Evidence Table 7. Studies Evaluating Association of LBW to Ophthalmologic Outcomes
Part I

Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Page 1993 94051493	Location: Canada Years of Birth: 1986-1987 Mean GA (range), wk: 27±1.8 (23-32) Mean BW (range), g: 942±197 (400-1250) Male: 38% Race: White 100% Enrolled: 138 Evaluated: 110 ? 50 Number of sites: 1	BW<1250 g admitted to Toronto's Hospital for sick children Survived the neonatal periods and had at least one eye examination between 28 and 42 of life that documented the severity of ROP	No 12-month follow-up reports	VLBW infants at 12-month follow-up (110) VLBW infants at 24-months follow-up (50)	Retrospective cohort (12, 24 months)
Cryo-ROP 1994 94304375 ***The original large population of CRYO-ROP**	Location: US Years of Birth: 1/1986 to 11/1987 Mean GA (range), wk: 26.0±1.9 to 29.6±2.1 Mean BW (range), g: 781±156 to 1061±144 Male: 48% Race: White 56%, Black 35%, Hispanic 6%, Other 3% Enrolled: 4099 Evaluated: 2759 Number of sites: 23	BW < 1251 g Survived at least 28 days No serious ocular anomaly, such as cataract, glaucoma, or chorioretinitis, and no major systemic malformations Parental consent Initial eye examination by a study-certified ophthalmologist by 49 days after birth	Death <28 days; serious ocular anomaly or systemic malformations, lack of consent; first eyes exam with 4 qd Death (264) Lost to follow-up (1076)	Zone and Stage of ROP (2759): Zone I (46) Zone II, stage 3+, 9-12 sectors (139) Zone II, stage 3+, 5-8 sectors (64) Zone II, stage 3+, 1-4 sectors (47) Zone II, stage 3 (241) Zone II, stage 2 (484) Zone II, stage 1 (500) Zone III (319) Other ROP (22) No ROP (896)	Prospective cohort (1 year)

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Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Keith 1995 95288128	Location: UK Years of Birth: 1977-1992 Mean GA (range), wk: Sample 1: 26.0±2.3 Sample 2: 26.1±2.2 Mean BW (range), g: Sample 1: 783±136 Sample 2: 786±133 Male: ND Race: ND Enrolled: 457 Evaluated: 434 Number of sites: 1	ELBW infants, BW < 1000g Survival to hospital discharge Eye exams done	ND Not seen by the ophthalmologist: transferred to another level-3 center for ongoing care (17); unknown reasons (6)	Sample 1: ELBW survivors born 1977-1984 (145) Sample 2: ELBW survivors born 1985-1992 (312)	Prospective cohort (16 years)
Foreman 1997 97271716	Location: UK Years of Birth: 4/1994-4/1996 Mean GA (range), wk: Cases: 29.38 Controls: 39.88 Mean BW (range), g: Cases: 1413±302 Controls: 3437±625 Male: 63% Race: ND Enrolled: 114 Evaluated: 16 (16 controls) Number of sites: 1	Healthy preterm infants GA 27 –32 weeks; weight within the normal range for GA Normal on all criteria of Standard child health surveillance program from 7.5 to 48 months Each could be matched with FT control on gender, post-natal age at testing, and on SEC. Healthy controls from School population Controls: children drawn from a school population who were known to have been full-term, normal delivered and whose uneventful medical and developmental histories were confirmed by parents, general practitioners, and teachers	ND	Healthy preterm infants (16) Controls: Matched full term controls (16)	Prospective cohort (6.1 years)

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Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Tin 1998 99046171 ***also in CNS table**	Location: North of England Years of Birth: 1983, 1990-1991 Median GA (range), wk: ND Mean BW (range), g: ND Male: ND Race: ND Enrolled: 1983 (230); 1990-1 (566) Evaluated: 1983 (230); 1990-1 (566) Number of sites: 5	GA 23-31 weeks	ND	1983 cohort (230): Child reviewed without difficulty (204) Child traced with difficulty (14) Child seen with difficulty after child was traced (12) 1990 to 1991 (566): Child reviewed without difficulty (505) Child traced with difficulty (26) Child seen with difficulty after child was traced (35)	Prospective cohort *2 Cohorts of different time periods
Dogru 1999 99168711	Location: Japan Years of Birth: 4/1994-4/1996 Mean GA (range), wk: Sample 1: 27.6±2.9 Sample 2: 26.9±1.4 Sample 3: 26.3±3.1 Controls: 29.6±2.6 Mean BW (range), g: Sample 1: 1016±207 Sample 2: 836±178 Sample 3: 874±218 Controls: 1193±241 Male: 49% Race: ND Enrolled: 144 Evaluated: 78 (66 controls) Number of sites: 1	Premature infants (BW < 1500 g, GA < 37 weeks) with ROP Controls: randomly selected premature subjects with no ROP	Physical and mental disabilities or any CNS and ocular disorder	Premature infants: (Sample 1, 2, and 3): Premature infants with ROP (78) Sample 1: ROP stage 1 (53) Sample 2: ROP stage 2 (11) Sample 3: ROP stage 3 (14) Controls: Premature infants without ROP (66)	Prospective cohort (18-24 months)

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Author, Year UI#	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Pennefather 1999 20002011 Pennefather 2000 20217908 *** This study also should be mentioned in multiple outcome and CNS table**	Location: UK Years of Birth: 1/1/90-12/31/91 Mean GA (range), wk: ND Mean BW (range), g: ND Male: ND Race: ND Enrolled: 566 Evaluated: 558 Number of sites: ND	All surviving children <32wk GA born in geographically deprived region in Northern UK Survived to 2 years old	No examined at age 2 years old	Preterm infants (558)	Prospective cohort and retrospective review of patient records (2-3 years)
Tin 2001 21143595 ***1990-1991 sample is same as 99046171**	Location: North of England Years of Birth: 1990-1994 Median GA (range), wk: 23-27 Mean BW (range), g: ND Male: ND Race: ND Enrolled: 1990-1 (781); 1992-1994 (ND) Evaluated: 249 (for current review) Number of sites: ND	GA < 28 weeks Surviving (born 1990-1991) when 2 years old Surviving (born 1992-1994) when 18 months Assessed for CP and ophthalmic For current review, only SpO_2 88-98% and SpO_2 70-90% groups were included	ND	Sample 1: Preterm infants, SpO_2 88-98% (123) Sample 2: Preterm infants, SpO_2 70-90% (126)	Prospective cohort

Evidence Table 7. Studies Evaluating Association of LBW to Ophthalmologic Outcomes
Part II

Author, Year	Predictors	Predictor Measures	Outcomes	Outcome Measures
Page 1993 94051493	*General predictors:* 1) Birth weight 2) GA *CNS predictors:* 1) Intracranial/ Intraventricular hemorrhage 2) Periventricular leukomalacia *Ophthalmology predictors:* 1) Retinopathy of prematurity 2) Myopic at 12 months post-term *Cardiovascular or pulmonary predictors:* 1) PDA 2) Days ventilated 3) Days in O_2	ROP - ICROP Others not defined Myopic - >0.25 D	**Ophthalmology outcomes:** Visual impairment Strabismus Refractive error Myopia Astigmatism	Myopia - spherical equivalent of ? 0.25 diopters High Myopia - spherical equivalent of ? 4.0 diopters Astigmatism - > 1 diopter in any meridian or cycloplegic refraction Anisometropia - spherical equivalent >2 D between eyes (both refracted)
Cryo-ROP 1994 94304375 ***The original large population of CRYO-ROP**	*Ophthalmology predictors:* Retinopathy of prematurity	ROP defined by examination according to the ICROP	**Ophthalmology:** Visual impairment Structural outcome	ROP outcomes (structural): I. Only peripheral changes, no mascular distortion II. Mascular displacement III. Retinal fold involving macula IV. Retrolental opacity entotal retinal detachment and/or total pupillary occlusion to retinal detachment Functional outcome: a. Normal fixation b. Presence/absence of nystagmus c. Strabismus d. Refractive error (spherical equivalence)

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Author, Year	Predictors	Predictor Measures	Outcomes	Outcome Measures
Keith 1995 95288128	*General predictors:* Birth cohort: 1977-1984 vs. 1985-1999	ND	***Ophthalmology outcomes:*** 1) blindness 2) severe ROP	Eye exam with ICROP classification. Sheridan-Gardner test - visual outcome. Snellen's eye chart - visual outcome.
Foreman 1997 97271716	GA	28-32 week prematurity vs. full term controls	**CNS** Attention skill **Ophthalmology** Visual-perceptual skills Visual-motor skills	Point-to-Target test Complex visual search test Cartoon comparison test Overlapping figures Goillin incomplete figures
Tin 1998 99046171 ***also in CNS table**	General: GA (23-31 wks)	ND	**CNS: CP** Neurodevelopmental: Mental retardation (IQ < 75) Other; disability (severe, sever sensorimotor) Other: development - assessed by Griffith's mental and developmental scales **Ophthalmology** Visual impairment Blindness Other: Severe ROP with Cryotherapy	Definition of "severe disability" and "severe sensorimotor disability" were not given in this article . They referred to the wrong reference for these definitions, therefore, I am unable to find the definitions. Reference population for Griffith's scales were "preterm babies in the study S serious sensorimotor disability"
Dogru 1999 99168711	ROP	Staging of retinopathy was based on International Classification of Retinopathy of Prematurity (The Committee for the Classification of Retinopathy of Prematurity, 1984)	**Ophthalmology:** Visual acuity	Preferential looking method

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Author, Year	Predictors	Predictor Measures	Outcomes	Outcome Measures
Pennefather 1999 20002011 Pennefather 2000 20217908 *** This study also should be mentioned in multiple outcome and CNS table**	*General Predictor:* GA CNS: 1) IVH 2) Periventricular leukomalacia 3) Ventriculomegaly/Ventricular Dilation Ophthalmology: 1) ROP 2) Refractive error Other: Family Hxg strabismus, Developmental disability, CP	ND	**CNS:** Cerebral palsy **Ophthalmology:** Visual impairment (cortical)(CVI) Cicatricial ROP Strabismus	Retrospective review of patient records Visual acuity, visual fields
Tin 2001 21143595 ***1990-1991 sample is same as 99046171**	*General predictors:* GA *Other predictors:* SpO_2 policies (88-98% vs.70-90%)	SpO_2 policies were obtained retrospectively	**CNS:** Cerebral palsy **Ophthalmology**: Blindness Severe ROP Rx with cryotherapy	Threshold ROP: (Cryo-ROP definition) stage 3 plus acute ROP extensive permanent cicatricial retinal scanning

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Part III

Author, Year	Associations found	Potential Biases	Comments
Page 1993 94051493	Outcome: Incidence of myopia at 12 mo postterm age: Overall incidence of myopia in cohort (BW<1251 g) was 15% (4.5% severe myopia) At 12 months age: Increased severity of ROP predicted increased severity of myopia (p=0.001) Overall, 16% of infants had myopia, and 4.5% had severe myopia at 12 months age. To show incidence of myopia according to severity of ROP: 10% of infants with No or Stage 1 ROP had myopia 54% of infants with Stage 3 ROP had myopia 23% of infants with Stage 3 ROP had severe myopia The likelihood of myopia at 12 months age doubled with each increment in ROP stage. - At 24 months age: 80% of 50 children showed deteriorating vision. - 13 of 16 (81%) showed worsening of their myopia after 12 months age. Overall, the incidence of myopia and severe myopia increased among 50 infants followed to 2 years: 38% had myopia 0.25-4 Diopters; 24% had myopia >4 Diopters. BW was negatively associated with incidence of myopia (p=0.002). BW<750 g 3.2 fold odds of myopia vs. 751-1000 g. - BW <750 g 10 fold odds of myopia vs. 1001-1250 g. Incidence of strabismus was positively associated with severity of ROP (e.g. no ROP 6% vs. Strabismus at 12 mo in infants who had Stage 3 ROP 38%). There was further increased diagnosis of strabismus at 24 months age. Months of age in infants who had had Stage 3 ROP (38% to 62%). 100% of infants who had Grade III or IV IVH had strabismus	Retrospective NB and ophthalmic chart review 36% eye reports available at 24 months. Also 24 month sample was biased toward children at greatest risk of myopia. Children with normal eye results at 12 months age were discharged from further follow-up at 18 months post-term age. This may have led to underdiagnosis of myopia due to lack of detection of progressive myopia. Infants born 1986-1987 (not a bias, but a limitation) Used other pop reference figures for norms	No data on funding source This study demonstrates the importance of low birth weight, ROP severity, and IVH in the development of myopia and strabismus.

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Cryo-ROP 1994 94304375 ***The original large population of CRYO-ROP**	The more posterior the zone of ROP and /or the greater the extent of Stage 3+ ROP, the worse the structural and functional ophthalmic outcomes. Zone II without plus disease, Zone III, or no ROP was associated with low rate of unfavorable outcome. CNS injury may affect ophthalmic function (e.g. nystagmus and strabismus). Visual function by ROP Classification ICROP Abnl.Fixation %Nystagmus %Strabismus Zone I …….44% ……..6%……25% Zone II Stage 3, 9-12 sectors 57%……..39%……33% Zone II, Stage 1……2%……1%……..10% No ROP…….1% ……1%……6% % of Eyes with refractive error (≥2 diopters myopia) by ROP severity No or Stage 1 ROP (<5%) Zone II, Stage3+, 9-12 sectors (62%) Zone I (40%)	(None)	Study was government and privately funded Biweekly or weekly eye exams until fully vascularized or until threshold ROP (>5 contiguous or 8 cumulative clock hours) stage 3 with plus disease. Only data from eyes that served as controls (untreated) are included in this segment.
Keith 1995 95288128	**Any ROP:** Birth Cohort 1977 –1984 (141) 68/141 48.2 % 1985-1992 (293) 105/293 35.6% OR=0.60 (0.40-0.90) P<0.02 **Severe ROP:** 1977 –1984 (141) 36/141 25.4 % 1985-1992 (293) 52/293 17.4% OR=0.62 (0.38-1.02) NS **Blindness:** 1977 –1984 (141) 2/141 1.4 % 1985-1992 (293) 2/293 0.6% OR=0.43 (0.05-3.5) NS	Data are from care center No outborn infants in either cohort so data are not generalizable to outborn ELBW infants Twenty-three surviving ELBW's could not be located to determine ROP status.	No data on funding source 16 year study; 1001 ELBW infants; 457 survived to discharge; 434 seen by same ophthalmologist. Twenty children not seen by ophthalmologist.

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Foreman 1997 97271716	***Visual-motor coordination:*** PT v. FT NS diff **Visual-spatial attention skill**: Significant difference between Preterm and Full term in complex visual search scores (failure to find figure and latency to find) and cartoon comparisons PT 2.94 FT 0.81 P<0.05 ***Visual-form perception***: NS difference between Preterm and full term in latency to respond to overlapping figure and Gollin incomplete figure tests. PT 22.2% FT 21.9% NS diff Compared to matched, FT controls, the PT school age group performed poorly on 2 measures visual-motor tests. Thus in the absence of detectable disability, prematurity is associated with visual-motor and attentional impairments that persist through 16 years age.	Small sample size Incomplete data analysis	No data on funding source
Tin 1998 99046171 ***also in CNS table**	*Result of 1983 cohort at 6 years:* ***Severe disability:*** Sample 1: 4.4%, Sample 2 : 2.1%, Sample 3: 50% *IQ < 75 without sensorimotor disability:* Sample 1 : 4.9%, Sample 2 : 0, Sample 3 : 25% *Severe sensorimotor disability:* Sample 1 : 5.9%, Sample 2 : 21.4%, Sample 3 : 41.7% *Severe sensorimotor or cognitive disability:* Sample 1 : 8.4% (5 - 13.1%, 95% CI) Sample 2 : 21.4% (4.7-50.8%) Sample 3: 41.7% (15.2-72.3%) **Result of 1990 cohort at 2 years:** *Severe disability:* Sample 1: 7.9%, Sample 2: 15.4%, Sample 3: 57.1% **High f/u rate is critical because it may underestimate incidence of the outcome.**	No definitions of outcome, incomplete methods description, wrong reference	Study was privately funded
Dogru 1999 99168711	Stage 3 ROP had significantly lower visual acuity scores compared to stage 1-2 or no ROP at 18-24 months (P<0.0001)	(None)	No data on funding source

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Author, Year	Associations found	Potential Biases	Comments
Pennefather 1999 20002011	Strabismus in 70/558 (12.5%) infants GA<32 week . **The incidence of strabismus increased with decreasing** GA (p=0.0004), increasing severity of ROP (p=0.0001), and decreasing general developmental quotient (GMDS) (p<0.0001).	Prospective evaluation but retrospective collection of neonatal data; therefore, probable incomplete collection of variable reason for present and absent data	No data on funding source
Pennefather 2000 20217908 *** This study also should be mentioned in multiple outcome and CNS table**	Stabismus present in 28 (52%) of patients with CP (P< 0.001) **OR (95% CI) of Strabismus if following predictor was present:** Cicatricial ROP: 4.94 (1.1-22.12), p0.037 Fam Hx of Strabismus: 4.15 (2.19-7.88), p<0.00005 Refractive Error: 2.71 (1.3-5.66), p=0.008 GMDS 78-100: 3.34 (1.46-7.64), p =0.004 GMDS <77: 46.2 (17.1-125), p<0.00005 This study confirms findings of other studies that strabismus is increased in premature infants with decreasing GA and is increased with increasing severity of ROP and CP. Independent factors related to strabismus are cicatricial ROP, refractive error, family hx of strabismus, and developmental delay (especially delayed hand-eye coordination)	No demographic data was report (the cohort was described elsewhere)	
Tin 2001 21143595 ***1990-1991 sample is same as 99046171**	Premature infants who had oxygen saturation range (SpO2) between 88-98% for at least first 8 weeks of life developed severe ROP requiring treatment with cryotherapy four times greater than infants who had SpO2 range between 70-90. Incidence of severe ROP with Cryotherapy (SpO2 range 88-98%)=28% Incidence of severe ROP with Cryotherapy (SpO2 range 70-80%)= 6% Incidence of Blindness in the two study groups: Premature infants with SpO2 range 88-98%: 4 / 65 Premature infants with SpO2 range 70-80%: 0 / 65 Incidence of CP in the two study groups: Premature infants with SpO2 range 88-98%: 17% Premature infants with SpO2 range 70-80% 15% The lower SpO2 range was not associated with difference in CP. Differences in SpO2 policies (70-90% vs. 88-98%) did have a major impact on the proportion who developed severe ROP, but had no effect on survival or on incidence of CP among premature survivors.	Different pulse oximeters No attempt to document real SpO_2 or how often SpO_2 fell outside recommended ranges (or vice versa). Narrow limits broached often > wider limits.	ROP screening conformed to national guidelines