In Reply We thank the authors for their interest in the Postnatal Growth and Retinopathy of Prematurity (G-ROP) studies. We previously reported development of the G-ROP criteria and more recently successful validation in a new cohort. The authors’ questions pertain to prediction model development. They question parameters for assessing discriminatory performance, which are associated with potential overfitting, and choice of predictive factors, which are associated with potential underfitting.

Screening for ROP represents a unique challenge. Because of the risk of blindness, sensitivity for treatment-requiring disease of proposed changes must be as high as current criteria (essentially 100%). Therefore, relevant parameters to judge new criteria are sensitivity for type 1 ROP (ensure all treatment-requiring cases are captured) and reduction in the number of infants requiring examinations (the benefit of new criteria). Thus, we chose criteria that maximally reduced the number of infants requiring examinations while maintaining 100% sensitivity for type 1 ROP. We were not interested in criteria with even marginally lower sensitivity; thus, some measures traditionally used during model development, such as the c index, were not applicable. We agree that developing a model by searching for various combinations of birth weight, gestational age, and weight gain can lead to optimistic estimates of sensitivity and reduction in the number of infants examined. However, the first study cohort was large (7483 infants) to minimize overfitting, and we tested for such bias through model validation using a second, independent cohort and demonstrated the estimates were not optimistically biased.

With regard to risk factor choice, the G-ROP criteria are a modification of current screening criteria, which are based only on birth weight and gestational age. While studies have identified other variables, invariably birth weight and gestational age have provided the greatest predictive information, with other factors adding minimal additional value. Screening decisions are a yes-or-no decision, so birth weight and gestational age are dichotomized into thresholds set high enough to capture all severe ROP. Among infants with higher birth weights and gestational ages, slow postnatal weight gain accurately predicts the few infants who develop type 1 ROP. This additional predictive information permits birth weight and gestational age thresholds to be lowered, saving many infants from examinations while maintaining 100% sensitivity. Based on development and then successful validation of the G-ROP criteria, the combination of birth weight, gestational age, and slow postnatal weight gain appears sufficiently robust to predict type 1 ROP without other factors. Also, we previously found that other factors were not necessary. In the development of Premature Infants in Need of Transfusion ROP, a predecessor to G-ROP, numerous factors were no longer significant when slow postnatal weight gain was included alongside birth weight and gestational age. Finally, screening criteria must be simple, or clinicians are unlikely to use them. Oxygen supplementation and nutritional status may be useful targets for ROP prevention, but both involve numerous complicated measures over time and are unlikely to be useful as screening criteria because of their complexity. Ultimately, successful validation of the G-ROP criteria in a second, diverse cohort, as we recently reported, provides evidence that the criteria were neither overfitted (in that sensitivity did not drop from 100%) nor underfitted (additional variables were not necessary) when they were developed in the first G-ROP study.

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CORRECTION

Update to Open Access Status: In the Brief Report titled “Reanalysis of Association of ProSOLee Substitution in Guanylate Cyclase Activating Protein-1 With Dominant Retinal Dystrophy,” published in the February issue of JAMA Ophthalmology, the authors updated the status of the article so that it is now Open Access. This article has been corrected online.