Term-3%,  $p<.0001$ ). In addition, adolescents with a history of BPD had significantly lower values in percent predicted  $FEV_1$ ,  $FEF_{25-75}$  and FVC than their term and VLBW peers ( $p$ 's  $<.004$ ).

B. Maternal outcomes. Our own studies of BPD infants through the first 3 years of life suggest that both sociodemographic and family factors are related to child risk status and outcomes, especially maternal psychological distress, coping mechanisms and social supports. In the neonatal period, mothers of BPD and VLBW infants self-reported increased distress, reflecting depression and anxiety, compared to mothers of term infants.<sup>75</sup> However, mothers of BPD and VLBW infants who experienced higher levels of social support did not differ from term mothers. Mothers of BPD and VLBW infants who were more depressed were less likely to respond actively to their infants during neonatal feedings.<sup>35</sup> While mothers of BPD and VLBW infants were initially more stimulating than term mothers neonatally, they were significantly less stimulating by 12 months and both BPD and VLBW preterm infants were less responsive than term infants. By child age of 2 and 3 years, the initially high psychological distress of VLBW infants had decreased while that of mothers of BPD infants did not, and less positive interactions were apparent in feeding and play through 2 years. Severity of maternal depressive symptoms postpartum was related to poorer child outcomes at 3 years in both the preterm and term groups.<sup>36</sup>

In an analysis of parent outcomes at eight years of age,<sup>81</sup> there were no group differences in mean scores of maternal psychological distress, although parents of term children reported more intrafamily strains ( $p < .02$ ). Levels of maternal education were different by group, with term mothers attaining higher education than either of the VLBW groups. Term mothers also reported a higher level of consensus with their partner/spouse than mothers of VLBW children with and without BPD. Mothers of children with BPD reported greater family and social impact, personal and financial strain on their families than mothers of term children, and experienced their children as more stressful, demanding, distractable and hyperactive, and less acceptable and adaptable than both mothers of VLBW children without BPD and mothers of term children. Multiple birth was found to relate to greater maternal social isolation, lower child IQ was related to higher parenting stress and higher maternal education was related to lower parenting stress. Mothers of children with BPD were less likely to use withdrawal/avoidant coping than mothers of term children. In a study currently under review,<sup>103</sup> the style of maternal coping was found to be significantly related to child outcomes at 8 years, with more positive coping styles relating to higher outcomes.

In the 14-year follow-up, initial analyses indicated the following:

*Demographic characteristics:* The sample of mothers seen at child age 14 were 49% African American, 56% married or living with a long-time partner, and 60% low socio-economic status (SES) (Hollingshead<sup>104</sup> categories of IV and V); however, groups did not differ in maternal race ( $p = .14$ ), marital status ( $p = .90$ ) or SES ( $p = .14$ ). Mothers of the three groups of children did not differ in measures of receptive vocabulary ( $p = .64$ ), but there was a non-significant trend for mothers of term children to have more education (BPD 13.8 years, VLBW 13.8 years, Term 14.6 years,  $p < .06$ ).

*Psychological Status:* At child age of 14 years, initial analyses indicate no difference in psychological status among groups (MANOVA results: Wilks'  $\lambda = 0.9482$ ,  $F = 0.63$ ,  $df = 18, 420$ ,  $p = 0.8770$ ). Mothers of children in all groups had similar overall levels of psychological stress (General Severity Index) on the BSI (BPD = .29, VLBW = .26 and Term = .36,  $p = .66$ ). Additionally, no significant differences were found in the numbers of mothers reaching clinical levels of symptoms between groups.

*Parenting Stress:* At child age of 14 years, preliminary analyses of the SIPA indicated no differences in the Parent Domain ( $p = 1.3$ ) or the Parent-Adolescent Relationship Domain ( $p = 0.17$ ) of the SIPA, however MANOVA results of the Adolescent Domain indicate significant group differences (Wilks'  $\lambda = 0.9122$ ,  $F = 2.88$ ,  $df = 8,490$ ,  $p < .004$ ). Further examination revealed that parents of adolescents with a history of BPD see their children as more socially isolated than parents of adolescents with a history VLBW without BPD ( $p < .007$ ). In addition, parents of term children rated their children higher in delinquency than did parents of adolescents with a history VLBW without BPD ( $p < .02$ ).

*Impact on Family:* Adolescents with a history of BPD are reported by parents to have a greater impact on the family than parents of term children (MANOVA results: Wilks'  $\lambda = 0.8903$ ,  $F = 2.93$ ,  $df = 10, 490$ ,  $p = 0.0014$ ). These preliminary findings indicate both positive and negative impact, in that family and social strains were higher for parents of children with a history of BPD, yet they experienced a greater sense of parenting competence (mastery) than term parents.

*Coping Style:* No significant differences emerged in coping styles between groups at child age 14 years.

*Social Support:* There were no significant group differences in feelings of social support reported by mothers.

*Life Stressors:* There was a non-significant trend for differences in groups on stressful life events in the past 12 months, with parents of term children having more stressors (BPD=8.5, VLBW=8.3, Term=11.0,  $p < .06$ ); however, no specific area of stress was significantly different between groups.

## **V. Discussion and Interpretation of Findings**

A. Conclusions to be drawn from findings (with reference to data supporting each). These initial analyses indicate that in adolescence, VLBW children without a history of BPD are no longer significantly different from their term peers in cognition, as measured by the WISC-IV, achievement (WJTA-III), language (CELF-3), memory and learning (CANTAB), and fine motor skills (Purdue Pegboard). However, those with a history of BPD continue to perform significantly below their term peers. In addition, VLBW adolescents with a history of BPD performed more poorly than their VLBW peers in the areas of Processing Speed, Perceptual Reasoning and Full Scale IQ of the WISC-IV, math and reading achievement (WJTA-III) and memory (CANTAB). Adolescents with a history of BPD were also more likely to be receiving special education services and physical, occupational and speech-language therapy than their VLBW and term peers. Children with a history of BPD also had more indications of impaired lung function than their VLBW and term peers. Thus,

children with a history of BPD continued to experience developmental delays well into adolescence above their VLBW and term peers. This supports our initial hypothesis on child outcomes.

Parents of VLBW adolescents without BPD reported fewer Internalizing behaviors than parents of either VLBW with BPD or term adolescents on the CBCL. Parents of adolescents with BPD reported higher anxiety in their children than parents of VLBW children without BPD on the CBCL. Interestingly, term adolescents were more likely to be enrolled in psychological therapy and rated themselves higher in Externalizing behaviors on the Youth Self Report, than either of their VLBW peer groups. On the SIPA, parents of term children reported more delinquency than parents of either VLBW group.

Parents of term children continued to differ from parents of the VLBW groups in the number of years of education attained. While no differences were found between groups on maternal psychological status, parents of adolescents with a history of BPD experienced their children as more socially isolated than parents of VLBW or term adolescents. They reported that their children had a high impact on their family more than did other parents, yet these mothers also reported a greater feeling of parenting competence. These findings do not support part of our hypothesis on parental outcomes, as no differences were found in psychological symptoms between groups, and VLBW parents actually experienced less family stress than term parents. However, our hypothesis that parents of adolescents with a history of BPD would continue to experience more parenting stress was supported.

#### B. Explanation of study limitations.

Findings of significant group differences may have been minimized because no descriptive data were collected on educational and psychosocial services received by the BPD group, although we documented that BPD children received more therapies and were enrolled for a longer time than the VLBW and control groups. Thus, interventions may have improved BPD outcomes, and had these special services been included as control variables, findings of group differences might have been even more robust. A limitation of this study is that it did not investigate types of interventions received by subjects, or their effects on child outcomes. Another limitation is that in exploring family stress and impact, only mothers were respondents. This did not allow for full examination of family stress, support and impact.

#### C. Comparison with findings of other studies.

*Cognition, Language, Achievement and Neuropsychological findings:* Our findings for children with a history of VLBW with BPD are consistent with findings of Saigal et al. (2000)<sup>105</sup> in their sample of ELBW, however their sample had no VLBW controls and did not control for oxygen duration in their analyses. Avchen et al. (2001)<sup>65</sup> and Litt et al. (2005)<sup>106</sup> found that risk of school-identified disabilities increase with decreasing birth weight, but did not control for neonatal or environmental factors. In a study that did control for neonatal characteristics, Taylor et al. (2004)<sup>45</sup> found oxygen exposure predicted the Wechsler scaled score and the synonyms subtest of the CASL and IED shift on the CANTAB, but not Spatial Span on the CANTAB. Our findings to date are in agreement with these findings, but go further in that our findings suggested differences for adolescents with a history of BPD on all composite scores of the WISC-IV, and suggest higher risk of special education placement and medical interventions based on a history of BPD.

*Behavior and Attention:* Several studies indicated that VLBW children and, especially those at lower birth weights are at risk for more behavioral and attention problems at school age and into adolescence.<sup>7, 107, 108</sup> Farel et al.<sup>109</sup> found VLBW children with a history of BPD to be at higher risk than VLBW peers for attention problems. This sample, however, was small and born before surfactant was in use. Our study indicated no group differences in risk for attention problems on either the Conner's Parent Report or the Brown ADD Scale - Adolescent Version. Grunau et al.<sup>108</sup> found that parents of ELBW teens reported more Internalizing, Externalizing and Total Problems on the CBCL at child age of 17 years. At 20 years, Hack et al.<sup>110</sup> reported that VLBW young adults self-reported more psychological disorders, but more risk avoidance on a different measure. Indredavik et al.<sup>80</sup> found that at child age of 14 years, VLBW teens did not report more emotional or behavioral problems than their term peers, although lower birth weight did increase the risk of these problems. Additionally, this cohort of VLBW infants reported their parents as more protective of them than term controls experienced. Our findings, in contrast, suggested that term children were at greater risk for externalizing problems, and that adolescents with a history of BPD were at similar risk of internalizing behavior as their term peers, while VLBW adolescents without BPD were at significantly lower risk for internalizing problems. Further analyses will help delineate factors that put children at greater or less risk for these problems in this cohort.

*Maternal Outcomes:* Very few studies have examined family impact and parental stress past the neonatal period of development. Saigal et al.<sup>105</sup> reported that although parents of ELBW teens felt that their child had a negative impact on some aspects of family functioning, the experience had made them feel more

positive about themselves as parents. Indredavik et al.<sup>80</sup> found that parents of VLBW teens did not report more psychological symptoms; however child disability impacted the parent's emotional status significantly. Our findings extend these reports in that although parents of teens with a history of BPD reported more impact on the family, and perceived their children as more socially isolated, it was the term parents in our cohort that had slightly more life stressors and perceived their children as more delinquent. This may reflect a delay or difference in risk-taking behaviors of VLBW children as suggested by Hack et al.'s<sup>110</sup> report, or the fact that VLBW children, both with and without a history of BPD receive more interventions throughout life, and that this more individualized attention somehow decreases risk of delinquent or externalizing problems.

D. Possible application of findings to actual MCH health care delivery situations (including recommendations when appropriate).

Our findings that children with a history of BPD continue to experience disproportionate levels of developmental and health impairments into adolescence demonstrate the need for education of parents, physicians and other professionals so that early treatments are employed to reduce risk for these children. In addition, the continued burden that families experience as a result of these impairments should be addressed and reduced as much as possible with supports and interventions to address these needs.

Our finding of fewer differences in outcomes between healthy VLBW children and their term peers in the adolescent period is also important. Findings from our current and previous studies show that healthy VLBW children received more school-based and other interventions than their term peers, and this indicates that the model of early interventions may help in this population to encourage "catch-up" in many areas.

E. Policy implications.

Government and other health care insurers need to provide comprehensive services for VLBW infants, especially those with chronic conditions such as BPD, through adolescence. Developmental intervention in infancy may prevent or compensate the negative educational and cognitive sequelae associated with VLBW birth.

F. Suggestions for further research.

VLBW children with a history of BPD should be followed into adulthood to determine the long-term implications of the cognitive and pulmonary deficits apparent in adolescence.

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## **VI. List of products:**

### **Peer Reviewed Articles:**

- Lewis BA, Singer LT, Fulton S, et al. Speech and language outcomes of children with bronchopulmonary dysplasia. *Journal of Communication Disorders* 2002;35:393-406.
- Eisengart SP. Coping and psychological distress in mothers of very low birth weight infants. In, *Dissertation Abstracts International Section A: Humanities and Social Sciences*; 2002:3204.
- Eisengart SP, Singer LT, Fulton S, Baley JE. Coping and psychological distress in mothers of very low birth weight young children. *Parenting: Science and Practice* 2003;3:49-72
- Short EJ, Klein NK, Lewis BA, et al. Cognitive and Academic Consequences of Bronchopulmonary Dysplasia and Very Low Birth Weight: 8-Year-Old Outcomes. *Pediatrics* 2003;112:e359
- Singer LT, Fulton S, Davillier M, et al. Effects of infant risk status and maternal psychological distress on maternal-infant interactions during the first year of life. *Journal of Developmental Behavioral Pediatrics* 2003;24:233-241.
- Eisengart SP, Singer LT, Kirchner HL, et al. Factor structure of coping: two studies of mothers with high levels of life stress. *Psychological Assessment* 2006;18:278-288.
- Short EJ, Kirchner HL, Asaad GR, et al. Developmental Sequelae in Preterm Infants Having a Diagnosis of Bronchopulmonary Dysplasia: Analysis Using a Severity-Based Classification System. *Archives of Pediatrics Adolescent Medicine* 2007;161:1082-1087.
- Lewis B, Fulton S, Short E, et al. A longitudinal case study of a child with mosaic trisomy 22: Language, cognitive, behavioral, physical, and dental outcomes. *American Journal of Medical Genetics A* 2007;143:2070-2074.
- Singer LT, Fulton S, Kirchner HL, et al. Parenting Very Low Birth Weight Children at School Age: Maternal Stress and Coping. *The Journal of Pediatrics* 2007;151:463-469.
- Short EJ, Kirchner HL, Asaad GR, et al. Long-term sequelae of postnatal surfactant corticosteroid therapies for BPD. *Journal of Perinatology* In Press, 2008.

### **Abstracts and Conference Proceedings:**

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- Weigand, K., Singer, L.T., Fulton, S., Short, E., Klein, N. The relationship between non-clinical language delay and behavior in 8-year-old sample. Poster presented at Society for Research in Child Development (SRCD) Biennial Meeting, April 25, 2003, Tampa, Florida.
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