

Innovative Multimodal Modelling for Predicting Clinical Outcomes and Understanding Drug Treatment Effects in Inflammatory Bowel Disease



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Background

- Inflammatory Bowel Disease (IBD) affects over 10 million people globally and is characterized by complex pathophysiology and heterogeneous treatment responses.
- Current therapies show in some patients limited efficacy or adverse effects, highlighting the need for data-driven, personalized approaches [1].

Main goal

- To develop a multimodal modeling framework that enhances the understanding of biomarker contributions to clinical endpoints and enables drug combination simulations.

Multimodal model framework

- We leveraged a multimodal comprehensive clinical trial dataset across multiple therapies, including baseline characteristics, longitudinal clinical outcomes, and log2 fold changes in biomarkers.
- Building on the MultiNODEs framework [2], we introduced modular encoders for clinical and biomarker trajectories. Their latent representations are used to define the initial conditions of a neural ODE [3], whose latent space dynamics was adapted incorporating dosing to capture drug effects.
- A unified decoder reconstructs both continuous and ordinal longitudinal variables, with loss functions tailored to each data type (see Figure 1)
- We carefully designed a rigorous evaluation protocol to assess performance across multiple scenarios, emphasizing robustness and generalizability (see validation scenarios)
- To avoid encoding of treatment effects into the initial conditions, an additional placebo classifier on the initial conditions penalizes identifiability using gradient reversal

Figure 1: Model Architecture

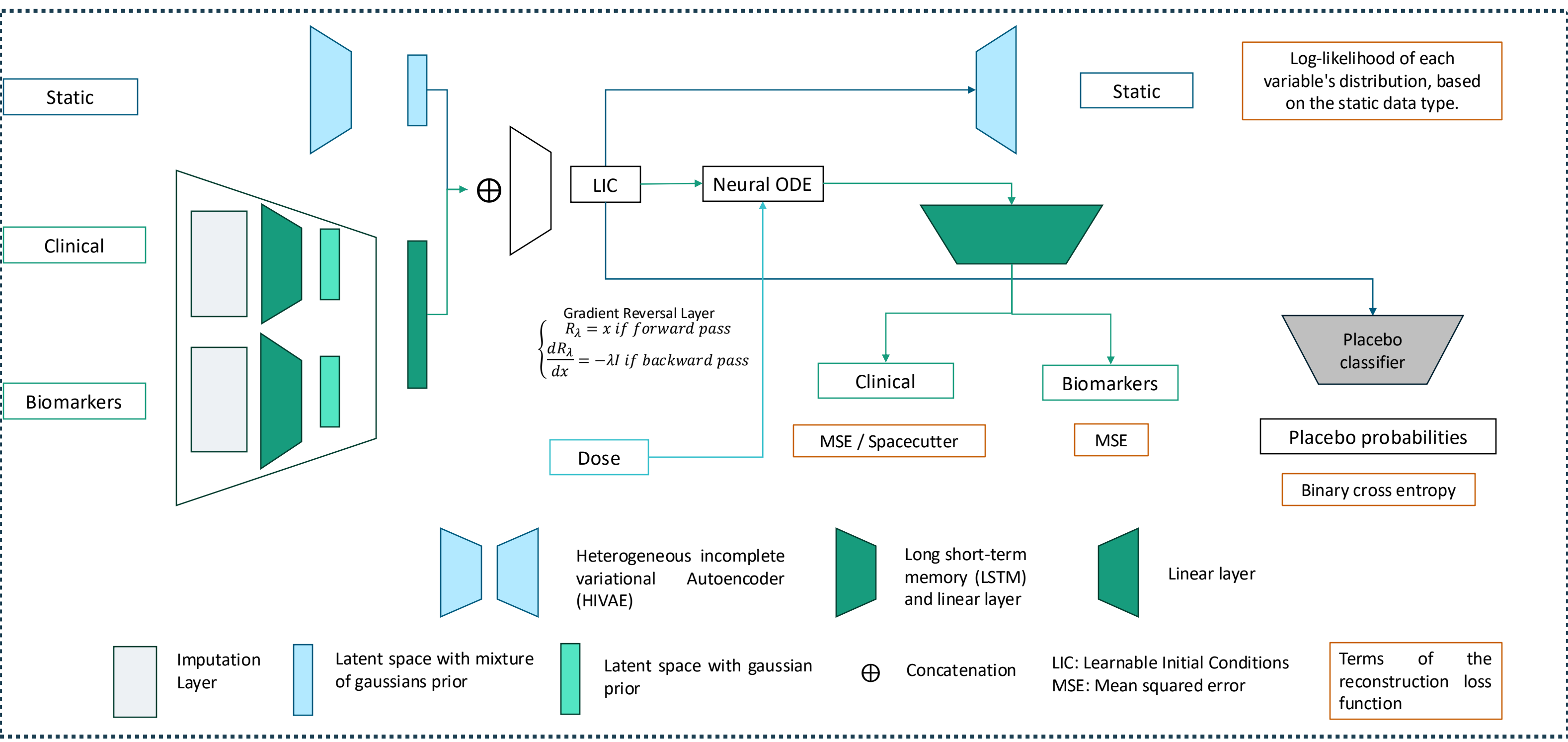
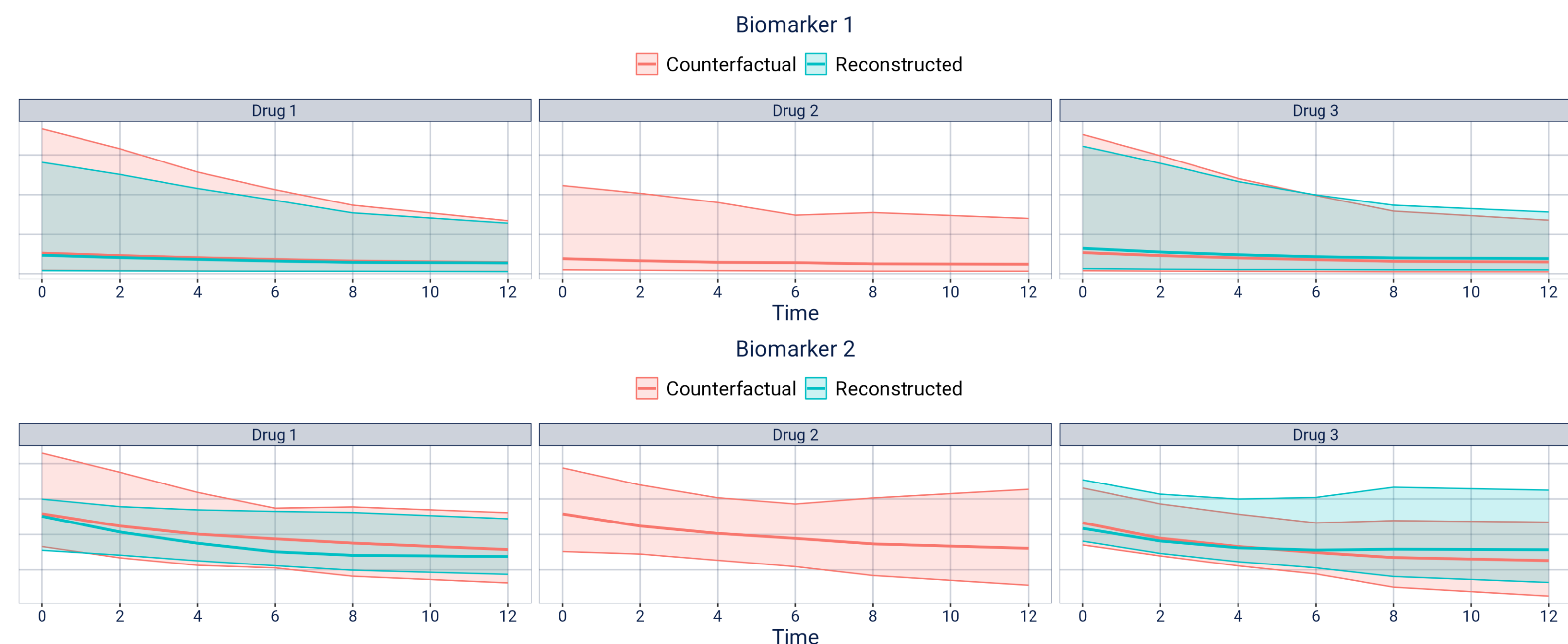


Table 1: Average class 1 F1 of clinical endpoints reconstruction at end of Induction and Maintenance across different studies for each drug

Endpoint	Drug 1		Drug 2		Drug 3	
	Induction	Maintenance	Induction	Maintenance	Induction	Maintenance
A	0.83	0.66	0.90	0.96	0.84	0.84
B	0.77	0.59	-	-	0.88	0.95
C	0.42	0.31	0.43	0.25	0.33	0.59
D	0.54	0.41	0.62	0.55	0.44	0.71

Figure 3: Placebo reconstruction and counterfactual simulation



Note: Counterfactual refers to a hypothetical scenario illustrating what would have happened if the treated patients had received a placebo instead.

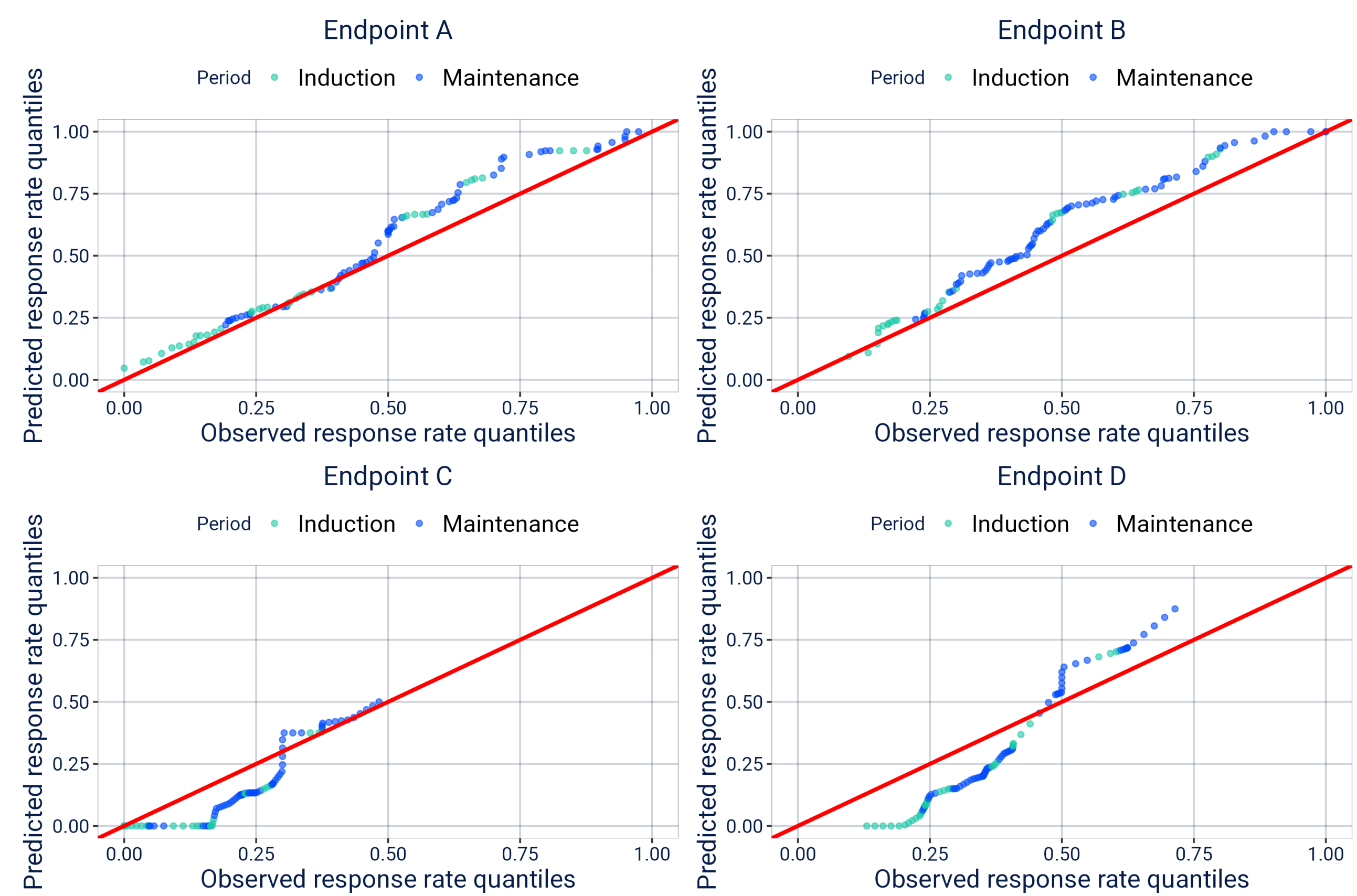
A comprehensive clinical dataset for IBD

- A diverse collection from clinical trials exploring multiple drugs
- Data revealing the intricate progression of therapeutic outcomes
- Rich demographic profiles across diverse populations
- Dynamic biomarker trajectories offering profound insights
- Patient baseline values capturing critical starting points
- Time dependent response rates for all drug dose groups

Validation Scenarios

- Do we learn a meaningful latent space?
 - Reconstruction using full time horizon
- Can we include patients with many missing values?
 - By encoding information with missing (not) at random
- Can we extrapolate over time?
 - By encoding induction information and predict across full time horizon
- Can we capture dose effects?
 - Counterfactual simulations focus on placebo effect
- Can we perform virtual clinical trials based on baseline values?
 - By encoding only baseline values and predict across full time horizon
- Can we capture the clinical time course when only encoding biomarkers?
 - Clinical data is assumed as missing values

Figure 2: QQ plots of the rates for clinical endpoints



Our model

- The model reveals a meaningful latent space that captures IBD dynamics, providing key insights into the disease through multimodal data.
- The model shows robustness against a high rate of missing values which is critical when processing clinical data
- Promising time extrapolation capabilities enable predictions of clinical trial phases, such as maintenance, from induction phase data—highlighting the power of multimodal data to drive accurate predictions.
- Our model captures distinct behaviors for each medication and shows that drug amount influences response differently in counterfactual scenarios.

Limitations

- Extrapolation from baseline characteristics remains suboptimal, emphasizing the need for richer data beyond baseline for precise trial simulation.
- Longitudinal data is an indispensable asset in capturing IBD's complexities

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A.V.P.B., C.M., I.W., S.M., and S.S are employees of AbbVie and may hold stock or options in the company. H.F sat on the Editorial Boards of the EPMA journal and Frontiers of Artificial Intelligence. D.V has no conflict of interest to declare.

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