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TITLE: Bayesian Weighted Prognostic Covariate Adjustment Using Digital Twins

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ABSTRACT:

Modern clinical trials face challenges due to enrollment difficulties, long durations, and high costs. At Unlearn, we are advancing artificial intelligence to solve these and other key pain points across clinical development. Our core technology, the Digital Twin Generator (DTG), uses generative AI on historical control data to create probabilistic forecasts, or digital twins, of participants' future clinical outcomes under the control condition. The DTG takes baseline data from prospective or retrospective RCT participants to generate these comprehensive forecasts. In this presentation, we introduce Bayesian Weighted Prognostic Covariate Adjustment (BW-PROCOVA), which leverages the means and variances of digital twins for prognostic covariate adjustment. It combines rich distributional information from digital twins as well as prior information from historical control participants, leading to trials with smaller sample sizes and shorter durations, or alternatively improved power and posterior precision compared to existing designs with a fixed sample size, while maintaining control of bias and Type I error rates in treatment effect inferences. BW-PROCOVA achieves desirable Frequentist properties by dynamically borrowing information from historical control participants using an additive mixture prior with both informative and non-informative components. This approach allows discounting of prior information when discrepancies between the trial and historical control participants arise, while leveraging digital twin data to recover any lost power and precision. Unlearn's Platform and statistical methods can ultimately transform the slow and expensive current approach in clinical trials and accelerate effective decision-making for drug development, as they incorporate the unique advantages of digital twins and satisfy regulatory desiderata.

This is joint work with Arman Sabbaghi (Unlearn.AI), Jon R. Walsh (Unlearn.AI), and Charles K. Fisher (Unlearn.AI).