Prematurity – what happens to the visual system later in childhood

Shivanand Sheth
Lionel Kowal

Prematurity

- WHO defines prematurity as "**babies born before 37 weeks from the first day of the last menstrual period"**

WHO Classification:

Extremely preterm (<28 weeks)

Very preterm (28 to <32 weeks)

Moderate to late preterm (32 to <37 weeks).

World Health Organization - Statistics

- Every year, an estimated **15 million babies** are born preterm and this number is rising.

- Over **1 million babies die** annually from preterm birth complications.

- Preterm birth is the leading cause of newborn deaths (babies in the first four weeks of life) and the ***second leading cause of death after pneumonia in children under five years***.

- Across 184 countries, the rate of preterm birth ranges from ***5% to 18%*** of babies born.

http://www.who.int/mediacentre/factsheets/fs363/en/

Australia statistics

- 8.3% (25,113) of babies were born preterm - most of which occurred at a gestational age of 32–36 completed weeks in Australia.

- This equates to approximately 25,000 babies each year.

**Australian Institute of Health and Welfare's Australia's 'Mothers and Babies' report (2011)*

Immediate/Short-term morbidity in pre-term babies

- Hypoglycemia
- Hypothermia
- Hypocalcemia
- Infection and Septicemia
- Respiratory distress syndrome
- Necrotising enteritis
- ***Intraventricular brain hemorrhage*** *(long term effects also)*
- ***Retinopathy of prematurity and blindness*** *(long term effects also)*

Long term problems of premature babies

- **Cerebral Palsy**
- ***Blindness and Low Vision***
- Hearing loss and Deafness
- Recurrent respiratory illnesses
- Recurrent hospital admissions
- Cognitive and neuro-motor impairments
- Attention Deficit Hyperactivity disorder
- Mental retardation

Pre-term babies survival - Australia

**Australian Institute of Health and Welfare's Australia's 'Mothers and Babies' report (2011)*

THE LANCET

An overview of mortality and sequelae of preterm birth from infancy to adulthood (2008)

Prof Saroj Saigal FRCP[C] a, Prof Lex W Doyle FRACP b c d

Non-ocular sequelae that could have a bearing on overall visual function

- **1/3rd of 7-year-old children** born between 32- 35 weeks had difficulties in motor skills, speaking, writing, mathematics, behaviour, and physical education.
- **Severe hearing impairment** in infancy was reported in **7%** of preterms
- **6% of 6-year-olds born before 26 weeks' gestation** were wearing hearing aids
- Very pre-term infants have central auditory processing difficulties, including difficulties discriminating simple speech sounds and worse auditory recognition than their full-term counterparts

THE LANCET

An overview of mortality and sequelae of preterm birth from infancy to adulthood (2008)

Prof Saroj Saigal FRCP[C] a, Prof Lex W Doyle FRACP b c d

Ocular Sequelae

- Blindness or severe visual impairment, or both
  - 1–2% (Gest Age 26–27 weeks)
  - 4–8% (Gest Age 25 weeks or below)

- Main causes of blindness and severe visual impairment
  - Retinopathy of prematurity
  - Perventricular Leukomalacia (Cortical visual loss)

- **Refractive errors arise in 1/4th of children** born before 28 weeks' gestation (Myopia > Hypermetropia)

- **24% of 6-year-old children** born before 26 weeks' gestation needed **prescription glasses versus 4% of term controls**.

	Gestational age range (weeks)	Years of birth	Age at assessment	Disability diagnosis	Rate of disability
Farooqi,[102] Sweden	23–25	1990–92	11 years	Moderate or disabling cerebral palsy, visual acuity <6/60 in at least one eye, sensorineural deafness with hearing aids, or special school education*	21% (18/86)
Doyle,[28] Victoria, Australia	23–27	1991–92	2 years†	Moderate or severe cerebral palsy, visual acuity <6/60 in better eye, sensorineural deafness with hearing aids, developmental quotient <–2 SD relative to controls	21% (46/219)
Bohin,[45] Trent region, UK	23–25	1991–93	18–24 months†	Cerebral palsy, visual acuity ≤6/24 in better eye, hearing loss more than 60 dB, Griffiths scale <70 or developmental quotient <–2 SD, any growth measurement <–2 SD, epilepsy requiring regular medication, any other serious condition	35% (19/55)
Tin,[18] northern region, UK	23-25	1991–94	1 year	Not stated	26% (13/50)
Sutton,[19] New South Wales, Australia	23–27	1992–93	1 year†	Cerebral palsy, visual acuity <6/60 in better eye, hearing aids, developmental quotient <–2 SD (Griffiths)	29% (74/255)
Wood,[22] UK, Ireland	22–25	1995	30 months†	Unable to walk without assistance, blind, impaired hearing uncorrected with hearing aids, no clear speech	23% (64/283)
Rijken,[47] Netherlands	23–26	1996–97	2 years†	Cerebral palsy, developmental quotient <–2 SD (Bayley I)	35% (9/26)
Mikkola,[48] Finland	22–26	1996–97	5 years	Moderate or severe cerebral palsy, severe visual impairment, deafness with hearing aids, epilepsy, shunted hydrocephalus, intelligence quotient <50	25% (25/102)
Doyle,[28] Victoria, Australia	23–27	1997	2 years†	Moderate or severe cerebral palsy, visual acuity <6/60 in better eye, sensorineural deafness with hearing aids, developmental quotient <–2 SD relative to controls (Bayley II)	28% (41/148)

*Outcomes assessed largely by questionnaires, with no formal cognitive assessment. †Corrected for prematurity.

***Table 2*: Neurological disability rates for survivors of borderline viability by gestational age from geographically defined cohorts**

THE LANCET

An overview of mortality and sequelae of preterm birth from infancy to adulthood (2008)

Prof Saroj Saigal FRCP[C] a, Prof Lex W Doyle FRACP b c d

	Gestational age range (weeks)	Years of birth	Age at assessment	Disability diagnosis	Rate of disability
Farooqi,[102] Sweden	23–25	1990–92	11 years	Moderate or disabling cerebral palsy, visual acuity <6/60 in at least one eye, sensorineural deafness with hearing aids, or special school education*	21% (18/86)
Doyle,[28] Victoria, Australia	23–27	1991–92	2 years†	Moderate or severe cerebral palsy, visual acuity <6/60 in better eye, sensorineural deafness with hearing aids, developmental quotient <–2 SD relative to controls	21% (46/219)
Bohin,[45] Trent region, UK	23–25	1991–93	18–24 months†	Cerebral palsy, visual acuity ≤6/24 in better eye, hearing loss more than 60 dB, Griffiths scale <70 or developmental quotient <–2 SD, any growth measurement <–2 SD, epilepsy requiring regular medication, any other serious condition	35% (19/55)
Tin,[18] northern region, UK	23-25	1991–94	1 year	Not stated	26% (13/50)
Sutton,[19] New South Wales, Australia	23–27	1992–93	1 year†	Cerebral palsy, visual acuity <6/60 in better eye, hearing aids, developmental quotient <–2 SD (Griffiths)	29% (74/255)
Wood,[22] UK, Ireland	22–25	1995	30 months†	Unable to walk without assistance, blind, impaired hearing uncorrected with hearing aids, no clear speech	23% (64/283)
Rijken,[47] Netherlands	23–26	1996–97	2 years†	Cerebral palsy, developmental quotient <–2 SD (Bayley I)	35% (9/26)
Mikkola,[48] Finland	22–26	1996–97	5 years	Moderate or severe cerebral palsy, severe visual impairment, deafness with hearing aids, epilepsy, shunted hydrocephalus, intelligence quotient <50	25% (25/102)
Doyle,[28] Victoria, Australia	23–27	1997	2 years†	Moderate or severe cerebral palsy, visual acuity <6/60 in better eye, sensorineural deafness with hearing aids, developmental quotient <–2 SD relative to controls (Bayley II)	28% (41/148)

*Outcomes assessed largely by questionnaires, with no formal cognitive assessment. †Corrected for prematurity.

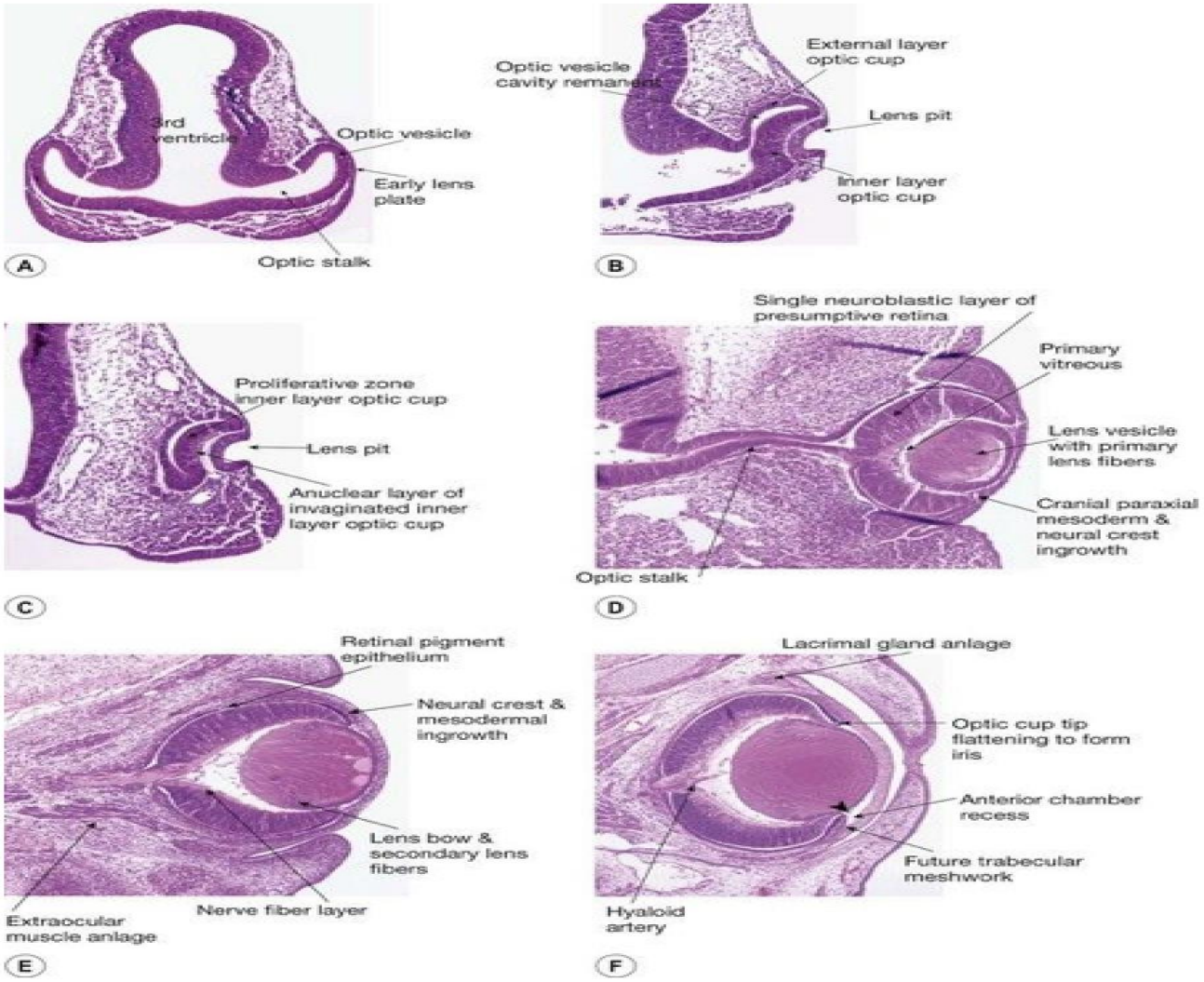
***Table 2*: Neurological disability rates for survivors of borderline viability by gestational age from geographically defined cohorts**

THE LANCET

An overview of mortality and sequelae of preterm birth from infancy to adulthood (2008)

Prof Saroj Saigal FRCP[C] a, Prof Lex W Doyle FRACP b c d

Normal eye development



Pediatr Clin North Am. 2003 Feb;50(1):1-23.

Anatomy, development, and physiology of the visual system.

Edward DP[1], Kaufman LM.

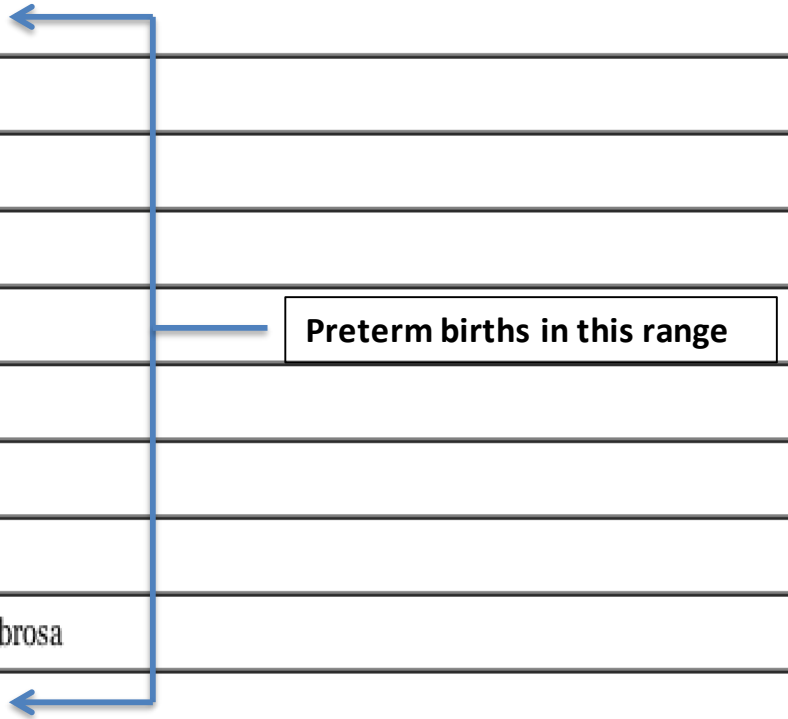
Gestational age	Developmental milestone
22 days	Optic primordia appears
2nd month	Hyaloid artery fills embryonic fissure
	Closure of embryonic fissure begins
	Lid folds appear
	Neural crest cells (corneal endothelium) migrate centrally; corneal stroma follows
	Choroidal vasculature starts to develop
	Axons from ganglion cells migrate to optic nerve
3rd month	Sclera condenses
	Lid folds meet and fuse
4th month	Retinal vessels grow into nerve fiber layer near optic disc
	Schlemm's canal appears
	Glands and cilia develop in lids

Pediatr Clin North Am. 2003 Feb;50(1):1-23.

Anatomy, development, and physiology of the visual system.

Edward DP[1], Kaufman LM.

5th month	Photoreceptors develop inner segments
	Lids begin to separate
6th month	Dilator muscle of iris forms
7th month	Central fovea thins
	Fibrous lamina cribrosa forms
	Choroidal melanocytes produce pigment
8th month	Iris sphincter develops
	Chamber angle completes formation
	Hyaloid vessels regress
	Retinal vessels reach periphery
	Myelination of optic nerve fibers is complete to lamina cribrosa
	Pupillary membrane disappears



Pediatr Clin North Am. 2003 Feb;50(1):1-23.

Anatomy, development, and physiology of the visual system.

Edward DP[1], Kaufman LM.

Normal newborn vs Adult Ocular parameters

	Newborn	Adult
Axial length	16.8 mm	23.0 mm
Mean keratometry	55 D	43 D
Optic nerve length	24 mm	30 mm
Corneal diameter	10 mm	10.6 mm (vertical) × 11.7 mm (horiz.)
Corneal thickness	581 µm	545 µm
Pars plana length	0.5–1.05 mm	3.5–4 mm
Orbital volume	7 cc	30 cc

Pediatr Clin North Am. 2003 Feb;50(1):1-23.

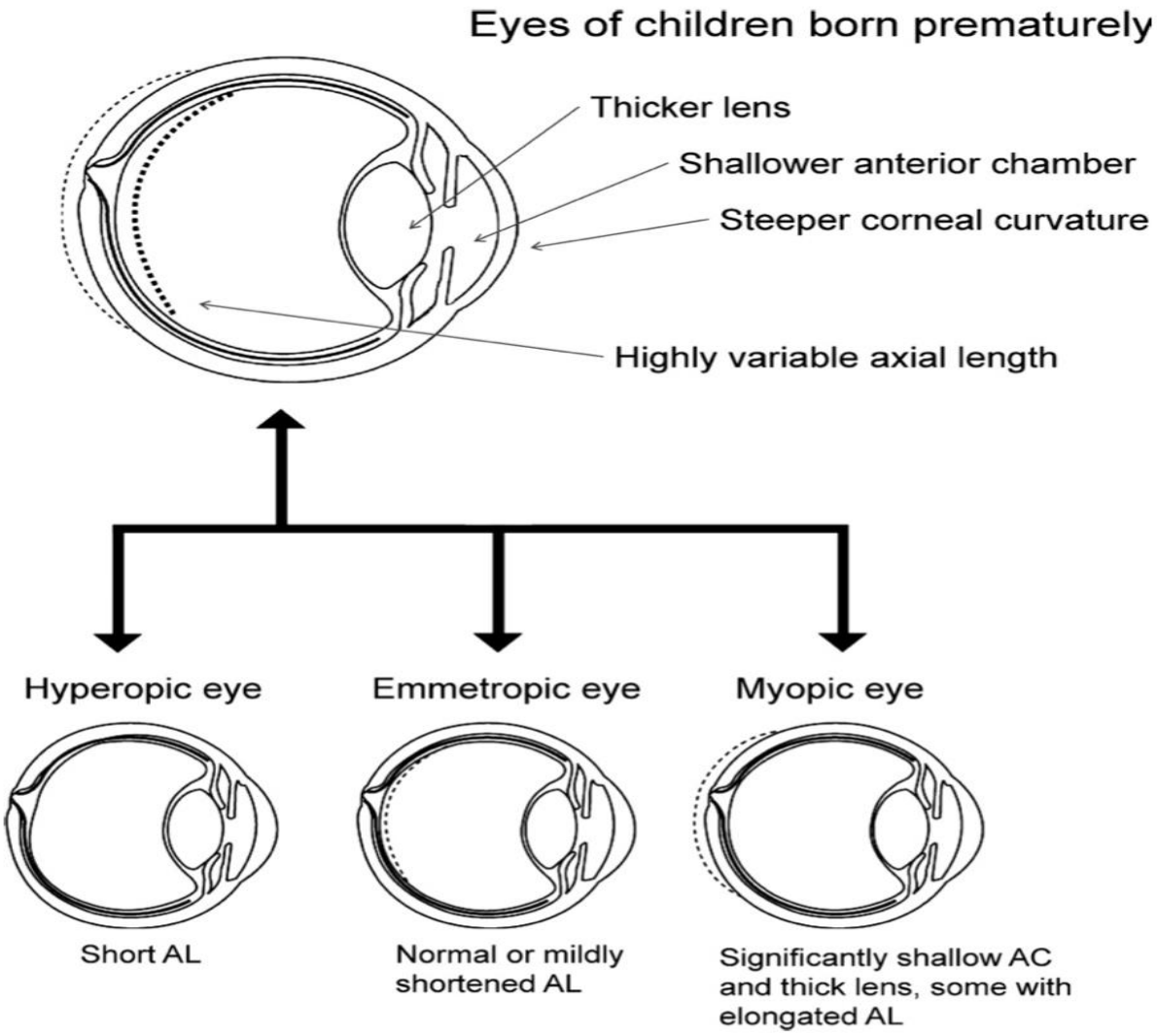
Anatomy, development, and physiology of the visual system.

Edward DP[1], Kaufman LM.

Long-term Evaluation of Refractive Status and Optical Components in Eyes of Children Born Prematurely

Ta-Ching Chen,[1] Tzu-Hsun Tsai,[1] Yung-Feng Shih,[1,2] Po-Ting Yeh,[1] Chang-Hao Yang,[1,2] Fu-Chang Hu,[3] Luke Long-Kuang Lin,[1,2] and Chung-May Yang[1,2]

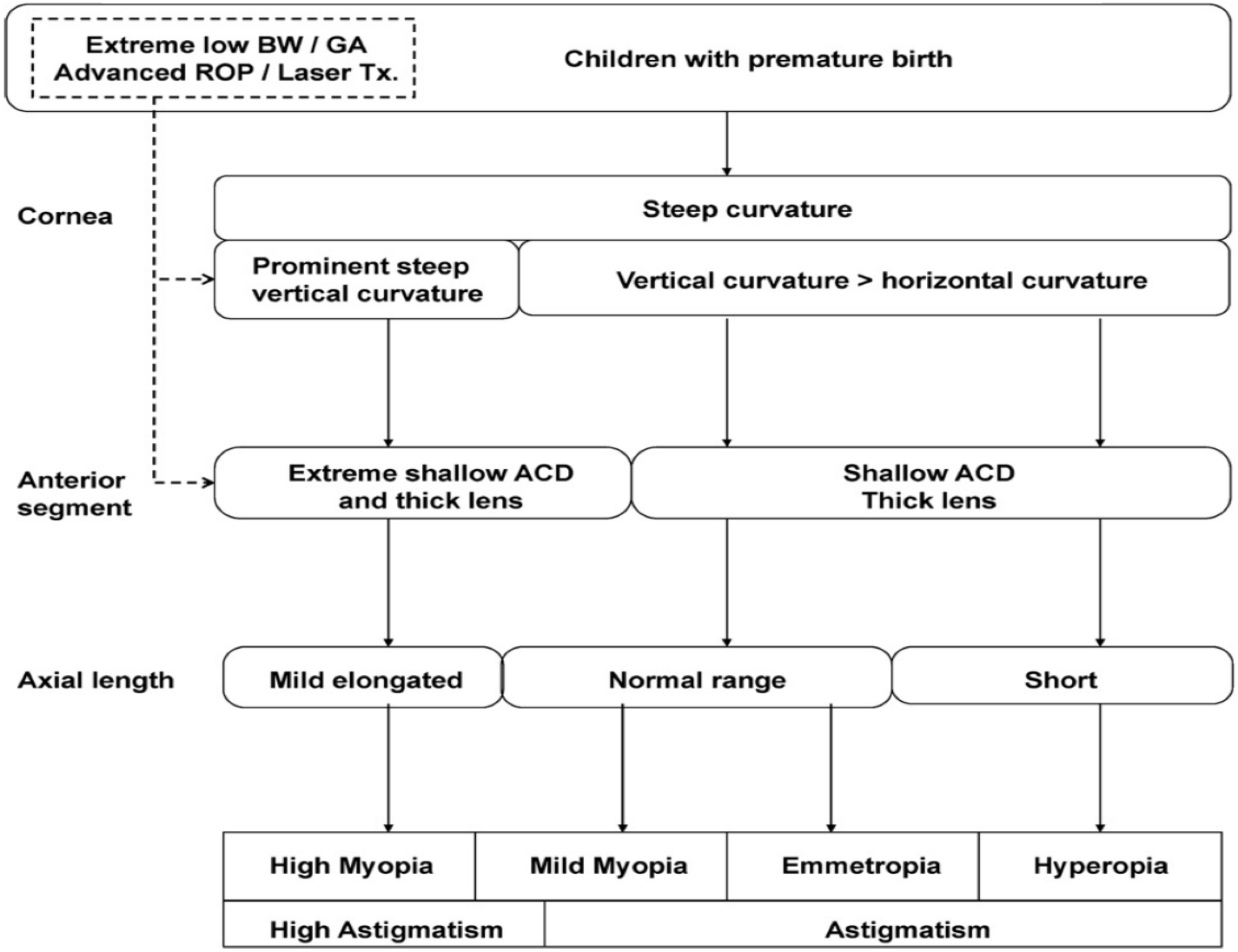
Investigative Ophthalmology & Visual Science, December 2010, Vol. 51, No. 12



Long-term Evaluation of Refractive Status and Optical Components in Eyes of Children Born Prematurely

Ta-Ching Chen,[1] Tzu-Hsun Tsai,[1] Yung-Feng Shih,[1,2] Po-Ting Yeh,[1] Chang-Hao Yang,[1,2] Fu-Chang Hu,[3] Luke Long-Kuang Lin,[1,2] and Chung-May Yang[1,2]

Investigative Ophthalmology & Visual Science, December 2010, Vol. 51, No. 12



BJO

Long term follow up of premature infants: detection of strabismus, amblyopia, and refractive errors

Nicoline E Schalij-Delfos, Mieke E L de Graaf, Willem F Treffers, et al.

Br J Ophthalmol 2000 84: 963-967
doi: 10.1136/bjo.84.9.963

Table 1 General characteristics of population (SD) arranged according to different age groups

	Group A GA <28 weeks	*Group B GA ⩾28, ⩽32 weeks*	*Group C GA >32, <37 weeks*	*p Values*	*Differences between groups*
No	32	64	34		
Mean gestational age (weeks)	26.9 (0.8)	29.9 (1.0)	34.4 (1.2)	<0.00	A-B-C
Mean birth weight (g)	936 (144)	1305 (298)	2089 (438)	<0.00	A-B-C
Artificial ventilation (days)	18.6 (12.7)	7.1 (9.4)	0.2 (0.8)	<0.00	A-B-C
Supplemental O_2 (days)	45.8 (35.8)	37.9 (85.2)	0.3 (0.8)	<0.00	(A=B)-C
Mean maximum O_2 administration (%)	67.4 (28.2)	66.2 (32.3)	22.2 (3.0)	<0.00	(A=B)-C
Mean duration of hospitalisation (days)	71.1(37.8)	54.2 (60.1)	22.3 (9.4)	<0.00	(A=B)-C
BPD (N (%))	16 (50%)	19 (29.7%)	0	<0.1	(A=B)-C
PDA (N (%))	14 (43.8%)	13 (20.3%)	0	<0.02	A-B-C
ROP (N (%))	21 (65.6%)	12 (18.7%)	0	<0.00	A-B-C

Continuous variables were tested by ANOVA on class differences and p values are listed in column 5. A Tukey post hoc procedure was performed to determine which age groups are really different from each other. A χ^2 test was performed on discrete variables Bronchopulmonary dysplasia (BPD), persistent ductus arteriosus (PDA), retinopathy of prematurity (ROP) of groups A and B.

BJO

Long term follow up of premature infants: detection of strabismus, amblyopia, and refractive errors

Nicoline E Schalij-Delfos, Mieke E L de Graaf, Willem F Treffers, et al.

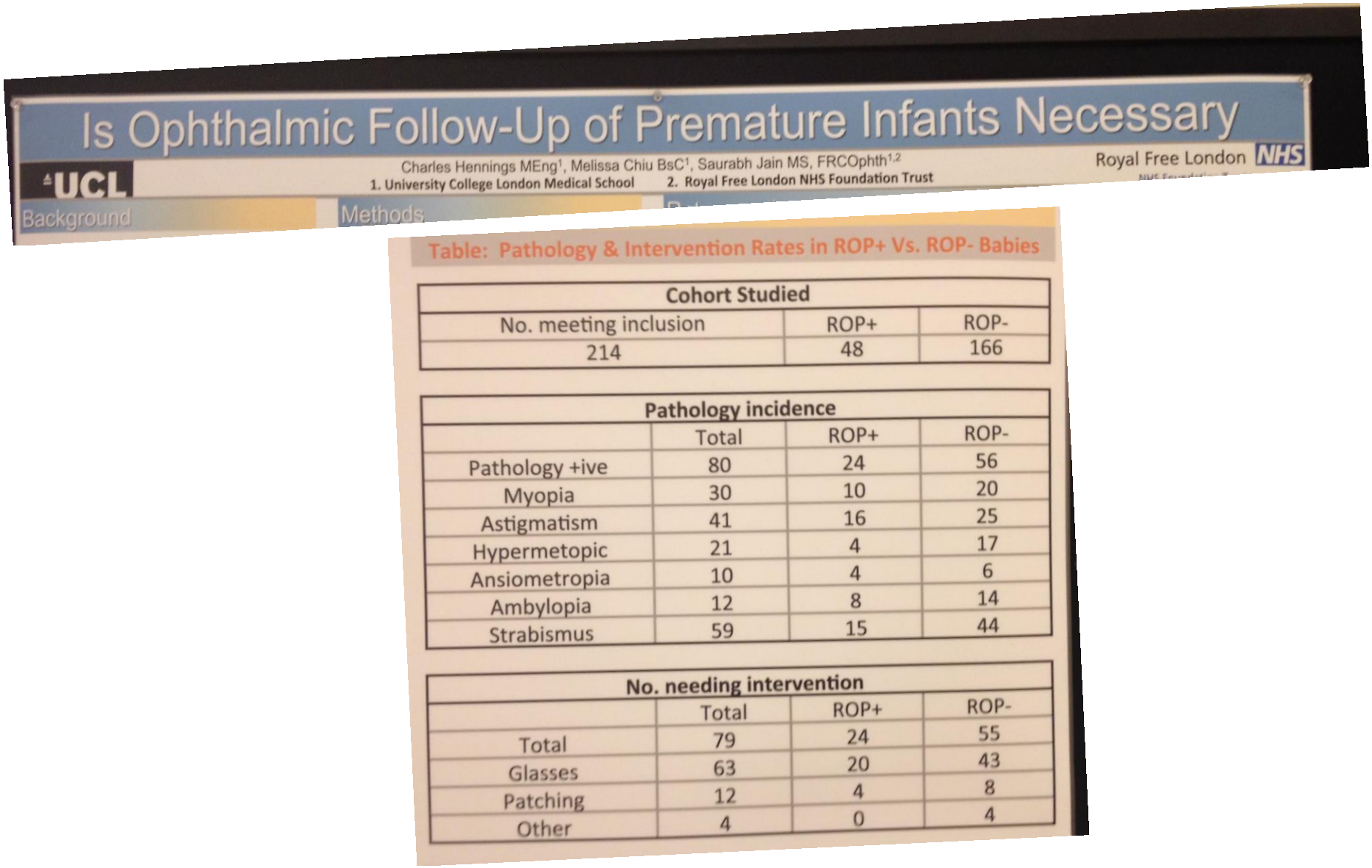
Br J Ophthalmol 2000 84: 963-967
doi: 10.1136/bjo.84.9.963

Table 2 Number and percentage of infants with strabismus, amblyopia, and refractive errors at the age of 5 years

	All infants	*Group A*	*Group B*	*Group C*
No	99	28	51	20
SAR	46 (46%)	16 (57%)	28 (55%)	2 (10%)
Strabismus	29 (22%)	11 (39%)	17 (33%)	1 (5%)
Amblyopia	22 (17%)	9 (32%)	11 (22%)	2 (10%)
Refractive errors	22 (17%)	8 (29%)	13 (25%)	1 (5%)

SAR = number of patients with strabismus and/or amblyopia and/or refractive errors.

AAPOS 2014 Meeting Palm Springs



Is Ophthalmic Follow-Up of Premature Infants Necessary

Charles Hennings MEng[1], Melissa Chiu BsC[1], Saurabh Jain MS, FRCOphth[1,2]
1. University College London Medical School 2. Royal Free London NHS Foundation Trust
UCL
Royal Free London NHS

Background Methods

Table: Pathology & Intervention Rates in ROP+ Vs. ROP- Babies

Cohort Studied		
No. meeting inclusion	ROP+	ROP-
214	48	166

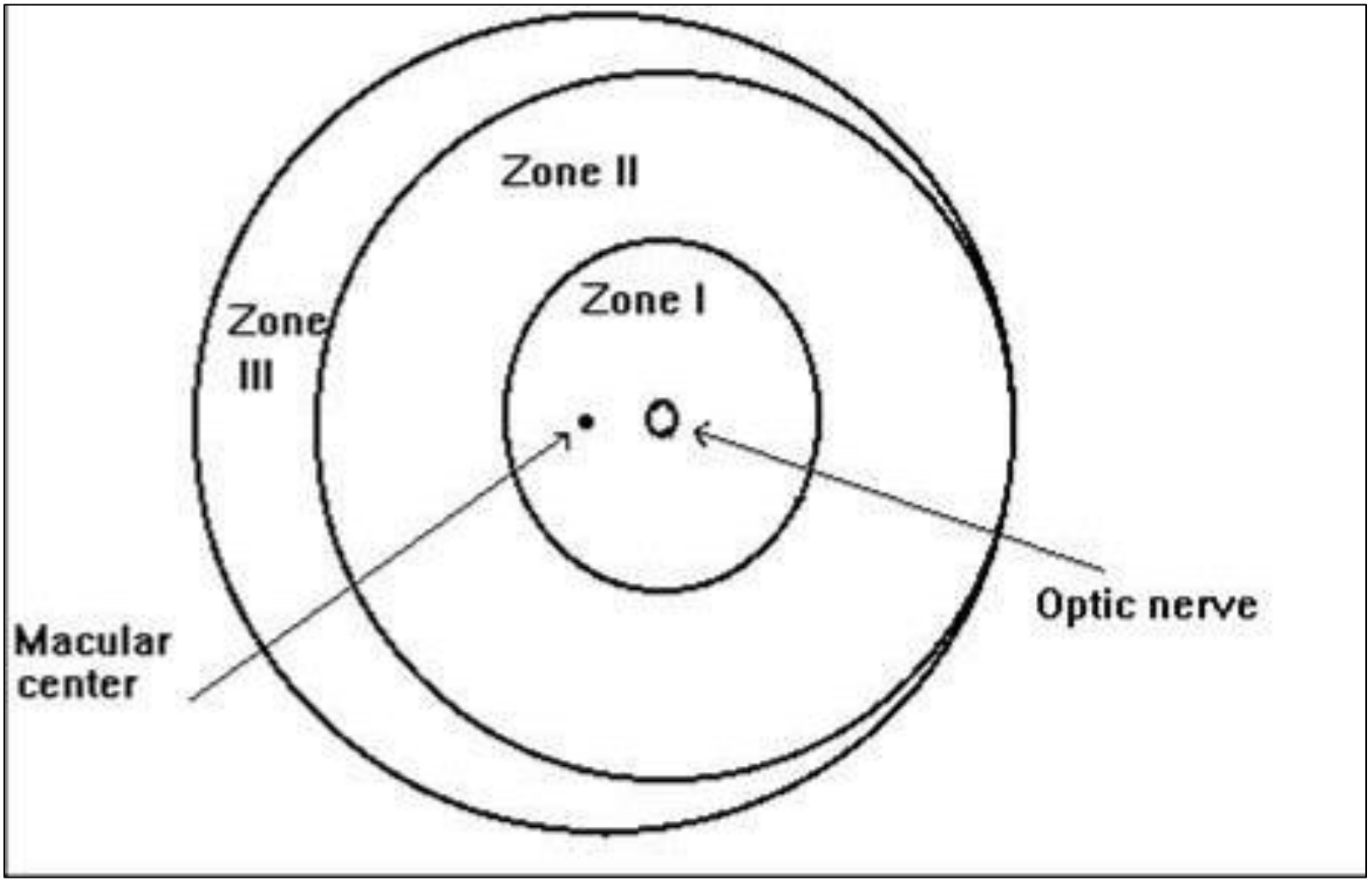
Pathology incidence			
	Total	ROP+	ROP-
Pathology +ive	80	24	56
Myopia	30	10	20
Astigmatism	41	16	25
Hypermetopic	21	4	17
Ansiometropia	10	4	6
Ambylopia	12	8	14
Strabismus	59	15	44

No. needing intervention			
	Total	ROP+	ROP-
Total	79	24	55
Glasses	63	20	43
Patching	12	4	8
Other	4	0	4

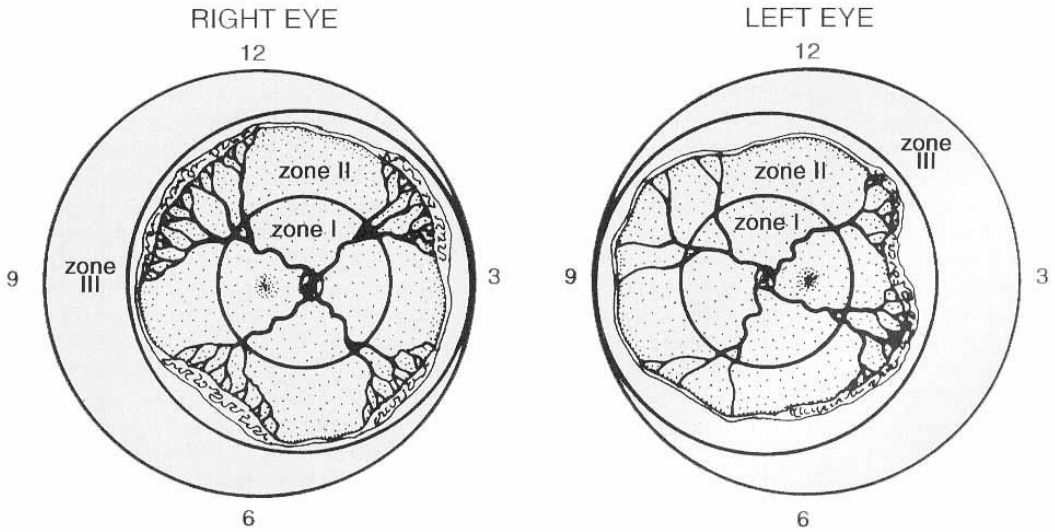
Retinopathy of Prematurity (ROP)

- Major cause of visual morbidity in pre-term children
- Untreated ROP itself can cause blindness by progressing to retinal detachment – surgical results poor. ***Major cause of childhood blindness in low socio-economic countries with poor ROP screening programs***
- Regressing ROP can cause dragging of macular area – can cause strabismus by affecting angle kappa.
- ROP can also cause strabismus by causing ametropia, astigmatism amblyopia
- ROP can cause high refractive errors – Myopia>> Hyperopia. ***ROP treated with lasers can cause greater myopia.***

ROP



ROP



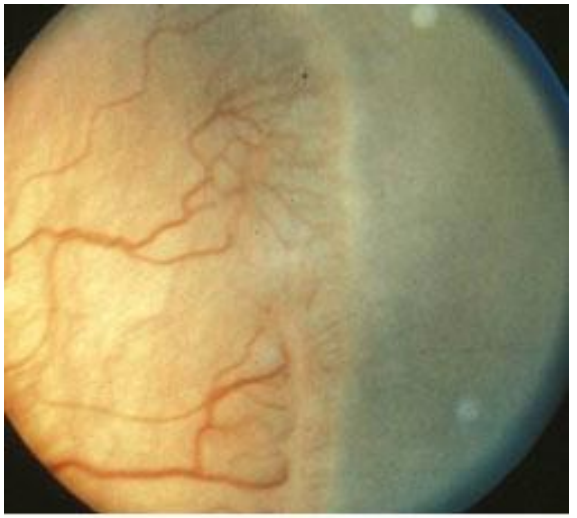


Fig. 3 Stage 3 ROP.

Table 1 - Classification of retinopathy of prematurity and treatment recommended for each stage

Stage	Retina alterations	Treatment - follow-up
Stage 1	White line between vascular and avascular retina	Weekly observation
Stage 2	Prominent ridge	Weekly observation
Stage 3	Fibrovascular proliferation from the ridge	Observation every 2 days
Stage 4	Proliferation may cause partial retinal detachment (4a if the fovea is spared and 4b if the fovea is involved)	Cyrocoagulation + scleral buckle and/or *pars* plana vitrectomy
Stage 5	Total retinal detachment (funnel shaped either open or closed at the anterior and posterior ends)	*Pars* plana vitrectomy
Threshold disease	Stage 3 retinopathy with plus disease across 5 contiguous hours or 8 separated hours of zone 1 or 2 (arteriolar dilation and venodilation)	Photocoagulation or cryotherapy of the avascular retina
Pre-threshold disease type 1	Zone 1 - any stage with plus disease Zone 1 - stage 3 wihtout plus disease Zone 2 - stage 2 or 3 with plus disease	Photocoagulation or cryocoagulation of the avascular retina
Pre-threshold disease type 2	Zone 1 - stage 1 or 2 without plus disease Zone 2 - stage 3 without plus disease	Observation every 2 days

ROP and Strabismus

J AAPOS. 2011 December ; 15(6): 536–540. doi:10.1016/j.jaapos.2011.07.017.

Prevalence and course of strabismus through age 6 years in participants of the Early Treatment for Retinopathy of Prematurity randomized trial

Deborah K. VanderVeen, MD[a], Don L. Bremer, MD[b], Rae R. Fellows, MEd[b], Robert J. Hardy, PhD[c], Daniel E. Neely, MD[d], Earl A. Palmer, MD[e], David L. Rogers, MD[b], Betty Tung, MS[c], and William V. Good, MD[f] on behalf of the Early Treatment for Retinopathy of Prematurity Cooperative Group*

[a]Children's Hospital Boston, Harvard Medical School, Boston, Massachusetts

[b]Nationwide Children's Hospital, The Ohio State University, Columbus, Ohio

[c]School of Public Health, University of Texas Health Science Center, Houston, Texas

[d]Department of Ophthalmology, Indiana University School of Medicine, Bloomington, Indiana

[e]Casey Eye Institute, Oregon Health & Science University, Portland, Oregon

[f]Smith-Kettlewell Eye Research Institute, San Francisco, California

Prevalence of strabismus at 9 months to 6 years examinations for patients in the randomized ETROP study

	Total	No. strabismus	No. normal	No. UA	% Strabismus
9 months	372	110	257	5	30.0
2 years	339	112	220	7	33.7
3 years	326	123	196	7	38.6
4 years	319	121	191	7	38.8
5 years	313	129	179	5	41.9
6 years	342	141	193	8	42.2

UA, unable to access: infants deemed unable to assess and not included in the percentage calculations.

ROP and Myopia

Ophthalmology: 2008

Progression of Myopia and High Myopia in the Early Treatment for Retinopathy of Prematurity Study

Findings to 3 Years of Age

*Graham E. Quinn, MD, MSCE,[1] Velma Dobson, PhD,[2] Bradley V. Davitt, MD,[3] Robert J. Hardy, PhD,[4] Betty Tung, MS,[4] Claudia Pedroza, PhD,[4] William V. Good, MD,[5] on behalf of the Early Treatment for Retinopathy of Prematurity Cooperative Group**

JAAPOS: 2013

Progression of myopia and high myopia in the Early Treatment for Retinopathy of Prematurity Study: Findings at 4 to 6 years of age

Graham E. Quinn, MD, MSCE,[a] Velma Dobson, PhD,[b] Bradley V. Davitt, MD,[c] David K. Wallace, MD, MPH,[d] Robert J. Hardy, PhD,[e] Betty Tung, MS,[e] Dejian Lai, PhD,[e] and William V. Good, MD,[f] on behalf of the Early Treatment for Retinopathy of Prematurity Cooperative Group*

Conclusions:

- **70%** of high-risk pre-threshold ROP eyes were myopic in early childhood, and the proportion with high myopia increased steadily between ages 6 months and 3 years.
- Timing of treatment of high-risk prethreshold ROP did not influence refractive error development.
- Approximately **two-thirds of eyes** with high-risk pre-threshold ROP during the neonatal period are **likely to be myopic** into the preschool and early school years

ROP and Myopia

Ophthalmology: 2008

Progression of Myopia and High Myopia in the Early Treatment for Retinopathy of Prematurity Study

Findings to 3 Years of Age

*Graham E. Quinn, MD, MSCE,[1] Velma Dobson, PhD,[2] Bradley V. Davitt, MD,[3] Robert J. Hardy, PhD,[4] Betty Tung, MS,[4] Claudia Pedroza, PhD,[4] William V. Good, MD,[5] on behalf of the Early Treatment for Retinopathy of Prematurity Cooperative Group**

JAAPOS: 2013

Progression of myopia and high myopia in the Early Treatment for Retinopathy of Prematurity Study: Findings at 4 to 6 years of age

Graham E. Quinn, MD, MSCE,[a] Velma Dobson, PhD,[b] Bradley V. Davitt, MD,[c] David K. Wallace, MD, MPH,[d] Robert J. Hardy, PhD,[e] Betty Tung, MS,[e] Dejian Lai, PhD,[e] and William V. Good, MD,[f] on behalf of the Early Treatment for Retinopathy of Prematurity Cooperative Group*

Table 1. Percentage of Eyes with Myopia and High Myopia at Corrected Ages 6 and 9 Months and Postnatal Ages 2 and 3 Years

Refractive Status	Treatment at High-Risk Prethreshold [n/N* (%)]	Conventionally Managed High-Risk Eyes		
		Total [n/N† (%)]	*Treatment at Threshold* [n/N (%)]	*Regressed, No Treatment* [n/N (%)]
Myopia ≥ 0.25 diopters				
6 mos	157/283 (55.5)	167/272 (61.4)	122/172 (70.9)	44/99 (44.4)
9 mos	197/304 (64.8)	198/280 (70.7)	140/172 (81.4)	57/107 (53.3)
2 yrs	198/281 (70.5)	181/253 (71.5)	128/155 (82.6)	53/98 (54.1)
3 yrs	191/268 (71.3)	174/243 (71.6)	124/149 (83.2)	49/93 (52.7)
Myopia ≥ 5 diopters				
6 mos	49/283 (17.3)	55/272 (20.2)	45/172 (26.2)	10/99 (10.1)
9 mos	74/304 (24.3)	74/280 (26.4)	62/172 (36.0)	12/107 (11.2)
2 yrs	91/281 (32.4)	86/253 (34.0)	73/155 (47.1)	13/98 (13.3)
3 yrs	102/268 (38.1)	92/243 (37.9)	76/149 (51.0)	16/93 (17.2)

*Refractive error data unavailable due to retinal detachment (RD), media opacity, pupillary miosis, or other difficulty in refracting (46 eyes at 6 mos, 15 eyes at 9 mos, 12 eyes at 2 yrs, and 13 eyes at 3 yrs) and due to exclusion of eyes that underwent vitrectomy, scleral buckling procedures, iridectomy, glaucoma procedures, or cataract surgery in an additional 1 eye at 6 mos, 17 eyes at 9 mos, 16 eyes at 2 yrs, and 16 eyes at 3 yrs.

†Refractive error data unavailable due to RD, media opacity, pupillary miosis, or other difficulty in refracting (50 eyes at 6 mos, 22 eyes at 9 mos, 21 eyes at 2 yrs, and 23 eyes at 3 yrs) and due to exclusion of eyes that underwent vitrectomy, scleral buckling procedures, iridectomy, glaucoma procedures, or cataract surgery in an additional 4 eyes at 6 mos, 27 eyes at 9 mos, 25 eyes at 2 yrs, and 21 eyes at 3 yrs.

ROP and Myopia

Ophthalmology: 2008

Progression of Myopia and High Myopia in the Early Treatment for Retinopathy of Prematurity Study

Findings to 3 Years of Age

*Graham E. Quinn, MD, MSCE,[1] Velma Dobson, PhD,[2] Bradley V. Davitt, MD,[3] Robert J. Hardy, PhD,[4] Betty Tung, MS,[4] Claudia Pedroza, PhD,[4] William V. Good, MD,[5] on behalf of the Early Treatment for Retinopathy of Prematurity Cooperative Group**

JAAPOS: 2013

Progression of myopia and high myopia in the Early Treatment for Retinopathy of Prematurity Study: Findings at 4 to 6 years of age

Graham E. Quinn, MD, MSCE,[a] Velma Dobson, PhD,[b] Bradley V. Davitt, MD,[c] David K. Wallace, MD, MPH,[d] Robert J. Hardy, PhD,[e] Betty Tung, MS,[e] Dejian Lai, PhD,[e] and William V. Good, MD,[f] on behalf of the Early Treatment for Retinopathy of Prematurity Cooperative Group*

Table 1. Percentage of eyes with myopia and high myopia at 4, 5, and 6 years postnatal age

Refractive status	Postnatal age, years	Treatment at high-risk prethreshold, n/N[a] (%)	Conventionally managed high-risk eyes: Total conventionally managed high-risk eyes, n/N[b] (%)	Conventionally managed high-risk eyes: Treatment at threshold, n/N (%)	Conventionally managed high-risk eyes: Regressed, no treatment, n/N (%)
Myopia ≥0.25 D	4	182/262 (69.2)	161/239 (67.4)	118/145 (81.4)	43/94 (45.7)
	5	175/255 (68.6)	151/233 (64.8)	110/141 (78.0)	41/92 (44.6)
	6	195/279 (69.9)	173/257 (67.3)	128/157 (81.5)	45/100 (45.0)
Myopia ≥5D	4	97/262 (37.0)	90/239 (37.7)	72/145 (49.7)	18/94 (19.1)
	5	90/255 (35.3)	86/233 (36.9)	71/141 (50.4)	15/92 (16.3)
	6	110/279 (39.4)	96/257 (37.4)	79/157 (50.3)	17/100 (17.0)

[a]Refractive error data unavailable because of retinal detachment, media opacity, pupillary miosis, or other difficulty in refracting (14 eyes at 4 years, 14 eyes at 5 years, and 15 eyes at 6 years) and because of exclusion of eyes that underwent vitrectomy, scleral buckling procedures, iridectomy, glaucoma procedures, or cataract surgery in an additional 13 eyes at 4 years, 16 eyes at 5 years, and 16 eyes at 6 years.
[b]Refractive error data unavailable because of retinal detachment, media opacity, pupillary miosis, or other difficulty in refracting (25 eyes at 4 years, 23 eyes at 5 years, and 26 eyes at 6 years) and because of exclusion of eyes that underwent vitrectomy, scleral buckling procedures, iridectomy, glaucoma procedures, or cataract surgery in an additional 18 eyes at 4 years, 20 eyes at 5 years, and 20 eyes at 6 years.

Other major studies also report similar myopia rates ranging from 60 - 80 %

ROP and Astigmatism

Ophthalmology: 2009

Astigmatism in the Early Treatment for Retinopathy of Prematurity Study

Findings to 3 Years of Age

Bradley V. Davitt, MD,[1] Velma Dobson, PhD,[2] Graham E. Quinn, MD, MSCE,[3] Robert J. Hardy, PhD,[4] Betty Tung, MS,[4] William V. Good, MD,[5] on behalf of the Early Treatment for Retinopathy of Prematurity Cooperative Group[6]

Ophthalmology: 2011

Astigmatism Progression in the Early Treatment for Retinopathy of Prematurity Study to 6 Years of Age

Bradley V. Davitt, MD,[1] Graham E. Quinn, MD, MSCE,[2] David K. Wallace, MD, MPH,[3] Velma Dobson, PhD,[4] Robert J. Hardy, PhD,[5] Betty Tung, MS,[5] Dejian Lai, PhD,[5] William V. Good, MD,[6] on behalf of the Early Treatment for Retinopathy of Prematurity Cooperative Group

Conclusions:

- By age 3 years,
  - **43%** of eyes treated at high-risk prethreshold ROP had astigmatism of **≥ 1.00D**
  - **20%** had astigmatism of **≥2.00 D**
- By 6 years of age,
  - **50%** of eyes with high-risk prethreshold ROP had astigmatism of **> 1.00D**
  - **25%** had astigmatism **≥2.00 D**
- Presence of astigmatism was not influenced by timing of treatment, zone of acute-phase ROP, or presence of plus disease.
- Most astigmatism was with-the-rule

Editorial

JAAPOS: 2013

There's more to ROP than ROP

Alistair R. Fielder, FRCP, FRCS, FRCOphth

- **At the 6-year ETROP examination:**
  - 11% had visual acuity of ≤ 20/200
  - 64% had an ophthalmoscopically normal fundus
  - 28% had straightening of the temporal retinal vessels with or without macular ectopia
  - 46% had optic atrophy
  - 8% had disk cupping (all of these in one or both eyes).
  - **Developmental status was normal in only 18%**
  - **77% of patients had Nystagmus**

- **Other conclusions:**
  - Cataracts commonly associated with end stage ROP, but can also be as a result of laser treatment for ROP – Can contribute to visual morbidity
  - Glaucoma is associated with end-stage ROP, but can develop in eyes with ROP sequelae and not be clinically evident for years

Prematurity and Cortical Visual Loss

Clinical characteristics of children with severe visual impairment but favorable retinal structural outcomes from the Early Treatment for Retinopathy of Prematurity (ETROP) study

JAAPOS: 2013

R. Michael Siatkowski, MD,[a] William V. Good, MD,[b] C. Gail Summers, MD,[c,d] Graham E. Quinn, MD, MSCE,[e] and Betty Tung, MS[f]

Conclusions:

- In 25 participants (7%) completing the 6-year examination***, cortical visual impairment was considered the primary cause of visual loss***.

- The remainder likely had components of both anterior and posterior visual pathway disease.

Prematurity and PVL

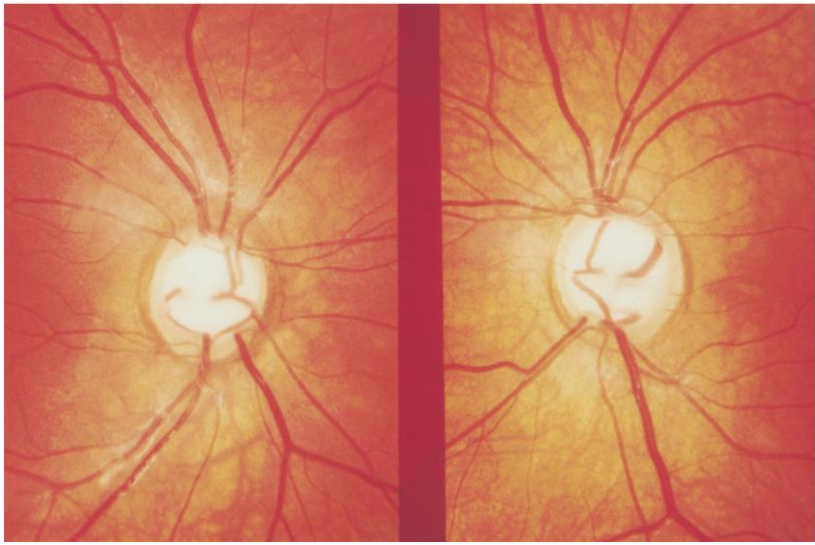
Periventricular Leukomalacia: An Important Cause of Visual and Ocular Motility Dysfunction in Children

Lena K. Jacobson, MD, PhD,[1] and Gordon N. Dutton, MD, FRCOphth[2]

[1]Karolinska Institutet, St Eriks Eye Hospital, Stockholm, Sweden, and [2]Royal Hospital for Sick Children, Yorkhill, Glasgow, United Kingdom

Survey Ophthal; 2000

- Visual acuity : Reduced grating acuity
- Visual fields: Non progressive constricted visual fields
- Cognitive Visual dysfunction: Poor in tasks requiring spatial and visuoperceptual abilities
- Optic disc cupping may be seen which can resemble glaucoma
- PVL can cause neurological strabismus, nystagmus, defective smooth pursuit movements and difficulty in performing visually guided saccades



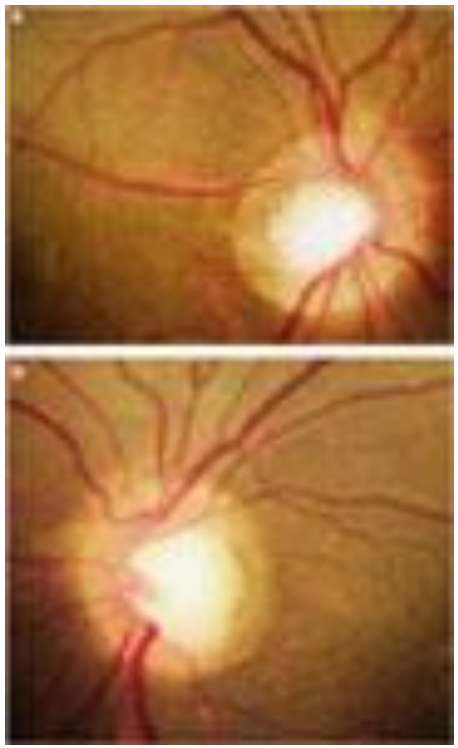
Prematurity and Optic disc morphology

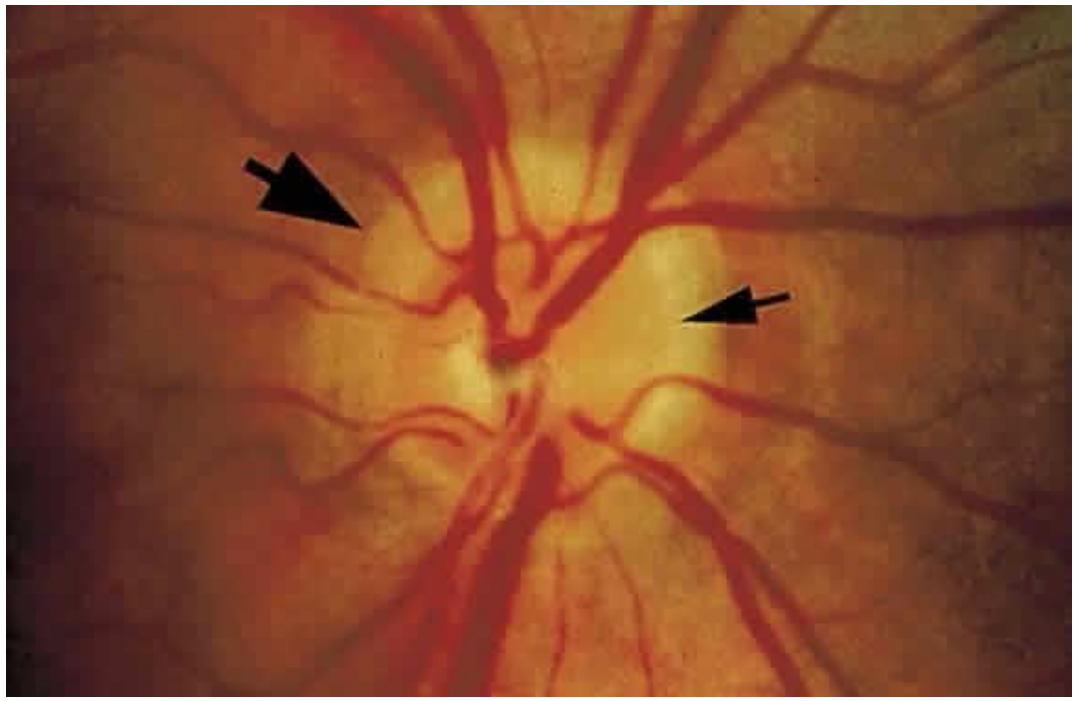
Optic disc morphology in premature infants

Sabine Hackl,[1] Florian Zeman,[2] Horst Helbig,[1] Isabel Maria Oberacher-Velten[1]

BJO 2013

75% of optic discs showed a double ring and 89% had visible disc cupping.





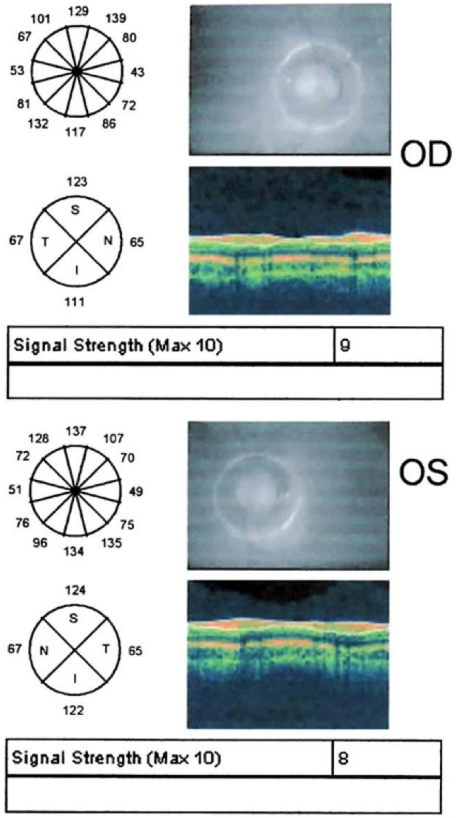
Prematurity and Retinal Nerve Fibre Layer

Retinal nerve fibre layer thickness in school-aged prematurely-born children compared to children born at term

Hanna Åkerblom, Gerd Holmström, Urban Eriksson, Eva Larsson

BJO; 2012

- The RNFL was reduced in prematurely-born children with severe ROP when compared to children born at term.
- Severe retinopathy as well as ablation of the retina with laser treatment or cryotherapy may affect the axons of the ganglion cells and thus reduce RNFL thickness.
- Prematurely-born children with low BW had a thinner RNFL, suggesting a negative effect of low birth weight on neural development.



Many other studies studying visual functions affected in prematurity

Effects of prematurity on the development of contrast sensitivity: Testing the visual experience hypothesis

Rain G. Bosworth *, Karen R. Dobkins

Visual field defects in prematurely born patients with white matter damage of immaturity: a multiple-case study

Lena Jacobson,[1,2] Olof Flodmark[2,3] and Lene Martin[2]

Alterations in the optic radiations of very preterm children—Perinatal predictors and relationships with visual outcomes ☆

Deanne K. Thompson [a,b,*], Dolly Thai [a], Claire E. Kelly [a], Alexander Leemans [c], Jacques-Donald Tournier [b], Michael J. Kean [d], Katherine J. Lee [a,e], Terrie E. Inder [f], Lex W. Doyle [a,g,h], Peter J. Anderson [a,e], Rodney W. Hunt [a,e,i]

Neurologic and Developmental Disability at Six Years of Age after Extremely Preterm Birth

Neil Marlow, D.M., Dieter Wolke, Ph.D., Melanie A. Bracewell, M.D., and Muthanna Samara, M.Sc., for the EPICure Study Group*

The NEW ENGLAND JOURNAL of MEDICINE

Developmental delay and magnocellular visual pathway function in very-low-birthweight preterm infants

Developmental Medicine & Child Neurology 2007

Summary

- The infant born preterm is at risk of developing a number of ophthalmic problems, not just in the eye but along the entire visual pathway and even beyond

- **Retina:** Preterm birth often causes retinopathy of prematurity (ROP) and can cause blindness, severe vision loss, strabismus, amblyopia, refractive errors

- **Central visual pathway:** Perinatal hypoxic-ischaemic events occurring between 24 and 34 weeks' gestation often cause a lesion of periventricular white matter, affecting the optic radiations, called periventricular leukomalacia (PVL) – Can cause cortical visual loss, strabismus, nystagmus and poor visual function

- More than half of preterm children have neuro-anatomical abnormalities as revealed by structural magnetic resonance imaging (MRI).

- **Visual perception:** Preterm infants born at very low gestation (≤30wks) and very low birth-weight (VLBW; ≤1500g) are at a greater risk of developing visual impairments, ***including deficits in acuity, contrast sensitivity, stereopsis, low- and high-level motion perception, motion-defined form, and visuo-motor control.***

Thank you