Machine learning approaches for prediction of major bleeding events in anticoagulated atrial fibrillation patients.

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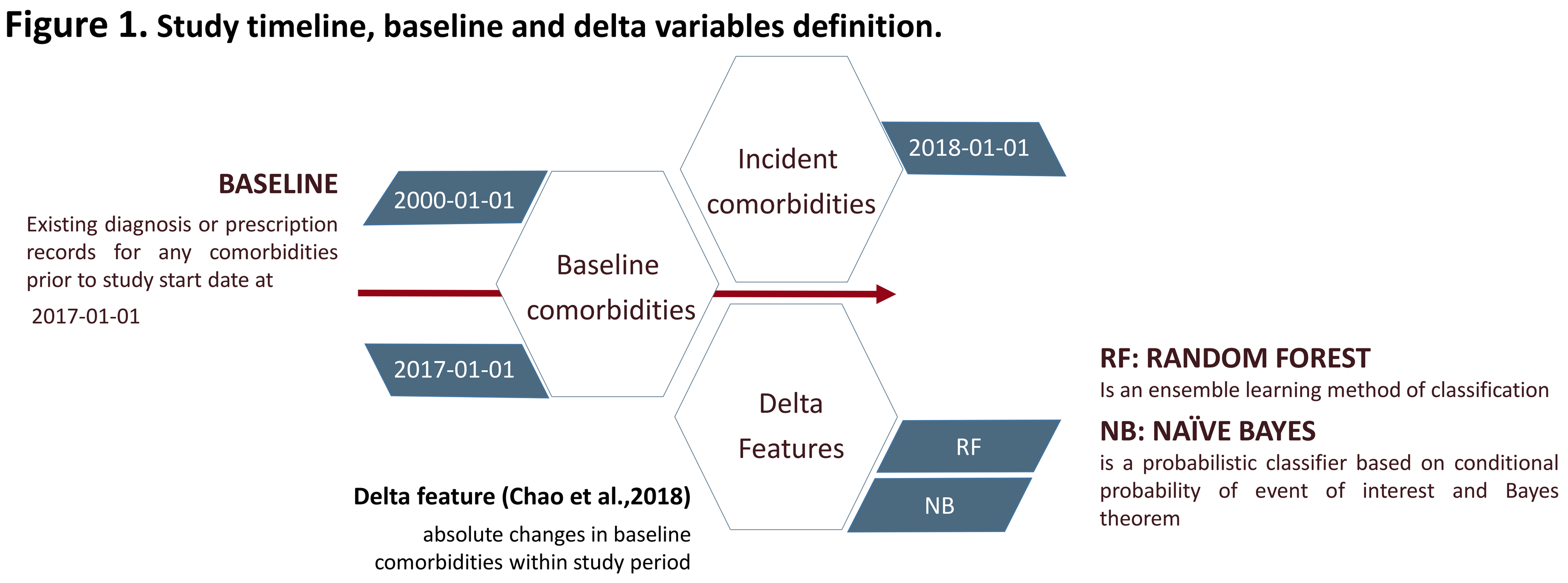
Introduction

Major bleeding events are the most serious complications of anticoagulation therapy (AC) in Atrial Fibrillation (AF) patients, with standardised bleeding risk scores used to guide therapy selection in practice. We explored whether a machine learning (ML) approach could improve bleeding risk modelling.

Methods

We developed two ML-based decision support systems and compared their performance with the HAS-BLED (the bleeding risk score used routinely in UK clinical practice) score for prediction of 1-year risk of major-bleeding events in the AC treated Welsh AF population. Multiple data sources were linked to capture potential contributing clinical variables. Figure 1 & 2

Figure 1. Study timeline, baseline and delta variables definition.

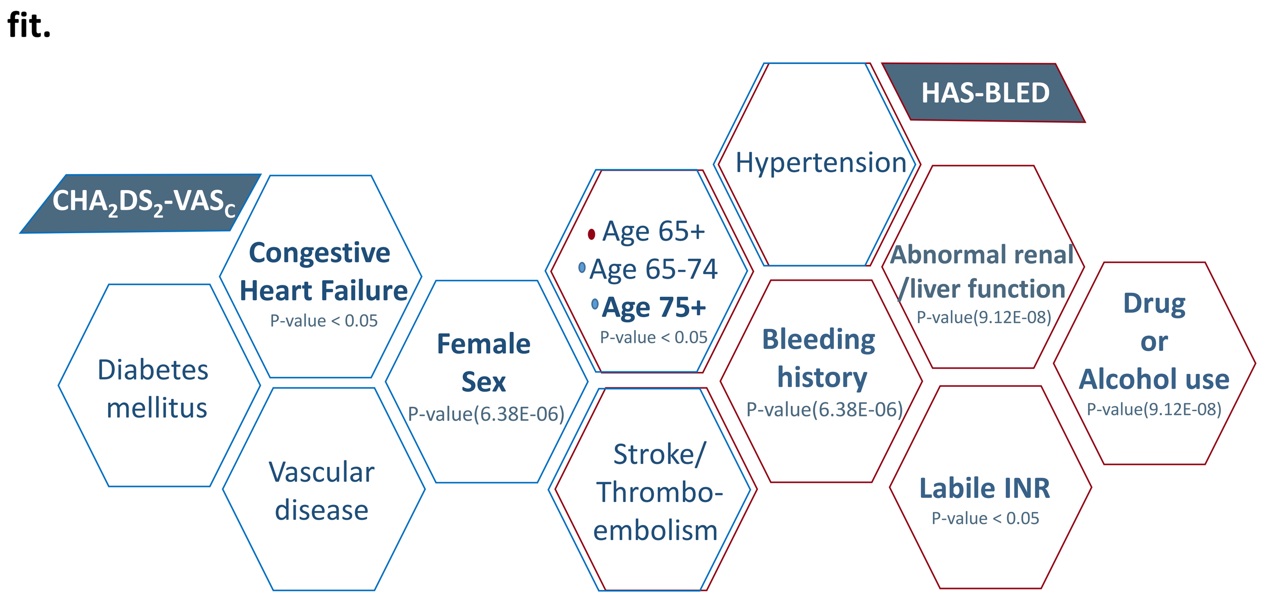


HAS-BLED was validated using multivariable logistic regression. Bootstrapping and 5-fold cross validation were used for development of Random Forest and Naïve Bayes algorithms. Incident event rate in relation to contributing clinical variables in the routinely used bleeding (HAS-BLED) and stroke (CHA_2DS_2VASc) risk scores were used for model optimization. Hazard ratios of the respective models were evaluated using Cox proportional hazard ratio modelling. McNemar test was used for evaluating marginal homogeneity of the final models.

Results

Clinical data were analysed throughout 2017 for 38,784 (43.5% female) AC treated AF patients (aged 76 ± 9.84years). Baseline HAS-BLED and CHA_2DS_2VASc scores were 2.18 (CI [2.17, 2.19]) and 3.45 (CI [3.44, 3.46]) respectively. Figure 3 illustrates variables in the models and statistical significance level in the logistic regression model.

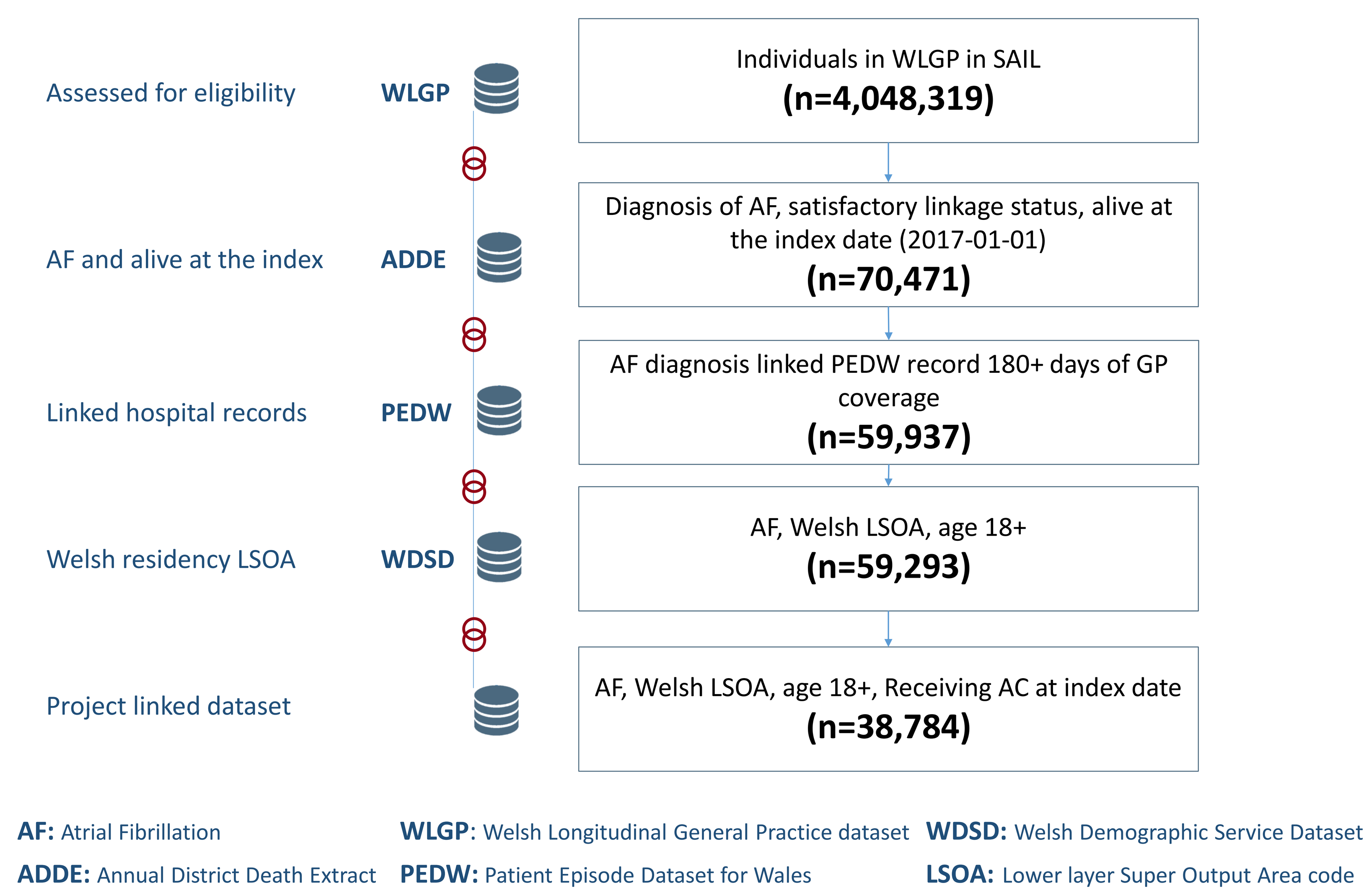
Figure 3. HAS-BLED and CHA_2DS_2-VASc variables used in the analysis and their level of significance in logistic regression fit.



Age>75 (P-value < 0.05), female-sex (P-value=6.38E-06), Incident and baseline congestive heart failure(P-value<0.05), baseline and incident bleeding (P-value<2e-16) and incident event of chronic kidney disease stage 4-5 (P-value=9.12E-08) , baseline measure of excessive alcohol intake (P-value<0.05), regular nonsteroidal anti-inflammatory drug use at the baseline (P-value=0.06), incident liver disease (P-value4.20E-14) and INR level above 5 (P-value<0.05) were significant predictors of bleeding.

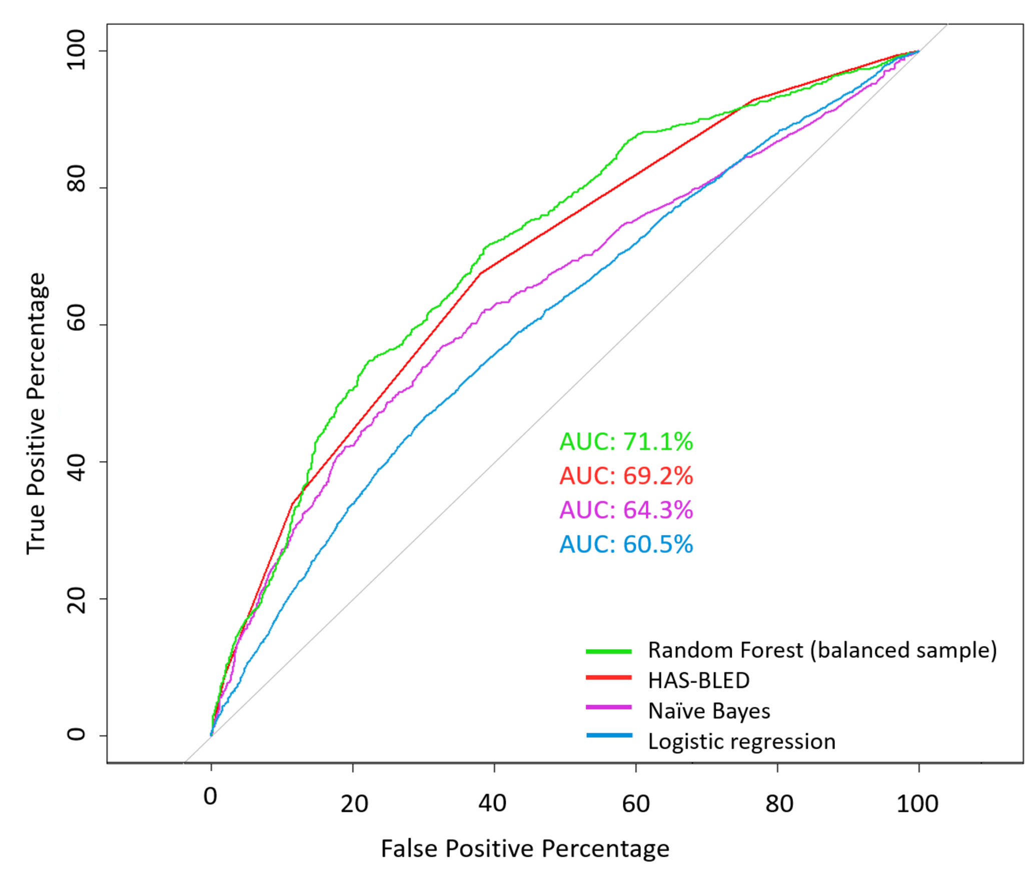
During 37,133 person-years 2,416 bleeding events occurred (6,506 per 100,000 patients/year).

Figure 2. Linked datasets and consort diagram of SAIL-AF cohort receiving AC therapy in 2017-01-01.



The Random Forest model achieved the highest AUC=71.1% compared to HAS-BLED (AUC=69.2%), Naïve Bayes (AUC=64.3%) and logistic regression (AUC=60.5%). (Figure 4)

Figure 4. ROC graph of true positive vs false positives for RF, Naïve Bayes, Logistic Regression and HAS-BLED scheme for prediction of bleeding events in atrial fibrillation population who are receiving anticoagulant drugs in Wales.



Conclusion

RF modelling achieved a small but significantly better prediction of bleeding than conventional HAS-BLED score, indicating a potential role for ML-based decision support algorithms to optimise evaluation of bleeding risk in AF patients on or considering AC treatment.

Future work

Using feature selection methods we were able to reach better performance with existing random forest models; we are evaluating predictive performance of other machine learning approaches and conducting a comparison between statistical modelling and machine learning classifications.

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SAIL DATABANK
PRINTED BY SCIENCEPOSTERS
ESC HEART & STROKE 2020