Published in final edited form as:

J Pediatr. 2015 February ; 166(2): 257–261.e2. doi:10.1016/j.jpeds.2014.09.069.

Retinopathy of Prematurity Risk Prediction for Infants with Birth Weight Less than 1,251 Grams

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Abstract

Objective—To predict retinopathy of prematurity (ROP) exam findings among infants with birth weight < 1,251 grams from 32 through 40 weeks post-menstrual age (PMA).

Study design—Secondary analysis of 3,714 eye exams from 1,239 infants.

Results—The likelihood of developing Type 1 ROP by 40 weeks PMA varied by GA ($p < 0.001$), from 33% for 25 weeks, 10% for 26 or 27 weeks, 4% for 28 or 29 weeks, and none for 30 weeks. By 40 weeks PMA, 51% with GA 27 weeks still needed subsequent exams. Previous exam findings, GA, and PMA were predictive of the development of Type 1 ROP (area under the curve, 0.78) or mature retina (area under the curve, 0.85).

Conclusions—This analysis provides the opportunity for development of an RO approach to estimate resource needs in the NICU and to facilitate communication with families when planning discharge or transfer.

MeSH Key Words

retinopathy of prematurity; very low birth weight infant; risk; decision modeling

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The authors declare no conflicts of interest.

Registered with ClinicalTrials.gov: NCT01264276

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Decreasing the incidence of blindness from retinopathy of prematurity (ROP) relies upon repeated ophthalmologic examination of infants based on gestational age (GA), birth weight (BW), and postmenstrual age (PMA), with subsequent treatment for those who develop specific retinal findings.¹ Most infants at risk will not develop significant ROP; however, even short delays in diagnosis can lead to blindness. In high-income countries such as the United States, fewer than 5% born with GA less than 32 weeks require treatment for ROP (ie, type 1 ROP).² The need for repeated timely eye exams is a challenge for many neonatal intensive care units (NICUs) because of the shortage of ophthalmologists who examine and treat ROP.³ In addition, families may become frustrated because of the inability to transfer infants to NICUs closer to home because of the inability to assure subsequent eye exams.³ Understanding the risk of developing significant ROP or the likelihood of no longer requiring eye exams for ROP detection could allow revision of management guidelines for efficient strategies for the detection of ROP and to inform families about the benefits of receiving timely eye exams.

Our goal was to develop a clinically useful model to predict the likelihood that the findings from an eye exam would lead to a treatment (ie, type 1 ROP), lead to subsequent eye exams (ie, immature retinae, mild ROP, type 2 ROP), or suggest that the infant is no longer at risk for developing ROP (ie, mature retinae). Many risk factors are associated with the development of ROP, including infant characteristics (eg, race, multiparity) and markers of severe illness (eg, use of supplemental oxygen therapy, prolonged mechanical ventilation, treatment with inhaled nitric oxide, sepsis, rate of early postnatal growth, prolonged NICU stay).^{4,5}

Not surprisingly, information about the status of the retinae can help predict the likelihood of developing ROP. The RM-ROP2 model, based on data published in 1991, used a wide array of infant characteristics, including previous eye exam findings, to predict the risk of progression from prethreshold ROP to unfavorable outcome at three-months post term for individual eyes.⁶ However, more recent risk-prediction models have focused on other clinical factors and did not include information about the previous status of the retina. For example, two studies found that BW, GA, and daily weight gain were sensitive risk predictors of significant ROP; however, the specificity was low.^{7,8} A more recent analysis from the Netherlands found that clinical characteristics could be used to decrease the number of infants with GA from 30 through 32 weeks by 29% without missing any cases of Type 1 ROP.⁹

We took advantage of recent longitudinal exam data from the Telemedicine Approaches to Evaluating Acute-Phase ROP (e-ROP) study, a prospective cohort study to compare eye examinations with remote evaluation of digital images. We used a subset of the data for those from 32 through 40 weeks PMA. Unlike earlier risk-prediction models, we considered the degree to which knowledge of the previous retinal exam findings predicted the subsequent development of ROP.

Methods

This is a secondary analysis of data from the e-ROP study. The e-ROP study was designed to enroll subjects with an increased likelihood of developing ROP. The study enrolled infants with BW < 1251 g from eleven clinical centers in the US and one in Canada from 2011 through 2013. Subjects included those born within each center or transferred from other NICUs for clinical management (e.g., chronic lung disease, necrotizing enterocolitis, post-hemorrhagic hydrocephalus, progressive ROP). The exclusion criteria included PMA > 39 weeks at the first opportunity for an eye exam within an e-ROP clinical center, admission to an e-ROP clinical center with treated or known regressing ROP, the presence of a significant media opacity precluding visualization of the retina, or major ocular or systemic congenital abnormality. Infants were included if their parents or guardians provided informed consent. Overall, 60% of eligible subjects were enrolled. The e-ROP study did not specify the timing of eye exams; instead, exams were conducted as indicated by the neonatologists and the study-certified ophthalmologists.

For this analysis, we included only those exams conducted from 32 through 40 weeks PMA or NICU discharge/transfer if that occurred first. We only evaluated the first exam in any particular week of PMA for infants who received more than one exam. We also excluded exams after infants were found to have Type 1 ROP because these infants would usually receive treatment and we excluded infants with mature retinæ bilaterally because these infants would no longer need routine eye exams for the detection of clinically significant ROP. The Duke University School of Medicine institutional review board and the institutional review boards from each of the clinical centers approved this study.

Classification of Eye Exams

Infants were classified as having mild, Type 2, or Type 1 ROP based on classification of the more severely affected eye.¹⁰ As previously described, we assumed that infants identified with type 1 ROP would be treated and infants with mature retina would no longer require subsequent exams for ROP. We also assumed that infants with type 2 ROP (ie, zone 1, stage 1 or 2 ROP without plus disease or zone II, stage 3 ROP without plus disease), mild ROP (ie, any degree of ROP that does not meet the criteria for type 2 ROP), or immature retinæ bilaterally would continue to need subsequent eye exams.

Predictor Variables

Potential predictor variables for ROP status included: GA, classified as 25 weeks, 26 or 27 weeks, 28 or 29 weeks, or 30 weeks; PMA in weeks; BW, classified as small for gestational age (SGA) or appropriate for gestational age (AGA);¹¹ multiparity, classified as singleton or multiple; sex; race/ethnicity, classified as non-Hispanic white, non-Hispanic black, Hispanic, other, and unknown, and relative average daily weight gain. The weight of all subjects within 24 hours of each eye exam was recorded. For the first examination, the relative average daily weight gain (g/kg/day) was based on the difference between the weight recorded at time of the eye exam and the birth weight normalized to the average of the two weights. For subsequent eye exams, the relative average daily weight gain (g/kg/

day) was based on the difference between the weight at the current eye exam and the weight at the previous exam normalized to the average of the two weights.¹²

In addition to these variables, we also considered whether knowledge of ROP status from previous exams was a predictor of current eye exam findings. To do this, we evaluated the eye exam from the previous week, classified as immature, mild or Type 2, or unknown if the infant did not have an exam in the study center in the previous week. We assumed that prior to 32 weeks PMA all subjects would have immature retina. In clinical management, infants with immature retina or mild ROP often wait for two weeks before the next exam. Therefore, we imputed the exam from the previous week with the results from two weeks earlier if the eyes were immature or had mild ROP.

Statistical Analyses

Chi-squared tests were used to assess for differences across categorical variables. The Spearman correlation coefficient was used to test the justification of categorizing infants at each exam based on the most severely affected eye. For these comparisons, we considered $P < 0.05$ to be statistically significant. Kaplan-Meier curves stratified by GA were constructed to determine the cumulative probability over time, based on PMA, that subjects would develop Type 1 ROP and thus need treatment, or mature retina and thus not require subsequent exams. Next, we developed separate logistic regression models to predict the odds of having Type 1 ROP and the odds of having mature retinæ. For these models, we separately assessed the association between each predictor variable and outcome adjusted to GA and PMA and the clustering of infants within each clinical site. We included those variables associated with $P < 0.20$ in univariate analyses. To assess the performance of the prediction models, goodness of fit was evaluated by measuring the area under the receiver operating characteristic curve (AUC). To simplify the model, predictors were then iteratively removed starting with the least strongly associated variable. The AUC between models was compared with evaluate whether further simplification was possible. We then combined these two models into a multinomial logistic regression model with robust variance estimates to predict the likelihood and 95% confidence intervals (CIs) of the following three outcomes from an exam: Type 1 ROP, mature retina, or the need for future exams (i.e., immature retina, mild ROP, or Type 2 ROP). Stata 12 statistical software (StataCorp LP; College Station, TX) was used for all analyses.

Results

There were 1,257 infants enrolled in the e-ROP study with eye examination data. Among these, 13 subjects were excluded because all exams were conducted before 32 weeks PMA and 5 were excluded because all exams were conducted after 40 weeks PMA, leaving 1,239 infants with a total of 3,714 eye exams conducted from 32 through 40 weeks PMA for this analysis. Among the subjects included in this analysis, 7 died. Causes of death included infection, respiratory failure, necrotizing enterocolitis, and encephalopathy. Among the subjects that did not develop Type 1 ROP or mature retinæ bilaterally by 40 weeks PMA or by exit from the study (i.e., death, discharge or transfer from the study center), the median PMA of the last exam was 37 weeks (IQR: 35-39 weeks).

Figure 1 (available at www.jpeds.com) illustrates the distribution of the number of eye exams by GA and PMA. For each subject, the median number of eye exams by week of PMA from 32 through 40 weeks PMA was 3 (interquartile range (IQR): 2-4). The overall median number of days between eye exams was 14 (IQR: 7-39). The median number of days between the 1,329 eye exams that occurred in consecutive weeks by PMA was 7 days (IQR did not vary), for the 1,047 exams that were performed at a 2-week interval was 14 days (IQR did not vary), and for the 89 exams that were performed at a 3-week interval was 20 days (IQR: 17-21 days). The median PMA for the final exam in the dataset was 37 weeks (IQR: 35-39 weeks). The Spearman correlation coefficient for inter-eye agreement of ROP findings at each exam was 0.93 (P for test of independence <0.001).

Among the 428 infants with GA ≥ 25 weeks, the GA was 22 weeks for 2 infants (0.5%), 23 weeks for 79 (18.5%), 24 weeks for 156 (36.5%), and 25 weeks for 191 (44.6%) (Table I). The median relative average daily weight gain was 13 g/kg/day (IQR: 10 g/kg/day -16 g/kg/day). Weight was missing for 24 ($<0.1\%$) of the eye exams. Eight of the subjects had Type 1 ROP at 32 weeks PMA, all of whom had GA ≥ 25 weeks (4 with GA of 23 weeks, 2 with GA of 24 weeks, and 2 with GA of 25 weeks).

Probability Developing Type 1 ROP, Mature Retina, or Needing Subsequent Exams

Figure 2 illustrates the cumulative likelihood of developing Type 1 ROP (i.e., needing treatment) by PMA stratified by GA. The development of Type 1 ROP was more likely among those with lower GA ($P < 0.001$). By 40 weeks PMA, 33% (95% CI: 27%-40%) of those with GA ≥ 25 developed Type 1 ROP. In contrast, Type 1 ROP developed among 10% (95% CI: 6%-15%) of those with GA of 26 or 27 weeks and 4% (95% CI: 1%-18%) of those with GA of 28 or 29 weeks. No cases of Type 1 ROP occurred among infants with GA ≥ 30 weeks.

Figure 3 illustrates the cumulative likelihood of having mature retinæ bilaterally by PMA stratified by GA. By 40 weeks PMA, the likelihood of having mature retina increased with GA, from 22% (95% CI: 16%-30%) among those with GA ≥ 25 weeks, to 42% (95% CI: 36%-49%) among those with GA of 26 or 27 weeks, to 73% (95% CI: 61%-84%) among those with GA of 28 or 29 weeks, and to 88% (95% CI: 74%-96%) among those with GA ≥ 30 weeks.

Figure 4 illustrates the cumulative likelihood of needing follow-up (i.e., immature, mild ROP, or Type 2 ROP). By 40 weeks PMA, about half of those with GA ≥ 27 weeks needed subsequent eye exams (GA ≥ 25 weeks: 51% (95% CI: 44%-58%); 26 or 27 weeks: 51% (95% CI: 45%-58%)). The proportion needing subsequent eye exams by 40 weeks PMA was lower among those with a GA of 28 or 29 weeks (26% (95% CI: 15%-37%)) or ≥ 30 weeks (12% (95% CI: 4%-26%)).

Model Development for Predicting Exam Findings

After adjusting for GA and PMA, the odds of developing Type 1 ROP was associated with previous eye exam findings (ie, immature, any ROP, unknown; $P < 0.001$), race (non-Hispanic Black vs. non-Hispanic White; $P = 0.02$), and being SGA ($P = 0.03$). The odds of

developing Type 1 ROP was not associated with multiparity ($P = 0.54$), sex ($P = 0.61$), average daily relative weight gain ($P = 0.87$), or being Hispanic ($P = 0.86$); these four variables did not meet criteria for inclusion in the development of the model. The AUC for the full model predicting Type 1 ROP, including GA, PMA, previous eye exam findings, race, and SGA status was 0.80 (95% CI: 0.76-0.83). However, a reduced model, including only GA, PMA, and previous exam findings had a similar AUC (0.78, 95% CI: 0.74-0.81).

After adjusting for GA and PMA, the odds of developing mature retinæ bilaterally were associated with previous exam findings ($P < 0.001$), SGA status ($P < 0.001$), and race (ie, non-Hispanic Black vs. non-Hispanic White; $P = 0.02$). Although not statistically associated with the odds of developing mature retina, ethnicity (i.e., Hispanic vs. non-Hispanic; $P = 0.07$), sex ($P = 0.09$) met the criteria ($p < 0.2$) for inclusion in model development. Multiparity ($P = 0.69$) and average daily relative weight gain ($P = 0.30$) were not included in model development. The AUC for the full model predicting mature retina, including GA, PMA, previous eye exam findings, race, ethnicity, and sex was 0.85 (95% CI: 0.84-0.87), which was similar to the reduced model including only GA, PMA, and previous exam findings (0.85, 95% CI: 0.83-0.87).

Predicted Probability of Type 1 ROP, Mature Retinæ, or Needing Subsequent Exams

Table II (available at www.jpeds.com) lists the predicted probability of finding type 1 ROP on a particular exam and Table III (available at www.jpeds.com) lists the predicted probability of finding mature retinæ bilaterally on a particular exam. The predicted probability of needing subsequent eye exams was similar across PMA by the categories of GA. As with the cumulative probability analysis, the predicted probability of finding type 1 ROP decreased with increasing GA. The predicted probability of finding type 1 GA generally increased with PMA, but the confidence intervals are wide because of the low incidence of type 1 ROP. The predicted probability also decreased if the previous exam was immature compared with the previous exam having any ROP (ie, mild, type 2). When the previous exam findings are unknown or cannot be imputed, the confidence intervals are wider than when specific information is available.

The predicted probability of finding mature retinæ bilaterally on a particular exam increases with GA and PMA. However, if the previous exam had any ROP or if the previous exam was unknown the predicted probability decreases. Among infants born ≥ 30 weeks GA, the previous exam findings had little impact on the predicted probability of having mature retina among those with GA ≥ 30 weeks because none of the infants in this group developed Type 1 ROP.

Discussion

Without early detection and timely treatment of serious disease, ROP may lead to blindness. Although there are many clinical factors associated with the development of ROP, risk stratification has been challenging. Current guidelines recommend eye exam frequency primarily on BW, with the first exam driven by GA and PMA. We found that prediction of the findings of an eye exam based on GA, PMA, and previous exam findings was at least as good as comparative models that include a wide array of clinical characteristics.

There are several strengths of this study. The findings were based on prospectively collected data. The e-ROP study did not mandate the timing or frequency of eye exams. As such, information including knowledge of the eye exam in the previous week reflects how care is typically provided in level III NICUs in US and Canada nowadays. There are, however, several limitations. We included eye exam data collected within the study centers from PMA of 32 through 40 weeks or NICU discharge/transfer, which restricts the range of prediction possible in this analysis. No eye exam data collected by study-certified ophthalmologists were available after discharge, including those infants discharged before 40 weeks PMA. However, of the 235 subjects who were discharged with immature retinæ bilaterally, follow-up examination information, including data from other ophthalmologists, was available for 163 (69.4%). Among these infants, none developed Type 1 ROP or received treatment for ROP. Still, there is a chance that one of the other infants developed ROP. The findings from this study should not be generalized beyond 40-weeks PMA. Another important limitation is that among the subjects included in the study, infants who stay in the NICU longer and who contributed more eye exam data might represent sicker infants who have a greater risk of developing ROP. If so, this could lead to overestimates of the risk of developing Type 1 ROP. The e-ROP study enrolled infants at greater risk of developing ROP (e.g., infants with BW < 1,251 grams, many of whom had more complex illness than typically seen in community NICUs). Thus, there were relatively fewer infants with greater GA (e.g., 30 weeks) and the overall risk of developing significant ROP was greater. Therefore, this study has limited generalizability to the entire “at risk” population as defined in the recommendations by the American Academy of Ophthalmology, the American Academy of Pediatrics, and the American Association for Pediatric Ophthalmology and Strabismus.¹

This study raises the question about whether current guidelines should be revised to not routinely recommend ROP exams for infants with GA of 30 weeks or greater unless some other specific risk factor is identified. No cases of Type 1 ROP, the current recommended severity of ROP requiring treatment, were identified among the 135 infants with GA 30 weeks. The survival-curve analysis found that among those with GA 30 weeks, about 50% will need follow-up eye exams after 38 weeks PMA, about 25% will need follow-up eye exams after 39 weeks PMA, and about 10% will need follow-up eye exams after 40 weeks PMA, ages when many infants have been safely discharged home. Future work should explicitly evaluate the tradeoffs in changing the recommendations for this group of infants before routine practice is changed. The full e-ROP study will help determine the circumstances under which a telemedicine approach to retinal imaging can be safely substituted for eye exams.

Findings from this study can help NICUs in resource management. Given the distribution of infants by GA and PMA within a NICU, neonatologists and ophthalmologists can estimate the likelihood that further eye care, including further exams or treatment, will be required after discharge or transfer. Neonatologists and ophthalmologists can use the tables from the risk-prediction model to facilitate communication with families about the expected outcome based on the PMA of the baby and the eye findings at a particular exam. This might also help with decisions around transfer or discharge. Of course, the limitations of these risk

predictions should be recognized: they were developed for a population at high risk and do not inform about outcomes after 40 weeks PMA.

Although our findings support a low risk for developing ROP requiring treatment for infants with GA $\geq$ 30 weeks, the ability to predict with a high degree of confidence the likelihood that any particular infant with GA $<$ 30 weeks will develop ROP that requires treatment remains elusive. Because of the risk of untreated Type 1 ROP, current care is necessarily inefficient, with many infants at low risk receiving repeated eye exams over time.

Acknowledgments

Supported by the National Institutes of Health (U10EY017014).

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Abbreviations

AGA	appropriate for gestational age
AUC	Area under the curve
BW	Birth Weight
e-ROP	Telemedicine Approaches to Evaluating Acute-Phase ROP
GA	Gestational Age
IQR	interquartile range
NICU	neonatal intensive care unit
ROP	retinopathy of prematurity
PMA	postmenstrual age
SGA	small for gestational age

Figure 1. (online). The number of eye exams included in e-ROP by postmenstrual age (PMA) and gestational age (GA), in weeks.

Figure 2.

The likelihood of developing Type 1 retinopathy of prematurity (ROP) over time, based on postmenstrual age (PMA) stratified by gestational age, in weeks. No cases of Type 1 ROP occurred in infants with GA ≥ 30 weeks.

Figure 3.
The probability of mature retinal over time, based on post-menstrual age (PMA), stratified by gestational age (GA), in weeks.

Figure 4. The probability of needing follow-up (i.e., immature, mild ROP, or Type 2 ROP) over time, based on post-menstrual age (PMA), stratified by gestational age (GA).

Table 1

Subject characteristics.

	N = 1,239* % (n)
GA	
25 weeks	35% (428)
26 or 27 weeks	33% (413)
28 or 29 weeks	21% (263)
30 weeks	11% (135)
BW	
SGA	15% (183)
AGA	85% (1,056)
Sex	
Male	51% (626)
Female	50% (613)
Parity	
Singleton	70% (870)
Multiple	30% (369)
Race/Ethnicity	
Non-Hispanic white	49% (611)
Non-Hispanic black	30% (366)
Hispanic	10% (120)
Other	5% (56)
Unknown	7% (86)
Final ROP Status [†]	
Immature	19% (235)
Mild	37% (464)
Type 2	7% (91)
Type 1	10% (124)
Mature	26% (325)

* Percentages may not add to 100% because of rounding.

[†] Final status by 40 weeks, NICU discharge/transfer, or first exam revealing Type 1 ROP or mature retinæ bilaterally.

Table 2

(online). Predicted probability (%) and 95% confidence interval of having Type 1 retinopathy of prematurity (ROP) by postmenstrual age (PMA) in weeks, stratified by gestational age (GA) in weeks and findings from the previous eye exam. No cases of Type 1 ROP occurred in infants with GA $\geq$ 30 weeks.

GA (weeks)			
	25	26 or 27	28 or 29
PMA (weeks)	Type 1 ROP		
Previous Exam Immature [*]			
32	3.6 (1.0-6.2)	0.7 (0.1-1.2)	0.1 (0-0.3)
33	0 (0-1.0)	0 (0-0.1)	0 (0-0)
34	0.5 (0-1.5)	0.1 (0-0.2)	0 (0-0)
35	0.6 (0-1.6)	0.1 (0-0.3)	0 (0-0.1)
36	0.7 (0-2.3)	0.1 (0-0.3)	0 (0-0.1)
37	0.7 (0-2.0)	0.1 (0-0.3)	0 (0-0.1)
38	0.8 (0-2.3)	0.1 (0-0.3)	0 (0-0.1)
39	0.5 (0-1.6)	0.1 (0-0.2)	0 (0-0)
40	0.6 (0-1.8)	0.1 (0-0.2)	0 (0-0)
Previous Exam Any ROP [†]			
33	4.4 (1.6-7.1)	1.3 (0.3-2.2)	0.3 (0-0.8)
34	4.9 (2.2-7.6)	1.4 (0.4-2.4)	0.4 (0-1.0)
35	4.8 (2.2-7.3)	1.4 (0.5-2.4)	0.4 (0-1.0)
36	7.1 (4.0-10.2)	2.1 (0.9-3.3)	0.6 (0-1.4)
37	6.2 (3.5-9.9)	2.0 (0.7-3.4)	0.6 (0-1.4)
38	6.7 (3.5-11.4)	2.3 (0.7-3.9)	0.7 (0-1.6)
39	5.3 (2.0-8.7)	1.6 (0.3-3.0)	0.4 (0-1.2)
40	5.9 (1.3-10.6)	1.9 (0.2-3.5)	0.5 (0-1.3)
Previous Exam Unknown [§]			
33	9.9 (5.5-14.2)	2.0 (0.9-3.0)	0.3 (0-0.8)
34	12.1 (5.8-18.5)	2.7 (0.9-4.6)	0.5 (0-1.2)
35	12.3 (6.3-18.4)	2.8 (1.0-4.6)	0.6 (0-1.3)
36	16.5 (8.5-24.5)	3.5 (1.3-5.8)	0.6 (0-1.6)
37	15.1 (7.1-23.0)	2.9 (0.8-5.1)	0.5 (0-1.2)
38	16.9 (7.1-26.7)	3.4 (0.7-6.1)	0.6 (0-1.5)
39	11.7 (3.6-19.9)	2.1 (0.2-4.0)	0.3 (0-0.9)
40	13.1 (2.5-23.6)	2.3 (0.1-4.6)	0.4 (0-1.0)

* The retinae were immature in the previous week or the retina were immature two weeks prior with no intervening eye exam. Prior to 32 weeks PMA, all retinae are assumed to be immature.

[†] The retinae had mild or Type 1 ROP in the previous week or mild ROP was present two weeks prior with no intervening eye exam. Prior to 32 weeks PMA, the retinae all are assumed to be immature.

[§]No exam data from the previous week and the exam could not be otherwise classified as immature or having any ROP.

Table 3

(online). Predicted probability (%) and 95% confidence interval of having mature retina by postmenstrual age (PMA) in weeks, stratified by gestational age (GA) in weeks and findings from the previous eye exam.

	GA (weeks)			
	25	26 or 27	28 or 29	30
PMA (weeks)	Mature Retina			
Previous Exam Immature*				
32	1.6 (0.5-2.7)	3.6 (1.4-5.8)	4.6 (1.9-7.2)	3.9 (1.4-6.5)
33	2.7 (1.2-4.2)	4.6 (2.4-6.9)	5.2 (2.5-7.8)	4.1 (1.7-6.5)
34	5.0 (2.6-7.3)	9.3 (5.7-13.0)	10.9 (6.9-15.0)	9.1 (5.2-13.1)
35	8.9 (5.3-12.5)	17.2 (12.3-22.1)	20.7 (14.7-26.7)	18.2 (12.2-24.2)
36	16.4 (10.5-22.3)	28.9 (21.7-36.1)	33.3 (25.7-40.9)	29.5 (21.1-37.9)
37	25.9 (17.5-34.3)	42.5 (33.8-51.2)	47.9 (38.4-57.4)	43.7 (32.7-54.8)
38	25.6 (16.4-34.8)	41.9 (32.2-51.7)	47.1 (36.8-57.3)	42.6 (31.0-54.2)
39	37.0 (25.7-48.4)	56.5 (45.0-68.0)	62.4 (50.4-74.3)	58.8 (44.5-73.0)
40	36.7 (22.8-50.6)	55.9 (42.2-69.6)	61.6 (47.5-75.7)	57.7 (41.3-74.1)
Previous Exam Any ROP†				
33	0.2 (0.1-0.3)	0.7 (0.3-1.1)	1.3 (0.5-2.2)	2.2 (0.7-3.7)
34	0.3 (0.1-0.4)	1.0 (0.4-1.5)	2.0 (0.9-3.0)	3.5 (1.4-5.6)
35	0.4 (0.2-0.7)	1.6 (0.9-2.2)	3.3 (1.7-4.9)	6.0 (2.8-9.2)
36	0.9 (0.4-1.3)	3.2 (1.8-4.6)	6.6 (3.7-9.6)	11.7 (5.8-17.6)
37	1.5 (0.7-2.2)	5.4 (3.2-7.5)	11.1 (6.3-15.8)	18.8 (10.1-27.5)
38	1.4 (0.6-2.2)	5.3 (2.9-7.6)	11.1 (6.0-16.2)	18.7 (9.5-28.0)
39	2.2 (1.1-3.2)	8.1 (4.7-11.4)	16.7 (9.7-23.6)	27.4 (15.8-39.1)
40	2.1 (0.8-3.5)	8.0 (3.8-12.3)	16.8 (8.2-25.3)	27.4 (13.9-40.8)
Previous Exam Unknown§				
33	2.2 (1.1-3.4)	5.4 (3.1-7.8)	7.1 (3.9-10.4)	6.4 (3.1-9.7)
34	3.4 (1.8-5.1)	9.3 (5.5-13.1)	13.3 (8.3-18.4)	13.3 (7.9-18.7)
35	5.7 (3.2-8.1)	15.8 (10.9-20.8)	23.2 (16.1-30.3)	24.5 (16.9-32.1)
36	10.5 (6.3-14.7)	27.3 (19.9-34.7)	37.3 (28.7-45.9)	38.3 (29.0-47.7)
37	16.9 (10.6-23.1)	39.9 (31.3-48.5)	51.9 (41.1-61.5)	53.3 (42.8-63.9)
38	16.0 (9.2-22.9)	39.3 (29.6-48.9)	51.3 (41.1-61.5)	52.4 (41.4-63.5)
39	24.5 (15.9-33.2)	52.5 (42.0-62.9)	65.1 (54.8-75.3)	67.2 (55.7-78.6)
40	23.9 (12.6-35.3)	52.0 (38.9-65.1)	64.6 (52.2-77.1)	66.4 (52.7-80.1)

* The retinae were immature in the previous week or the retina were immature two weeks prior with no intervening eye exam. Prior to 32 weeks PMA, all retinae are assumed to be immature.

† The retinae had mild or Type 1 ROP in the previous week or mild ROP was present two weeks prior with no intervening eye exam. Prior to 32 weeks PMA, the retinae all are assumed to be immature.

§ No exam data from the previous week and the exam could not be otherwise classified as immature or having any ROP.