Supplementary material

**Table S1. ROC\_AUC for four different machine learning models during the model development process (prediction of biochemical hypoglycemia)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Model | | | |
| Dataset | Logistic regression | XG Boost | Decision trees | Gradient Boosting |
| Baseline dataset (IH) | 0.71 | 0.78 | 0.72 | 0.78 |
| Insulin dose dataset (IH+) | 0.72 | 0.81 | 0.75 | 0.80 |
| Previous hypo dataset (PH) | 0.73 | 0.96 | 0.81 | 0.96 |

**Table S2. Variable ranking by their contributions to the predictions of the XGBoost model.**

|  |  |
| --- | --- |
| **Variable** | **Ranking score (from highest to lowest)** |
| previousLowGlucose<4mmol/l | 0.8282 |
| previousLowGlucose<3mmol/l | 0.6599 |
| Albumin level | 0.6361 |
| Type 2 diabetes | 0.6044 |
| Intravenous insulin | 0.5954 |
| Long acting insulin analogue | 0.5922 |
| Dose of long acting insulin analogue | 0.5909 |
| Procedure | 0.5835 |
| Rapid acting insulin analogue | 0.5710 |
| Dose of rapid acting insulin analogue | 0.5706 |
| Oxygen saturation\* | 0.5619 |
| Temperature\* | 0.5526 |
| Weight | 0.5518 |
| Type 1 diabetes | 0.5512 |
| Ethnicity\_White | 0.5507 |
| Dose of rapid human insulin | 0.5457 |
| Rapid human insulin | 0.5456 |
| BMI | 0.5446 |
| Metformin | 0.5428 |
| Age | 0.5418 |
| Heart rate\* | 0.5409 |
| Gender | 0.5361 |
| Morphine\* | 0.5330 |
| Height | 0.5258 |
| Long human insulin | 0.5232 |
| Dose of long human insulin | 0.5218 |
| Dose of mixed human insulin | 0.5207 |
| Systolic blood pressure\* | 0.5198 |
| Mixed human insulin | 0.5195 |
| Dose of mixed human insulin | 0.5141 |
| Mixed insulin analogue | 0.5137 |
| Sulfonylurea | 0.5134 |
| Prednisolone | 0.5051 |
| Diastolic blood pressure\* | 0.5050 |
| Amitriptyline\* | 0.5040 |
| Ethnicity\_Asian | 0.5027 |
| Pregabalin\* | 0.5009 |
| Dexamethasone | 0.5009 |
| GLP-1 | 0.5002 |
| Bisoprolol\* | 0.5002 |
| DPP-4 | 0.5000 |
| Pioglitazone | 0.4998 |
| Ethnicity\_Black | 0.4992 |
| Ethnicity\_Mixed | 0.4973 |
| Creatinine | 0.4925 |
| Hemoglobin | 0.4885 |
| CRP | 0.4884 |
| Potassium | 0.4853 |
| Sodium | 0.4840 |
| White cells | 0.4780 |
| eGFR | 0.4777 |

Variables designated (\*) are novel predictors of inpatient hypoglycaemia, not investigated in previous studies.

**Table S3. Coefficient of the logistic regression model (arranged in descending order of statistical significance for clinically significant hypoglycemia)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Predictors | Biochemical hypoglycemia (blood glucose < 4 mmol/l) | | | | Clinically significant hypoglycemia (blood glucose <3 mmol/l) | | | |
|  | Coefficient | Standard error | P-value | z | Coefficient | Standard error | P-value | z |
| **(+)PrevLowGlucose3** | 3.842 | 0.086 | **<0.001** | **28.42** | 4.021 | 0.047 | **<0.001** | **20.39** |
| **(-)Albumin** | -0.078 | 0.003 | **<0.001** | **-27.22** | -0.074 | 0.004 | **<0.001** | **-19.51** |
| **(+)Intravenous insulin** | 0.639 | 0.041 | **<0.001** | **15.43** | 0.501 | 0.051 | **<0.001** | **9.82** |
| **(-)Type of diabetes(type 2)** | -0.820 | 0.060 | **<0.001** | **-13.68** | -0.656 | 0.083 | **<0.001** | **-7.88** |
| **(+)Procedure indication** | 0.485 | 0.033 | **<0.001** | **14.87** | 0.339 | 0.050 | **<0.001** | **6.81** |
| **(-)Weight** | -0.010 | 0.001 | **<0.001** | **-7.42** | -0.012 | 0.002 | **<0.001** | **-6.38** |
| **(+)Sulfonylurea** | 0.572 | 0.040 | **<0.001** | **14.24** | 0.311 | 0.058 | **<0.001** | **5.35** |
| **(+)Insulin (long human)** | 0.011 | 0.002 | **<0.001** | **4.77** | 0.010 | 0.003 | **<0.001** | **5.35** |
| **(+)Oxygen saturation** | 0.059 | 0.009 | **<0.001** | **6.31** | 0.067 | 0.013 | **<0.001** | **5.30** |
| **(-)Metformin** | -0.212 | 0.035 | **<0.001** | **-6.02** | -0.258 | 0.051 | **<0.001** | **-5.02** |
| **(-)Temperature** | -0.061 | 0.027 | 0.022 |  | -0.163 | 0.036 | **<0.001** | **-4.45** |
| **(-)Diastolic blood pressure** | -0.008 | 0.003 | 0.005 |  | -0.014 | 0.004 | **<0.001** | **-3.68** |
| **(+)**Amitriptyline | 0.192 | 0.059 | 0.001 |  | 0.227 | 0.076 | 0.003 |  |
| **(+)**Ethnicity(black) | 0.377 | 0.114 | 0.001 |  | 0.424 | 0.154 | 0.006 |  |
| **(-)**Sex | -0.061 | 0.033 | 0.068 |  | -0.126 | 0.047 | 0.007 |  |
| **(+)**Insulin (long analogue) | 0.003 | 0.001 | 0.047 |  | 0.005 | 0.002 | 0.008 |  |
| **(-)**Height | -0.000 | 0.002 | 0.980 |  | 0.006 | 0.003 | 0.020 |  |
| **(+)Insulin (mixed analogue)** | 0.007 | 0.002 | **<0.001** | **3.67** | 0.004 | 0.002 | 0.060 |  |
| **(+)**Insulin (mixed human) | 0.006 | 0.002 | 0.007 |  | 0.005 | 0.003 | 0.060 |  |
| **(+)**Morphine | 0.101 | 0.036 | 0.005 |  | 0.087 | 0.048 | 0.070 |  |
| **(-)**Dexamethasone | -0.234 | 0.091 | 0.010 |  | -0.211 | 0.122 | 0.084 |  |
| **(-)**Age | -0.001 | 0.001 | 0.160 |  | 0.002 | 0.002 | 0.150 |  |
| **(-)**Potassium | -0.005 | 0.003 | 0.090 |  | -0.004 | 0.004 | 0.230 |  |
| **(+)Insulin (rapid human)** | 0.023 | 0.006 | **<0.001** | **4.11** | 0.007 | 0.006 | 0.285 |  |
| **(+)**Insulin (rapid analogue) | 0.005 | 0.002 | 0.022 |  | 0.002 | 0.003 | 0.370 |  |
| **(+)**PrevLowGlucose4 | 0.030 | 0.086 | 0.750 |  | 0.059 | 0.049 | 0.420 |  |
| **(-)**White cells | -0.003 | 0.003 | 0.230 |  | -0.003 | 0.004 | 0.470 |  |
| **(-)**Bisoprolol | -0.027 | 0.036 | 0.460 |  | -0.030 | 0.049 | 0.530 |  |
| **(+)**Pregabalin | 0.088 | 0.091 | 0.330 |  | 0.070 | 0.117 | 0.553 |  |
| **(-)**Hemoglobin | -0.002 | 0.003 | 0.440 |  | 0.002 | 0.004 | 0.610 |  |
| **(-)**Sodium | -0.001 | 0.003 | 0.650 |  | -0.002 | 0.004 | 0.680 |  |
| **(-)**Creatinine | -0.002 | 0.003 | 0.480 |  | -0.001 | 0.004 | 0.710 |  |
| **(-)**Pioglitazone | -0.033 | 0.160 | 0.840 |  | 0.070 | 0.221 | 0.750 |  |
| **(-)**eGFR | -0.003 | 0.003 | 0.350 |  | -0.001 | 0.004 | 0.760 |  |
| **(+)**C-Reactive Protein | 0.001 | 0.003 | 0.680 |  | 0.001 | 0.004 | 0.800 |  |
| **(-)**Systolic blood pressure | -0.001 | 0.001 | 0.443 |  | -0.001 | 0.000 | 0.800 |  |
| **(-)**GLP-1 | -0.273 | 0.151 | 0.071 |  | -0.050 | 0.203 | 0.807 |  |
| **(-)**Heart rate | -0.005 | 0.002 | 0.001 |  | -0.001 | 0.000 | 0.810 |  |
| **(-)**DPP-4 | -0.122 | 0.075 | 0.102 |  | 0.018 | 0.103 | 0.863 |  |
| **(+)**Prednisolone | 0.032 | 0.053 | 0.540 |  | 0.003 | 0.071 | 0.970 |  |

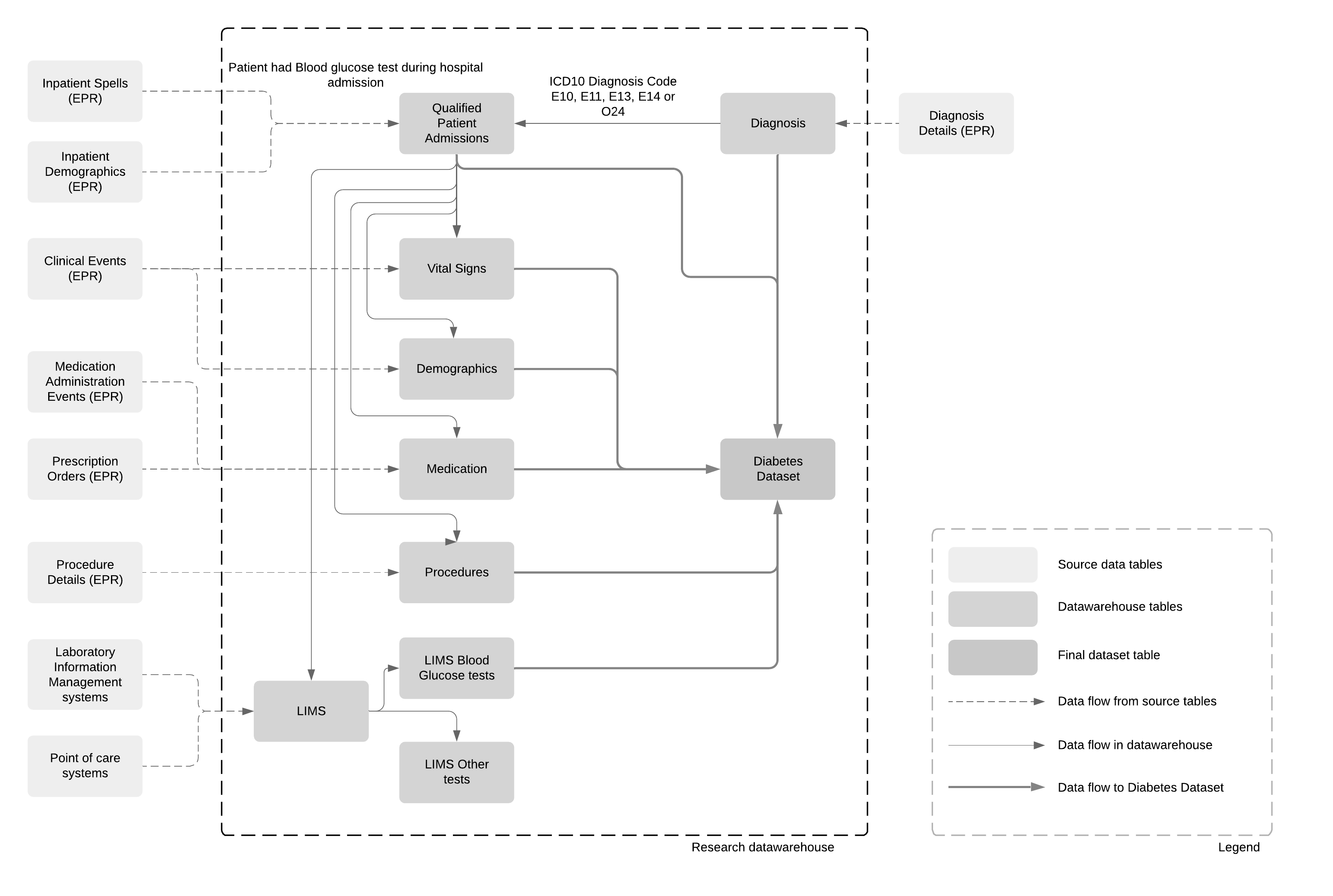
Predictors with P-values less than 0.001 are highlighted in bold-face. The Coefficient reflects the effect size of the variable and the z score reflects the statistical significance of the variable

PrevLowGlucose3 indicates previous admission within 6 months with glucose below 3mmol/L

PrevLowGlucose4 indicates previous admission within 6 months with glucose below 4mmol/L

Factors with a positive Coefficient value increase the risk of hypoglycaemia and factors with a negative Coefficient value decrease the risk of hypoglycaemia. Eg an increase in albumin value reduces the risk of hypoglycaemia and people with Type 2 diabetes have an decreased risk of hypoglycaemia. A (+) or (–) sign is given to each of the factors to indicate the effect direction.

**Figure S1. Data flow from the electronic health records to the final dataset used in the predictions models. EPR: electronic patient records; LIMS: laboratory information management system.**



**Table S4. Normalized confusion matrix for logistic regression, gradient boosting, XGBoost and decision trees models. True positive and true negative rate are shown at coordinates (0,0) and (1,1), respectively, in each confusion matrix.**

Logistic regression Gradient boosting

|  |  |  |  |
| --- | --- | --- | --- |
|  | | predicted label | |
| 0 | 1 |
| true label | 0 | 0.94 | 0.06 |
| 1 | 0.32 | 0.68 |

|  |  |  |  |
| --- | --- | --- | --- |
|  | | predicted label | |
| 0 | 1 |
| true label | 0 | 0.97 | 0.03 |
| 1 | 0.29 | 0.71 |

XGBoost Decision trees

|  |  |  |  |
| --- | --- | --- | --- |
|  | | predicted label | |
| 0 | 1 |
| true label | 0 | 0.98 | 0.02 |
| 1 | 0.29 | 0.71 |

|  |  |  |  |
| --- | --- | --- | --- |
|  | | predicted label | |
| 0 | 1 |
| true label | 0 | 0.92 | 0.08 |
| 1 | 0.29 | 0.71 |