Evidence Table 10. Studies Evaluating Association of LBW and Bone and Growth Outcomes
Part I

Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Forslund 1992 93044002	Location: Sweden Years of Birth: ND Median GA (range), wk: ND Mean BW (range), g: ND Male: ND Race: ND Enrolled: ND Evaluated: 41 (24 controls) Number of sites: ND	ND	ND	Cases: Preterms (41) Controls: Term infants (24)	Unclear (the study design was described in detail in previous papers)
Chye 1995 95314864	Location: Australia Years of Birth: 1989 to 1990 Mean GA (range), wk: Cases: 28±1.58 Controls: 28.63±1.26 Mean BW (range), g: Cases: 1055± 234 Controls: 1077±215 Male: 56% Race: ND Enrolled: 80 Evaluated: 78 (78 controls) Number of sites: 1	Cases: 26-33 week GA infants with BPD and discharged home Controls: 26-32 week GA infants without BPD admitted to the hospital within 1 year of the cases, matched for BW with the cases in broad categories (<1000 g, 1000-1499 g and =1500 g)	Cases: Trisomy 21 (2)	Cases: Preterm infants with BDP (78) Sample 2: Preterm infants without BPD (78) Subgroups of cases at 12 months corrected age follow-up: Sample 1: BPD no Home O_2 (58) Sample 2: BPD with Home O_2 (20)	Case-control study
DeReignier 1997 98041177	Location: Netherlands Years of Birth: 1/1/1987-12/31-1991 Median GA (range), wk: 27.5 Mean BW (range), g: 1015 Male: 48% Race: 38% Black Enrolled: 678 Evaluated: 174 Number of sites: 1	VLBW infants , BW < 1500 g, survived until discharge Matched sever CLD and no CLD infants to mild CLD infants for BW, race, and sex.	Condition independent of CLD known to adversely affect neurosensory status, development, growth; significant congenital anomalies; congenital viral infections; SGA; NEC requiring enterostomy	Matched VLBW infants (89): No CLD (58) Mild CLD (58) Severe CLD (58)	Retrospective cohort (followed until 1 year adjusted age)

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Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Gosch 1997 97379896	Location: US Years of Birth: 1989 to 1994 Mean GA (range), wk: Cases: 27.6 (26-29) Controls: 39 (36-40) Mean BW (range), g: Cases: 880 Controls: 3466 Male: 50% Race: ND Enrolled: 5 (5 controls) Evaluated: 5 (5) Number of sites: 1	Participants in a early intervention and family care for blind infants and preschoolers Blind children	ND	Cases: Blind children born preterm (5) Controls: Blind children born full term (5)	Retrospective cohort (24, 36, 48, and 58 months)
Ladd 1998 98357452	Location: US Years of Birth: 1980-1995 Mean GA (range), wk: 30 (23-42) Mean BW (range), g: 1500 (272-4840) Male: 53% Race: ND Enrolled: 249 Evaluated: 249 Number of sites: 1	249 babies with NEC who had their initial surgical care at the James Whitcomb Riley Hospital for Children Indiana University Medical Center campus, with the diagnosis of NEC from 1/1/1908-12/31/1995 were included in the study	Infants with focal, isolated perforations of the ileum were excluded	Infants with NEC (249)	Retrospective cohort (16 years)

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Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Wang 1998 98244087	Location: Canada Years of Birth: 1/1977 to 5/1992 Mean GA (range), wk: 27.7±2.3 Mean BW (range), g: 954.6±185.9 Male: 48% Race: Caucasian 88.5% SES: low SES category (Blishen index=40) 47.2% Enrolled: 1007 Evaluated: 514 Number of sites: 1	VLBW infants, BW<1250g, survived to NICU D/C	Missing more than one measurement	VLBW infants (514)	Prospective cohort (36 months)
Connors 1999 99250892	Location: Australia Years of Birth: 1/1987 to 12/1992 Mean GA (range), wk: 27±2.2 Mean BW (range), g: 822.8 ±125 Male: 45% Race: ND Enrolled: 226 Evaluated: 198 Number of sites: 1	ELBW survived infants, BW <1000 g	Died by 2 years corrected age (1) Lost to follow-up (12) Transferred interstate and limited information was available (4)	ELBW infants (198): Sample 1: ELBW with low perinatal risk factors (128) Sample 2: ELBW with high perinatal risk factors (70)	Prospective cohort (2 year CA)

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Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
French 1999 99115141 (CNS + Growth+ All)	Location: Australia Years of Birth: 1990-1992 Median GA (range), wk: Sample 1: 30 (26-32) Sample 2: 29 (27-31) Sample 3: 30 (28.5-31.5) Sample 4: 31 (29-32) Mean BW (range), g: Sample 1: 1435 (905-1810) Sample 2: 1345 (1000-1735) Sample 3: 1517.5 (1210-1660) Sample 4: 1455 (1080-1715) Male: total 57% Race: ND Enrolled: 652 Evaluated: 477 Number of sites: 1	Singleton live-born infants GA <33 weeks	ND	Sample 1: Antenatal steroids x 0 course (311) Sample 2: Antenatal steroids x 1 course (123) Sample 3: Antenatal steroids x 2 courses (20) Sample 4: Antenatal steroids x > 3 courses (23)	Prospective cohort (3 years)
Ford 2000 20380862 ***overlapped sample with Doyle, 2001 21064379 in Lung table**	Location: Australia Years of Birth: 1/1977 to 3/1982 Mean GA (range), wk: Sample 1: 27.5 ±2.3 Sample 2: 29.6 ±1.5 Controls: 39.9 ±1.0 Mean BW (range), g: Sample 1: 859±100 Sample 2: 1248±145 Controls: 3420±427 Male: 56% Race: ND Enrolled: 206 (60 controls) Evaluated: 179 (42 controls) Number of sites: 1	Cases: Preterm ELBW infants (<1500g) who survived to discharge Control: Full term NBW (BW>2499g) infants group who survived to discharge	Children with CP at age 14 years Lost to follow-up	At 14-year follow-up: Cases (Sample 1&2): Preterm ELBW infants (179) Sample 1: Preterm infants, BW<1000g (79) Sample 2: Preterm infants, BW 1000-1499g (100) Control: Full term NBW infants (42)	Prospective cohort (14 years)

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Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Morley 2000 20167446	Location:UK Centers:5 Enrollment period: ND Age at assessement:7.5-8 yrs Trial 1: conducted in 3 centers Total enrolled in trial 1 and 2: N=926 infants with BW< 1850 g Long term f/up at 7.5-8 yrs of age: N=781 of 833 (94%) survivors	Premature BW< 1850 g Survivors of participants in the two RCTs with 2 parallel arms each (assessing effect of different neonatal diets of growth) Age 7.5-8 yrs	ND	GroupA: Prematures/ fed banked breast milk until weight 2000 g or discharge from the NICU N=207 Mean BW: 1397±297 Mean GA:31.1 % of SGA:30% Males: 53% Group B: Prematures/ preterm formula N=213 Mean BW:1387 ±278 Mean GA:31 % of SGAs:35% Males:52% (both groups included 2 parallel arms with or without supplementation with mother's own milk)	Two Randomized clinical trials Trial 1 and 2, with 2 parallel arms in each trial (The results for each trial are presented for the combination of the 2 parallel arms) Trial 1 had : Follow up At 9 mo At 18 mo At 7.5-8 yrs

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Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Avila-Diaz 2001 21334039	Location: Mexico Years of Birth: ND Mean GA (range), wk: Sample 1: 39±0.9 Sample 2: 30±2.6 Mean BW (range), g: Sample 1: 3195±323 Sample 2: 1294±167 Male: 51% Race: ND Enrolled: 82 Evaluated: 82 Number of sites: 1	Informed consent 48 full-term "healthy" infants and 34 pre-term infants who were predominantly breast-fed	ND	Sample 1: Full term infants (48) Sample 2: Preterm infants (34)	Prospective cohort (6 months)

Evidence Table 10. Studies Evaluating Association of LBW and Bone and Growth Outcomes
Part II

Author, Year	Predictors	Predictor Measures	Outcomes	Outcome Measures
Forslund 1992 93044002	General: GA	Not given, resulted from previous papers of study with same group	**CNS:** Neurodevelopmental Motor delay **Growth** in height, weight and head circumference	Motor performance was tested by a physiotherapist: used TMI (test of motor impairment) Measurement of height Weight and head circumference by an experienced RN.
Chye 1995 95314864	Bronchopulmonary dysplasia BPD with Home O_2 BPD without Home O_2	Diagnoses of BPD was based on Bancalari' BPD definition Home oxygen therapy program – infants who were well, feeding satisfactorily and gaining weight, but were unable to maintain adequate oxygenation (93-97% saturation) in room air, and were therefore discharged from hospital under the home oxygen therapy	Growth Re-hospitalization	Growth was based on sex-specific National Center of Health Statistics growth chart
DeReignier 1997 98041177	General: GA Cardiovascular/Pulmonary: Chronic lung disease Gastrointestinal: Necrotizing "enterocolitis" Other: Osteomalcia = Socioeconomic status	No CLD- room air at 28 days Mild CLD- requiring 02 at 28 days but not at 36 wks PCA. Severe CLD- requiring 02 at 28 days and 36 wks PCA Not included in CLD if 02 used only for prevention of apnea	**CNS:** Motor delay Cerebral palsy Cognitive delay Mental retardation **Growth:** Weight Height Head circumference **Other** : Hospital readmissions	Motor and cognitive delay: corrected MDI or PDI scores were >2SD below mean (ie correct score <68) Mental retardation Growth: Weight, Length, Head circumference Development: Pediatrician & physical therapist agreed on presence of definitely abnormal position & posture from impaired neuromotor function Hospital readmission in 1st year

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Author, Year	Predictors	Predictor Measures	Outcomes	Outcome Measures
Gosch 1997 97379896	Ophthalmology 1) Other: Blind ELBW 2) Other: blind Term (term control) Other Predictors 1) Nutrition/Growth-lead circumference(cm) 2) Other: days spent in hospital after delivery	Self-explanatory	**CNS:** Other: BDTB (Bielefeld developmental test for blind infants and pre-schoolers at age 18-48 months) **Growth:** Weight Height Head circumference Body mass index	The scales of BDTB including numbers of items and maximum scores listed on table 1
Ladd 1998 98357452	Gastrointestinal: 1) Short gut 2) Necrotizing "enterocolitis" 3) Presence of ileocecal valve 4) Length of bowel reserve	ND	Growth predictors: growth	ND
Wang 1998 98244087	BW	VLBW = 1250 g	Growth Weight Height	At the specified age and reference
Connors 1999 99250892	Birth weight (i.e. ELBW=BW <1 kg) Postnatal Nutrition Growth: <3%tile, 3-9%tile, ≥10%tile)	High perinatal risk: PVH>Grade 2 + ventriculomegaly, NEC, Home O2. Low perinatal risk: none of the above risk factors	CNS: CP Other adverse neurodevelopmental outcome Neurological Exam	Neurodevelopmental outcome assessed by Griffith's Developmental Scales, Motor outcome assessed by Neurosensory Motor Developmental Assessment [NMDA].
French 1999 99115141 (CNS + Growth+ All)	Other: Number of courses of antenatal steroids	ND	**CNS**: Neurodevelopmental CP **Growth:** Weight ratio Height ratio Head circumference ratio Disability	ND Weight, height, or HC compared to national standard "Any disability" = cerebral palsy, IQ< 85, deafness, or visual acuity worse than 6/60

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Author, Year	Predictors	Predictor Measures	Outcomes	Outcome Measures
Ford 2000 20380862 ***overlapped sample with Doyle, 2001 21064379 in Lung table**	Birth weight	VLBW < 1500g (<1kg and 1-1.5 kg) vs Normal BW (>2.4 kg)	Growth outcome: Height Weight Head circumference Pubertal development	Growth scores and variables
Morley 2000 20167446	Trial 1: Type of diet in early neonatal period: • Banked donor breast milk vs Preterm formula (with or without supplementation with its mother's milk) Trial 2: • Preterm formula vs term formula (with or without supplementation with mother's milk)	Not further specified	Trial 1: Growth: Assessment at 9 and 18 months post-term: • Weight (kg) • Length (cm) • HC • Subscapular skinfold thickness • Body mass index Assessment at 7.5 –8 yrs: • All of the above • Also weight to hip ratio Trial 2: • Growth at 18 mo • Growth at 7.5-8 yrs	Not further specified
Avila-Diaz 2001 21334039	*General predictors:* 1) birth weight 2) preterm vs. full-term	ND	*Other outcomes:* 1) bone mineral contents (BMC) 2) bone area 3) changes in bone mineral content over time	BMC was measured monthly for full-term infants during the first 5 months of extrauterine life and bimonthly for pre-term infants during the first 6 months of extrauterine life

Evidence Table 10. Studies Evaluating Association of LBW and Bone and Growth Outcomes
Part III

Author, Year	Associations found	Potential Biases	Comments
Forslund 1992 93044002	Growth and motor performance assessed in preterm children at 8 years of life. • Differences for mean values for weight, height and head circumference not significant • Relationship exists between findings in TMI (test of motor impairment at 4 and 8 years) suggests possibility of identifying motor problems before school age.	A specific population in a certain are that has been studied before Lack of data regarding the population, stated birth weight significant but not listed anywhere	Study was privately funded Cannot generalize, general lack of data The population studied and the study design have been described in detail in previous paper

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Part III

Author, Year	Associations found	Potential Biases	Comments
Chye 1995 95314864	Rehospitalization rate (overall) BPD (78) 58% Control (75) 35% RR 1.7 (1.2-2.4) Rehospitalization for respiratory illness BPD (78) 39% Control (75) 20% RR 1.9 (1.1- 3.2) Rehospitalization for poor growth BPD (78) 14% Control (75) 1% RR=1.4 (1.7-82) Rehospitalization for failure to thrive BPD on home O_2 (20) 30% Control no home O_2 (58) 9% RR=3.3 (1.2-8.9) **Growth (wt in kg) :** NS diff between BPD and control BPD M 9.08 F 8.4 Control M 9.37 F 8.82 **Growth (Ht in cm):** NS diff BPD M 73.0 F 72.1 Control M 74.4 F 72.6 **Growth (HC in cm):** NS diff BPD M 46.7 F 46.0 Control M 47.0 F 454. There was a significant increase in **any** rehospitalization in 1st year of life in preterm infants with BPD vs. preterm infants with no BPD. There was a significant increase (2-fold) in rehospitalization for **respiratory illness** in the 1st year of life in preterm infants with BPD vs. preterm infants with no BPD. BPD infants with Home O2 (N=20) had ~3 fold increased re-hospitalization for failure to thrive. Growth failure was common in both preterm groups (i.e. in infants with no BPD and with BPD <10% in weight at 1 yr age). Re-hospitalization was high in both preterm groups (with and without BPD).	(None)	Study was privately funded

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Author, Year	Associations found	Potential Biases	Comments
DeReignier 1997 98041177	Sensorineural Hearing Loss: CLD: No:0 Mild:0 Severe: 3 P<0.05 Low MDI (Bayley Scale): CLD: No: 0 Mild:4 Severe:5 P<0.05 Low PDI (Bayley Scale): CLD: No: 1 Mild:4 Severe:7 P<0.05 Cerebral Palsy No CLD vs Any CLD: Odds ratios: 6.4 95% CI: (1.05-139.8) Weight 2-Score: CLD: No: 2 score Severe: signify lower weight HC+ Length 2-Score: No, Mild, Severe: No significant difference	(None)	No data on funding source
Gosch 1997 97379896	Blind ELBW infants have developmental delay of 1.5 to 2 years that of term blind controls. **At 48 mos, ELBW blind vs Term blind BDTB scores:** Overall score: 169.4±62.4 vs 270.6±50.7, p <0.05 Neuromotor skills: not significant Social maturity: 42± 13.4, 67.4± 10.1, p < 0.05 Cognition: 16.8 ±22.5, 47.5 ±19.7, p< 0.05 Linguistic abilities: 11.2± 11.7, 29.2 ±12.5, p< 0.05 Socioemotional behavior:33±9.6, 44.8±6.3, NS Orientation and mobility: 35.6 ±10.7, 50.8± 5.9, p< 0.05 **ELBW blind infants had significantly lower weight,** height, head circumference and body-mass index than term blind infants.	Extremely small number of subjects only 5, so statistics not reliable Validity of BDTB scale still in question Does not state whether the evaluators were blinded to the groups or whether they were the same throughout the length of study.	No data on funding source

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Author, Year	Associations found	Potential Biases	Comments
Ladd 1998 98357452	Death rate of children with NEC was 49% 148 subjects with follow-up more than 2 years was evaluated for the impact of the ICV on severe growth retardation (<10 %tile) found that no association between length of bowel resected or status of the ICV, and sever growth retardation.	Extraordinary poor study Populations at follow-up times not described or compared Time of follow-up given only for 1 outcome Massive Bias Results not interpretable	No data on funding source
Wang 1998 98244087	More VLBW infants were classified as "subnormal growth" based on chronologic age vs. adjusted age through 36 months. The % of VLBW children with subnormal growth is therefore affected by adjustment for corrected age through 36 months and varies according to growth references (especially at younger ages 4-8 months). Regardless of adjusted or chronologic age or growth reference, the mean weight and mean height were significantly lower in VLBW (<1250 gm) than term infants at 4 through 36 months age. As infants approach 18 and 36 months age, the deviation from full term infants is less.	Large number of infants were not included in the analyses. They were slightly differed from the study sample in that they had higher BW and GA and less BPD and CP in follow-up	Study was privately funded
Connors 1999 99250892	Weight percentile was strongly associated with lower general growth quotient and lower motor abilities in ELBW infants. Low weight percentile at 2 year was related to adverse developmental outcome in ELBW infants at high perinatal risk or with neurological impairment. There was minimal association between postnatal low weight percentile and adverse neurodevelopmental outcome in ELBW infants who were at low perinatal risk and who had normal neurological exam. This study confirms strong association between low postnatal weight and adverse neurodevelopmental outcome. This association is stronger in infants with high perinatal risk factors and in infants with CNS impairment	(None)	No data on funding source
French 1999 99115141 (CNS + Growth+ All)	No significant association between antenatal corticosteroids and cerebral palsy, weight ratio at 3 years (median, IQR), height ratio median (IQR), head circumference ratio (median, IQR), and any disability (number, %)	Differential loss to follow-up not assessed Small number in severe group	No data on funding source

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Part III

Author, Year	Associations found			Potential Biases	Comments
Ford 2000 20380862 ***overlapped sample with Doyle, 2001 21064379 in Lung table**	Pubertal development was similar in VLBW and Normal BW infants. At all ages (2,5,8,14 yrs) the children who were VLBW were significantly smaller Wt/ Ht/ HC than normal BW children. Differences in Ht/ Wt/ improved over time, between VLBW and NBW, but VLBW remained smaller than Normal BW.			(None)	No data on funding source
Morley 2000 20167446	Trial 1 There was no association between the neonatal diet (banked donor milk vs preterm formula) and the 6 anthropometrics at any follow up point (9 mo, 18 mo and 7.5-8 yrs)	Group A: Fed Banked donor milk (with or without supplementation with mother's milk)	Group B: Fed preterm formula:(with or without supplementation with mothers' milk)		
	(Growth at 9 mo)	N=195	N=174		
	(Growth at 18 months)	N=221	N=217		
	(Growth at 7.5-8 yrs)	N=206	N=214		
	Trial 2 There was no association between neonatal diet (term vs preterm formula) and the Weight, Height, HC and skinfold thicknesses at any follow up point (18 mo and 7.5 yrs) Except for a significantly lower waist to hip ratio at 7.5 yrs in infants fed preterm vs term formula solely (without supplementation with mother's milk) (0.86 vs 0.89, p<0.001)				
	(Growth at 18 mo)	N= 168	N=166		
	(Growth at 7.5-8 yrs)	N=181	N=178		

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Author, Year	Associations found	Potential Biases	Comments
Avila-Diaz 2001 21334039	Study of bone mineral density using DEXA scan. Outcomes at 5 to 6 months; well preterms vs. fullterm. Full term infants (n = 16) had significantly higher ($P < 0.05$) bone mineral content and bone area in comparison to preterm infants (n = 26). Preterm infants had a significantly higher rate of increase in bone mineral content per day than full term infants suggesting incomplete “catch-up”.	Only "healthy" premature infants enrolled Short duration of follow-up - six months Not clear that all preterms were VLBW	Study was government funded A study of bone mineralization in preterm vs. full-terms. Not clear if all preterms were less than 1500 g.