CORRESPONDENCE OPEN

Check for updates

Correspondence to "Prediction of severe retinopathy of prematurity in 24–30 weeks gestation infants using birth characteristics"

Journal of Perinatology (2022) 42:416–417; https://doi.org/10.1038/s41372-021-01150-2

TO THE EDITOR:

We read with great interest Journal Club publication entitled *Prediction of severe retinopathy of prematurity in 24–30 weeks gestation infants using birth characteristics* by Dr. R. E. Zackula and Dr. T. S. Raghuveer [1]. We are grateful for the thorough review of DIGIROP-Birth, our prediction model for ROP treatment (ROPT), and for having its appropriateness evaluated by the newly developed PROBAST instrument assessing potential risks of bias [2–4]. Below we provide justifications to the raised questions with highest concern.

WERE ALL INCLUSIONS AND EXCLUSIONS OF PARTICIPANTS APPROPRIATE? (DEVELOPMENT AND VALIDATION)

DIGIROP-Birth was based on 6947 infants born 2007–2017 at gestational age (GA) 24–30 weeks included in SWEDROP, the Swedish ROP registry. Of those, 289 (4.2%) had ROPT. From the development group, 94/7041 (1.3%) infants were excluded for missing data or date inconsistencies, 3 had ROPT. GA at birth and sex were similarly distributed in the excluded vs development group, 28.4 (SD 1.8) vs 28.3 (SD 1.9) weeks, and 47.9 vs 45.1% girls.

SWEDROP does not include race/ethnicity. A thorough validation of a model is a prerequisite for clinical implementation. If required, the model selection and/or parameter estimates might be re-evaluated for a specific population or clinical setting.

WERE THERE A REASONABLE NUMBER OF PARTICIPANTS WITH THE OUTCOME? (VALIDATION)

Although separately evaluated in our publication, 153/2122 (7.2%) infants had ROPT in the Swedish, German and US validation datasets. Per the PROBAST instrument, validation with ≥100 events is recommended [4].

WERE PARTICIPANTS WITH MISSING DATA HANDLED APPROPRIATELY? (DEVELOPMENT AND VALIDATION)

Reducing the effective sample by 1% (3/292 excluded events) and having no indication of infant selection in the excluded group, biased estimates were not expected. Internal validation including cross-validation and calibration plots, and external validations were affirmative.

WAS SELECTION OF PREDICTORS BASED ON UNIVARIABLE ANALYSIS AVOIDED? (DEVELOPMENT)

DIGIROP-Birth aimed to include few well-known risk factors available for all infants at birth; GA, sex and birth weight (BW) (*z*-score). Hence, univariable analyses were not required. The model was consecutively extended, starting with GA.

Concern was raised regarding multicollinearity for GA and BW *z*-score. We expect high correlation between GA and BW, $r = 0.79$ in this cohort. However, BW *z*-score extracts rest of the immaturity effect beside GA (and sex), $r = -0.06$. Therefore, we did not expect multicollinearity problem.

WERE RELEVANT MODEL PERFORMANCE MEASURES EVALUATED APPROPRIATELY? (VALIDATION)

In the DIGIROP-Birth publication the optimal cut-offs were not investigated. We identified cut-offs in our publication for the extended model incorporating ROP progression data (DIGIROP-Screen), proposing a clinical decision support tool [5]. Pre-specified cut-offs were defined using development group and 100% sensitivity. Applying those cut-offs on DIGIROP-Birth external validation cohort, sensitivity 149/153 (97.4%) and specificity 886/1969 (45.0%) were achieved. Further improvement of DIGIROP-Birth adding other known neo- and perinatal risk factors is planned in near future. Including more variables in a model increases the need for consideration of robust regression techniques that might reduce the potential risk for under- and overfitting.

We sincerely encourage and are thankful for all the efforts put on the validations and discussions of our work.

Aldina Pivodic [1]✉ and Ann Hellström [1]

[1] *Department of Clinical Neuroscience, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.* ✉*email: aldina.pivodic@gu.se*

REFERENCES

1. Zackula RE, Raghuveer TS. Prediction of severe retinopathy of prematurity in 24-30 weeks gestation infants using birth characteristics. J Perinatol. 2021;41:351–5.
2. Pivodic A, Hård AL, Löfqvist C, Smith LEH, Wu C, Bründer MC, et al. Individual Risk Prediction for Sight-Threatening Retinopathy of Prematurity Using Birth Characteristics. JAMA Ophthalmol. 2020;138:21–9.

Received: 16 June 2021 Revised: 22 June 2021 Accepted: 6 July 2021
Published online: 24 July 2021

3. Wolff RF, Moons KGM, Riley RD, Whiting PF, Westwood M, Collins GS, et al. PROBAST: a Tool to Assess the Risk of Bias and Applicability of Prediction Model Studies. Ann Intern Med. 2019;170:51–8.
4. Moons KGM, Wolff RF, Riley RD, Whiting PF, Westwood M, Collins GS, et al. PROBAST: a Tool to Assess Risk of Bias and Applicability of Prediction Model Studies: Explanation and Elaboration. Ann Intern Med. 2019; 170:W1–33.
5. Pivodic A, Johansson H, Smith LEH, Hård AL, Löfqvist C, Yoder BA, et al. Development and validation of a new clinical decision support tool to optimize screening for retinopathy of prematurity. Br J Ophthalmol. 2021:bjophthalmol-2020-318719. https://doi.org/10.1136/bjophthalmol-2020-318719. [Epub ahead of print].

AUTHOR CONTRIBUTIONS

Concept and design: AP and AH. Acquistion of data: AH. Statistical analysis and/or interpretation of data: AP and AH. Drafting of the letter: AP. Critical revision of the letter: AP and AH. Approval of the final letter: AP and AH.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

Correspondence and requests for materials should be addressed to A.P.

Reprints and permission information is available at http://www.nature.com/reprints

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.