



15.482 Healthcare Finance

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Unit 6, Part 3: Bayesian Adaptive
Clinical Trials

Unit Outline

- Overview of the Drug Development Process
- Randomized Clinical Trial Design
- Size, Power, and Cost
- Formal Statistical Analysis

Bayesian Adaptive Clinical Trials

Adaptive Designs

“An *adaptive design clinical study* is defined as a study that includes a prospectively planned opportunity for modification of one or more specified aspects of the study design and hypotheses based on analysis of data (usually interim data) from subjects in the study.”

FDA Guidance for Industry (2010)

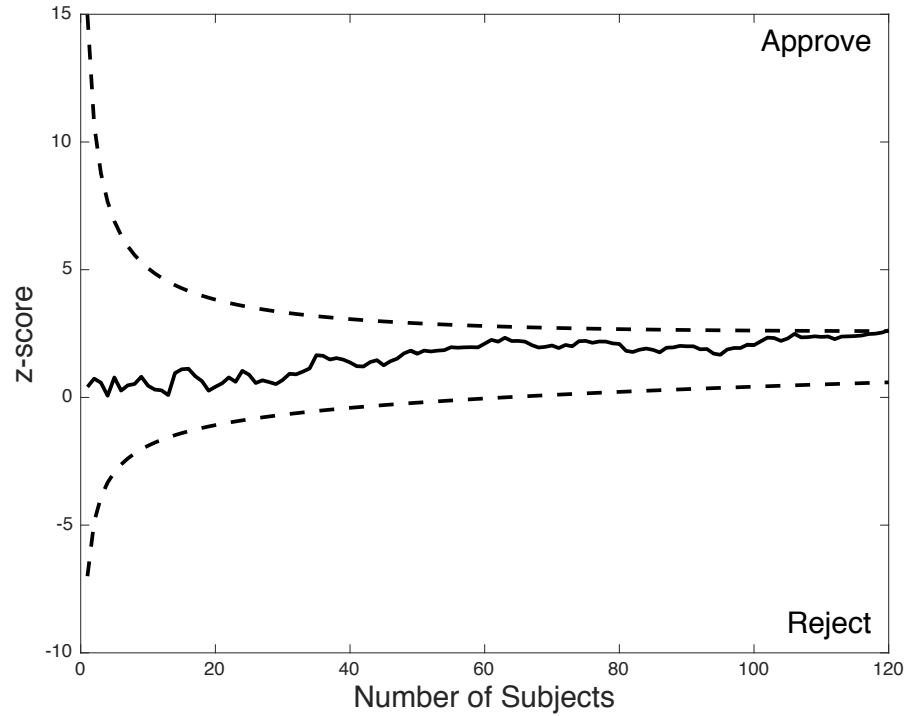
Examples include:

- Adaptive randomization
- Sample size re-estimation
- Adaptive dose finding
- Biomarker-adaptive design
- Adaptive-endpoint design
- Adaptive treatment-switching
- Seamless Phase II/III trials
- etc.

Adaptive Designs: Example

- Non-Adaptive (n fixed)
 1. Collect fixed sample
 2. Compute Z_n
 3. If $Z_n > Z_{\alpha/2}$, approve
If $Z_n \leq Z_{\alpha/2}$, reject
- Adaptive Test (n variable)
 1. Collect variable sample
 2. Compute Z_k for each new patient
 3. If $Z_k > Z_{u,k}$, approve
If $Z_{l,k} < Z_k < Z_{u,k}$ collect more data
If $Z_k \leq Z_{l,k}$, reject
- Adaptive test can achieve the same Type I and Type II error rates with smaller expected sample sizes

Adaptive Designs: Example



The Role of Behavior in Clinical Trial Design

- Suppose you are a small biotech startup
 - What are your objectives?
 - Are you likely to be over/under-confident in your drug?
 - Are you likely to be cash-constrained or not?
 - How are you likely to choose power (hence sample size n)?
- Suppose you are a large pharma company
 - What are your objectives?
 - How would senior management and shareholders react?
 - Are you likely to under/over-power your clinical trial?

The Role of Behavior in Clinical Trial Design

Biotech Target Accrual Pharma Target Accrual

Phase	Oncology	Metabolic Disorders	Autoimmune Disorders
I	74%	103%	90%
I/II	62%	97%	86%
II	82%	75%	91%
III	66%	87%	72%

Source: Pharma intelligence | informa dataset (sample of 14,681 trials)