Artificial intelligence-based flare prediction in patients with Systemic Lupus Erythematosus (SLE): leveraging seven SLE clinical trial data from TransCelerate.

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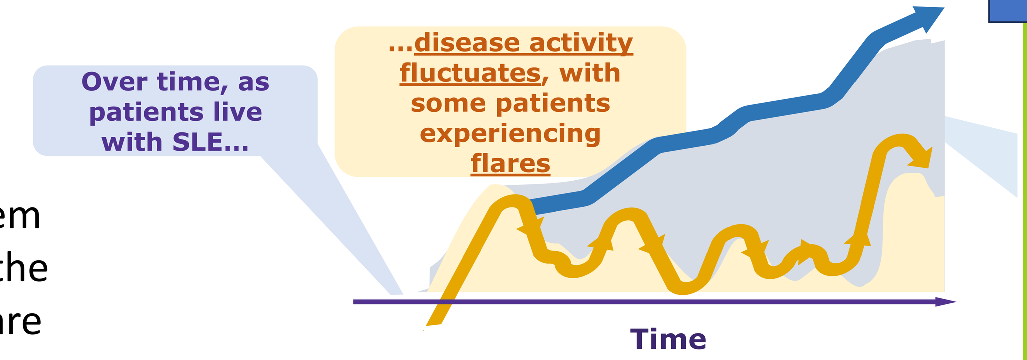
INTRODUCTION

- Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease characterized by significant heterogeneity in immunological features and clinical manifestations, impacting multiple organ systems.
- SLE is characterized by recurring bouts of increased disease activity (flares), mild to life-threatening in severity. Measuring SLE disease activity accurately remains a challenging and demanding task given the complex, multi-system nature of the disease. SLE flares derived from the British Isles Lupus Assessment Group (BILAG) are a key component of response assessment [1].



OBJECTIVES

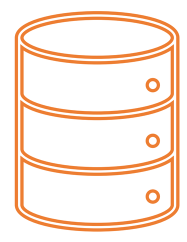
Leveraging a large longitudinal, multivariable dataset of SLE patients using state-of-the-art Machine Learning (ML) methods to forecast SLE flares.

Such predictive algorithm could enhance clinical trial design and interpretation and serve the physician to predict the likelihood of a patient to flare.

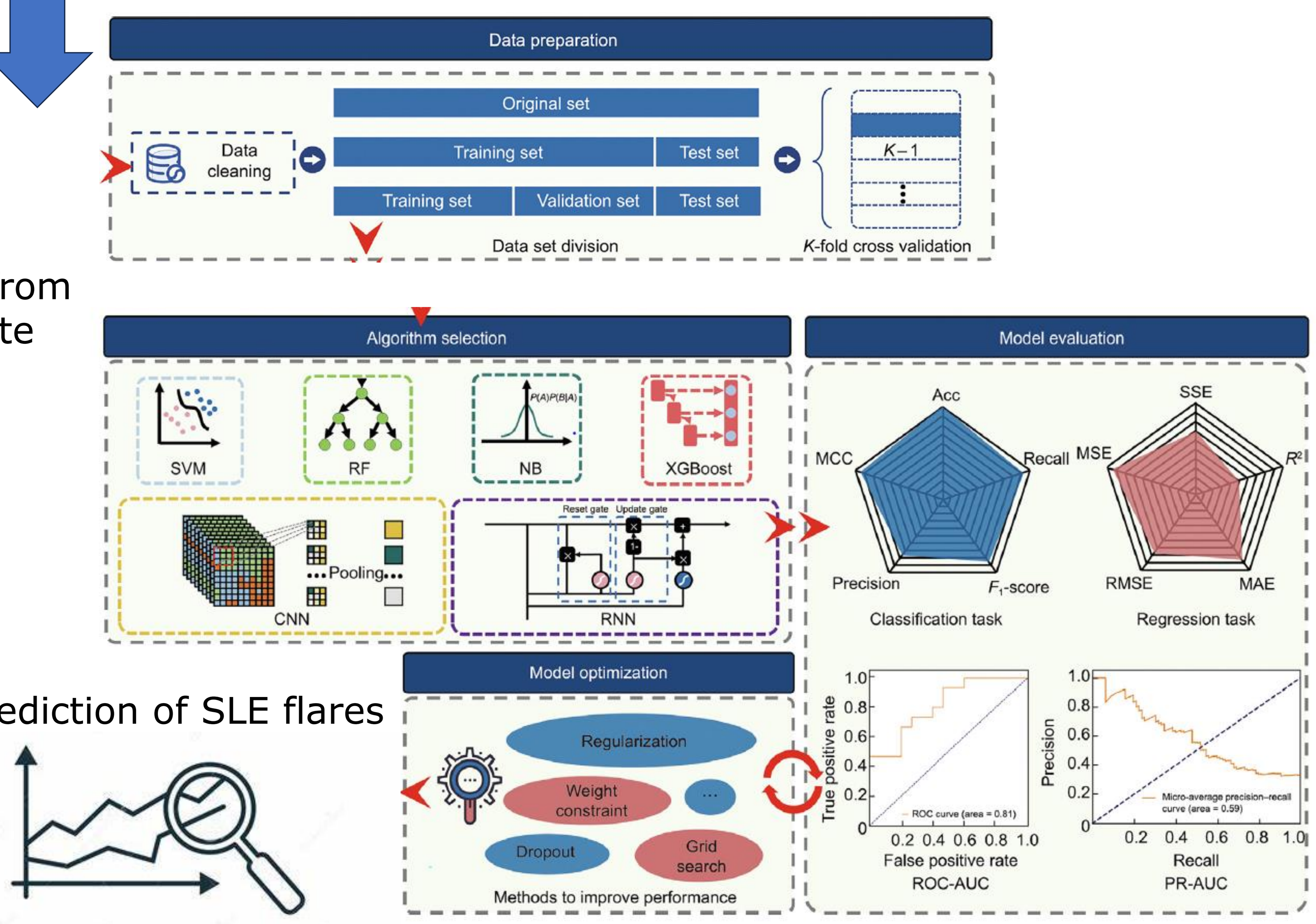
METHODS

TransCelerate Dataset

Study	Short title	Treatment	N	Duration
EMBODY1	Study of Epratuzumab Versus Placebo in Subjects With Moderate to Severe General SLE	Epratuzumab	263	48 weeks
EMBODY2	Study of Epratuzumab Versus Placebo in Subjects With Moderate to Severe General SLE	Epratuzumab	263	48 weeks
BLISS-52	A Study of Belimumab in Subjects With SLE	Belimumab	287	52 weeks
BLISS-76	A Study of Belimumab in Subjects With SLE	Belimumab	275	76 weeks
ILLUMINATE-1	A Study of LY2127399 (Tabalumab) in Participants With Systemic Lupus Erythematosus	Tabalumab	387	52 weeks
ILLUMINATE-2	A Study of LY2127399 (Tabalumab) in Participants With SLE	Tabalumab	376	52 weeks
SLE Anifrolumab NCT02446899	A Multicentre, Randomised, Double-blind, Placebo-controlled, Phase 3 Study Evaluating the Efficacy and Safety of Anifrolumab in Adult Subjects With Active SLE	Anifrolumab	82	52 weeks



Placebo arm from TransCelerate dataset

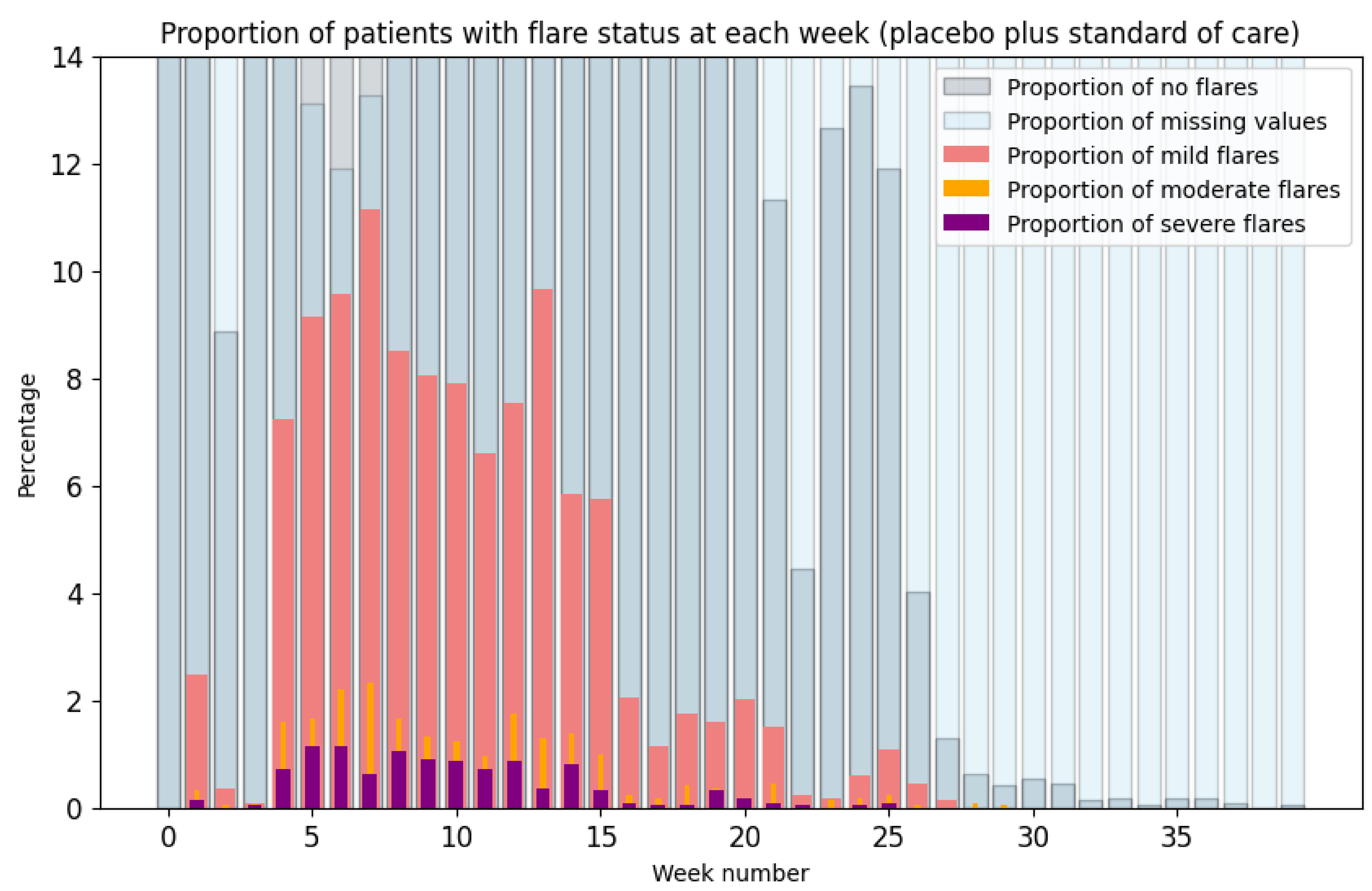


Prediction of SLE flares

Flare prediction pipeline on placebo arm of TransCelerate dataset (partially adopted from [3]).

- The dataset coming from the TransCelerate program, an initiative for sharing historical data across biopharma companies, includes patient-level data in the placebo plus standard of care arms of 7 randomized controlled trials involving 1933 patients.
- A set of 290 constant and time varying covariates including demographic data, disease specific biomarkers, immunology variables, measurements from urinalysis, vital signs, variables from Electrocardiograms (ECG) signal, and hematological variables are collected up to 52 weeks.
- BILAG score across three main involved organs (mucocutaneous, musculoskeletal and renal) were used to derive the SLE flare status defined as moderate, severe and no flare across all organs [2].

RESULTS



		Hidden test set results (20% of data is left out for test)				Cross validation results	
Prediction model	Positive class/negative class (N) (ratio)	Precision (+/-) Average (%)	Recall (+/-) Average (%)	F-score (+/-) Average (%)	AUCPRC	AUCPRC (mean) K=9	AUCPRC (std) k=9
Prediction of moderate or severe flares.	455 / 1478 (30%)	93 93 93	75 98 93	83 95 92	0.91	0.76	0.19

- The ML based flare prediction algorithm achieved promising results in prediction of flares (AUCPRC of 0.91 with consistent performance across all 7 clinical trial data) including 1933 patients across 290 covariates.
- This performant ML flare prediction model for SLE could provide valuable insights for enhancing clinical trial design and interpretation. Additionally, such a model can assist physicians in predicting a patient's likelihood of experiencing a flare.

[1] Ceccarelli F, Perricone C, Massaro L, Cipriano E, Alessandri C, Spinelli FR, Valesini G, Conti F. Assessment of disease activity in Systemic Lupus Erythematosus: Lights and shadows. Autoimmunity reviews. 2015 Jul 1;14(7):601-8.
[2] Isenberg DA, Allen E, Farewell V, D'Cruz D, Alarcon GS, Aranow C, Bruce IN, Dooley MA, Fortin PR, Ginzler EM, Gladman DD. An assessment of disease flare in patients with systemic lupus erythematosus: a comparison of BILAG 2004 and the flare version of SELENA. Annals of the rheumatic diseases. 2011 Jan 1;70(1):54-9.
[3] Lu, M., Yin, J., Zhu, Q., Lin, G., Mou, M., Liu, F., ... & Zhu, F. (2023). Artificial intelligence in pharmaceutical sciences. Engineering, 27, 37-69.

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