Disease Diagnosis and Severity Prediction: Artificial Intelligence Application in Hemophilia A

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Background

- Hemophilia A, also called factor VIII deficiency or classic hemophilia, is a genetic disorder caused by missing or defective factor VIII (FVIII), a clotting protein[1]. In 2021, 185,318 hemophilia A patients were reported worldwide.[2] Hemophilia A was severe in 50% to 60%, moderate in 25% to 30% and mild in 15% to 20% cases.[3]
- The diagnosis of hemophilia A includes clotting factor test, prothrombin time, partial thromboplastin time, genetic test and inflammatory markers identification.[4]
- Despite recent advances, the hemophilia A diagnosis accuracy in claims/clinical settings remains unknown.
- Machine learning (ML) has encouraging results in hemophilia diagnosis, severity prediction, user-centered app, gene therapy, myocardial infarction risk estimation, identification of factor V and CRISPR/Cas9 nuclease off-treatment target.
- Artificial Intelligence (AI) is an emerging reality that has the potential to bring a paradigm shift in hemophilia A diagnosis and severity prediction.

Objective

- To identify and evaluate current AI-based algorithm use in Hemophilia A diagnosis and severity prediction, a targeted literature review (TLR) was conducted

Methods

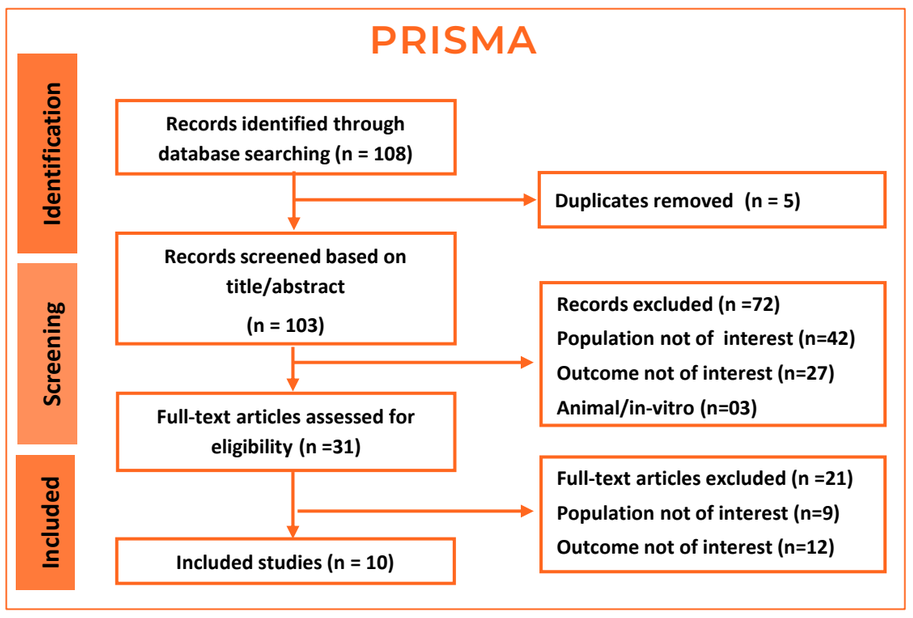
- The TLR was conducted based on the PRISMA guidelines. PubMed, Embase and desk search was done to identify the studies that reported the use of AI in hemophilia A diagnosis and severity prediction.

Eligibility criteria

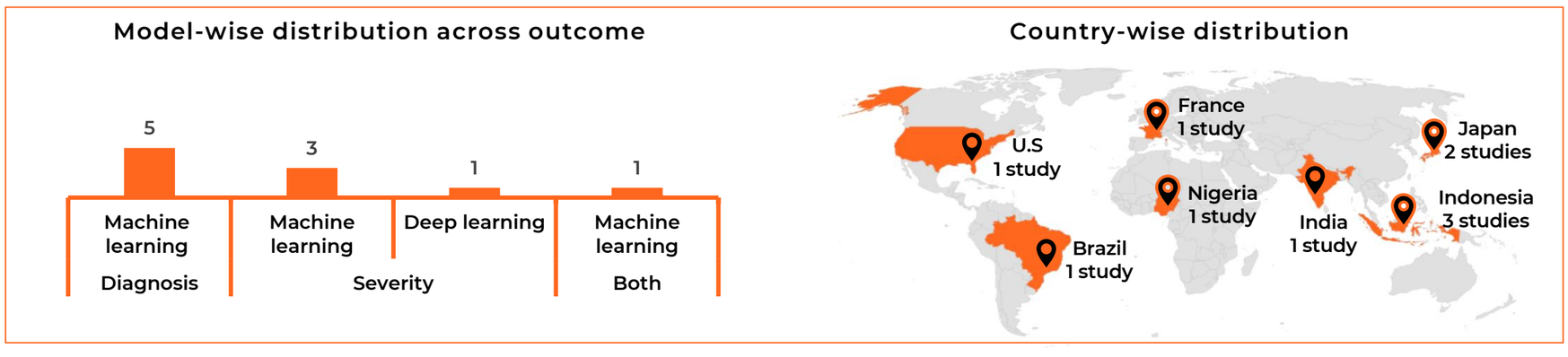
Population	Hemophilia A patients
Intervention/ comparator	NA
Outcomes	AI based diagnostic and severity prediction models, Diagnostic and severity efficacy (Accuracy, sensitivity, specificity, Recall, Precision, False positive rate (FPR), Positive predictive value (PPV), Similarity, F-Measure etc.)
Study design	Any • Observational studies • Disease-specific registry/database • Records (medical records or charts)/ Surveys • Model based studies
Geography	Any

Results

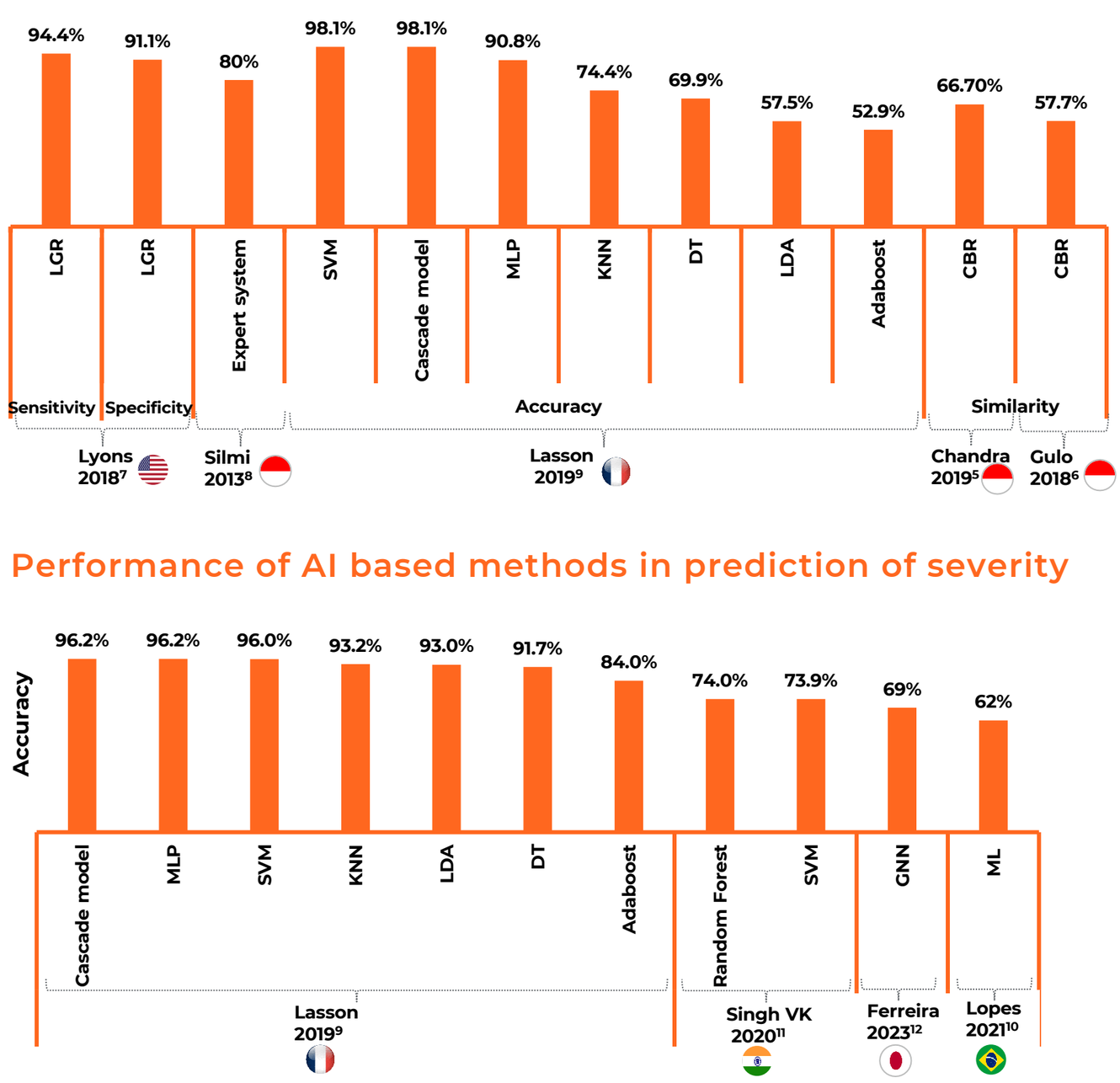
- Of the 108 hits, ten studies utilized AI for diagnostic decision-making (n=5), severity prediction (n=4), and both (n=1) in hemophilia A
- Different AI models included ML (Case-Based Reasoning, Expert system, Haemaxpert, Hema-class, etc.) and Deep learning (DL) (Graph-based neural network)
- Validation was described by four studies. Reference standards included biological thrombin generation assay and genetic testing
- ML model accuracy for severity prediction ranged between 62%-73.86%; for diagnosis ranged between 80-95.57% with 65% positive predictive value
- At a probability threshold of 0.6, 94.4% sensitivity, and 90.1% specificity were seen
- A cascade of ML models accurately diagnosed hemophilia (99.18%), its type (98.1%), and severity (96.23%)
- Among the different methods of ML (Decision tree, Adaboost, K-Nearest Neighbors, Linear Discriminant Analysis, Support Vector Machines (SVM), and MultiLayer Perceptron (MLP)), highest accuracy, recall, precision, F-measure and lowest FPR was seen with SVM for diagnosis and MLP for severity prediction in Hemophilia
- Random Forest and SVM ML classifiers gave better precision and recall value for most of the Position-Specific Mutation based approaches in comparison to One-Hot Encoding
- DL model accuracy for severity prediction was 69% with F1 value of 0.44

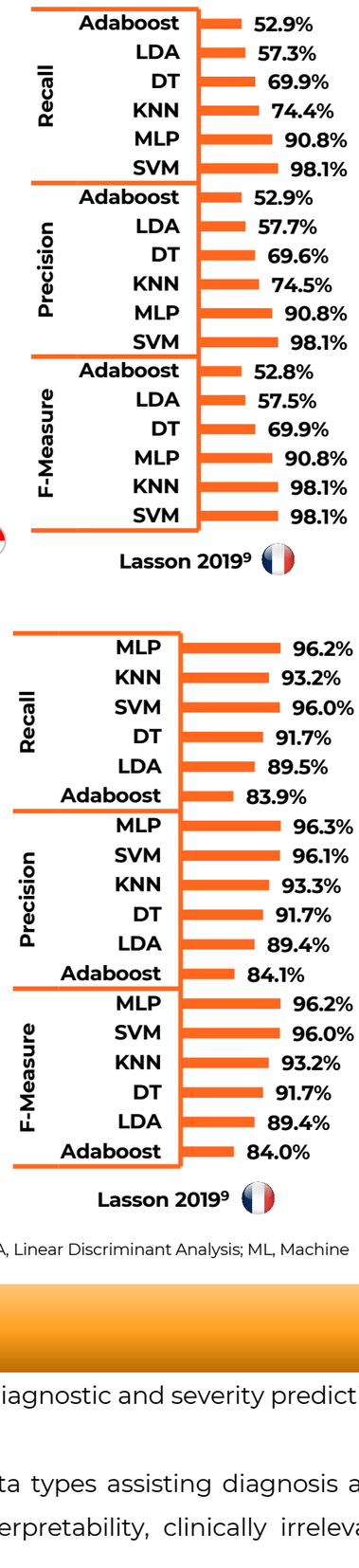


Distribution of studies



Performance of AI based methods in diagnosis





Performance of AI based methods in prediction of severity

Abbreviations: CBR, Case Based Reasoning; DT, Decision Tree; GNN, Graph Based Neural Network; KNN, K-Nearest Neighbors; LGR, Lasson Regression; LDA, Linear Discriminant Analysis; ML, Machine Learning; MLP, MultiLayer Perceptron; NA: Not Available; PPV: Positive Predictive Value; SVM: Support Vector Machines

Conclusion

- The findings of the review suggest that AI based models have shown mixed results across different diagnostic and severity prediction parameters in hemophilia A
- Though AI models for hemophilia A can deal with highly abstract data features and different data types assisting diagnosis and severity prediction, they lack comprehensive quality datasets and face operational, ethical, interpretability, clinically irrelevant performance metrics, and methodological research concerns
- To endorse best practices for AI in hemophilia A, it is crucial to develop critical safeguards, transparent policies, and robust data infrastructure. Further research on adapting AI models for implementation in clinical practice is warranted

References:

1. https://www.hemophilia.org/bleeding-disorders-a-z/types/hemophilia-a. 2. https://wfh.org/research-and-data-collection/annual-global-survey/ 3. https://www.rarediseaseadvisor.com/disease-info-pages/hemophilia-epidemiology/. 4. https://www.verywellhealth.com/hemophilia-a-diagnosis-5208550 5. Chandra et. al, Indonesia Journal of Artificial Intelligence and Data Mining, 2019. 6.Gulo et. al, Pelita Informatics Journal, 2018 7. Lyons et. al, Value in Health 21, 2018.. 8. Silmi et. al, Journal of Informatics and Technology, 2013. 9.Lasson et. al, Advances in Computational Intelligence. IWANN, 2019. 10. Lopes et. al, NPJ systems biology and applications, 2021. 11.VK Singh et. al, Genomics, 2020. 12. Ferreira et. al, Frontiers in Bioinformatics, 2023. 13.Aoki K et. al, International Conference on Artificial Life and Robotics, 2015. 14. Olusayo et. al, Annals. Computer Science Series, 2018.