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Delirium Screening in an acute care setting with a Machine Learning Classifier Based on Routinely Collected Nursing Data: A Model Development Study

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Delirium Screening in an acute care setting with a Machine Learning Classifier Based on Routinely Collected Nursing Data: A Model Development Study

Abstract

Delirium screening in acute care settings is a resource intensive process with frequent deviations from screening protocols. A predictive model relying only on daily collected nursing data for delirium screening could expand the populations covered by such screening programs. Here, we present the results of the development and validation of a series of machine-learning based delirium prediction models. For this purpose, we used data of all patients 18 years or older which were hospitalized for more than a day between January 1, 2014, and December 31, 2018, at a single tertiary teaching hospital in Zurich, Switzerland. A total of 48,840 patients met inclusion criteria. 18,873 (38.6%) were excluded due to missing data. Mean age (SD) of the included 29,967 patients was 71.1 (12.2) years and 12,231 (40.8%) were women. Delirium was assessed with the Delirium Observation Scale (DOS) with a total score of 3 or greater indicating that a patient is at risk for delirium. Additional measures included structured data collected for nursing process planning and demographic characteristics. The performance of the machine learning models was assessed using the area under the receiver operating characteristic curve (AUC). The training set consisted of 21,147 patients (mean age 71.1 (12.1) years; 8,630 (40.8%) women|) including 233,024 observations with 16,167 (6.9%) positive DOS screens. The test set comprised 8,820 patients (median age 71.1 (12.4) years; 3,601 (40.8%) women) with 91,026 observations with 5,445 (6.0%) positive DOS screens. Overall, the gradient boosting machine model performed best with an AUC of .933 (95% CI, .929 - .936). In conclusion, machine learning models based only on structured nursing data can reliably predict patients at risk for delirium in an acute care setting. Prediction models, using existing data collection processes, could reduce the resources required for delirium screening procedures in clinical practice.

Keywords: delirium, machine learning, prediction model, screening

1 **Delirium Screening in an acute care setting with a Machine Learning**
2 **Classifier Based on Routinely Collected Nursing Data: A Model**
3 **Development Study**
4

5

6 **Introduction**

7 Delirium is a severe neuropsychiatric syndrome characterized by fluctuations in alertness and

8 cognition with an acute onset. Up to one third of hospitalized patients develop delirium during their

9 hospital stay (Inouye et al., 2014; Schubert et al., 2018). Although delirium has been under-diagnosed

10 for a long time, its association with a broad range of negative outcomes (e.g., prolonged

11 hospitalization and increased mortality) has been well documented (Siddiqi et al., 2006). To minimize

12 the negative impact of delirium on these and additional outcomes, its early detection and non-

13 pharmacological treatment are of crucial importance (Kim et al., 2020; Oh et al., 2017). Thus, daily

14 screening of patients at risk for delirium are recommended by current guidelines (Young et al., 2010)

15 and have been established in many acute care facilities (de Wit et al., 2016; Rudolph et al., 2016).

16 Because most screening procedures need to be carried out by qualified health care providers (i.e.,

17 nursing staff or clinicians) the costs of such procedures are relatively high and thus, screening is often

18 restricted to high-risk populations (De and Wand, 2015). Despite these efforts, delirium remains

19 under-diagnosed and under-treated (McCoy et al., 2016).

20 To optimize existing delirium screening processes, numerous delirium prediction models have

21 been developed over the last two decades (Chua et al., 2021; Lindroth et al., 2018). Early models were

22 designed as screening tools in form of a questionnaire. Therefore, such models had to balance their

23 precision with the resources required to obtain the necessary information (e.g., clinical assessments).

24 Other predictive models focused on risk stratification aiming to predict the severity of delirium based

25 on a few easy-to-obtain items (Inouye et al., 1993). More recently, the wide use of electronic health

26 records (EHR) and the advancements in predictive modeling using machine learning (ML) algorithms

27 paved the way for a new generation of delirium prediction models (Lindroth et al., 2018). These novel

28 models make use of data collected routinely and stored in the EHR to optimize the precision of their

29 prediction. Consequently, such models include several dozens to hundreds of different predictor

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30   variables. For example, the authors of one study used EHR data available in the first 24 hours after

31   patient admission to an acute care facility to predict the onset of delirium using a series of ML models.

32   Their models achieved excellent performance (Wong et al., 2018). Yet, each of their ML models

33   included almost 800 different clinical variables. Notably, other predictive models with a similar

34   performance also incorporate hundreds of variables (Chua et al., 2021; Jauk et al., 2020).

35   　　　While many of these ML-based delirium prediction models typically achieve reliable

36   performance, their clinical applicability is limited in two fundamental ways. First, although these

37   models usually rely on routinely collected data, many of the included variables will not be collected

38   for every patient during every hospitalization. For example, in one study, laboratory results of a

39   comprehensive metabolic panel (e.g., including ammonia) were among the variables with the highest

40   predictive value (Wong et al., 2018). However, such a panel is likely only collected from a minority of

41   patients. Consequently, the utility of a model incorporating such variables is limited in clinical

42   practice. Second, the type, structure, and quality of the data obtained and stored in EHRs vary across

43   different hospital networks (and sometimes even within the same facility). Since most of the

44   developed ML-based delirium prediction models try to use the full source of data, these models are

45   affected by the standard operating procedures of the study site. Consequently, many of these models

46   are highly generic and it is doubtful that they can be used in a clinical setting other than the one in

47   which they were trained – at least not without extensive site-specific model retraining and reevaluation

48   (Jauk et al., 2020; Sun et al., 2021).

49   　　　Hence, the clinical applicability of a delirium prediction model across different sites requires

50   standardized patient data collection at each hospitalization regardless of its location if substantial

51   retraining and validation at every new site should be avoided. Nowadays, many hospitals use the same

52   standardized tools to plan and document the care processes for each patient. Data obtained by these

53   tools are therefore similar across different sites. Consequently, a delirium prediction model based on

54   such data might therefore be more generalizable to multiple sites. The aim of the current study was to

55   provide a proof-of-principle that a delirium prediction model based on such standardized nursing data

56   can achieve good performance. Therefore, we aimed to develop a ML-based delirium prediction model

57   using data collected with standardized nursing instruments at a single study site.

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Materials and methods

60

61 **Procedure**

62 This study included data extracted from the EHR of all patients who were hospitalized at the

63 University Hospital Zurich in Switzerland for more than 24 hours between January 1, 2014, and

64 December 31, 2018. Data collected during the calendar year of 2014 (January 1 to December 31) were

65 part of a research program approved by the ethics committee of the Canton of Zurich (see (Schubert et

66 al., 2018)). The investigation was carried out in accordance with the Declaration of Helsinki. Data

67 collected between January 1, 2015, to December 31, 2018, were obtained for quality control reasons.

68 Under Swiss federal law and local regulations, such data is waived from the requirement of written

69 informed consent by individual participants.

70

71 **Measures**

72 Demographic information was extracted from the EHR of individual patients, including patients' age

73 and sex. Information on self-reported race and ethnicity is not routinely collected in Switzerland and

74 was therefore not available.

75 Delirium presence or absence was determined using the Delirium Observation Scale (DOS)

76 (Koster et al., 2009). The DOS is a 13-item scale developed to assess the presence of delirium as

77 defined by the fourth edition of the Diagnostic and Statistical Manual of Mental Disorder (DSM-IV)

78 and administered by nursing staff (Scheffer et al., 2011). Items reflect disturbances in the patient's

79 level of consciousness, attention, thought processes, orientation, memory, psychomotor behavior, and

80 affect (e.g., a sample item "The patient is picking, disorderly, restless"). All items are rated with a

81 dichotomous response format, three items are reversely coded. Individual item ratings are summed to a

82 total score ranging from 0 to 13, with higher scores indicating higher probability of delirium. A total

83 score of three or more is considered to be indicative for delirium (Gemert van and Schuurmans, 2007).

84 The DOS has been previously validated in a variety of populations (Gavinski et al., 2016; Koster et al.,

85 2009). In this study Cronbach's alpha was 0.8 indicating good internal consistency.

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86   Standardized documentation of nursing processes was carried out with the Electronic Patient

87   Assessment-Acute Care® (ePA-AC®). The ePA-AC® is a 56-item nursing instrument developed to

88   measure abilities and impairments of patients in 11 domains (e.g., state of consciousness or motor

89   skills). Individual items are rated dichotomously or on four-point Likert scales and can be used to

90   calculate a variety of scores (for more information see (Hunstein, 2012)). In the current analysis, only

91   the raw scores of the 56 items were included.

92

93   **Study population**

94   During the study period all patients of 65 years or older, as well as patients younger than 65

95   years old with delirious symptoms or a known neurological disorder or cognitive impairments, were

96   included in the delirium screening program. Delirium screening with the DOS was conducted 3 times

97   a day (observations) until screening was negative for three consecutive days, the patient died or was

98   discharged. Standardized nursing documentation was completed for every patient once every 24 hours

99   at the end of the morning shift (at 4 pm). The results of each patient's delirium screening events were

100   included in the study sample (i.e., observation) when the standardized nursing documentation was

101   completed for the same assessment day. Consequently, up to three screening events per patient per day

102   could be included, with all three referring to the same nursing documentation. We conducted a

103   complete-case analysis (i.e., if one of the 13 DOS or 56 ePA-AC® items was missing, the whole scale

104   was missing for this observation).

105   Overall, 48,840 patients with cumulatively 536,233 screening events between January 1, 2015,

106   and December 31, 2018, were considered for this study. Of these, 18,846 (38.7%) patients and

107   212,183 (39.6%) screening events were excluded due to missing data. The remaining 324,050

108   outcome observations were split into: (1) **Training Set** comprising of 233,024 (71.9%) observations

109   from 21,147 patients screened between January 1, 2015, and December 31, 2017; (2) **Test Set-**

110   comprising of 91,026 (28.1%) screening observations from 8,820 patients obtained between January 1,

111   2018, and December 31, 2018.

112

113   **Model development & statistical analysis**

4

114   The outcome of each model was coded as a binary variable with two levels, delirium presence defined

115   as a DOS total score ≥ 3) and delirium absence (DOS total score < 3). Model predictors included sex,

116   age (as a continuous predictor) and all 56-items of the ePA-AC® in their original coding.

117   Model training and validation followed procedures were adapted from similar publications

118   (Wong et al., 2018). The performance of the following models was tested (implemented in the

119   following package): non-regularized logistic regression (LR; *glm*), penalized logistic regression (PLR;

120   *glmnet*), random forest (RF; *randomForest*), linear support vector machine (SVM; *e1071*), gradient

121   boosting machine (GBM; *gbm*), and an artificial neural network with a single hidden layer (Nnet;

122   *nnet*). Because the outcome was highly imbalanced with less than 7% of outcome observations

123   indicating delirium presence, we used down sampling to balance the training set. We then first

124   optimized the hyperparameters of each model using three repeats of five-fold cross-validation. In a

125   second step, the optimized models were trained using the full training data set. Third, model

126   performance was assessed using the area under the receiver operating characteristic curve (AUC). In

127   addition, sensitivity, specificity, positive predictive values (PPV), and negative predictive value (NPV)

128   are reported. Exact binomial confidence intervals were calculated for sensitivity, specificity, PPV, and

129   NPV. Confidence intervals for AUC were obtained using a bootstrapping procedure. Fourth, AUCs

130   were compared using DeLong's test for correlated receiver operating characteristic curves (DeLong et

131   al., 1988). Fifth, the relative importance of the included predictors was calculated for all models but

132   the linear support vector machine.

133   In a sensitivity analysis, we assessed the performance of a series of models limited to ten

134   predictors. We selected ten predictors based on their variable importance in the full models aiming to

135   choose predictors with top variable importance in more than one full model (see Table S3). Training,

136   testing, and evaluation of these models followed the same procedure as outlined above.

137   The α-level was set at .05 and all tests were conducted two-sided. Because the analysis was

138   not aimed at formal hypothesis testing, the resulting *P* values were not adjusted for multiple testing.

139   We followed the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis

140   or Diagnosis guideline (TRIPOD) (Collins et al., 2015). All analyses were carried out in the R

141   statistical environment with R version 4.0.2 (R Core Team, 2020).

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142

143   **Results**

144   A demographic description of the dataset including delirium prevalence is provided in Table 1.

145   Overall, 40.8% of the patients were female and mean age was 71.1 years (SD = 12.2). In n = 21,612

146   (6.1%) of included observations, DOS total scores were ≥ 3. The relative share of observations with a

147   DOS total score ≥ 3 differed between the training (6.9%) and test set (6.0%).

148   The performance of all included models is presented in Table 2 and visualized in Figure 2. The

149   GBM model had the highest AUC of .933 (95% CI, .929 - .936) significantly outperforming all other

150   models. However, all models had comparable accuracy and performance metrics, apart from the neural

151   net model (Nnet) which performed the worst. Positive predictive values ranged from .986 (95% CI,

152   .865 - .870; Nnet) to .990 (95% CI, .989 - .991; GBM), and negative predictive values ranged from

153   .278 (95% CI, .271 - .285; Nnet) to .326 (95% CI, .318 - .334; PLR).

154   The variables with the highest predictive value mainly included variables assessing

155   quantitative and qualitative aspects of consciousness as well as basic bodily and motor functions. For

156   example, orientation (person, place, time, and situation), attention. and a history of falls were among

157   the ten most predictive variables in several of the assessed predictive models. The performance of the

158   series of models restricted to a selection of ten predictors is also shown in Table 2. Overall, these

159   models performed similarly to the full models except for the random forest model which had lower

160   performance than the corresponding model with all predictors. Additional information including

161   confusion matrices and the relative importance of the included variables are outlined in the

162   supplementary materials (Table S4-Table S19).

163

164

165   **Discussion**

166   Our findings demonstrate that a machine learning classifier solely based on daily collected structured

167   nursing data can be used to reliably identify patients at risk for delirium. Although the GBM model

168   performed significantly better than the models based on other algorithms, the differences in

169   performance between the models were minimal (except for the artificial neural net model). The models

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170 developed and validated in this study rely exclusively on data that were routinely collected in the same

171 standardized manner in many hospitals. If replicated in an independent dataset, these models could be

172 readily implemented across different hospitals to optimize delirium screening protocols.

173 All developed models (with an exception of the artificial neural net model) performed

174 similarly well and achieved a better or similar performance as the best delirium prediction models

175 currently available (Chua et al., 2021; Lindroth et al., 2018). For example, Wong et al (2018) reported

176 an AUC of 0.855 for their gradient boosting model, and Jauk and colleagues' (2020) random forest

177 model achieved an AUC of 0.86. Notably, the models presented in this study relied on fewer

178 predictors suggesting that nursing data can be used effectively in a parsimonious model for delirium

179 prediction. There are multiple reasons why this could be the case. First, all nursing staff was trained in

180 collecting structured and standardized data, which reduces the measurement error, increases inter-rater

181 reliability, and results in higher data consistency (Weiskopf and Weng, 2013). Second, the staff

182 collecting these data do rely on them for numerous clinical and documentation tasks. This minimizes

183 the loss of data and increases the representativeness of the collected data for the study population.

184 Third, some items included in the nursing assessment ask for a clinical judgment. Compared to results

185 from a blood analysis or a patient's administrative arrival (e.g., from home or a nursing home (Zipser

186 et al., 2022)), the clinical assessment of a patient's alertness is much more complex and might contain

187 more relevant information. Fourth, the fact that different algorithms achieved similar performance

188 with similar variables among those with top importance further emphasizes the high information value

189 of these variables for delirium prediction. Taken together, this underscores that structured nursing data

190 is a rich resource for delirium prediction models.

191 The variables with the highest predictive value included symptoms and known risk factors for

192 delirium, emphasizing the clinical plausibility of the prediction models. For example, several items

193 included in the nursing assessment cover the quantitative and qualitative state of consciousness,

194 including changes in attention, a key diagnostic criterion for delirium (American Psychiatric

195 Association, 2013). Similarly, other items with high predictive value include assessments of basic

196 neuropsychiatric functions, such as interpersonal interaction or the need for support in daily activities,

197 which are often disturbed in patients with delirium (Inouye et al., 2014). Individuals' age, a well-

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198   documented risk factor for delirium (Oh et al., 2017), was also among the ten variables with the

199   highest predictive value in several of the developed models. Moreover, the relative importance of the

200   five most important variables was greatly higher than the importance of the remaining variables. In

201   accordance, the sensitivity analyses of a second series of delirium prediction models which were

202   solely based on the ten predictors with highest predictive value across all assessed models revealed

203   comparable performance like the full models.

204   Although the current findings highlight the clinical potential of a nursing data-based delirium

205   prediction model, additional research is needed before such a model can be implemented in clinical

206   practice. First, several studies demonstrated lower performance of predictive models at other clinical

207   sites than the ones in which the models were developed (Zech et al., 2018). We would also expect a

208   decrease in predictive precision of our models at another site, for example due to differences in the

209   underlying hospital population. However, because our models are based on structured nursing data

210   collected in the same standardized and structured manner at many different sites, our models should

211   generalize well. Second, any implementation of a delirium prediction model in a clinical setting should

212   be tested for its efficacy (i.e., whether it outperforms current screening protocols in a controlled study),

213   as well as for its cost-effectiveness (Labarère et al., 2014; Salazar de Pablo et al., 2021) Still, the

214   current findings provide a proof-of-principle for the use of clinical nursing data to reliably predict

215   delirium and are therefore the first of many steps towards this goal.

216

217   **Limitations**

218   This study is subject to several limitations. First, the use of highly structured clinical data limits the

219   generalizability and applicability of our models to sites using the same standardized nursing

220   assessment (ePA-AC©). However, this specific nursing assessment is being used in hundreds of

221   hospitals representing a population of millions of patients in which our prediction model could be

222   employed. Nonetheless, the use of additional or alternative data sources could help to increase the

223   number of sites in which such a delirium prediction model could be implemented. Furthermore, the

224   use of additional data sources could also increase the performance and reliability of the prediction

225   models. Second, the rate of outcome observations indicating delirium in our sample (6.1%) was lower

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226   than the prevalence of delirium documented in other large cohort studies (7-35%) (Boettger et al.,

227   2020; Inouye et al., 2014; Siddiqi et al., 2006). Therefore, it is likely that some patients in our cohort

228   were screened false negatively for delirium. Our predictive models are thus likely affected by this bias

229   as well. Third, the generalizability of our findings is limited by using data from a single clinical site.

230   As studies have shown that predictive models designed at a single site can have substantially worse

231   performance at another clinical site (Beede et al., 2020), future research should aim to develop a

232   predictive model that includes data from multiple sites. Fourth, the exclusion of patients with missing

233   data (see methods) further limits the generalizability. However, we did not aim to develop a predictive

234   model that is readily transferable into clinical use but designed this study to provide proof-of-principle

235   for the utility of using structured nursing data. Given this proof, future work should focus on

236   optimizing the model for maximal generalizability (e.g., also including data from different sites) and

237   clinical utility. Fifth, our main outcome measure (i.e., presence of delirium based on total DOS scores

238   ≥ 3) indicated that a patient is at-risk for delirium and does not correspond to the clinical diagnosis of

239   delirium, which can only be made by structed interview with a certified clinician. Nevertheless, this

240   DOS cut-off score has been validated as a delirium screener in numerous studies (Scheffer et al., 2011;

241   Zipser et al., 2022) to determine presence or absence of delirium and therefore represents a widely

242   used outcome in delirium research. Apart from these limitations, the current study has several

243   important strengths. First, more than 200,000 complete observations of the outcomes and the

244   predictors were used to train the models, providing a sufficiently large pool of training data. Second,

245   in addition to the machine-learning models, a simpler logistic regression model was also trained and

246   evaluated, which performed comparably to the more complex models. Although much attention has

247   been paid to machine-learning models, simpler, more interpretable models are preferred in clinical

248   practice and therefore they should be included in the prediction model development process. In

249   conclusion, ML-based prediction models relying only on structured nursing data collected daily can

250   reliably identify patients at risk for delirium. The models presented in this study achieved similar

251   performance as more complex delirium prediction models. Yet, the presented models are likely more

252   easily transferable to other hospitals collecting the same structured nursing data. However, validation

253   across different sites is necessary before the models can be implemented in clinical practice.

9

Conflict of Interest Disclosures

There are no conflict of interests.

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Data Sharing Statement: Data are subject to legal restrictions on confidential data of the University Hospital Zurich (USZ) and cannot be shared by the authors. Free access to the data can be requested from the USZ, however, access might be denied. The corresponding author can be contacted for further information.

Disclaimer: The views expressed in this article are solely those of the authors and do not reflect an endorsement by or the official policy or position of the U.S. Department of Veterans Affairs or the United States Government.

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Figure legends

Figure 1.

Legend: GBM, Gradient boosting machine; LR, Logistic regression; Nnet, Artificial neural network with a single hidden layer; PLR, Penalized logistic regression; SVM, Support vector machine.

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Tables

Table 1. Demographics and Delirium Presence by Data Set

Variable	Data set, No (%) of Patients		
	Overall (N = 29,967)	**Training data (n = 21,147)**	**Testing data (n = 8,820)**
Age, mean (SD), y	71.1 (12.2)	71.1 (12.1)	71.1 (12.4)
Gender			
Woman	12,231 (40.8)	8,630 (40.8)	3,601 (40.8)
Man	17,736 (59.2)	12,517 (59.2)	5,219 (59.2)
	No (%) of Observations		
DOS total score ≥ 3	21,612 (6.1)	16,167 (6.9)	5,445 (6.0)
DOS total score < 3	324,050 (93.9)	216,857 (93.1)	85,581 (94.0)

Abbreviations: DOS, Delirium observation scale.

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Table 2. Model Performance Metrics

	Full models[a]					
	LR	PLR	RF	SVM	GBM	Nnet
Variable						
Sensitivity	.890 (.887 - .891)	.890 (.887 - .892)	.889 (.887 - .891)	.888 (.887 - .891)	.874 (.872 - .876)	.868 (.865 - .870)
Specificity	.838 (.828 - .847)	.838 (.828 - .848)	.843 (.833 - .852)	.841 (.832 - .852)	.863 (.854 - .872)	.800 (.789 - .810)
NPV	.989 (.988 - .989)	.989 (.988 - .989)	.989 (.988 - .990)	.989 (.988 - .990)	.990 (.989 - .991)	.986 (.985 - .986)
PPV	.324 (.316 - .332)	.326 (.318 - .334)	.326 (.318 - .333)	.325 (.317 - .333)	.304 (.297 - .311)	.278 (.271 - .285)
AUC	.931 (.928 - .935)	.931 (.928 - .935)	.928 (.924 - .932)	.930 (.927 - .934)	.933 (.929 - .936)	.904 (.900 – .909)
	Restricted models[b]					
Sensitivity	.889 (.886 - .891)	.889 (.886 - .891)	.867 (.864 - .868)	.882 (.880 - .884)	.874 (.871 - .876)	.874 (.872 - .876)
Specificity	.844 (.834 - .853)	.844 (.834 - .853)	.814 (.804 - .824)	.835 (.825 - .845)	.863 (.853 - .872)	.863 (.854 - .872)
NPV	.989 (.988 - .990)	.989 (.988 - .990)	.987 (.986 -.987)	.988 (.987 - .989)	.990 (.989 - .991)	.990 (.989 -. 991)
PPV	.325 (.317 - .333)	.325 (.317 - .333)	.279 (.272 -.286)	.311 (.303 - .318)	.303 (.295 - .310)	.303 (.296 - .311)
AUC	.931 (.927 - .935)	.931 (.927 - .935)	.909 (.905 - .913)	.929 (.925 - .933)	.932 (.928 - .935)	.928 (.925 - .932)

Abbreviations: AUC, Area under the receiver operating characteristic curve; GBM, Gradient boosting machine; LR, Logistic regression; Nnet, Artificial neural network with a single hidden layer; NPV, Negative predictive value; PLR, Penalized logistic regression; PPV, Positive predictive value; SVM, Support vector machine.

[a]Models including all available predictors (56 ePA-AC® items, age, gender)
[b]Models including ten predictors with the highest variable importance

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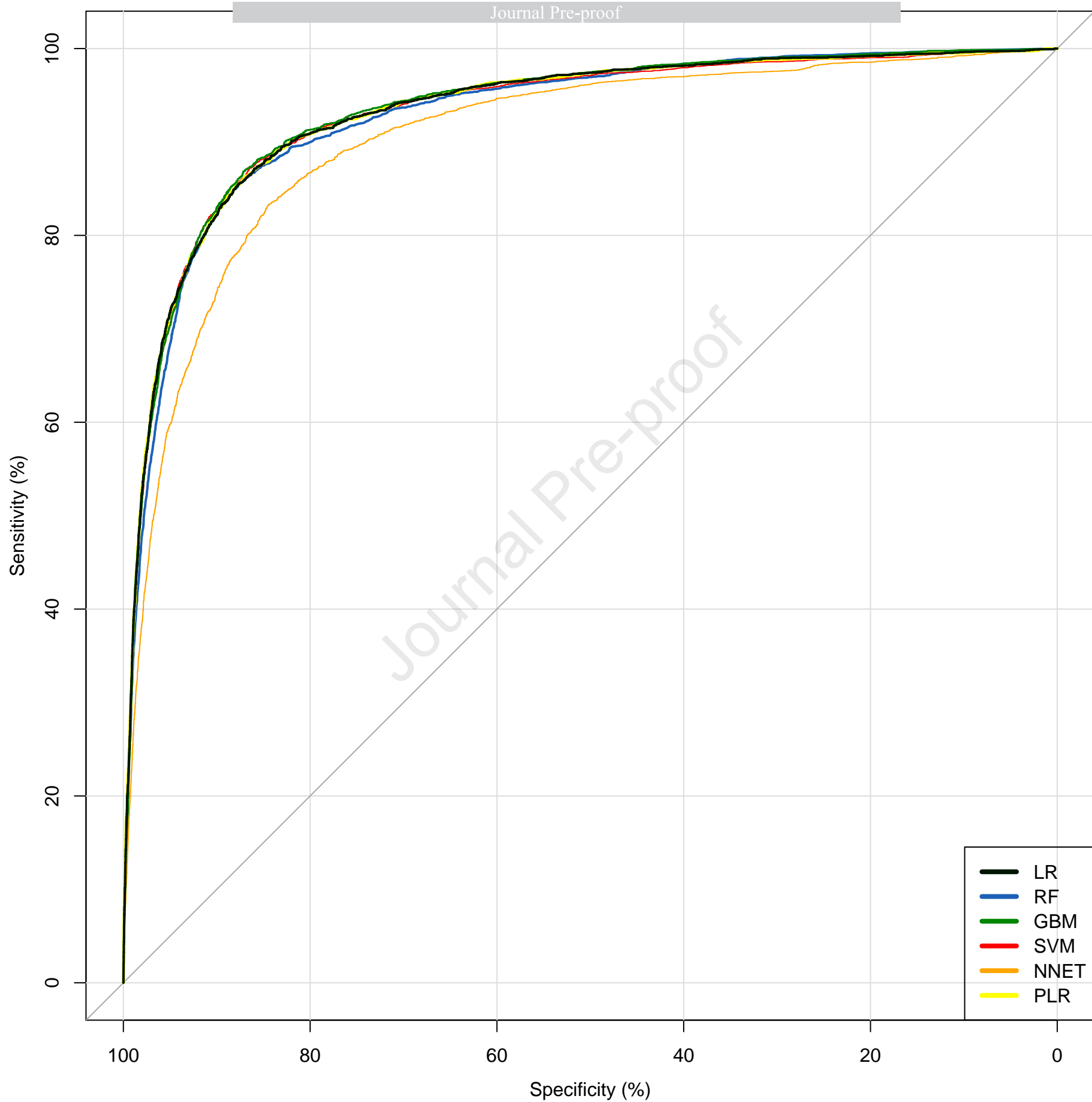
Highlights

1. Delirium can be reliably predicted with machine-learning models using nursing data

2. Delirium prediction models with few predictors can perform as well as more

Conflict of Interest Disclosures

There are no conflict of interests.