Colorado retinopathy of prematurity model: a multi-institutional validation study

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PURPOSE The Colorado retinopathy of prematurity (ROP) prediction model (CO-ROP), developed using a cohort of infants from Colorado, calls for ROP examination of infants meeting all of the following criteria: gestational age of ≤30 weeks, birth weight of ≤1500 g, and a net weight gain of ≤650 g between birth and 4 weeks of age. The purpose of this study was to perform an external validation to assess the sensitivity and specificity of the CO-ROP model in a larger cohort of babies screened for ROP from four academic institutions in the United States.

METHODS The medical records of neonates screened for ROP according current national guidelines was conducted at 4 US academic centers were retrospectively reviewed. Sensitivity, specificity, and respective 95% confidence intervals in detecting ROP using CO-ROP were calculated for type 1, type 2, and any grade of ROP.

RESULTS A total of 858 cases were included. The CO-ROP algorithm had a sensitivity of 98.1% (95% CI, 93.3%-99.8%) for type 1 ROP, 95.6% (95% CI 78.0-99.9%) for type 2 ROP, and 95.0% (95% CI, 93.1-97.4%) for all grades of ROP. The CO-ROP model would have reduced the total number of infants screened by 23.9% compared to current 2013 screening guidelines.

CONCLUSIONS CO-ROP demonstrated high sensitivity in predicting ROP and would have greatly reduced the number of infants needing examination. (J AAPOS 2016;20:220-225)

Retinopathy of prematurity (ROP) is an adverse complication of preterm birth that is characterized by abnormal vascularization of the immature retina.[1] It is the most common preventable cause of blindness in the developed world and the third leading cause of blindness in children.[2] The Multicenter Trial of Cryotherapy for Retinopathy of Prematurity (CRYO-ROP) and Early Treatment for Retinopathy of Prematurity (ETROP) studies demonstrated a reduction of unfavorable anatomical and visual outcomes through timely detection and treatment of infants with severe ROP.[3,4] Current (January 2013) United States screening guidelines recommend ROP examinations under the following conditions: "infants with a birth weight of ≤1500 g, infants with a gestational age 30 weeks or less (as defined by the attending neonatologist), and select infants with a birth weight between 1500 and 2000g or gestational age of >30 weeks with an unstable clinical course, including those requiring cardiorespiratory support and who are believed by their attending pediatrician or neonatologist to be at high risk for ROP."[5] While this screening algorithm is very sensitive, <10% of the total number of infants identified for examinations eventually require treatment for ROP.[6-8]

Several investigators have proposed alternative models for screening babies at risk for ROP, with the goal of improving efficiency and reducing the number of infants requiring stressful and costly ROP examinations.[6,8,9] The Colorado ROP model (CO-ROP)[10] is a novel ROP screening model designed to maintain high sensitivity for all cases of ROP while reducing the number of

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examinations performed for low-risk infants. The Colorado model calls for ROP examination in an infant meeting all of the following criteria: gestational age of ≤30 weeks, birth weight of ≤1500 g, and a net weight gain of ≤650 g between birth and 4 weeks of age.[10] Using these three simple objective criteria, CO-ROP aims to reduce the number of examinations. The purpose of the present study was to validate the model and to assess its sensitivity and specificity of CO-ROP in a larger and more demographically diverse population than that in which the model was first tested.

Subjects and Methods

The records of infants included in the analytic dataset were screened for ROP at the following 4 institutions: University of California–Los Angeles (institution A), University of California–San Diego (institution B), Baylor College of Medicine (institution C), and Vanderbilt University (institution D). This multicenter study was approved by the Colorado Multiple Institutional Review Board (COMIRB). Each contributing institution also obtained local institutional review board approval.

ROP was graded using the International Classification of ROP criteria.[11] For the purposes of this study, the maximum grade of ROP was defined as the highest stage and lowest zone of ROP noted in the worse eye during any ROP examination. Patients with type 1 ROP (stage 1 or 2 ROP in zone I with plus disease, stage 3 ROP zone I with or without plus disease, or stage 2 or 3 ROP in zone II with plus disease) were treated in accordance with recommendations from the Early Treatment of Retinopathy of Prematurity Randomized Trial (ETROP).[4] Type 2 ROP was also defined according to ETROP criteria: stage 1 or 2 ROP in zone I without plus, or stage 3 ROP in zone II.[4] For the purposes of this study, infants who develop type 1 or type 2 ROP were grouped as "high grade" ROP. All infants who developed ROP that did not meet type 1 or type 2 criteria were grouped as "low grade" ROP.

Data Collection

The medical records of neonates screened for ROP at each of the 4 institutions were reviewed retrospectively. Data collected included sex, gestational age, birth weight, ROP outcome (stage, zone, presence of plus disease), and weight at 1 month of age (defined as chronological 28th day of life). Gestational age was conservatively estimated by rounding down to the nearest week. For example, an infant born at 30 weeks and 6 days was counted as 30 weeks gestational age.

Eligible subjects included in the study were consecutive neonates screened for ROP at each individual institution using current (January 2013) national guidelines (all neonates with birth weight of ≤1500 g or gestational age of ≤30 weeks; or select infants with a birth weight of 1500–2000 g or gestational age of >30 weeks).[5] To be included, each infant had to meet 2013 screening guidelines, have a known weight on chronologic day of life 28, and have a known ROP outcome. Infants who did not meet all three criteria were excluded.

The records of this cohort of infants were reviewed with respect to CO-ROP criteria: gestational age of ≤30 weeks, birth weight of ≤1500 g, and a net weight gain of ≤650 g between birth and 4 weeks of age.[10]

Statistical Analysis

Demographic information across groups was compared using χ^2 tests for categorical variables and Kruskall-Wallis for continuous variables. CO-ROP was assessed by calculating sensitivities and specificities for detection of high grade ROP, low grade, and overall ROP.[12] Corresponding 95% confidence intervals were calculated using exact Clopper-Pearson confidence limits for binomial proportions. Statistical analysis was performed using SAS version 9.4 software (SAS Institute Inc, Cary, NC, 2013).

Results

A total of 858 infants were included in the analysis. Of these, 83 (9.7%) developed type 1 ROP, 23 (2.7%) developed type 2 ROP, 135 (15.7%) developed low-grade ROP, and 617 (71.9%) did not develop any ROP. The median net weight gain at 1 month of age across all institutions was 220 g (range, −70 to 860 g) for high-grade ROP (type 1 and 2), 265 g (range, −135 to 805 g) for low-grade ROP, and 416 g (range, −30 to 987 g) for infants who did not develop ROP ($P < 0.01$). Baseline demographics for each cohort appear in Table 1. There were no statistically significant differences in the birth weight and gestational age across the 4 institutions. There were differences in net weight gain at 1 month of age and distribution of ROP severity among the 4 institutions. Institution A had a higher rate of ROP, which could likely be explained by the lower net weight gain.

The CO-ROP model signaled an alarm in 653 (76.1%) infants who were otherwise screened using current national guidelines as being at risk for ROP (Table 2). The CO-ROP algorithm had a sensitivity of 98.8% (95% CI, 93.5%-100%) for type 1 ROP, 95.7% (95% CI, 78.1%-99.9%) for type 2 ROP, and 95.0% (95% CI, 91.5%-97.4%) for all grades of ROP (Table 3). Similar sensitivities were observed across all 4 institutions. The CO-ROP model would have reduced the total number of infants screened with no ROP by 31.3% compared to current 2013 screening guidelines.

The 23% of infants who were deemed low risk after applying the CO-ROP model had a mean birth weight of 1443 g, gestational age of 30.6 weeks, and net weight gain of 520 g between birth and 1 month of age. Using the CO-ROP model, 1 infant with type 1 ROP, 1 with type 2 ROP, and 10 infants with low-grade ROP were missed compared to current guidelines (Table 4). Applying the CO-ROP model would have reduced the overall number of infants being examined by 23.9% ROP screening examinations based on current ROP screening recommendations.

Table 1. Demographics of 858 infants screened for ROP

Characteristics	Institution[a]				*P* value
	A (n = 177)	B (n = 210)	C (n = 190)	D (n = 281)	
Female, N (%)	80 (45.2%)	103 (49.1%)	90 (47.4%)	130 (46.3%)	0.88
GA, weeks, median (IQR)	28 (26-30)	29 (26-30)	28 (26-30)	28 (26-30)	0.46
BW, g, median (IQR)	1025 (775-1360)	1110 (839-1340)	1040 (780-1315)	980 (790-1290)	0.32
Net weight gain 28 days, g, median (IQR)	270 (160-420)	390 (250-505)	349 (235-449)	420 (325-550)	<0.01
ROP type					<0.01
High-grade[b]	39 (22.0%)	22 (10.5%)	14 (7.4%)	31 (11.0%)	
Low-grade[c]	45 (25.4%)	28 (13.3%)	33 (17.4%)	29 (10.3%)	
No ROP	93 (52.5%)	160 (76.2%)	143 (75.3%)	221 (78.7%)	

BW, birth weight; *GA*, gestational age; *IQR*, interquartile range; *ROP*, retinopathy of prematurity.
[a]Institution A, University of California–Los Angeles; institution B, University of California–San Diego; institution C, Baylor College of Medicine; institution D, Vanderbilt University. Values presented are n (%) or median (IQR).
[b]Infants who developed type 1 or type 2 ROP as defined by the Early Treatment for Retinopathy of Prematurity study.
[c]Infants who developed any degree of ROP that did not meet type 1 or type 2 criteria.

Table 2. The Colorado ROP model reduced the total number of infants screened by 23.9%

Institution[a]	Type 1 ROP		Type 2 ROP		Low-grade ROP[d]		No ROP	
	Alarm[b]	No alarm[c]	Alarm[b]	No alarm[c]	Alarm[b]	No alarm[c]	Alarm[b]	No alarm[c]
A	29	0	9	1	40	5	56	37
B[e]	15	0	7	0	27	1	110	50
C	8	0	6	0	32	1	103	40
D[f]	30	1	–	–	26	3	155	66
Total	82	1	22	1	125	10	424	193

[a]Institution A, University of California–Los Angeles; institution B, University of California–San Diego; institution C, Baylor College of Medicine; institution D, Vanderbilt University.
[b]Infants who met Colorado-ROP model's screening criteria.
[c]Infants who did not meet Colorado ROP model's screening criteria.
[d]Infant who developed any grade of ROP that did not meet type 1 or type 2 criteria as defined in the Early Treatment for Retinopathy of Prematurity study.
[e]No zone 3 data available.
[f]No type 2 ROP data available.

Discussion

The Colorado ROP model was developed in a cohort of 499 infants at a single academic tertiary referral institution in Colorado. CO-ROP suggests that infants born at a gestational age of ≤30 weeks, having a birth weight of ≤1500 g, and achieving a net postnatal weight gain of ≤650 g between birth and 1 month of age be screened for ROP. Applying CO-ROP to the original 499 infants had a sensitivity of 100% (95% CI, 92.1%-100.0%) for high-grade ROP, 96.4% (95% CI, 92.3%-98.7%) for all grades of ROP, and reduction in infants screened compared to 2013 screening guidelines by 23.7%.[10]

In the current study of 858 infants, the model showed good sensitivity for all grades of ROP in 4 large, academic referral centers (98.1% of high-grade ROP, and 95.0% of all infants with any degree of ROP). We also demonstrated that use of this model would have reduced the number of infants screened by 23.9% compared to 2013 screening criteria. Despite a geographically diverse population, the sensitivity of each subset of ROP populations (type 1, type 2, high-grade, low-grade, any ROP) analyzed remained similar within each individual institution. The reduction in total ROP examination burden at each individual institution was also consistent and significant (range, 21.6%-24.9%). Thus, the CO-ROP model demonstrated good generalizability, a trait crucial to the success of any ROP screening model.[8]

ROP prediction models incorporating postnatal weight gain were developed in response to extensive research on the subject of postnatal weight gain and its value as a predictor of the development of ROP. Landmark studies show that insulin growth factor-1 (IGF-1) acts as a permissive factor for vascular endothelial growth factor–induced retinal vascularization.[1,13-15] Subsequent studies have shown that postnatal weight gain, a proposed surrogate marker for serum IGF-1 levels, can be utilized to predict the development of ROP.[14,16-18]

Two major models incorporating postnatal weight gain include the Weight, IGF-1, Neonatal ROP (WINROP)[9] and Children's Hospital of Philadelphia Postnatal Weight Gain, Birthweight, and Gestational Age ROP Risk Model (CHOP-ROP).[6] In previous studies, implementation of the WINROP model reduced the number of infants screened by 21.6-84%[6,17,19-22]; CHOP-ROP, by 49%. Both WINROP and CHOP-ROP were developed to detect high-grade ROP. Both models require serial

Table 3. The Colorado ROP model maintained sensitivity for all grades of ROP while reducing total number screened by 23.9%

Institution[a]	No. patients	High-grade ROP[b] (n = 106)	Type 1 ROP (n = 83)	Type 2 ROP (n = 23)	Low-grade ROP (n = 135)	Any ROP (n = 241)	No ROP (n = 617)	% reduction no. screened
		Sensitivity (95% CI)					Specificity (95% CI)	
A	177	97.4% (86.5-99.9)	100% (88.1-100)	90.0% (55.5-99.7)	88.9% (75.9-96.3)	92.9% (85.1-97.3)	39.8% (29.8-50.5)	24.3%
B	210	100% (84.6-100)	100% (78.2-100)	100% (59.0-100)	96.4% (81.7-99.9)	98.0% (89.4-99.9)	31.3% (24.2-39.0)	24.3%
C	190	100% (76.8-100)	100% (63.1-100)	100% (54.1-100)	97.0% (84.2-99.9)	97.9% (88.7-99.9)	28.0% (20.8-36.1)	21.6%
D	281	96.8% (83.3-99.9)	96.8% (83.3-99.9)	N/A	89.7% (72.6-97.8)	93.3% (83.8-98.2)	29.9% (23.9-36.4)	24.9%
Total	858	98.1% (93.4-99.8)	98.8% (93.5-100)	95.7% (78.1-99.9)	92.6% (86.8-96.4)	95.0% (91.5-97.4)	31.3% (27.6-35.1)	23.9%

CI, confidence interval; *ROP*, retinopathy of prematurity.
[a]Institution A, University of California–Los Angeles; institution B, University of California–San Diego; institution C, Baylor College of Medicine; institution D, Vanderbilt University.
[b]Type 1 ROP or type 2 ROP.

Table 4. Clinical features of Infants with ROP not detected by the Colorado ROP model

Infant	Institution[a]	Sex	GA, weeks	BW, g	NWG, g	Comorbidities[b]						ROP				
						NEC	Vent	PDA	Cx+[c]	IVH	Gene[d]	Type[e]	Stage	Zone	Plus	Tx
1	D	M	30	1080	860	–	–	–	–	–	Y	1	3	2	Y	Y
2	A	F	29	1575	455	N	N	Y	Y	N	N	2	2	1	N	N
3	A	F	27	985	805	Y	N	N	Y	N	N	Low	2	3	N	N
4	A	M	31	1345	665	N	N	N	N	Y	N	Low	1	3	N	N
5	A	M	30	1690	520	N	N	N	N	N	N	Low	1	2	N	N
6	A	M	29	1600	80	Y	Y	N	Y	N	N	Low	1	2	N	N
7	A	F	30	1690	78	N	Y	N	Y	N	N	Low	1	3	N	N
8	B	M	30	1365	679	N	N	N	N	N	N	Low	1	2	N	N
9	C	M	32	1216	314	N	N	N	N	N	N	Low	1	2	N	N
10	D	F	23	600	730	–	–	–	–	–	–	Low	1	2	N	N
11	D	M	29	2170	420	–	–	–	–	–	–	Low	2	2	N	N
12	D	M	29	1550	440	–	–	–	–	–	–	Low	1	2	N	N

BW, birth weight; *Cx+*, blood/cerebrospinal fluid culture–positive sepsis or serious culture-proven infection; *GA*, gestational age; *Gene*, genetic disorder or anomaly; *IVH*, intraventricular hemorrhage (grade 3 or higher); *NEC*, necrotizing enterocolitis; *NWG*, net weight gain between birth and 1 month of age; *PDA*, patent ductus arteriosus requiring surgical ligation; *Tx*, treatment; *Vent*, positive pressure ventilation >14 days.
[a]Institution A, University of California–Los Angeles; institution B, University of California–San Diego; institution C, Baylor College of Medicine; institution D, Vanderbilt University.
[b]Cormorbidity data was not available from Institution D.
[c]Excluding urinary tract infection and tracheitis.
[d]Confirmed or clinical suspicion warranting a chromosomal or mircroarray analysis.
[e]Low-grade ROP: any grade of ROP that did not meet type 1 or type 2 criteria as defined by the Early Treatment for Retinopathy of Prematurity study.

longitudinal weekly weight gain calculations for an indeterminate number of weeks (a challenge especially for infants transferred between hospitals) and require calculations using a more complex equation (CHOP-ROP) or proprietary application (WINROP). In contrast, CO-ROP is simple one-time application formula designed to identify infants at risk of any grade of ROP in a timely manner (4 weeks).

We found 1 infant who developed type 1 ROP who was missed by the CO-ROP model. This infant was born at a gestational age of 30 weeks, had a birth weight of 1080 g, and net weight gain of 860 g at 1 month of age (infant A, Table 4). The neonate's clinical course was notable for a noncardiac congenital anomaly requiring multiple surgical interventions, prolonged ventilation, and had significant edema with fluctuating weights requiring diuresis. The baby's weight at 1 month of age was therefore nonphysiologic.

The infant in question presents an important outlier. Adjustment of the screening parameters in the CO-ROP model to trigger screening of infants with any instead of all of the three screening criteria (birthweight, gestational age, and net weight gain at 28 days of life) would have resulted in minimal reduction in the total number of infants screened compared to current national guidelines. Neither the CO-ROP, CHOP-ROP, nor the WINROP models are designed to predict ROP risk in infants with nonphysiologic weight gain, and none of these models would have captured this infant. The WINROP model specifically indicates that infants with nonphysiologic weight gain (grossly represented by a net weight gain of >400 g in 1 week) be automatically screened for ROP because such infants cannot be adequately assessed using the WINROP algorithm. Thus, this infant underscores the need for further refinement in how postnatal weight gain, nonphysiologic weight, and infants with obvious unstable clinical course are incorporated in ROP risk models.

Aligned with current national screening guidelines, CO-ROP was designed to capture as many infants who develop any degree of ROP as possible. We therefore included in

our analysis neonates who developed low-grade ROP. We feel that inclusion of these babies in our model is important, because previously published studies have shown that infants who develop low-grade ROP are at increased incidence of visual sequelae including refractive error (particularly myopia), strabismus, and amblyopia, compared to their low-birth-weight cohorts who do not develop any ROP.[23,24] Furthermore, recognition of long-term vitreoretinal sequelae have begun to emerge as the earliest surviving preterm infants are now entering their fifth and sixth decades of life.[23,25,26] A further in-depth discussion of the pros and cons of developing a model calibrated to detect all grades of ROP (eg, current screening guidelines, CO-ROP) versus just those with high-grade ROP (eg, WINROP and CHOP-ROP), at the expense of eliminating infants with low-grade ROP from screening examinations, is a subject that merits discussion but is beyond the scope of this paper. However, we believe that reduced sensitivity for low-grade ROP may limit a models' use in predicting overall future visual disability.

This study was limited both by its retrospective nature and by the difficulties of extracting data from multiple institutions. Infants who did not have a known ROP outcome or who did not have available weight data at 28 days were not included in the data analysis. While the year(s) of the available data varied between institutions, all data obtained were contemporary (composed of infants screened within 5 years of study initiation), and each individual dataset was composed of consecutive infants screened at that institution. Data for zone 3 ROP was not available at institution B, and data on type 2 ROP infants was not available at institution D (Table 2). Furthermore, our study was limited by the relatively low number of neonates who developed ROP requiring treatment.[8] This is in line with previous published studies from the United States, where fewer than 10% of the total number of infants screened eventually develop ROP. We chose to focus our discussion of confidence intervals using all infants available, acknowledging that continued refinement through studies encompassing hundreds of infants with severe ROP will be needed to raise the lower boundary of the 95% confidence interval for high-grade ROP to a level nearing 100%.[6,8] In the interim we strongly emphasize that all alternatively proposed ROP screening models, including the CO-ROP model in its current formulation, can only serve as an adjunct to current ROP screening guidelines. Application of any novel ROP screening model prior to extensive study places one at risk of missing infants with ROP. At this stage, therefore, this model should be used only with intent to further stratify infants at risk of developing ROP.

Notwithstanding the limitations described above, our study contributes to a growing body of evidence that postnatal weight gain can be a discriminating and useful predictor of ROP and may be useful in the continued advancement in ROP screening guidelines. This study indicates that the Colorado model maintained excellent sensitivity for all grades of ROP and demonstrated generalizability in a large cohort of geographically diverse, academic, tertiary-referral institutions within the United States. At minimum, CO-ROP is a simple set of criteria that can be easily implemented as an adjunct to current ROP screening programs to assess ROP risk. Additional larger cohort studies will be needed to further refine any proposed ROP screening model incorporating postnatal weight gain prior to implementation.

References

1. Hellstrom A, Smith LE, Dammann O. Retinopathy of prematurity. Lancet 2013;382:1445-57.
2. Kong L, Fry M, Al-Samarraie M, Gilbert C, Steinkuller PG. An update on progress and the changing epidemiology of causes of childhood blindness worldwide. J AAPOS 2012;16:501-7.
3. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Multicenter trial of cryotherapy for retinopathy of prematurity. Snellen visual acuity and structural outcome at 5 1/2 years after randomization. Arch Ophthalmol 1996;114:417-24.
4. Good WV, Early Treatment for Retinopathy of Prematurity Cooperative Group. Final results of the Early Treatment for Retinopathy of Prematurity (ETROP) randomized trial. Trans Am Ophthalmol Soc 2004;102:233-48. discussion 48-50.
5. Fierson WM, American Academy of Pediatrics Section on Ophthalmology, American Academy of Opthalmology, American Association for Pediatric Ophthalmology and Strabismus, American Association of Certified Orthoptists. Screening examination of premature infants for retinopathy of prematurity. Pediatrics 2013;131:189-95.
6. Binenbaum G, Ying GS, Quinn GE, et al. The CHOP Postnatal Weight Gain, Birth Weight, and Gestational Age Retinopathy of Prematurity Risk Model. Arch Ophthalmol 2012;130:1560-65.
7. Wu C, Vanderveen DK, Hellstrom A, Lofqvist C, Smith LE. Longitudinal postnatal weight measurements for the prediction of retinopathy of prematurity. Arch Ophthalmol 2010;128:443-7.
8. Binenbaum G. Algorithms for the prediction of retinopathy of prematurity based on postnatal weight gain. Clin Perinatol 2013;40:261-70.
9. Hellstrom A, Hard AL, Engstrom E, et al. Early weight gain predicts retinopathy in preterm infants: new, simple, efficient approach to screening. Pediatrics 2009;123:e638-45.
10. Cao JH, Wagner BD, McCourt EA, et al. The Colorado-retinopathy of prematurity model (CO-ROP): postnatal weight gain screening algorithm. J AAPOS 2016;20:19-24.
11. International Committee for the Classification of Retinopathy of Prematurity. The International Classification of Retinopathy of Prematurity revisited. Arch Ophthalmol 2005;123:991-9.
12. Loong TW. Understanding sensitivity and specificity with the right side of the brain. BMJ 2003;327:716-19.
13. Hellstrom A, Perruzzi C, Ju M, et al. Low IGF-I suppresses VEGF-survival signaling in retinal endothelial cells: direct correlation with clinical retinopathy of prematurity. Proc Natl Acad Sci U S A 2001;98:5804-8.
14. Hellstrom A, Engstrom E, Hard AL, et al. Postnatal serum insulin-like growth factor I deficiency is associated with retinopathy of prematurity and other complications of premature birth. Pediatrics 2003;112:1016-20.
15. Smith LE, Shen W, Perruzzi C, et al. Regulation of vascular endothelial growth factor-dependent retinal neovascularization by insulin-like growth factor-1 receptor. Nat Med 1999;5:1390-95.
16. Wallace DK, Kylstra JA, Phillips SJ, Hall JG. Poor postnatal weight gain: a risk factor for severe retinopathy of prematurity. J AAPOS 2000;4:343-7.
17. Wu C, Lofqvist C, Smith LE, VanderVeen DK, Hellstrom A, WINROP Consortium. Importance of early postnatal weight gain for normal retinal angiogenesis in very preterm infants: a multicenter study analyzing weight velocity deviations for the prediction of retinopathy of prematurity. Arch Ophthalmol 2012;130:992-9.

18. Lundgren P, Wilde A, Lofqvist C, Smith LE, Hard AL, Hellstrom A. Weight at first detection of retinopathy of prematurity predicts disease severity. Br J Ophthalmol 2014;98:1565-9.
19. Lundgren P, Stoltz Sjostrom E, Domellof M, et al. WINROP identifies severe retinopathy of prematurity at an early stage in a nation-based cohort of extremely preterm infants. PLoS One 2013;8:e73256.
20. Eriksson L, Liden U, Lofqvist C, Hellstrom A. WINROP can modify ROP screening praxis: a validation of WINROP in populations in Sormland and Vastmanland. Br J Ophthalmol 2014;98:264-6.
21. Zepeda-Romero LC, Hard AL, Gomez-Ruiz LM, et al. Prediction of retinopathy of prematurity using the screening algorithm WINROP in a Mexican population of preterm infants. Arch Ophthalmol 2012; 130:720-73.
22. Lofqvist C, Andersson E, Sigurdsson J, et al. Longitudinal postnatal weight and insulin-like growth factor I measurements in the prediction of retinopathy of prematurity. Arch Ophthalmol 2006;124: 1711-18.
23. Smith BT, Tasman WS. Retinopathy of prematurity: late complications in the baby boomer generation (1946-1964). Trans Am Ophthalmol Soc 2005;103:225-34. discussion 34-36.
24. Gursoy H, Basmak H, Bilgin B, Erol N, Colak E. The effects of mild-to-severe retinopathy of prematurity on the development of refractive errors and strabismus. Strabismus 2014;22:68-73.
25. Fledelius HC, Jensen H. Late subsequent ocular morbidity in retinopathy of prematurity patients, with emphasis on visual loss caused by insidious 'involutive' pathology: an observational series. Acta Ophthalmol 2011;89:316-23.
26. Tufail A, Singh AJ, Haynes RJ, Dodd CR, McLeod D, Charteris DG. Late onset vitreoretinal complications of regressed retinopathy of prematurity. Br J Ophthalmol 2004;88:243-6.