UNLEARN

Digital Twins in Clinical Trials

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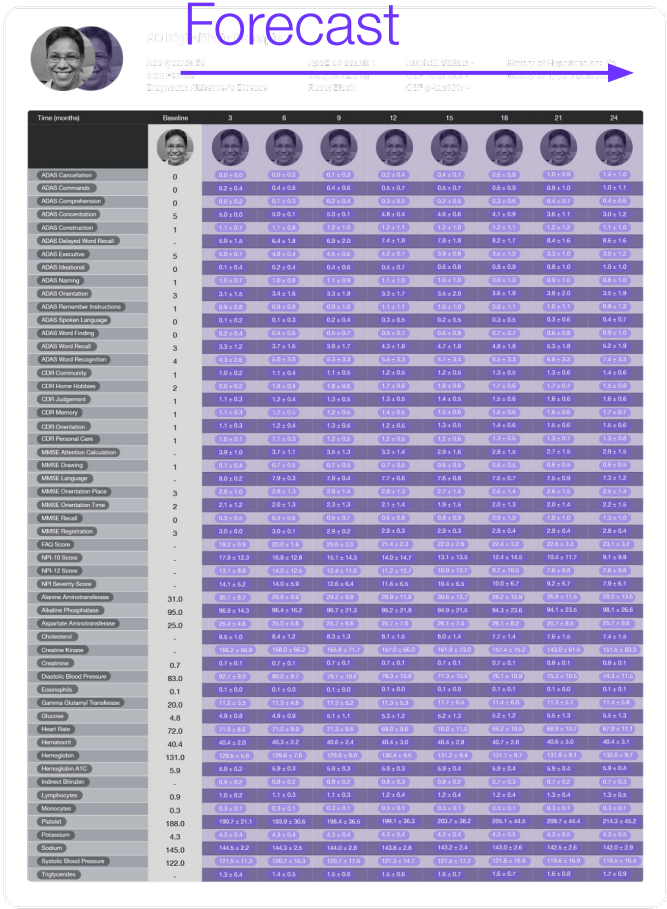
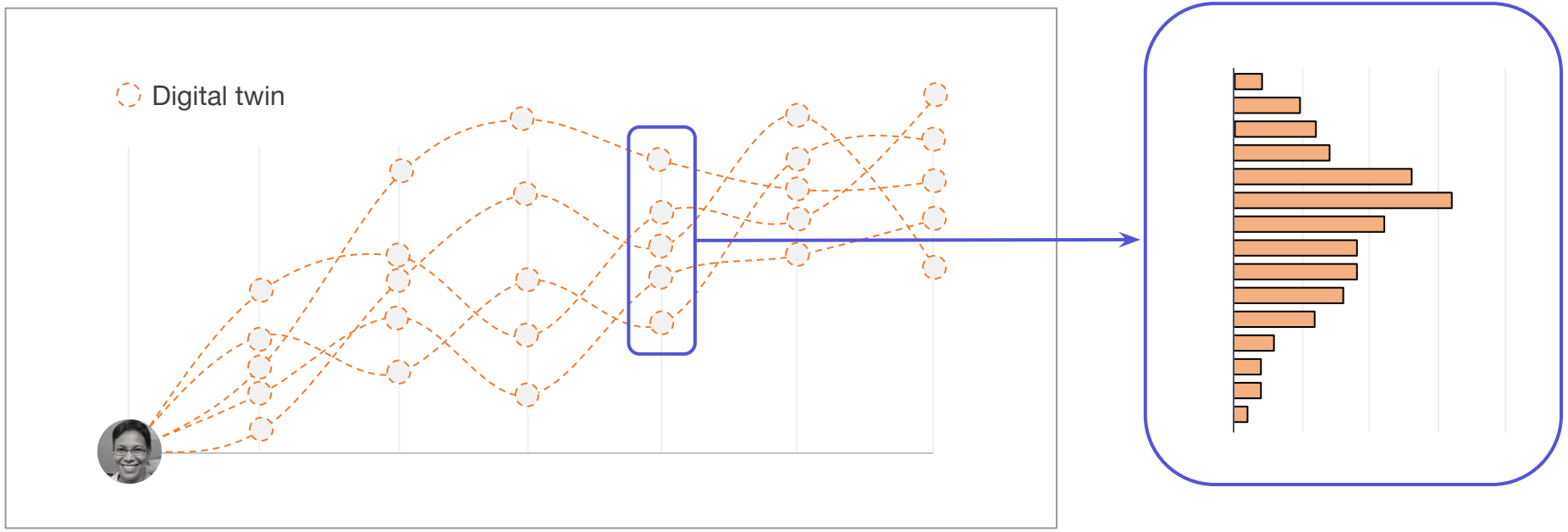
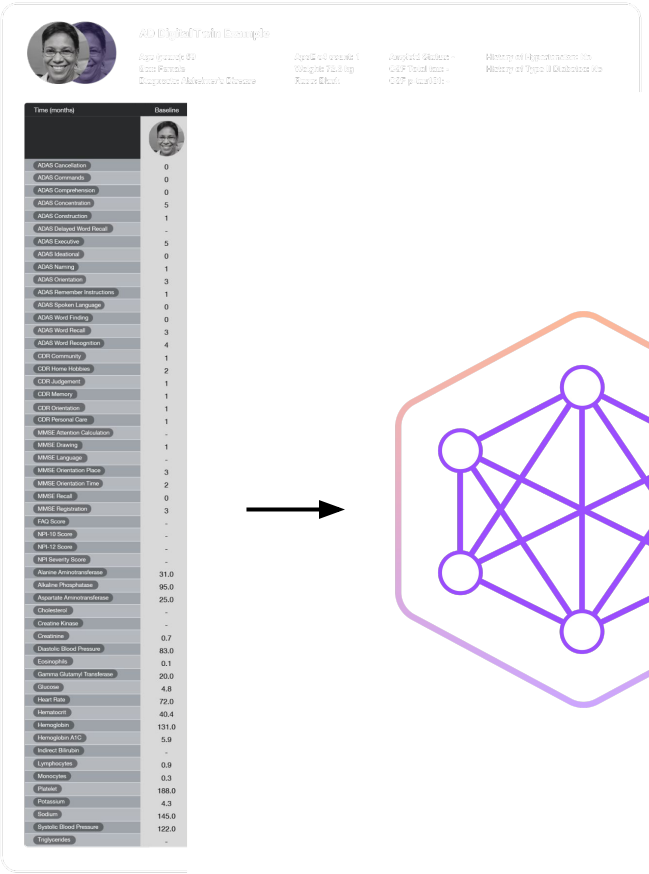
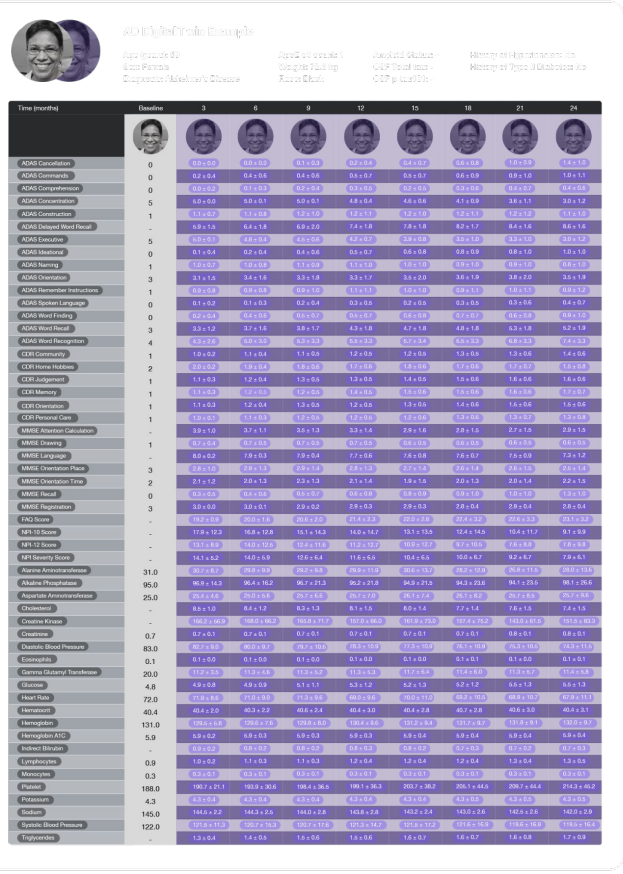
Digital Twins are
comprehensive,
computationally generated,
probabilistic predictions
of a patient's outcomes

They predict a patient's expected outcomes on a standard of care









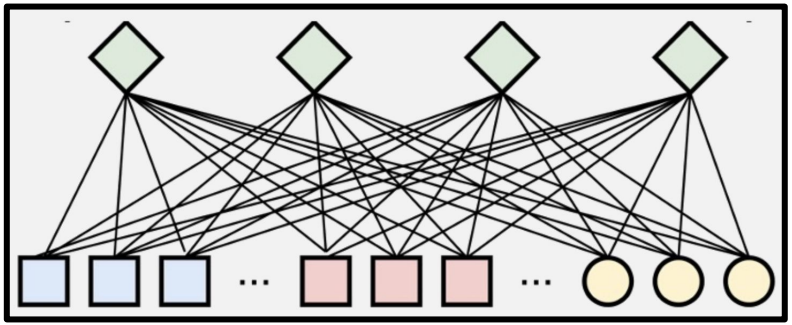
Our model architectures are purpose-built for clinical data

key properties of clinical data:

- longitudinal
- multimodal
- missingness is common
- data is not abundant
- data-taking conditions vary

probabilistic neural networks
(e.g., restricted Boltzmann machines)

hidden variables



visible variables

Defining the context of use is critical

“Pre-trial deliberations should identify those covariates and factors expected to have an important influence on the primary variable(s), and should consider how to account for these in the analysis in order to improve precision and to compensate for any lack of balance between treatment groups.”

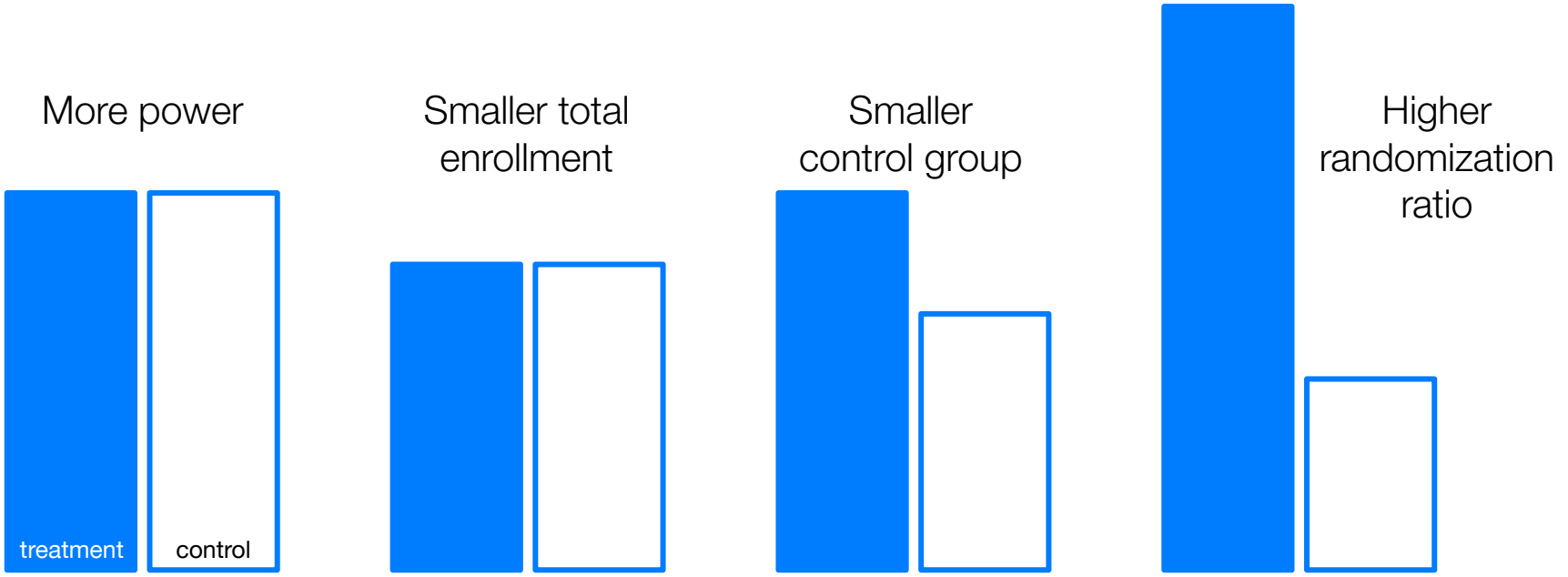
- ICH Guidance, “Statistical Principles for Clinical Trials”

Defining the context of use is critical

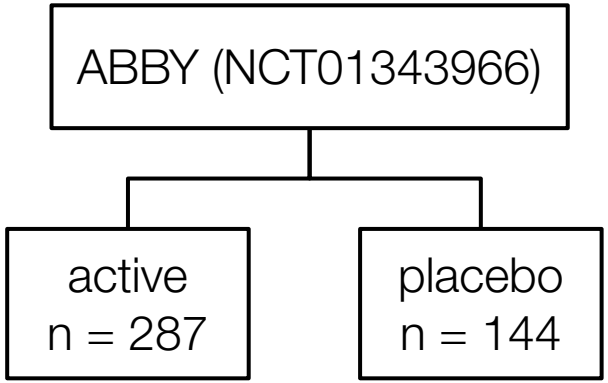
PROCOVA (Prognostic Covariate Adjustment)
Use a complex model applied to pre-randomization data to produce an optimal covariate for adjustment

PROCOVA is qualified by EMA for use in Phase 2 and 3 trials for added power or sample size reduction. It offers a way to meaningfully apply AI models and digital twins in clinical trials.

Digital twins can be used to improve standard RCTs



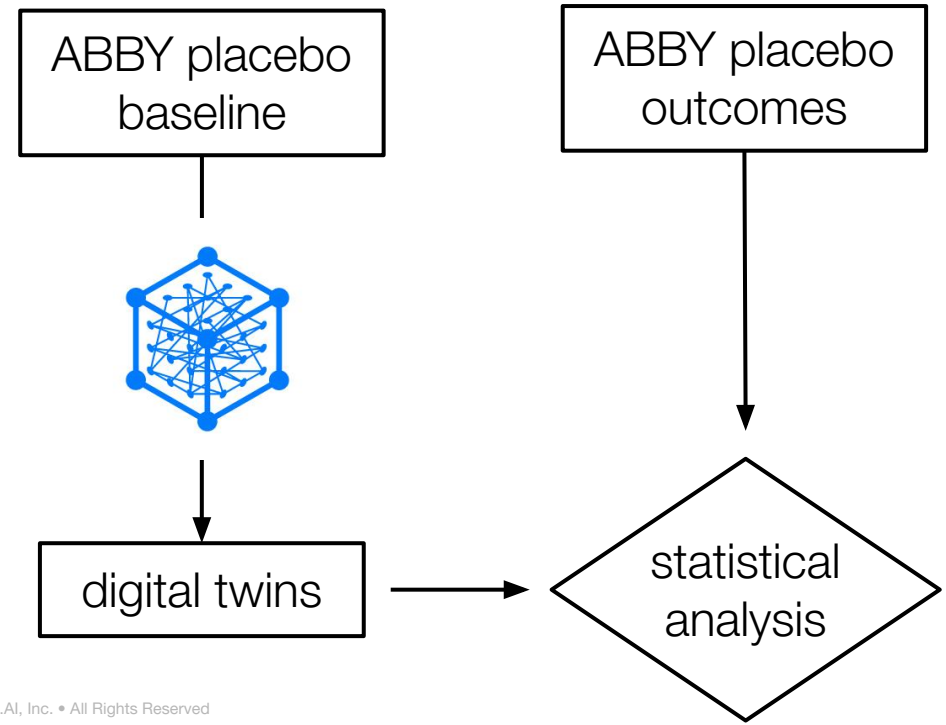
The goal of our collaboration was to evaluate the quality of digital twins using a previously completed clinical trial



ABBY

- Alzheimer's Disease Phase 2 trial
- 431 participants, randomized 2:1
- Cognitive (ADAS-Cog12) and functional (CDR-SB) primary endoints
- 18-month follow-up
- Study conducted 2011-2014

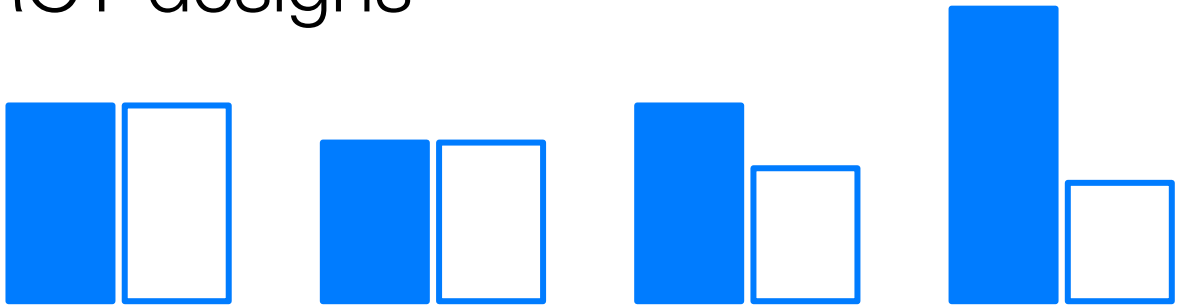
We used data from the placebo arm to create digital twins and compare to observed outcomes



We evaluate the prognostic quality of the digital twins using the correlation between the predicted and observed outcomes

Endpoint	Correlation, baseline score	Correlation, digital twins
ADAS-Cog12 change from baseline at 18 months	0.11	0.46
CDR-SB change from baseline at 18 months	-0.05	0.37

This translates to meaningful improvements for different RCT designs



Endpoint	Power (from 80%)	Sample size reduction	Control arm reduction	Higher randomization ratio
ADAS-Cog12	**88.4%**	**21%**	**35%**	**5:2**
CDR-SB	**85.4%**	**14%**	**24%**	**2:1**

table assumes an initial 1:1 design

Thank you!

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