Predicting Declines in Lung Function with the US CF Registry: Impact of Initiating Highly Effective Modulator Therapy
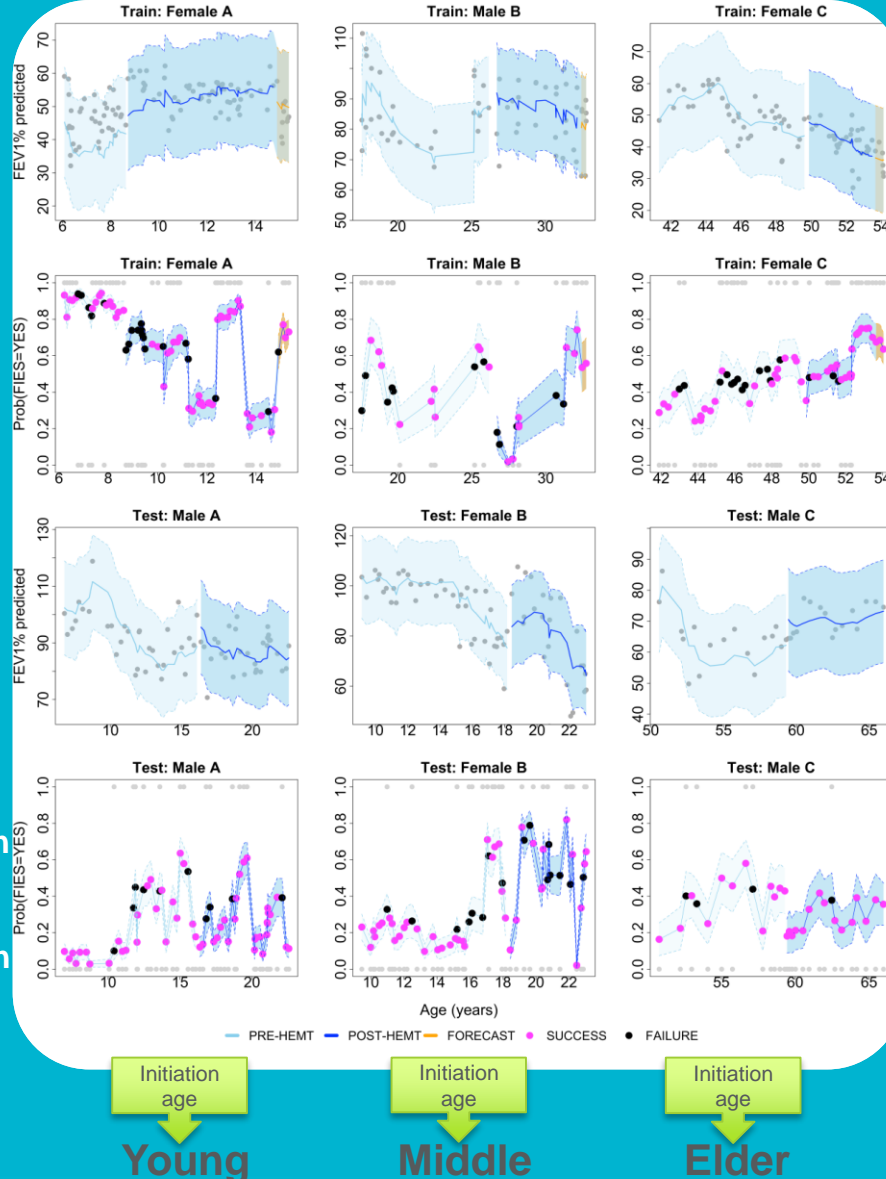
Objective

To demonstrate how robust predictions of lung function in post-highly effective modulator therapy (HEMT) era are.

Background

- KALYDECO®(Ivacaftor) which is one of HEMTs continues to improve lung function trends in 90% of CF patients in US
- The predictive accuracy of FEV1% pred decline models for post-HEMT, is unknown
- Particularly of interest is the identification of pulmonary exacerbation (PE) events defined by the CF Foundation's FEV1-indicated exacerbation score (FIES).

PRE-HEMT   POST-HEMT   FORECAST   SUCCESS   FAILURE

Young   Middle   Elder

Initiation age   Initiation age   Initiation age

Methods

- Apply the LME model with nonstationary stochastic process
- Add a change point to modify the slope
- Utilize the target function to predict probability of FIES

Results

	FEV1% pred: RMSE*		FIES: AUC* (95% CI)	
	PRE-HEMT	POST-HEMT	PRE-HEMT	POST-HEMT
FITTING (N=694)	8.31	7.7	0.79 (0.78, 0.79)	0.82 (0.81,0.83)
FORECASTING (N=694)	NA	7.38	NA	0.87 (0.85, 0.89)
TESTING (n=173)	7.83	7.2	0.81 (0.79, 0.82)	0.83 (0.81, 0.84)

*RMSE: root mean square error(☺smaller), AUC: area under curve(☺larger)

Conclusions

- The change point is a significant effect & corroborates the positive impact of initiating HEMT
- Our optimal model exhibits impressive predictive performance with an overall accuracy of 80% for FIES events in post-HEMT era

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Abbreviations: CF, cystic fibrosis; FEV1% pred, percent predicted forced expiratory volume in 1 second ; LME, linear mixed effects.

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