Evidence Table 6A. Studies Evaluating Association of LBW to Behavioral Disorders
Part I

Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Nadeau 2001 21163667	Location: Canada Years of Birth: 1987-1990 Median GA (range), wk: Cases: 27.4±1.1 Control: 39.8±1.6 Median BW (range), g: Cases: 1024.3±204.2 Control: 3453.4±497.8 Male: Cases: 51% Control: 50% Race: ND Enrolled: 129 Evaluated: 86 ? 61 (50 controls) Number of sites: 1	Cases: GA<29 weeks, BW<1500 g Controls: Normal BW children , born at the same hospital during the same time period	Cases: Lost to follow-up at 5 years 9 months: families had moved away (33), parents' refusal (10) Lost to follow-up at age 7: families had moved away (10), parents' or school's refusal (13)	Cases: EP/VLBW infants (86? 61)	Prospective cohort (at 18 months, 5 years 9 months, and age 7)
Robson 1997 9055145	Location: Canada Years of Birth: ND Mean GA (range), wk: 32.6±3.4 Mean BW (range), g: 1758.7±521.7 Male: 36% Race: ND Enrolled: 132 Evaluated: 85 Number of sites: 2	LBW cohort: ≤ 2500 g Admitted to neonatal intensive care units at 2 hospitals in a mid-sized Canadian city. English-speaking mothers. Families lived within 100 km of either hospital. Assessments at 7 mos and 12 mos of age.	Significant visual or motor impairments or any other gross neurological or physical anomalies.	Cases: 85 LBW infants No control group	Prospective single-arm cohort study

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Breslau 1996 8836807	Location: US Years of Birth: 1983-1985 Mean GA (range), wk: ND Mean BW (range), g: Urban LBW: 14.7%<1500 g, 21.4% 1501-2000 g, 63.9% 2001-2500 g. Suburban LBW: 17.4%<1500 g, 17.9% 1501-2000 g, 64.7% 2001-2500 g. Urban NBW: ND Suburban NBW: ND Male: Urban LBW: 42% Suburban LBW: 52% Urban NBW: 48% Suburban NBW: 54% Race (% African-American): Urban LBW: 80% Suburban LBW: 11% Urban NBW: 48% Suburban NBW: 3% Enrolled: 1095 Evaluated: 823 Urban LBW: 238 Suburban LBW: 235 Urban NBW: 176 Suburban NBW: 174 Number of sites: 2	LBW cohort: ≤ 2500 g NBW cohort: > 2500 g Born between 1983-85, 6- 7 yrs old during 1990-92 when the fieldwork took place. From 2 major hospitals in southeast Michigan: one urban and one suburban. (In each hospital, random samples of LBW and NBW children were drawn).	From the target sample: Children with severe neurologic impairment: severe mental retardation, severe cerebral palsy, blindness.	At 6 yrs (823): Cases: LBW 473: Urban LBW (238) Suburban LBW (235) Controls: NBW 350: Urban NBW (176) Suburban NBW (174)	Nonrandomized comparison study (6 years)

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Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Breslau 2000 20298367	Location: US Years of Birth: 1983-1985 Mean GA (range), wk: ND Mean BW (range), g: ND Male: ND Race (% African-American): Urban LBW: 80% Suburban LBW: 11% Urban NBW: 74% Suburban NBW: 3% Enrolled: 1095 Evaluated: 823→717 Number of sites: ND	LBW cohort: ≤ 2500 g NBW cohort: > 2500 g Born between 1983-85, 6- 7 yrs old during 1990-92; when the initial assessment took place. Follow-up assessment at age 11 (1995-1997). From 2 major hospitals in southeast Michigan: one urban and one suburban. (in each hospital, random samples of LBW and NBW children were drawn).	From the target sample: Children with severe neurologic impairment: severe mental retardation, severe cerebral palsy, blindness.	At 11 yrs (717): Cases: LBW 411: Urban LBW (217) Suburban LBW (194) Controls: NBW 306: Urban NBW (164) Suburban NBW (142)	Nonrandomized comparison study (11 years)

Evidence Table 6A. Studies Evaluating Association of LBW to Behavioral Disorders
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Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Hille 2001 21319264	Location: US, Canada, Germany, Netherlands Years of Birth: US: 1984-1987 Canada: 1977-1982 Germany: 1985-1986 Netherlands: 1983 Mean GA (range), wk: US: 27±2.3 Canada: 27±2.3 Germany: 29±2.0 Netherlands: 29±2.3 Mean BW (range), g: US: 853±114 Canada: 834±126 Germany: 888±101 Netherlands: 882±105 Male: US: 40% Canada: 45% Germany: 45% Netherlands: 42% Race: White 93% Enrolled: 523 Evaluated: 408 Number of sites: 1	Survivors from 4 population based cohorts of ELBW infants in 4 countries: US – the neonatal brain-hemorrhage cohort (NBH): BW<2000 g Canada – McMaster ELBW cohort (McM): BW<1000 g Germany – Bavarian longitudinal study of children at biological risk (BLS): BW<1500 g and GA<32 weeks Netherlands – the project on preterm and small for gestational age infants (POPS): BW<1500 g and GA<32 weeks	No assessments of CBCL at age 8-19	Cases: ELBW infants from 4 population based cohorts in 4 countries (108): USA (80) Canada (150) Germany (78) Netherlands (100) Controls/Normative Samples: USA had 1200 4 – 11 year old normative controls. Netherlands had 1172 11 year old normative controls. Canada had 145 full-term controls Germany had 335 full-term controls.	Prospective single-arm cohort study

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Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Katz 1996 97145056	Location: UK Years of Birth: 5/83- 4/85 Median GA (range), wk: 29.2±2.5 (26-34) Mean BW (range), g: 1227.5±341.4 (740-2240) Male: Cases: 52% Controls: 55% Race: Cases: 75% White, 19% Black, 6% Asian Controls: 75% White, 12.5% Black, 12.5% Asian Enrolled: 212 Evaluated: 64 (40 controls) Number of sites: 2	≤34 weeks, no major congenital anomaly, 3 cranial u/s in first week of life	Lost to follow-up Too impair due to multiple cognitive, sensory, or motor disabilities, to complete testing	Cases: Preterm infants (64) Controls: Full-term comparison sample (40)	Prospective cohort (6-8 years)
Sajaniemi 1998 99041674	Location: Finland Years of Birth: 1989-1991 Mean GA: Sample 1: 28.9 (23-35) Sample 2: 39.4 (36-43) Mean BW: Sample 1: 1205 (560-2360) Sample 2: 3461 (2510-5360) Male: ND Race: ND Enrolled: ND Evaluated : 160 Number of sites: 1	For Preterm Group (sample 1): GA: 23-34 wks Mother referred to University Central Hospital of Helsinki for threatened preterm delivery Born between 1989-1991 For Full term group (Sample 2): Born in Metropolitan Helsinki Visiting pediatric services in Helsinki for acute infectious diseases	For Preterm group If mothers had chorioamnionitis If mother had insulin dependent diabetes Children with congenital anomalies, by U/S For Full term group Chronic diseases Developmental delay	Sample 1: Preterm infants (80) Sample 2 Full term enrolled at: 20-28 mo of age (80)	Retrospective comparative study (24 mo CA)

Evidence Table 6A. Studies Evaluating Association of LBW to Behavioral Disorders
Part II

Author, Year UI#	Predictors	Predictor Measures	Outcomes	Outcome Measures
Nadeau 2001 21163667	General: GA Other: Family adversity Index	Evaluated at 5 years 9 months, was developed using SES data such as the family status (two-parent, single-parent, blended), age of each parent, their respective levels of education, and professional occupations. 0=low ~ 7=high	**CNS:** Neurodevelopmental: Motor function Cognitive delay Behavioral disorders **Behavior**	Neuromotor development index: Huttenlocher neurological task test McCarthy Scales of Children's Abilities Behaviors wre assessed by peers, teachers, and parents: RCP, TRF, parent's CBCL
Robson 1997 9055145	Developmental status Quality of home environment Early Medical risk Infant temperament	Development measured by The Bayley Scales of Infant Development Quality of Home environment at 7 and 12 mos of age: The HOME Inventory, paternal education, The Blishen Index, preschool version of the HOME Inventory in early childhood Early Medial Risk measured by the Morbidity Scale Infant Temperament and Development: The Carey Infant Temperament Questionnaire when the infants are 7 months of age corrected for prematurity.	Behavior at 5.5 years of age: Inattention Impulsivity	McCarthy Scales of Children's Abilities by the examiner Parental report from the Child Behavior Checklist Task performance test, vigilance tasks Matching Familiar Figures Test
Breslau 1996 8836807	General: 1) LBW (vs Normal BW= NBW) 2) Urban (vs suburban setting) 3) Maternal smoking during pregnancy	BW <2500g Racial composition, whether mothers completed high school, marital status, maternal smoking during pregnancy, maternal substance abuse/dependence during pregnancy.	ADHD (attention deficit hyperactivity disorder) Separation anxiety disorder Simple phobia Overanxious disorder Oppositional defiant disorder	The National Institute of Mental Health Diagnostic Interview Schedule for Children-Parent Teacher Report Form

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Author, Year UI#	Predictors	Predictor Measures	Outcomes	Outcome Measures
Breslau 2000 20298367	General: 4) LBW (vs Normal BW= NBW) 5) Urban (vs suburban setting) 6) Maternal smoking during pregnancy	BW <2500g Racial composition, whether mothers completed high school, marital status, maternal smoking during pregnancy, maternal substance abuse/dependence during pregnancy.	Behavior assessment at 11 yrs of age. (Assessment at 6 yrs: reported in 1996 publication) 1) Behavioral problems in 3 domains: Attention, Externalizing behaviors, Internalizing behaviors 2) Severe attention problems (above a cutoff point of 67)	Mother's rating was done with: Child Behavior Checklist (CBCL) Teacher's rating was done with Teacher Report Form (TRF) (teachers were blind to the BW information of the child) Assessments at 11 yrs were conducted blindly to the results of assessments at 6 yrs (reported in another publication) 1) Attention problem subscale; 20 items 2) Externalization problem subscale: 2 subclasses 3) Internalization problem subscale: 3 subclasses
Hille 2001 21319264	Birth weight	ND	Behavior Attention	CBCL – Parents: Total problem score Internalizing behavior (anxious, Socratic), Externalizing behavior (aggressive and delinquent), Social, thought, attention problems
Katz 1996 97145056	General: GA CNS: 1) Intracranial/ Intraventicular hemorrhage 2) Periventricular leukomalacia (cystic PVD) 3) PVD (if unilateral or bilateral periventicular echogenic lesions present on at least 3 scans)	IA IVH: no lesion= consistently NC scans. Mild lesion = germinal hem or small IVH or PVD or mild vent dilation without hem. Severe lesion: blood distends the vents or in parenchyma, or multicystic PVC.	**CNS:** Neurodevelopmental: Attention IQ	Measured by CPT test (Continuous Performance Test), measuring errors of omission or commission. Is also measured by CBCC (Child Behavior Check List): parents check off behavior related to attention and hyperactivity. Measured by British Abilities Scale

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Author, Year UI#	Predictors	Predictor Measures	Outcomes	Outcome Measures
Sajaniemi 1998 99041674	General: 1) Prematurity per se 2) Premature with BW< 1000 g vs premature with BW > 1000 g 3) Preeclampsia 4) SGA 5) Duration of NICU stay **CNS:** 1) PVL 2) IVH **Pulmonary:** 1) Duration of ventilation	Not further specified	**CNS:** Neurologic outcome Developmental outcome Temperament profile Behavioral profile	Neurologic outcome: 1) Cerebral palsy 2) Free of major disabilities Developmental outcome: 1) Bayley Scales of Infant Development 2) Mental Development Index (MDI) Temperament: Toddler Temperament questionnaire (TTQ) (contains 97 statements) 9 temperament dimensions: 1) Activity 2) Rhythmicity 3) Approach 4) Adaptability 5) Intensity 6) Mood Persistence 7) Distractability 8) Threshold Behavior: Infant Behavior Record: 1) Social responsiveness 2) Attention 3) Affect 4) Energy level 5) Goal directedness during the test (24 mo CA)

Evidence Table 6A. Studies Evaluating Association of LBW to Behavioral Disorders
Part III

Author, Year	Associations found	Potential Biases
Nadeau 2001 21163667	EP/ VLBW, n = 61 and controls, n = 44. EP/ VLBW / Control / Significance Normal neuromotor function: 67% / 97% / NS Abnormal neuromotor function: 33% / 3% McCarthy IQ [mean (SD)]: 100.3 (19.1) / 112.8 (16.2) / P < 0.01 Behavioral ratings at 7 years age: Peers rated EP/ VLBW's as significantly more sensitive/ isolated than controls Teachers rated EP/ VLBW's as significantly more inattentive than controls Parents rated EP/ VLBW's as more hyperactive than controls Significantly = P < 0.01	No data on funding source Data on neuromotor and intellectual functioning only collected once Data on behavior collected once
Robson 1997 9055145	• Developmental status and the quality of the home environment correlate with hyperactivity. • Medical risk, infant temperament, quality of home environment and developmental status correlate with attention. • A nurturing home environment fosters development of self-regulating behaviors in LBW.	Internal validity B
Breslau 1996 8836807	• LBW was significantly associated with ADHD but not with separation anxiety disorder, simple phobia, overanxious disorder, or oppositional defiant disorder. • Both the mothers' and teachers' ratings significantly correlated with increased ADHD in LBW infants and this relationship is stronger in urban than in suburban communities. • LBW children with the lowest IQ have highest incidence of ADHD. • The urban group was primarily black, more mothers had not completed high school and more were single. However, maternal marital status, history of substance abuse/dependence and smoking during pregnancy were not associated with ADHD.	Parent ratings, questionnaire results are biased but corroborated by teachers who are blinded to BW of children helps to corroborate. Internal validity B

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Part III

Author, Year	Associations found	Potential Biases
Breslau 2000 20298367	1) Information from mothers and teachers on children's **behavior problems** at age 11 revealed that the effect of LBW on attention problems differed between urban and suburban settings. 2) LBW children had an excess of **attention problems** in the urban disadvantaged communities and not in the suburban middle class communities. 3) LBW infants in the urban setting had twice as high incidence of attention problems than in urban NBW. 4) In suburban setting there was no difference in severe attention problems between LBW and NBW children. 5) LBW children had externalizing problems both in the urban and suburban settings (however this effect was mainly accounted for by maternal smoking in pregnancy). 6) No LBW effect was observed with respect to internalizing problems 7) Regardless of LBW status, maternal smoking during pregnancy was associated with an increase in externalizing problems 8) No association found between maternal smoking during pregnancy and internalizing or attention problems OVERALL SCORES — Attention scores / Internalizing / Externalizing MOTHER'S SCORES Urban • LBW (n=217) 58.8 52.7 52.2 • NBW (n=164) 55.8 51.5 50.4 Suburban • LBW (n=194) 55.1 50.4 48.4 • NBW (n=142) 53.8 48.6 46.3 TEACHER'S SCORES Urban • LBW (n=186) 56.9 50.3 53.9 • NBW (n=151) 54.7 48.8 48.5 Suburban • LBW (n=180) 53.7 49.0 48.5 • NBW (n=135) 54.0 48.7 48.3	1) Recollection bias: The Hx of maternal smoking during pregnancy was elicited when the child was 6 yrs old. This bias would have resulted in underestimation of the confounding effect of smoking during pregnancy. 2) Diagnosis bias: Although there was correspondence of the findings of teachers reports (who were blind to the LBW status of children) and the mothers reports, mothers report could have definitely been biased (worse scores from mothers of LBW infants)
Hille 2001 21319264	ELBW vs. Controls Total problem score: Boys: 3.3-9.8 points higher in ELBW vs. norm/ control Girls: 3.7-5.9 points higher in ELBW vs. norm/ control Social, thought, and attention difficulty scales were 0.5-1.2 SD higher in ELBW children vs. norm/control Internalizing and externalizing behavior scores: no difference for all 4 groups (except for one cohort for internalizing scores) ELBW children had higher total problem scores than normative/control children (statistical significance in European countries). Study identified similar types of behavioral problems in all 4 countries in ELBW infants. This suggests that problems with attention, social, and thought problems are a function of experiences of children who were born ELBW, and not to cultural differences.	(None) Study was privately funded

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Author, Year	Associations found	Potential Biases	
Katz 1996 97145056	Attention deficit is measured by the CPT test (error of omission). Hyperactivity and impulsivity is measured by the CPT test (error of commission). There were no differences among the preterm infants with mild, moderate and severe intracranial lesions. However, there was a significant increase in both errors of commission and omission in preterm with mild lesions compared to full term infants as well as in preterm with severe lesions compared to full term infants. With increasing severity of lesions in preterm infants, increasing percentage in each group commit errors of commission. Even in the absence of detectable intracranial lesions, preterm infants are still at higher risk for developing attention deficits than full term infants.	Exactly how FT controls were selected in an unbiased way is not described.	No data on funding source This study does not explore relationship of attention deficits identified with CPT test with actual school performance and achievement in this group of preterm infants. This study includes older preterm 26-34 weeks and does not include the extremely preterm 24-25 wk infants.

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Author, Year	Associations found			Potential Biases
Sajaniemi 1998 99041674	The neurological outcome of preterm infants was:			• Post hoc multiple comparisons were done between preterms and full terms for the multiple individual items of the tests used. • Cannot exclude selection bias • No matching between groups cannot exclude the presence of confounders. • Interactions between • Predictor may have masked some real associations; Possible interactions were not formally tested • Cannot exclude Diagnosis bias, as no information is given on the blinding of the personnel doing the outcome evaluation, of the child's PMHx.
	For Cerebral palsy:	Free from major disabilities	MDI	
	1) All prematures: 17.5%	82.5%	103	
	2) Prematures < 1000 gs: 23.5%	23.5%	98	
	3) Prematures > 1000 gs: 13.5%	85.6%	107	
	The developmental outcome: Preterm infants had significantly lower MDI scores when compared to full terms (Full terms 124) When temperament was considered: the premature children were significantly less active; more adaptive; less intensive; more positive in mood and had lower sensory threshold than the healthy control term children. When behavior was assessed (Infant's Behavior Records): the preterms were significantly less goal directed; less attentive, and had lower endurance than the controls. When Bayley neurodevelomental was assessed: 1) the preterms performed significantly less well than the controls. 2) Low Bayley scores correlated with temperament scores of high rhythmicity, positive mood, low persistence and high threshold 3) Low Bayley scores correlated with IBR scores 4) No strong relationship between temperament characteristics and cognitive performance. Preterm infants had significantly lower MDI compared to full terms: • Preterm infants were different in 5/9 items of temperament profile compared to full terms: less active ($p<0.008$), more adaptive ($p<0.02$), less intense ($p<0.01$), more positive in mood ($p<0.0004$), lower in threshold to respond ($p<0.0003$) • Preterm infants were different in 3/5 items in IBR profile when compared to full terms: less goal directed, less attentive, lower in endurance Predictors evaluation: • From the perinatal risk factors: preeclampsia, SGA, PVL and IVH were not associated with developmental outcome or temperament profiles. • PVL, IVH were associated with shorter attention span (1/5 items in IBR profile); when preterms compared to full terms. • Duration of NICU stay was not associated with Bayley score • Duration of ventilation was not associated with Bayley score • Duration of ventilation and days in NICU were associated with the 5 items of IBR profile; Duration of ventilation was associated with 1/9 items of temperament profile			