

Prediction of preeclampsia Complications

In the study by Peter von Dadelszen and co-authors on the prediction of pre-eclampsia complications (Jan 15, p 219),¹ for most predictors the worst values recorded during the first 48 h after eligibility—such as the lowest platelet count and the highest liver enzyme concentrations—were used to predict complications within the same 48-h timeframe. In practice, a model based exclusively on information available at the time of admission would be more helpful, because it would allow sufficient time for effective intervention.

Another minor but still important matter of concern is the optimism in model construction. 54 predictors were considered in a dataset with a relatively small number of events: 106 in 1935 patients. Von Dadelszen and colleagues were aware of potential overfitting and used bootstrapping to correct for that. However, it is unclear from the paper and the study website whether all steps of model development, including univariable screening, assessment of linearity, finding of proper nonlinear functional forms, and testing of interactions, were also considered in the validation process.² Insufficient adjustment for optimism is known to lead to flattered estimates of model performance.

We would therefore like to suggest a more cautious interpretation of the performance of this promising model. Introduction into clinical practice as an online risk calculator, before further validation and in the absence of evidence of improved outcome through effective measures, seems premature.

We declare that we have no conflicts of interest.

* *Parvin Tajik, Katrien Oude Rengerink, Wessel Ganzevoort, Aeilko H Zwinderman, Ben Willem Mol, Patrick M Bossuyt*
p.tajik@amc.uva.nl

Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Center Amsterdam, 1105 AZ Amsterdam, Netherlands (PT, AHZ, PMB); and Department of Obstetrics and Gynecology, Academic Medical Center Amsterdam, Amsterdam, Netherlands (PT, KOR, WG, BWM)

References:

1. von Dadelszen P, Payne B, Li J, et al. Prediction of adverse maternal outcomes in pre-eclampsia: development and validation of the fullPIERS model. *Lancet* 2011; **377**: 219–27.
2. Steyerberg EW, Bleeker SE, Moll HA, Grobbee DE, Moons KG. Internal and external validation of predictive models: a simulation study of bias and precision in small samples. *J Clin Epidemiol* 2003; **56**: 441–47.

Authors' reply

It is not uncommon for risk prediction tools to be based on the “worst” data from the first 24 h after admission for critical care (eg, APACHE and SNAP-II-PE for adult and neonatal critical care, respectively). Use of admission data for risk prediction represents a cross-sectional approach and facilitates a quick management response,¹ whereas use of the worst data from the first several hours provides a more longitudinal perspective, probably yielding more robust risk estimates. For the reasons described in the paper,² we based our prediction model on data obtained (before outcome occurrence) from the first 48 h, especially to permit incorporation of 24-h urine results.

We re-examined the fullPIERS database to determine how the published fullPIERS model performed for prediction of outcomes within 48 h of admission using data from 1398 women collected on admission (area under the receiver operating characteristic curve [AUC] 0.857, 95% CI 0.804–0.911), and within 12 h and 24 h of admission (n=1767, AUC 0.863, 0.818–0.908; and n=1865, AUC 0.870, 0.828–0.912, respectively).

Our model development strategy balanced statistical and clinical considerations. For example, given highly correlated predictors, our approach was to include the most clinically relevant of the group in the model—a process that cannot be automated and is not suitable for bootstrapping. Therefore, our internal validation assessed the potential for overfitting at the level of the stepwise backwards regression modeling (which included specification of nonlinear variables and assessment of a-priori-specified interaction terms). Internal validation showed that the prediction equation had modest optimism and performed well. However, internal validation strategies have their limitations, and overfitting can only be excluded definitively through external validation. We have invited, and are facilitating, external validation of the fullPIERS model.

How should the clinical community manage women with pre-eclampsia before external validation of the fullPIERS model? The fullPIERS model was developed and internally validated using independently predictive variables from a standardised assessment and surveillance regimen associated with lower rates of adverse maternal events, institutionally and provincially.^{3,4} The alternative to using the fullPIERS model in clinical practice relies on deeply flawed definitions of “severe” preeclampsia.⁵ We believe that use of the fullPIERS model represents the better management option at present and have, therefore, hosted an open-access calculator to facilitate risk estimation and minimise the chance of calculation errors.

We declare that we have no conflicts of interest.

**Peter von Dadelszen, Beth A Payne, Jennifer A Hutcheon, K S Joseph, Laura A Magee, for the PIERS Study Group*
pvd@cw.bc.ca

Department of Obstetrics and Gynaecology, University of British Columbia and the Child & Family Research Institute, Vancouver, BC V6H 3N1, Canada (PvD, BAP, JAH, KSJ, LAM); School of Population and Public Health, University of

British Columbia, Vancouver, BC, Canada (PvD, JAH, KSJ, LAM); and Department of Medicine, University of British Columbia, Vancouver, BC, Canada (LAM)

References:

1. Angus DC, Laterre PF, Helterbrand J, et al. The effect of drotrecogin alfa (activated) on long-term survival after severe sepsis. *Crit Care Med* 2004; **32**: 2199–206.
2. von Dadelszen P, Payne B, Li J, et al. Prediction of adverse maternal outcomes in pre-eclampsia: development and validation of the fullPIERS model. *Lancet* 2011; **377**: 219–27.
3. Menzies J, Magee LA, MacNab YC, et al. Instituting surveillance guidelines and adverse outcomes in preeclampsia. *Obstet Gynecol* 2007; **110**: 121–27.
4. von Dadelszen P, Sawchuck D, McMaster R, et al. The active implementation of pregnancy hypertension guidelines in British Columbia. *Obstet Gynecol* 2010; **116**: 659–66.
5. Menzies J, Magee LA, Li J, et al. Current CHS and NHBPEP criteria of severe pre-eclampsia do not uniformly predict adverse maternal or perinatal outcomes. *Hypertens Pregnancy* 2007; **26**: 447–62.