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Validation of the Colorado Retinopathy of Prematurity Screening Model

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Key Points

Question

What is the sensitivity and specificity of the Colorado Retinopathy of Prematurity (CO-ROP) model for predicting severe ROP in a large, diverse cohort of premature infants?

Findings

In this validation study, the CO-ROP model demonstrated high but not 100% sensitivity for severe ROP and missed infants who might require treatment. Most of the infants not predicted by the CO-ROP model had obvious deviation in expected weight trajectories or nonphysiologic weight gain.

Meaning

These findings suggest that the CO-ROP model needs to be revised before considering implementation into clinical practice.

Abstract

Importance

The Colorado Retinopathy of Prematurity (CO-ROP) model uses birth weight, gestational age, and weight gain at the first month of life (WG-28) to predict risk of severe retinopathy of prematurity (ROP). In previous validation studies, the model performed very well, predicting virtually all cases of severe ROP and potentially reducing the number of infants who need ROP examinations, warranting validation in a larger, more diverse population.

Objective

To validate the performance of the CO-ROP model in a large multicenter cohort.

Design, Setting, Participants

This study is a secondary analysis of data from the Postnatal Growth and Retinopathy of Prematurity (G-ROP) Study, a retrospective multicenter cohort study conducted in 29 hospitals in the United States and Canada between January 2006 and June 2012 of 6351 premature infants who received ROP examinations.

Main Outcomes and Measures

Sensitivity and specificity for severe (early treatment of ROP [ETROP] type 1 or 2) ROP, and reduction in infants receiving examinations. The CO-ROP model was applied to the infants in the G-ROP data set with

all 3 data points (infants would have received examinations if they met all 3 criteria: birth weight, <1501 g; gestational age, <30 weeks; and WG-28, <650 g). Infants missing WG-28 information were included in a secondary analysis in which WG-28 was considered fewer than 650 g.

Results

Of 7438 infants in the G-ROP study, 3575 (48.1%) were girls, and maternal race/ethnicity was 2310 (31.1%) African American, 3615 (48.6%) white, 233 (3.1%) Asian, 40 (0.52%) American Indian/Alaskan Native, and 93 (1.3%) Pacific Islander. In the study cohort, 747 infants (11.8%) had type 1 or 2 ROP, 2068 (32.6%) had lower-grade ROP, and 3536 (55.6%) had no ROP. The CO-ROP model had a sensitivity of 96.9% (95% CI, 95.4%-97.9%) and a specificity of 40.9% (95% CI, 39.3%-42.5%). It missed 23 (3.1%) infants who developed severe ROP. The CO-ROP model would have reduced the number of infants who received examinations by 26.1% (95% CI, 25.0%-27.2%).

Conclusions and Relevance

The CO-ROP model demonstrated high but not 100% sensitivity for severe ROP and missed infants who might require treatment in this large validation cohort. The model requires all 3 criteria to be met to signal a need for examinations, but some infants with a birth weight or gestational age above the thresholds developed severe ROP. Most of these infants who were not detected by the CO-ROP model had obvious deviation in expected weight trajectories or nonphysiologic weight gain. These findings suggest that the CO-ROP model needs to be revised before considering implementation into clinical practice.

Introduction

Retinopathy of prematurity (ROP) is a proliferative retinal vascular disorder affecting premature infants and a leading cause of childhood visual impairment in the United States and worldwide. The Cryotherapy for ROP and Early Treatment for ROP studies demonstrated improved visual and retinal outcomes in infants with severe ROP when treated; thus, detecting clinically significant ROP is essential.

The current guidelines for ROP examinations in the United States (birth weight [BW] of <1501 g, gestational age at birth [GA] of 30 weeks or less, or an “unstable clinical course”) have low specificity in detecting ROP, with fewer than 10% of infants examined needing treatment for ROP. Significant interest in improving screening efficiency for infants at risk for ROP has led to the development of several proposed prediction models that incorporate slow postnatal weight gain, which is associated with the subsequent development of ROP. One of these models is the Colorado Retinopathy of Prematurity (CO-ROP) model.

The CO-ROP model requires that both BW and GA criteria be met rather than 1 criterion, as well as an additional weight gain criterion measured at age 4 weeks (28 days) to improve the prediction of the development of ROP. The model proposed ROP examinations be performed only for infants with a GA of 30 weeks or less, a BW of less than or equal to 1500 g, and a net postnatal weight gain less than or equal to 650 g between birth and age 4 weeks. This model showed promise to improve screening efficiency for ROP in an original cohort of 499 Colorado infants at risk for ROP, an expanded cohort of 1225 Colorado infants, and a cohort of 858 infants at risk for ROP from 4 geographically diverse centers. Sensitivity for severe ROP in these studies was 100% (95% CI ,92.1%-100.0%), 100% (95% CI, 97.1%-100%), and 98.1% (95% CI, 93.4-99.8); and specificities were 33.7% (95% CI, 28.7%-39.1%), 39.2% (95% CI, 35.8%-42.7%); and 31.3% (95% CI, 27.6%-35.1%), respectively. These studies were limited by sample sizes that were too small to provide precise estimates of sensitivity, as represented by the sensitivity confidence intervals, and by the limited degree of diversity of the infants studied.

We sought to evaluate the performance of the CO-ROP model in a much larger sample and more diverse patient population by applying the CO-ROP model to the cohort of infants in the Postnatal Growth and

Retinopathy of Prematurity (G-ROP) study, a contemporary cohort of infants that included 7483 infants from 29 North American hospitals. Secondarily, we considered whether any revisions to the model would improve its performance.

Methods

We performed a secondary analysis of data from the G-ROP Study, which was a National Eye Institute–sponsored study of infants who received ROP examinations at 29 North American hospitals between January 2006 and June 2012. Data collection for the G-ROP Study was performed retrospectively between 2013 and 2015. Institutional review board approval for the G-ROP study was obtained and a waiver of informed consent was granted at the study headquarters (Children's Hospital of Philadelphia), the study data-coordinating center (University of Pennsylvania), and at all study hospitals (see the Acknowledgments), and the study was carried out according to the principles of the US Health Insurance Portability and Accountability Act.

Participants

All 7483 infants in the G-ROP Study had a known ROP outcome, GA, and BW. Retinal examinations were completed by a fellowship-trained pediatric ophthalmologist or retinal specialist with expertise in ROP diagnosis and familiarity with describing ROP using International Classification of ROP terms. The GA of the patient was determined by the best obstetrical estimate when available and alternatively by neonatologist estimation based on physical examination. Birth weights in grams were obtained from the labor and delivery notes and, if not available, from the patient's admission note. An additional inclusion criteria for the primary analysis of the CO-ROP validation was an available weight measurement at age 28 days (day of life 29). Weight measurements were abstracted from the nursing flow sheet in the patient's medical record.

Statistical Analysis

In the primary analysis of this study, the CO-ROP model was applied to the subcohort of infants who met the previously mentioned inclusion criteria. Infants with a BW of 1500 g or less, a GA at delivery of 30 weeks and 6 days or less, and a weight gain of 650 g or less between birth and age 28 days (day of life 29) would be identified as high risk and would undergo ROP examinations. All 3 criteria would have to be met for an infant to be identified as high risk. Gestational age was rounded down so that an infant who was 29 weeks and 6 days old was included as 29 weeks, consistent with previous ROP studies. In a secondary analysis, all infants in the G-ROP Study were included in the analysis, and infants with missing weight measurement data at 28 days (day of life 29) were treated as if their weight gain was less than 650 g. This secondary analysis was performed because in a hypothetical clinical application of the model, missing weight data would be treated in this fashion.

The primary outcome measures for the analysis were the sensitivity for severe ROP and the reduction in infants who would have received examinations by using the CO-ROP model. The Wilson method was used for calculating the 95% confidence interval. Retinopathy of prematurity for each infant was defined as the highest-stage and lowest-zone ROP in the more affected eye at the examination with the most severe ROP. Severe ROP was defined as type 1 or type 2 ROP, according to the recommendations from the Early Treatment of Retinopathy of Prematurity (ET-ROP) randomized clinical trial. Retinopathy of prematurity not meeting type 1 or type 2 criteria was categorized as "low-grade" ROP. All analyses were performed using SAS statistical software, version 9.3 (SAS Institute).

An a priori plan was established to examine the available medical histories of any infants with severe ROP who were not detected by the CO-ROP model to gain insight into the characteristics of such infants and to

identify potential modifications to the CO-ROP model that might improve its performance. Weight gain is a critical covariate in the CO-ROP model, and we recently observed that deviations in expected weight gain are a risk factor for ROP. Therefore, an assessment was made for factors that could have contributed to a nonphysiologic weight gain, such as surgery, sepsis, hydrocephalus, twin-to-twin transfusion syndrome, intraventricular hemorrhage, chromosomal abnormalities, other systemic or genetic diagnoses, or heart disease. Additionally, because infants who are small for GA are at increased risk for severe ROP and other ROP risk prediction models failed to detect infants at the higher end of expected BW for age, the birth percentiles of infants not detected by the CO-ROP model were examined to identify infants at extremes of expected BW. Finally, the Fenton growth curve for premature infants was used to understand where the infants missed by the CO-ROP model were on their expected growth curve; weight percentages for age using the Fenton growth curve were determined at birth and at age 1 month.

Results

For the 7483 infants in the G-ROP Study, the mean (SD) GA was 28 (2.6) weeks, mean (SD) birth weight was 1100 (363) g, and 3575 infants (47.8%) were girls. Maternal race/ethnicity was white for 3615 (48.3%), African American for 2310 (30.9%), Asian for 233 (3.1%), American Indian/Alaskan Native for 40 (0.5%), Pacific Islander for 93 (1.2%), other for 526 (7.0%), and unknown for 666 (8.9%) (Table 1).

A total of 6351 infants (84.9%) had an available weight measurement at 28 days (day of life 29) and were included in the primary evaluation of the CO-ROP model. Among these 6351 infants, 352 (5.5%) had type 1 ROP, 395 (6.2%) had type 2 ROP, 2068 (32.6%) had low-grade ROP, and 3536 (55.7%) did not have ROP (Table 2). When compared with the infants without weight measurements at 28 days, the infants with weight data at 28-days-old had statistically significantly lower BW, were born at a younger GA, and a higher percentage had severe ROP (eTable in the Supplement).

In this cohort, the CO-ROP model correctly predicted 724 of 747 infants (96.9%) with severe ROP (Table 3). The sensitivity for severe ROP was 96.9% (95% CI, 95.4%-97.9%) and the specificity was 40.9% (95% CI, 39.3%-42.5%). Application of the CO-ROP model in this cohort of infants would have eliminated ROP examinations for 1655 infants (26.1%) (95% CI, 25.0%-27.2%).

In a secondary analysis, infants with missing weight data at 28 days (day of life 29), were treated as having a weight gain of less than 650 g. With these infants included in the analysis, the CO-ROP model correctly predicted 908 of 931 infants (97.5%) with severe ROP (Table 4). The sensitivity for severe ROP was 97.5% (95% CI, 96.3%-98.4%) and using the CO-ROP model in this fashion would have eliminated ROP examinations for 2154 infants (28.8%) (95% CI, 27.8%-29.8%).

Application of the CO-ROP model in this cohort would have missed 23 infants (3.1%) with severe ROP (14 infants with type 1 ROP and 9 infants with type 2 ROP). The characteristics of these 23 infants appear in Table 5. Eleven infants (48%) had a history suggestive of nonphysiologic weight gain. Specifically, these infants had hydrocephalus, anasarca, necrotizing enterocolitis with or without perforation, complex congenital heart disease, or twin-to-twin transfusion syndrome. Of the remaining 12 infants without a history suggestive of nonphysiologic weights, 11 infants were either born in the top 20% or bottom 20% of expected weight for GA and/or were in the top 20% or bottom 20% of expected weight at 28 days on the Fenton growth curve for premature infants. One infant with severe ROP missed by the CO-ROP model did not have obvious deviations in expected weight (Table 5).

Discussion

We evaluated the CO-ROP model in a large, diverse cohort of premature infants and found the sensitivity of the model for severe ROP was high but not 100%. The CO-ROP model was developed initially in 499 infants at a single tertiary academic center in Colorado with the goal of investigating the relationship of

weight gain at 1 time (age 4 weeks) on the risk of ROP. The current study built on previous, smaller validation studies of this model and facilitated a greater understanding of the model's potential to screen for severe ROP. The G-ROP Study data provided a more ethnically, racially, and geographically diverse population and many infants at risk for ROP.

In this study, the CO-ROP model performed well, with a sensitivity for detecting severe ROP of 96.9%. However, the lower boundary of the 95% confidence interval was 95.4%, and the CO-ROP model missed identifying 23 infants (3.1%) with severe ROP. An ideal ROP prediction model must have extremely high sensitivity for detecting clinically significant ROP, approaching 100% with a narrow confidence interval, to ensure no missed cases of treatment-requiring ROP.

Several models have been proposed in recent years to incorporate postnatal weight gain to predict ROP in the hopes of improving ROP screening efficiency. While these models have 100% sensitivity for severe ROP in small development or validation cohorts, they all have reduced sensitivity when studied in larger cohorts. The weight, insulin-like growth factor 1, neonatal, ROP (WINROP) group from Sweden developed a proprietary formula that initially also used insulin-like growth factor 1 levels to predict ROP. This model was later revised to use only weight gain as a surrogate for insulin-like growth factor 1 levels to predict ROP but excluded infants with nonphysiologic weight. The WINROP formula has been studied in multiple populations with generally good, but somewhat variable results. The WINROP model initially demonstrated 100% sensitivity for severe ROP, but in a larger validation study, it demonstrated a drop in sensitivity similar to the CO-ROP model. The first ROP prediction model from the United States to study weight gain and ROP was Premature Infants in Need of Transfusion model. During model development in a high-risk cohort, the investigators evaluated multiple risk factors in addition to weight gain, including race/ethnicity, sex, medications, and neonatal complications, but they concluded that weight gain, GA, and BW were the only variables that remained predictive in a multivariable model. They then expanded their model to a broader-risk cohort to develop the Children's Hospital of Philadelphia (CHOP)–ROP model, which had an identical structure that consisted of a logistic regression equation with 3 factors. The CHOP-ROP model has been validated in 2 different populations with high sensitivity but did miss some infants with severe ROP when applied to a cohort from Colorado and most recently demonstrated a sensitivity of 98.5% when tested in the G-ROP data set. Another equation-based ROP prediction model, ROP score, was developed in Brazil and includes BW, GA, weight gain at 6 weeks, blood transfusion, and the use of oxygen. Retinopathy of prematurity score was developed using 474 infants and demonstrated a sensitivity of 98% for detecting treatment-requiring ROP in the development study. In the 1 published validation study of this model, which involved 445 Italian infants at risk for ROP, ROP score performed well, with 100% sensitivity. Notably, the CHOP-ROP model also had 100% sensitivity of detecting severe ROP in this same cohort.

Any model suitable for clinical use would be easy to use, accessible, and have widespread acceptance by ophthalmologists and neonatologists. In this regard, 2 strengths of the CO-ROP prediction model are its ease of use and transparency. The CO-ROP model has a simple structure, similar to current ROP guidelines. However, an important distinction is that all 3 criteria must be met in the CO-ROP model, whereas current ROP guidelines require only 1 criterion to be met. As a result, the CO-ROP model did not identify all cases of severe ROP when applied to this very large and diverse cohort. Nevertheless, this study provided valuable insight into why infants were missed, how to modify the CO-ROP model, and generally what to consider in developing an ROP predictive model.

We examined the medical histories of the infants for which the CO-ROP model did not predict severe ROP to understand which infants might develop ROP despite significant (>650 g) weight gain at age 4 weeks. We sought to identify patterns that might help revise the model, as well as better understand which infants are at risk of severe ROP. Three characteristics emerged among the 23 infants missed by the model: (1)

conditions causing nonphysiologic weight gain, such as twin-to-twin transfusion syndrome, necrotizing enterocolitis, anasarca, and complex cardiac disease; (2) a weight percentage less than or greater than what was expected at 28 days; and (3) a BW in the top or bottom 20% for GA at birth. All but 1 infant (baby 18; Table 5) had 1 or more of these findings. Therefore, adding criteria to CO-ROP that provide for examinations when there is a neonatologist concern for nonphysiologic weight gain or when there are extremes of BW or extremes of weight gain at 28 days could potentially make the model more suitable for clinical use. Based on the G-ROP study data, modifying the CO-ROP model to incorporate screening infants with 1 or more of these factors would improve the model's sensitivity for detecting severe ROP to 99.9% (95% CI, 99.3%-100%). However, doing so would also probably decrease the beneficial reduction in the number of infants requiring examinations. We reviewed the medical records of these 23 infants. It was not feasible to review the medical records of all infants in the G-ROP study in the same fashion, so we could not calculate the magnitude by which the reduction in infants requiring examinations would decrease. Finally, any modification of the model requires additional validation before clinical use.

Limitations

There are limitations to our study to consider. Although data collection was retrospective, the relevant clinical data, including BW, GA, weight measurements, and ROP examination results, are likely reliable and represent the general variation that might arise in clinical practice with regard to these specific data. Retinopathy of prematurity examinations were performed by ophthalmologists with expertise in ROP using standardized terminology. Moreover, the representation of clinical variations in the data set is important for improving the value of a prediction model validation study, as the data allow the investigators to better understand how the model might perform if applied clinically. Similarly, the large number and wide geographic distribution of the participating hospitals in the G-ROP Study are representative of differences in clinical practice across the United States and Canada. Finally, the CO-ROP model would not be expected to perform well in countries with developing neonatal care systems where oxygen use plays a more dominant role in the pathophysiology of ROP and larger-BW and older-GA infants develop severe ROP. Similar predictive models have performed poorly in such settings.

Weight gain–based predictive models may help to reduce the number of infants requiring examinations to identify treatment-requiring ROP. Such models potentially could also be applied to reduce the frequency of ROP examinations for infants receiving examinations, as suggested by WINROP, ROPscore, and CHOP-ROP; they could also be applied in combination with a telemedicine system, recently described as a "Tiered Approach to Retinopathy of Prematurity" by the evaluating acute-phase ROP and G-ROP study groups. However, the widespread adoption of a new model of ROP screening ideally should require that a consensus be reached among ophthalmologists and neonatologists regarding the acceptable performance of the model, as represented by a high sensitivity for detecting severe ROP and a simple, readily available, and easy-to-use validated model. With a large and diverse patient sample, the G-ROP Study cohort may provide an excellent cohort from whom to develop or validate a potential model.

Conclusions

The CO-ROP model had high, but not 100%, sensitivity for detecting severe ROP in this large validation study. Most infants who were not detected by the CO-ROP model had nonphysiologic weight gain or extremes in their BW or weight trajectories, a somewhat expected finding in a model centered around weight and weight gain. Revisions of this model seem warranted before it is suitable for clinical practice.

Notes

Supplement.

eTable. Characteristics of Infants With and Without Weight Data at 28 days

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Figures and Tables

Table 1.

Characteristics of Infants in the Postnatal Growth and Retinopathy of Prematurity Study (N = 7483)

Characteristic	ROP, No. (%)		
	None (n = 4259)	Low-grade (n = 2293)	Severe (Types 1 and 2) (n = 931)
Birth weight, g			
Mean (SD)	1274 (329)	927 (273)	731 (199)
Median (range)	1265 (400-3000)	880 (364-2880)	695 (310-1692)
Gestational age, full wk			
Mean (SD)	29.4 (2.1)	26.7 (2.1)	25.0 (1.6)
Median (range)	30.0 (23.0-35.0)	27.0 (22.0-35.0)	25.0 (22.0-32.0)
Female, No. (%)	2030 (47.7)	1139 (49.7)	406 (43.6)
Maternal ethnicity, No. (%)			
Hispanic or Latino	322 (7.6)	159 (6.9)	83 (8.9)
Not Hispanic or Latino	3038 (71.3)	1653 (72.1)	560 (60.2)
Unknown	899 (21.15)	481 (21.0)	288 (30.9)
Maternal race, No. (%)			
White	1995 (46.8)	1166 (50.9)	454 (48.8)
Asian	164 (3.9)	42 (1.8)	27 (2.9)
Black	1312 (30.8)	733 (32.0)	265 (28.5)
American Indian/Alaskan native	27 (0.6)	9 (0.4)	4 (0.4)
Pacific islander	74 (1.7)	14 (0.6)	5 (0.5)
Other	302 (7.1)	148 (6.5)	76 (8.2)
Unknown	385 (9.0)	181 (7.9)	100 (10.7)
Birth location, No. (%)			
Inborn	3375 (79.2)	1601 (69.8)	536 (57.6)
Outborn	884 (20.8)	692 (30.2)	395 (42.4)

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Abbreviation: ROP, retinopathy of prematurity.

Table 2.

Birth Weight, Gestational Age, and Weight Gain at 28 Days by Severity of Retinopathy of Prematurity Among Infants With Weight Data at 28 Days (N = 6351)[a]

Characteristics	ROP		
	None (n = 3536)	Low-grade (n = 2068)	Severe (Types 1 and 2) (n = 747)
Birth weight, g			
Mean (SD)	1248 (329)	925 (272)	740 (205)
Median (range)	1230 (400 to 3000)	880 (364 to 2880)	700 (372 to 1692)
Gestational age, wk			
Mean (SD)	29.2 (2.0)	26.7 (2.1)	25.1 (1.7)
Median (range)	30.0 (23.0 to 35.0)	27.0 (22.0 to 35.0)	25.0 (22.0 to 32.0)
Weight change from birth at 28 d, g			
Mean (SD)	467 (186)	341 (168)	279 (149)
Median (range)	460 (−565 to 1450)	320 (−964 to 1441)	260 (−100 to 1085)
Change <650 g, No. (%)	2992 (84.6)	1977 (95.6)	731 (97.9)

Abbreviation: ROP, retinopathy of prematurity.

[a]From analysis of variance for comparison across 3 ROP groups.

Table 3.

Prediction of Retinopathy of Prematurity Using the Colorado Retinopathy of Prematurity Model Criteria Among 6351 Infants in the Postnatal Growth and Retinopathy of Prematurity Study With Known Weight Measurement at 28 Days (Day of Life 29)

	ROP					
	Severe (Type 1 and Type 2)	Type 1	Type 2	Low-grade	Any	None
No.	747	352	395	2068	2815	3536
Alarm-positive	724	338	386	1881	2605	NA
Sensitivity, % (95% CI)	96.9 (95.4-97.9)	96.0 (93.4-97.6)	97.7 (95.7-98.8)	91.0 (89.6-92.1)	92.5 (91.5-93.5)	NA
Alarm-negative	NA	NA	NA	NA	NA	1445
Specificity, % (95% CI)	NA	NA	NA	NA	NA	40.9 (39.3-42.5)

Abbreviations: NA, not applicable; ROP, retinopathy of prematurity.

Table 4.

Prediction of Retinopathy of Prematurity Using the Colorado Retinopathy of Prematurity Model Criteria Among 7483 Infants in the Postnatal Growth and Retinopathy of Prematurity Study[a]

	ROP					
	Severe (Type 1 and Type 2)	Type 1	Type 2	Low-grade	Any	None
No.	931	459	472	2293	3224	4259
Alarm-positive	908	445	463	2083	2991	NA
Sensitivity, % (95% CI)	97.5 (96.3-98.4)	97.0 (95.0-98.2)	98.1 (96.4-99.0)	90.8 (89.6-92.0)	92.8 (91.8-93.6)	NA
Alarm-negative	NA	NA	NA	NA	NA	1921
Specificity, % (95% CI)	NA	NA	NA	NA	NA	45.1 (43.6-46.6)

Abbreviations: NA, not applicable; ROP, retinopathy of prematurity.

[a]Infants with missing weight measurements at 28 days (day of life 29) were treated as having a weight gain of less than 650 g.

Table 5.

Characteristics of 23 Infants Incorrectly Predicted as Being at Low Risk for Severe Retinopathy of Prematurity by the Colorado Retinopathy of Prematurity Model

Patient	Fenton BW %	Fenton % at 28 d	Potential Causes of Nonphysiologic Weight	GA, d	BW, g	Weight Gain at 28 d, g	Race/Ethnicity	ROP Type
1[a]	0	54	NA	25	381	799	W	2
2[a]	4	0	NA	32	1050	330	O	2
3[a]	6	26	NA	27	586	677	W	1
4[a]	7	1	NA	31	1045	520	A	2
5[a]	14	35	TTTS, multiple courses of diuretics, postoperative infection	28	760	776	W	1
6[a]	16	17	NA	30	1080	790	AA	1
7	25	69	Sepsis	25	610	675	W/H	1
8	42	74	TTTS	26	762	733	W/U	1
9	44	18	Congenital hydrocephalus, cardiac abnormalities	31	1530	575	W	1
10	46	41	Large hemangioma, nec with perforation	29	1200	730	W/U	1
11[a]	50	81	NA	25	740	699	W	1
12	54	4	Multiple cardiac abnormalities, VATER	31	1515	250	A	2
13	60	72	Congenital diaphragmatic hernia, did not meet 2013 screening criteria	31	1660	1085	W	1
14	63	63	Anasarca, complex cardiac anomalies, died	29	1309	841	AA	1
15[a]	63	14	NA	31	1590	330	AA	2
16[a]	64	92	NA	24	689	691	AA	2
17	64	64	Nec and sepsis	29	1248	788	W	2
18	69	58	NA	28	1190	669	O	1

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Abbreviations: A, Asian; AA, African American; BW, birth weight; GA, gestational age; NA, not applicable; nec, necrotizing enterocolitis; O, other; ROP, retinopathy of prematurity; TTTS, twin-to-twin transfusion syndrome; U, unknown; VATER, vertebral anomalies, anal atresia, cardiac defects, tracheoesophageal fistula and/or esophageal atresia, renal & radial anomalies and limb defects association; W, white and non-Hispanic; W/H, white and Hispanic.

[a]Infants with Fenton birth percentages in the top or bottom quintiles at birth or at 28 days.