Evidence Table 2. Randomized Controlled Trials for LBW Infants and Multiple Outcomes: CNS, Eye, Lung, Growth, etc.
Part I

Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Casiro 1995 95264245	Location: Canada Years of Birth: 1988- 1990 Mean GA (range), wk: Experiment: 25.8±1.6 Control: 24.8±1.1 Mean BW (range), g: Experiment: 652±64 Control: : 661±52 Male: Experiment: 40% Control: 40% Race: White Experiment: 6% Control: 14% Enrolled: 113 (111 controls) Evaluated: 47 (42 controls) Number of sites: 13	BW 500-749 g Informed consent Mechanical ventilation required within 24 hr. b/o RDS A/A PO2 ratio< 0.22	"Exclusion criteria for this study were the same as those used in an earlier trial of synthetic surfactant" (Long W, Thompson T, et al., 1991) Died by age of 1 year	Experiment: Exosurf (47) Control: Placebo (42)	Randomized Controlled Trial

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Gerdes 1995 95264241	Location: US Years of Birth: 3/1989-4/1990 Mean GA (range), wk: Experiment 1: 27.2±1.7 Experiment 2: 27.2±1.8 Mean BW (range), g: Experiment 1: 907±121 Experiment 2: : 911±125 Male: Experiment 1: 55% Experiment 2: 56% Race: Experiment 1: White 55%, Black 37%, Hispanic 4%, Other 5% Experiment 2: White 60%, Black 30%, Hispanic 5%, Other 5% Enrolled: 826 Evaluated: 508 Number of sites: 33	Mothers who were expected to deliver premature infants with BW 700-1100 g	All exclusion prenatal. 1) Proven fetal lung maturity 2) Known malformation or chromosome anomaly 3) Fetal growth retardation 4) Hydrops 5) Purulent amnionitis 6) Maternal heroin addiction 7) Obstetric decision not to support fetus Postnatal exclusions: 1) Major malformation 2) ≥3 minor anomalies 3) Hydrops	Experiment 1: One doses surfactant (244) Experiment 2: Three doses surfactant (264)	Randomized comparison trial (1 year)

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Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
O'Shea 1998 98167528 98190123 ***also in CNS table** ***overlapped sample as 98049056**	Location: US Years of Birth: 1978-89; 1990-94 Mean GA (range), wk: Born in 1978-1989: Cases: 28(24-33) Unmatched controls: 29 (23-39) Matched controls: 28 (24-34) Born in 1990-1994: 28.0±2.9 Mean BW (range), g: Born in 1978-1989: Cases: 1021 (520-1500) Unmatched controls: 1150 (580-1490) Matched controls: 1095 (580-1490) Born in 1990-1994: 1039±291 Male: Born in 1978-1989: Cases: 54% Unmatched controls: 50% Matched controls: 51% Born in 1990-1994: 51% Race: Born in 1978-1989: Cases: 45% African-American Unmatched controls: 35% African-American Matched controls: 32% African-American Born in 1990-1994: 56% White Enrolled: 1978-1989 (1559); 1990-1994 (1264) Evaluated: 1978-1989 (80 cases, 240 controls); 1990-1994 (723) Number of sites: 2	BW 500-1500g, admitted to the 2 intensive care nurseries that served the 17 countries in NW N. Carolina. Birth at only tertiary OB center in region Survived to age 1 year corrected age Cases: diagnosis of any subtypes of cerebra palsy Controls: VLBW infants born closest in time to the respective case, who after examination at 1 year of age were felt to be free of any signs of cerebra palsy	Major congenital anomaly	Born in 1978-1989: Cases: CP (80) Unmatched controls (160) Matched controls (80) Born in 1990-1994: VLBW infants: 723	Case-control study (1 year corrected age)

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Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
O'Connor 2001 21376723	Location: US Years of Birth: 1996-1998 Mean GA (range), wk: 29 (27-31) Mean BW (range), g: 1253 (965-1543) Male: 39% Race: ND Enrolled: 376 Evaluated: 246 (126 controls) Number of sites: 8	GA < 33 weeks and BW 750-1805 g Completed the study to 12 months' CA	Serious congenital abnormalities, major surgery prior to enrollment/ randomization. PVL/IVH > grade II Maternal Incapacity Liquid ventilation Severe asphyxia Uncontrolled systemic infection at enrollment	Sample 1: EHM-T fed infants (43), reference group only, not included in analyses At 12 months: Sample 2: AA+OHA (fish/fungal) (120) Sample 3: AA+DHA (egg-TG/fish) (126) Control: formula-fed infants (126)	Randomized controlled trial (12 months)

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Part II

Author, Year	Predictors	Predictor Measures	Outcomes	Outcome Measures
Casiro 1995 95264245	Cardiovascular/Pulmonary: Exosurf vs. placebo	ND	**CNS:** Motor delay Cerebral palsy Cognitive delay Severity impairment **Ophthalmology**: ROP **Growth**: Height, weight, head circumference **Other:** Re-hospitalization in 1st year of life	Bayley Scales of Infant Development: MDI and PDI The details of ophthalmologic examination, 1-year follow-up, health status evaluation were described in elsewhere (Courtney SE, Long W, et al., 1995)
Gerdes 1995 95264241	Cardiovascular or Pulmonary: Surfactant use	ND	**CNS:** Cerebral palsy Cognitive delay Mental retardation **Ophthalmology:** Visual impairment, Blindness **Audiology:** Hearing Disorder, Deafness **Pulmonary:** Asthma e/o CLD Respiratory support @ 1yr **Growth**: Height, Weight, HC **Other**: hospital re-admissions, h/o surgery	Mental retardation Bayley Scales MDI<69

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Part II

Author, Year	Predictors	Predictor Measures	Outcomes	Outcome Measures
O'Shea 1998 98167528 98190123 ***also in CNS table** ***overlapped sample as 98049056**	General predictors: Birth weight GA CNS predictors: IVH White matter disorder Periventricular leukomalacia Ventriculomegaly/Ventricular dilation Other: Infectious disease Perinatal factors	Hemorrhage disease diagnosed by Cranial US finding	**CNS:** CP	CP including spastic hemiplegia (involvement of an arm and leg on the same side of the body), spastic diplegia (involvement of the both legs with minimal to no involvement of the arms); and, spastic quadriplegia (involvement of all four extremities)
O'Connor 2001 21376723	Other: Nutrition/growth	ND	**CNS:** Motor delay Cognitive delay Other: information processing languages **Ophthalmology:** Visual Acuity **Growth:** Weight Length Head circumferences	 Bayley scales – PDI; MDI Teller visual acuity cards

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Part III

Author, Year	Associations found	Potential Biases	Comments
Casiro 1995 95264245	Assessed at one year corrected age. No significant differences between placebo group and Exosurf group for: Bayley MDI (Placebo 79 ± 22 vs. Exosurf 87 ± 20) Bayley PDI (Placebo 73 ± 18 vs. Exosurf 81 ± 19) Percent of patients with Bayley MDI < 69 (22% vs. 21%) Percent of patients with Bayley PDI < 69 (29% vs. 19%) No significant differences between placebo and Exosurf groups for: No impairment (38% vs. 55%, Placebo vs. Exosurf) Any impairment (62% vs. 45%, Placebo vs. Exosurf) Serious impairment (41% vs. 32%, Placebo vs. Exosurf) No significant differences between placebo and Exosurf groups for: Bilateral sensorineural deafness: 7% vs. 9%, Placebo vs. Exosurf) Blindness: (7% vs. 2%, Placebo vs. Exosurf) No significant difference in height, weight or head circumference.	All patients had RDS requiring mechanical ventilation	No data on funding source

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Author, Year	Associations found		Potential Biases	Comments
Gerdes	Severe ROP:		25% loss to follow up, equal in both groups 1	No data on funding source
1995	1 dose: 47(16)	3 dose: 35(11)	year follow up does not predict long term	
95264241	Physical evidence of CLD:		outcome from all infants	
	1 dose: 43(18)	3 dose: 40(15)		
	Medication for CLD:			"Prenatal and postantal
	1 dose: 35(14)	3 dose: 30(11)		exclusion criteria were
	Medication for chronic neurologic disease:			identical to those used in an
	1 dose: 12(5)	3 dose: 3(1)		earlier prophylactic trial of
	Index<2 SD (%):			this synthetic surfactant"
	1 dose: 29(15)	3 dose: 30(13)		Died by 1-year adjusted age
	Impairment present:			Lost to follow-up
	1 dose: 106(44)	3 dose: 92(35)		
	No impair ment:			
	1 dose: 123(51)	3 dose: 155(59)		
	Severity of impairment:			
	Mild/moderate:			
	1 dose: 40(17)	3 dose: 39(15)		
	Serious:			
	1 dose: 66(27)	3 dose: 53(20)		
	Types of impairments:			
	MDI<69:			
	1 dose: 40(16)	3 dose: 38(14)		
	Moderate/severe CP:			
	1 dose: 22(9)	3 dose: 16(6)		
	Bilateral sensorineural deafness:			
	1 dose: 5(2)	3 dose: 10(2)		
	Deafness not requiring amplification:			
	1 dose: 5(2)	3 dose: 2(1)		
	Bilateral blindness:			
	1 dose: 10(4)	3 dose: 4(2)		
	Visual defect:			
	1 dose: 24(10)	3 dose: 22(8)		

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Author, Year	Associations found				Potential Biases	Comments
O'Shea		*Dexamethasone*	*Placebo*	*P*	(None)	Study was government funded
1998	Definite Cerebral Palsy:	12	3			
98167528	Possible CP:	5	2			
98190123	Overall CP:	17	5	0.006		
	Neuro exam severe					
***also in CNS**	Abnormal:	4	2			
table	Mild abnormal:	16	6			
***overlapped**	Overall abnormal					
sample as	Neuro exam:	20	8	0.03		
98049056	Authors analyze associations between prenatal factors and cerebral palsy in 80 infants with weights 500-1500g who were born in 1978-1989 to a resident of northwest region of Carolina. Factors that were strongly associated with increased risk of CP were: multiple gestation, chorioamnionitis, maternal antibiotics, antepartum vaginal bleeding, and labor lasting less than 4 hours. Pre-eclampsia and delivery without labor were associated with decreased risk of CP.					
O'Connor 2001 21376723	Growth (Wt, Ht, HC) no difference among the 4 pretem groups in terms of gm/kg/day for weight ; mm/wk for Ht and HC. Bayley at 12 months MDI range 92.2- 93.4 (no difference among 4 groups) PDI range 85.9-87.2 (no difference among 4 groups) For infants with BW<1250 gm Control group: PDI 81.8 which was sig less than PDI in AA-DHA (fish/fungal) (90.6)or AA-DHA (egg) (84.7) groups Language vocabulary comprehension at 14 mo. Comprehension: 97-101.6 (no difference among 4 groups) Production: 96.6-98.3 (no difference among 4 groups) Results support benefit in PDI of supplementing formulas for premature infants with AA+DHA from either fish/fungal or egg/fish source from first enteral feeding through 12 months in infants BW<1250 g				(None)	No data on funding source