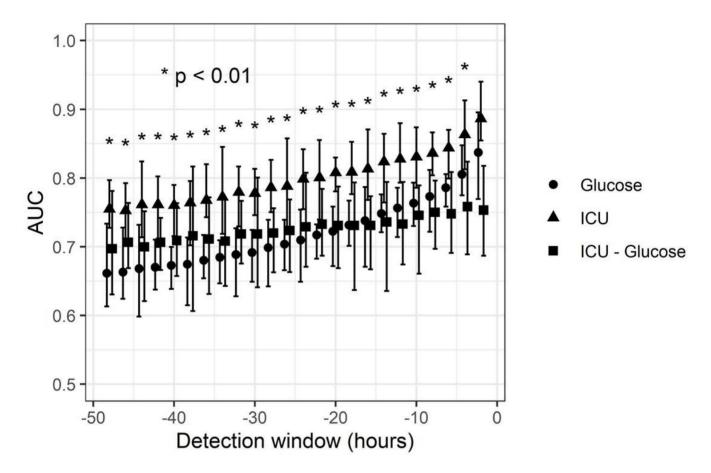
**Supplemental Figure.** Cross-validated area under the receiver operating characteristic curve (AUROC) values by event detection window. At -10 hours, for example, a positive prediction within -10 to 0 hours before event is considered a true positive. *ICU* ( $\blacktriangle$ ) represents the aggregate ICU hypoglycemia model; *Glucose* ( $\bigcirc$ ) represents the model with serum glucose alone (i.e., all other laboratory, hemodynamic, and electrophysiological variables removed); and *ICU-glucose* ( $\blacksquare$ ) represents the ICU hypoglycemia model without serum glucose. The aggregate ICU hypoglycemia model demonstrated significantly higher AUROC than the other models at every detection window tested (Wilcoxon rank sum test,  $\alpha$ =0.05. (AUC= area under the receiver operating characteristic curve).



## TRIPOD Checklist: Prediction Model Development and Validation

| Section/Topic                   | Item |     | Checklist Item                                                                                                                                                                                        | Page                     |
|---------------------------------|------|-----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|
| Title and abstract              |      |     | Identify the study as developing and/or validating a multivariable prediction model, the                                                                                                              |                          |
| Title                           | 1    | D;V | target population, and the outcome to be predicted.                                                                                                                                                   | 1                        |
| Abstract                        | 2    | D;V | Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.                                               | 2                        |
| Introduction                    | T    |     |                                                                                                                                                                                                       |                          |
| Background and objectives       | 3a   | D;V | Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.      | 4, 12, & 13              |
|                                 | 3b   | D;V | Specify the objectives, including whether the study describes the development or validation of the model or both.                                                                                     | 4                        |
| Methods                         |      | 1   |                                                                                                                                                                                                       |                          |
| Source of data                  | 4a   | D;V | Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.                               | 4 & 5                    |
|                                 | 4b   | D;V | Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.                                                                                        | 4 & 5                    |
| Participants                    | 5a   | D;V | Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.                                                          | 4                        |
|                                 | 5b   | D;V | Describe eligibility criteria for participants.                                                                                                                                                       | 4                        |
|                                 | 5c   | D;V | Give details of treatments received, if relevant.                                                                                                                                                     | 4 & 5                    |
| Outcome                         | 6a   | D;V | Clearly define the outcome that is predicted by the prediction model, including how and when assessed.                                                                                                | 5                        |
|                                 | 6b   | D;V | Report any actions to blind assessment of the outcome to be predicted.                                                                                                                                | 5                        |
| Predictors                      | 7a   | D;V | Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.                                                         | 5-6                      |
|                                 | 7b   | D;V | Report any actions to blind assessment of predictors for the outcome and other predictors.                                                                                                            | 5-6                      |
| Sample size                     | 8    | D;V | Explain how the study size was arrived at.                                                                                                                                                            | 4                        |
| Missing data                    | 9    | D;V | Describe how missing data were handled (e.g., complete-case analysis, single                                                                                                                          | 6                        |
| Ū                               | 10a  | D   | imputation, multiple imputation) with details of any imputation method.<br>Describe how predictors were handled in the analyses.                                                                      | 6 & 7                    |
| Statistical<br>analysis methods | 10b  | D   | Specify type of model, all model-building procedures (including any predictor selection),<br>and method for internal validation.                                                                      | 5-7                      |
|                                 | 10c  | V   | For validation, describe how the predictions were calculated.                                                                                                                                         | 7                        |
|                                 | 10d  | D;V | Specify all measures used to assess model performance and, if relevant, to compare multiple models.                                                                                                   | 7                        |
|                                 | 10e  | V   | Describe any model updating (e.g., recalibration) arising from the validation, if done.                                                                                                               | 7                        |
| Risk groups                     | 11   | D;V | Provide details on how risk groups were created, if done.                                                                                                                                             | N/A                      |
| Development vs. validation      | 12   | V   | For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.                                                                         | 7                        |
| Results                         |      | 1   |                                                                                                                                                                                                       |                          |
| Participants                    | 13a  | D;V | Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful. | 7                        |
|                                 | 13b  | D;V | Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.    | 7 & 16                   |
|                                 | 13c  | V   | For validation, show a comparison with the development data of the distribution of                                                                                                                    | 7 & 16                   |
|                                 | 14a  | D   | important variables (demographics, predictors and outcome).<br>Specify the number of participants and outcome events in each analysis.                                                                | 7 & 19                   |
| Model<br>development            | 14b  | D   | If done, report the unadjusted association between each candidate predictor and                                                                                                                       | 8, 9, 20, & 21           |
| Model<br>specification          | 15a  | D   | outcome.<br>Present the full prediction model to allow predictions for individuals (i.e., all regression                                                                                              | 8-11                     |
|                                 | 15b  | D   | coefficients, and model intercept or baseline survival at a given time point).<br>Explain how to the use the prediction model.                                                                        | 11 & 12                  |
| Model                           | 16   | D;V | Report performance measures (with CIs) for the prediction model.                                                                                                                                      | 11 & 12                  |
| performance<br>Model-updating   | 17   | V   | If done, report the results from any model updating (i.e., model specification, model                                                                                                                 | 10 & 11                  |
| Discussion                      | I    |     | performance).                                                                                                                                                                                         |                          |
| Limitations                     | 18   | D;V | Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).                                                                                      | 13                       |
| Interpretation                  | 19a  | V   | For validation, discuss the results with reference to performance in the development data, and any other validation data.                                                                             | 9                        |
|                                 | 19b  | D;V | Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.                                                        | 9-12                     |
| Implications                    | 20   | D;V | Discuss the potential clinical use of the model and implications for future research.                                                                                                                 | 12-14                    |
| Other information               |      |     |                                                                                                                                                                                                       |                          |
| Supplementary information       | 21   | D;V | Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.                                                                         | Supplemental<br>Material |
| Funding                         | 22   | D;V | Give the source of funding and the role of the funders for the present study.                                                                                                                         | 15                       |

TRAPOD