Biomarker prioritization and power analysis

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Problem statement

- Treatment and placebo groups
- 10 patients each
- Baseline, then 5 days follow-up
- 4000 biomarkers measured

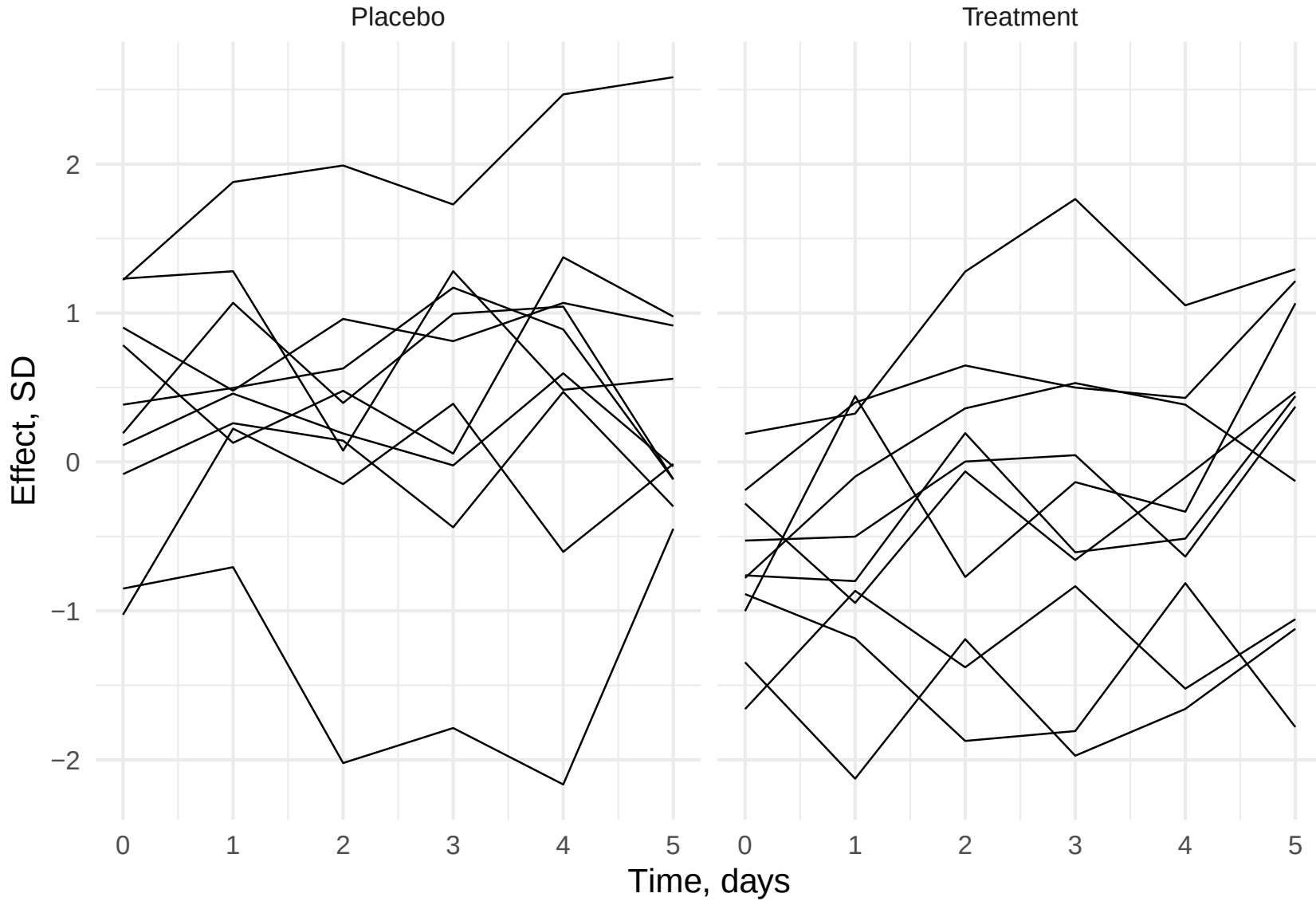
Potential approaches

- Repeated measures ANOVA
  - Appropriate, but no effect indication
- Linear mixed model
  - Effect size inference, significance testing
- Bayesian linear model
  - Appropriate with limited data, but priors are hard to choose
- Machine learning
  - Performant, but hard to interpret

Data pre-processing

- Log-transformation
  - Necessary if biomarker varies over degrees of magnitude
- Z-score standardization
  - 0-centered
  - Units of standard deviations

Simulated dataset



Mixed-effects model

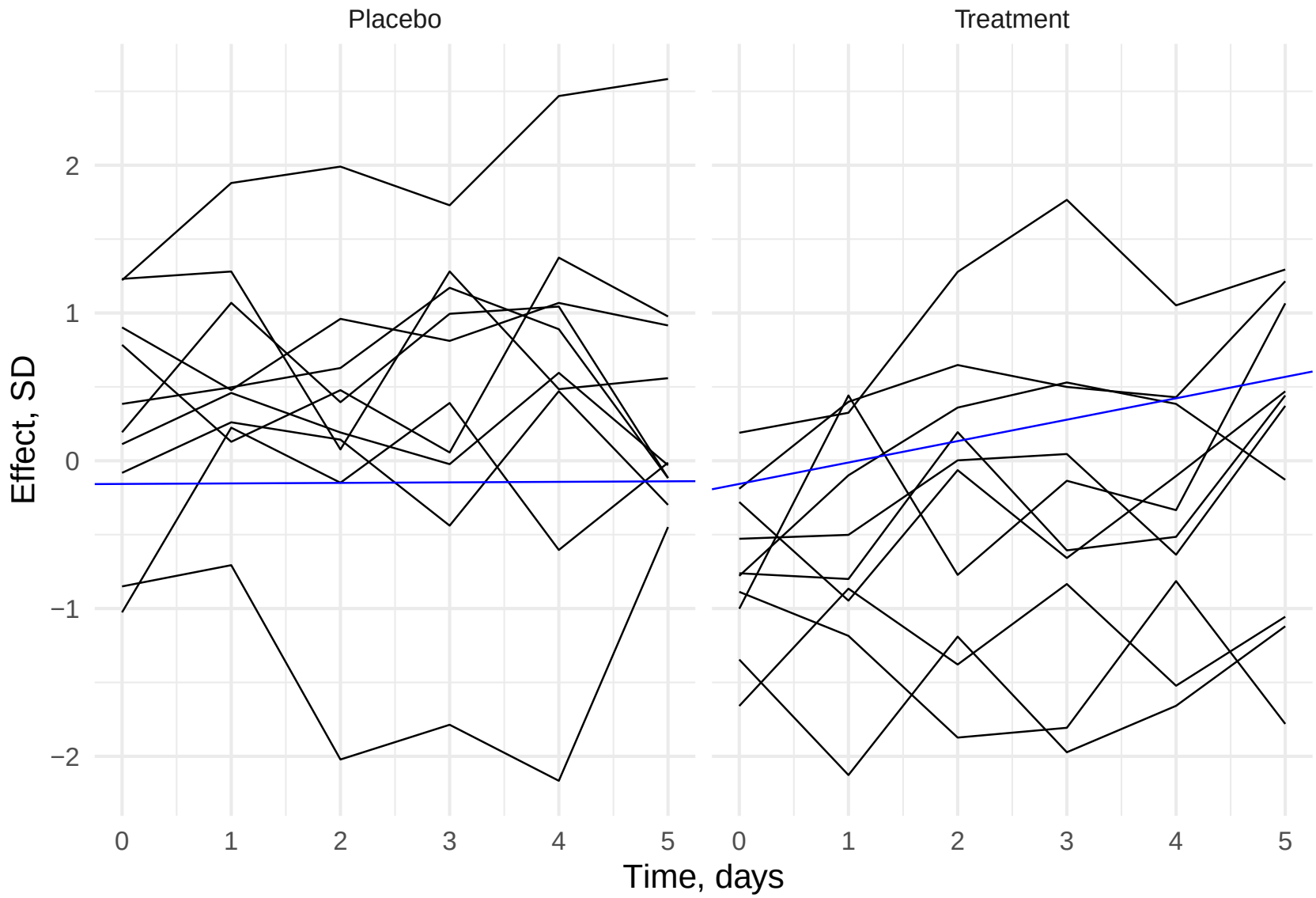
- Fixed effects
  - On average, baseline is zero (standardized)
  - Biomarker activity increases over time (only with treatment)
- Random effects
  - Baseline is different for each patient
  - Individual response to drug is different

Inference

Table 1: Inferblue effects

Fixed effect	Estimate	Std. Error	df	t value	p value
(Intercept)	-0.157	0.196	19.221	-0.799	0.434
t:groupPlacebo	0.004	0.040	33.172	0.089	0.930
t:groupTreatment	0.145	0.040	33.172	3.618	0.001

Inference



Multiple testing correction

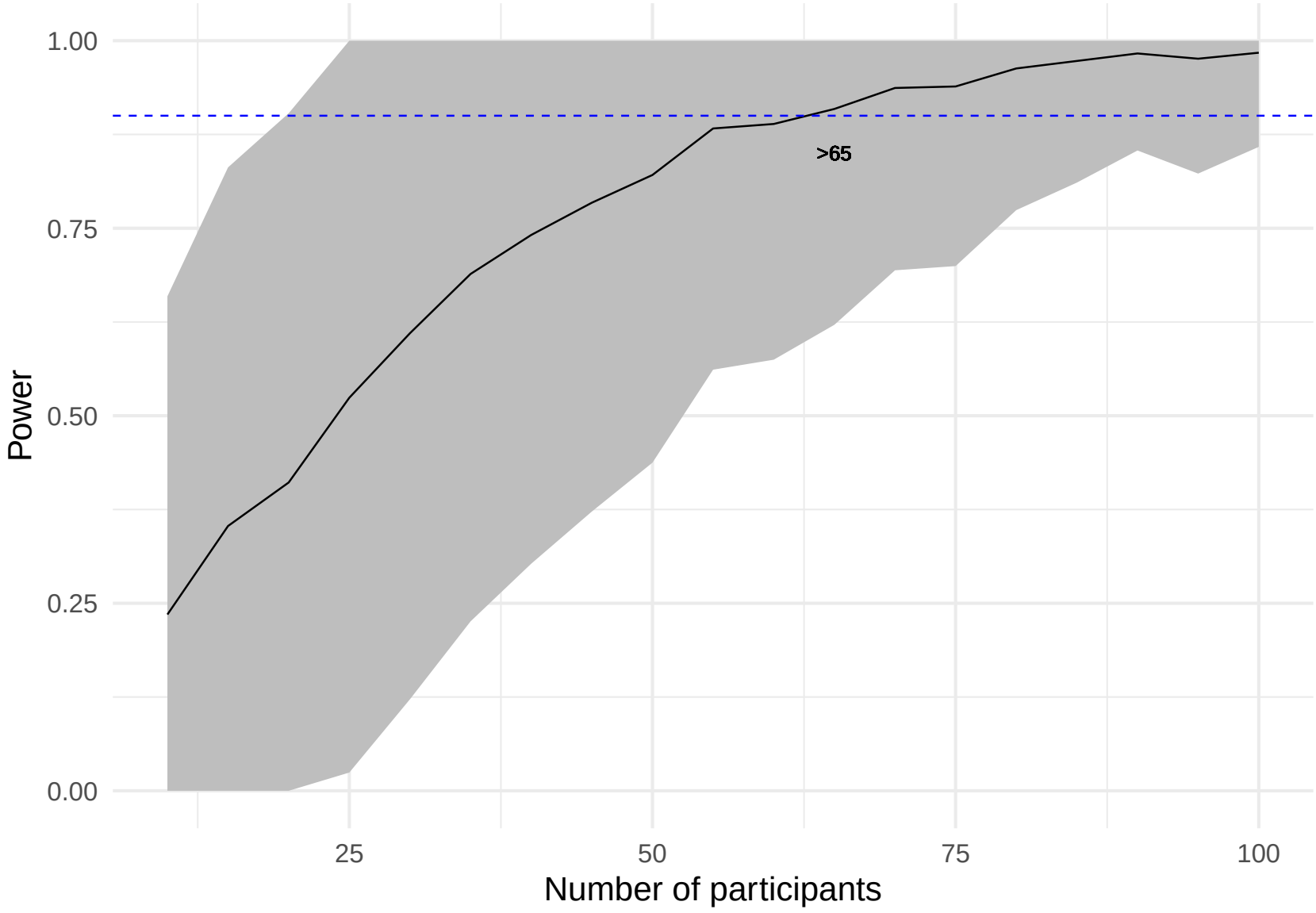
- Benjamini-Hotchberg False discovery rate
  - Controls for the false positives in the entire experiment
  - Less stringent than Bonferonni correction

Power

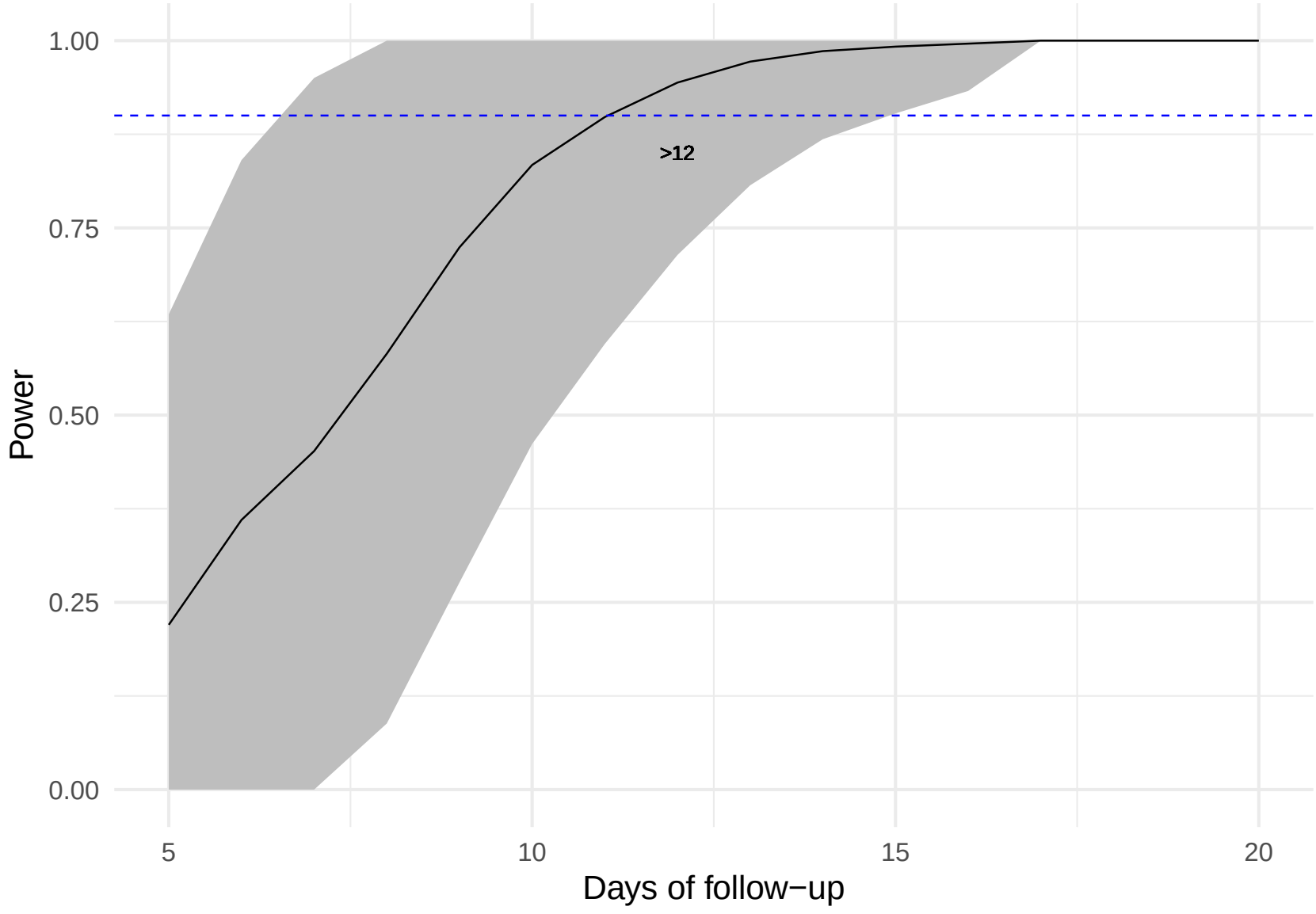
Power of the test

- Can we detect an effect if it actually exists?
- How many days of follow-up do we need?
- How many patients do we need per group?

Participant number



Days of follow-up



Further directions

- Smaller placebo group - 20 participant may be sufficient
- Effect of the drug concentration

Code available at github.com/ivan-krukov/biomarker-discovery

Questions?

Assumptions about effect

- With treatment, biomarker level changes 0.05 SD per day
- 2% improvement per day
- 93rd percentile after 30 days of treatment