Research Advocacy Network
AdvocateInstitute

Understanding Clinical Trial Design: *A Tutorial for Research Advocates*

Part II

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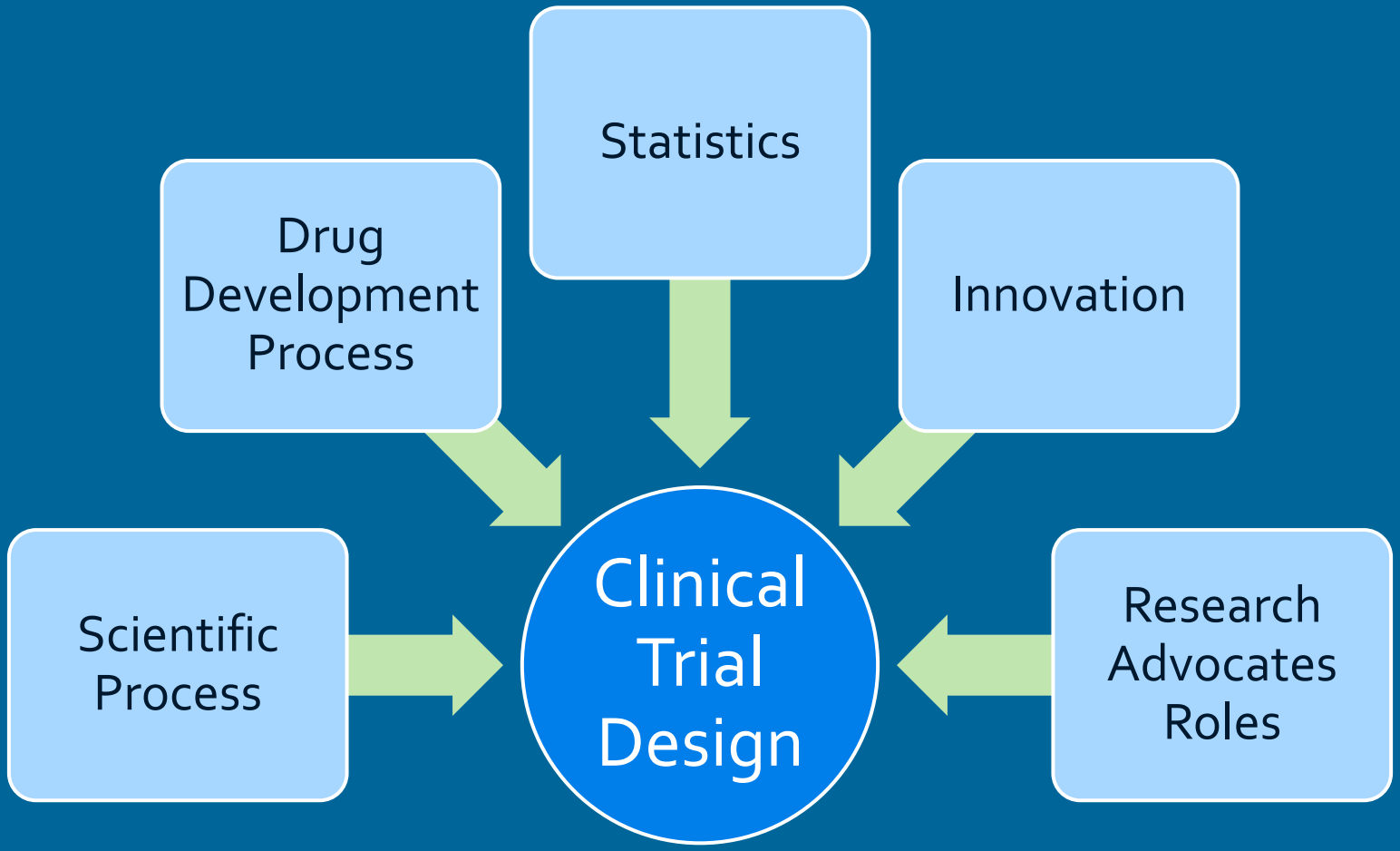
Clinical Trial Design



Part II Topics

- Why Innovation?
- Bayesian Approaches to Statistical Inference
- Adaptive Trial Designs
- Patient Enrichment Strategies
- What Research Advocates Can Do

Clinical Trial Design: Balancing Multiple Priorities

- **Effective:**
  - Avoid errors
  - Answer the right primary question definitively
  - Provide evidence about secondary questions
- **Satisfy the Needs of Multiple Stakeholders**

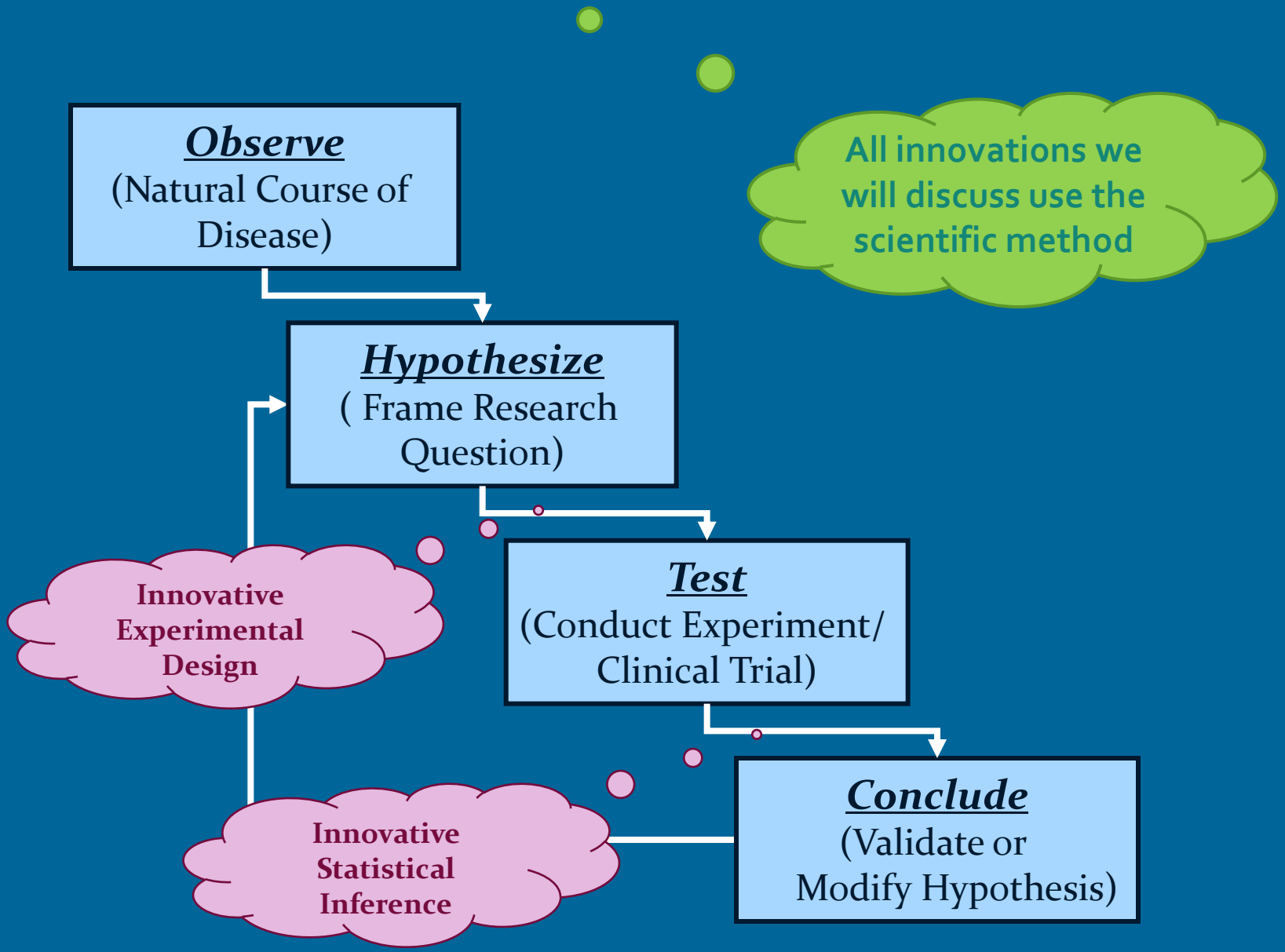
- **Efficient:**
  - Minimize Costs
  - Speed Results
  - Increase Accrual
- **Ethical:**
  - Minimize harm and maximize benefit to participants

Can we design more efficient trials, without compromising other priorities?

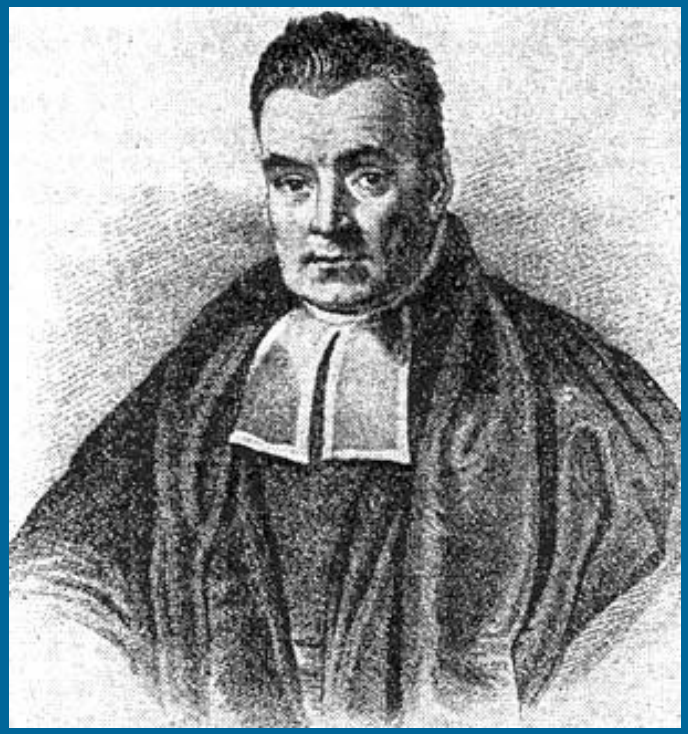
The Current Picture of Drug Development

- Only ~9% of drugs that go into clinical trials are ever approved
- It takes >10 years for drugs that do be approved
- It costs about $1.3B to bring a new drug to market
- Only ~6% of clinical trials meet their accrual schedules
- Only ~3% of adult cancer patients participate in clinical trials

Scientific Method



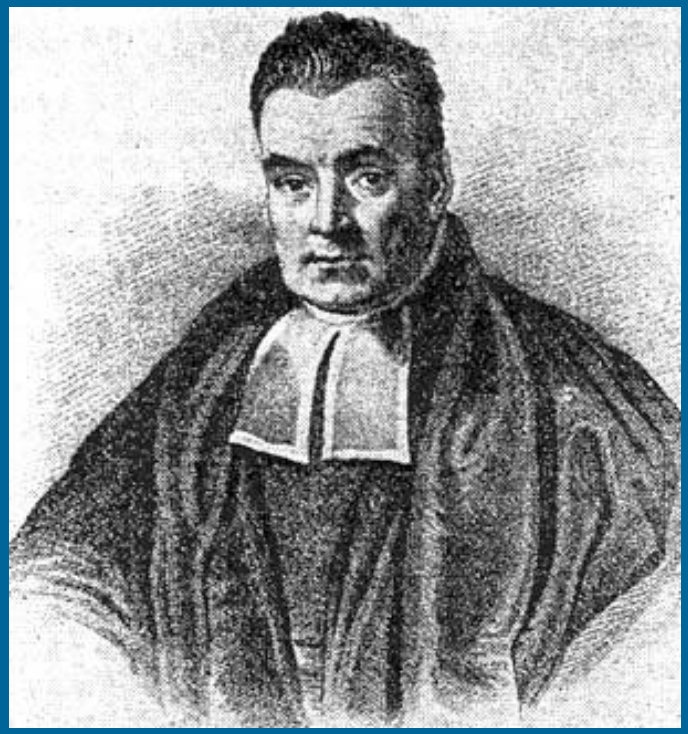
Bayesian Approach to Statistical Inference



Thomas Bayes
1702 - 1761

- Bayesians ask somewhat different questions than frequentists
  - *Frequentist:* Can I reject the null hypothesis?
  - *Bayesians:* How likely is my real hypothesis?

Bayesian Approach to Statistical Inference



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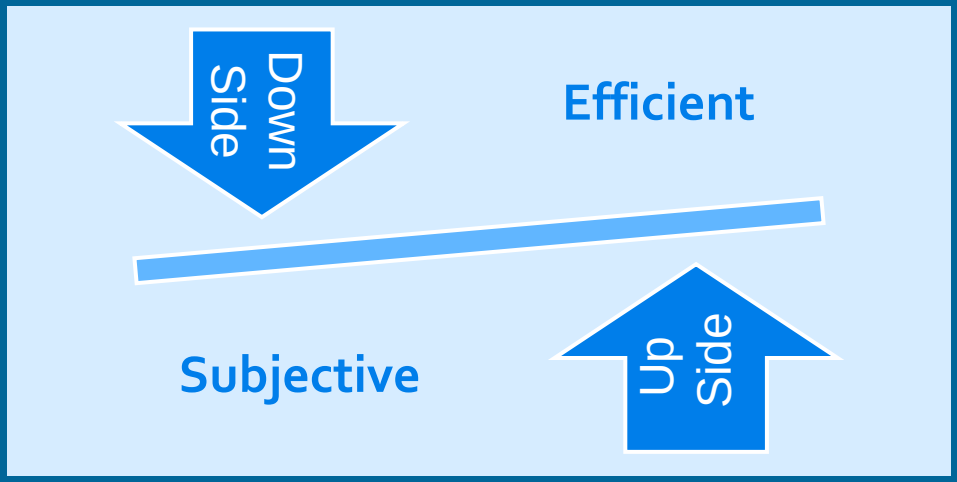
- Allows researchers to incorporate prior knowledge into their analyses



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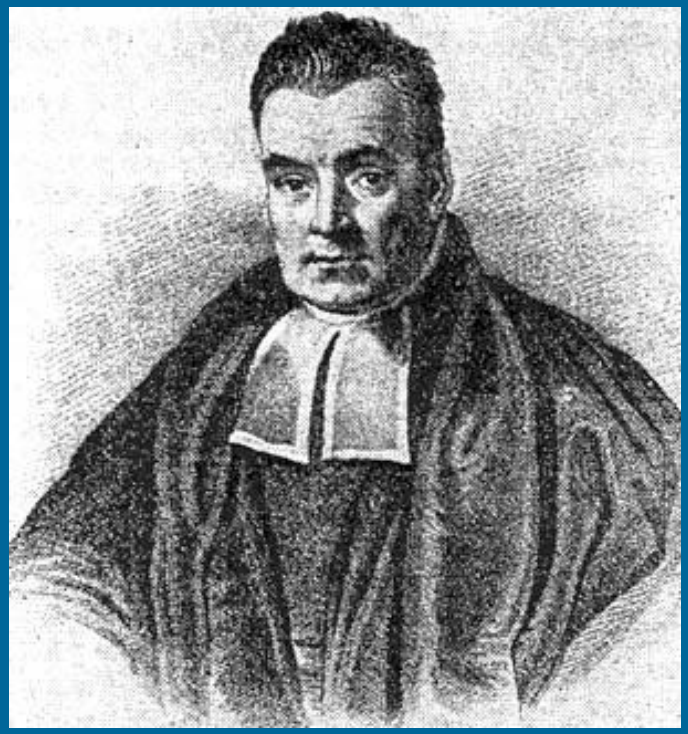

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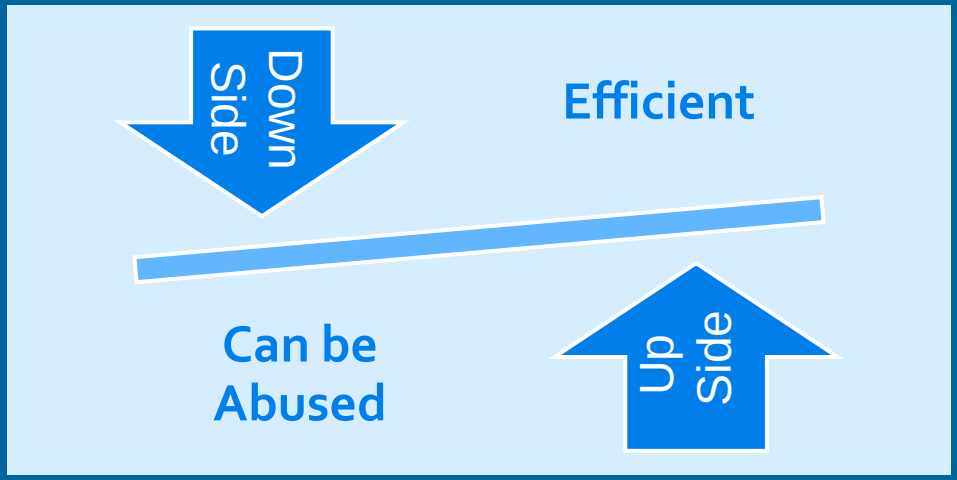


- Allows researchers to continuously look at their data, and modify their trials

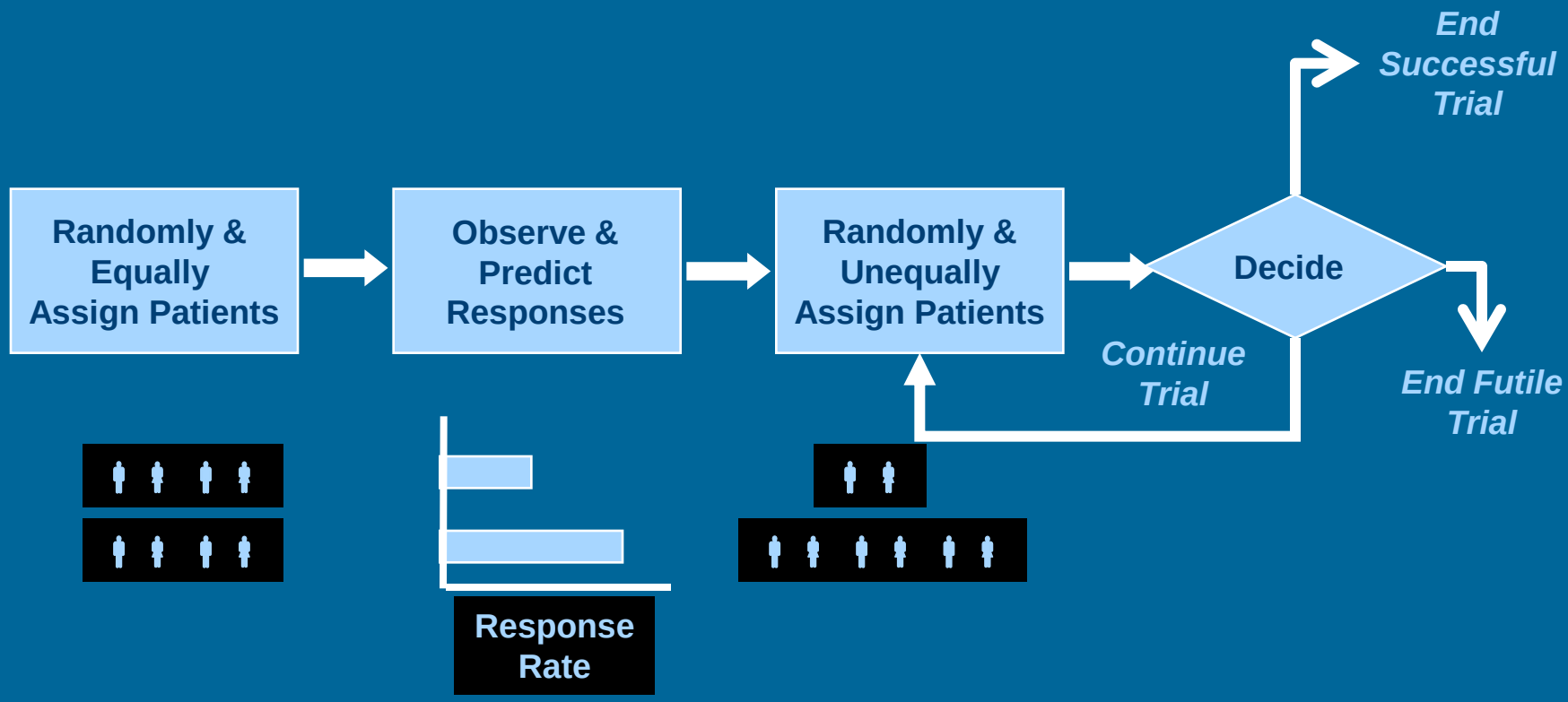
Adaptive Trial Designs

- Multi-stage designs, in which some aspects of later stages depend upon outcomes in earlier stages
- All *adaptation rules* ***must*** be fully specified prior to starting the trial
- At least some parts of the trial include *randomization*
- Are generally more efficient and attractive to patients

Do You Have to Be Bayesian to Use Adaptive Designs?

- Traditional *frequentists* use *multi-stage designs* but:
  - They are not really consistent with their paradigm
  - Using them reduces statistical power and diminishes gains in efficiency
- Continuous data monitoring and adaptation is natural to *Bayesians*

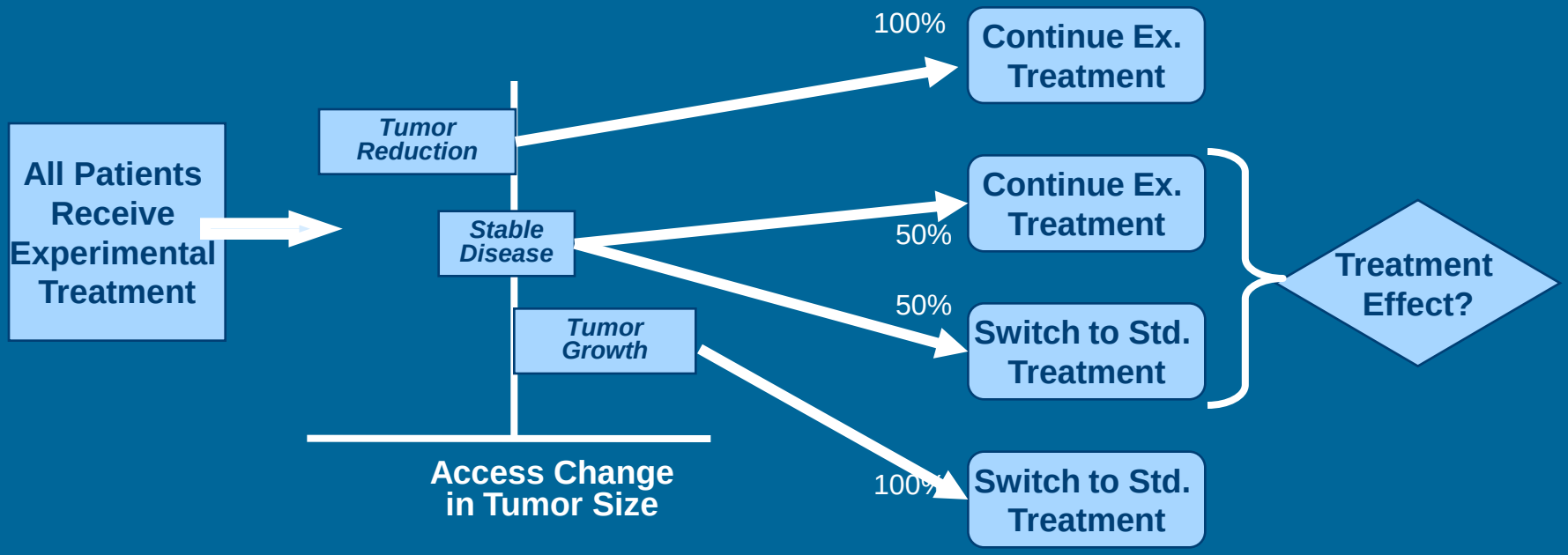
Patient Allocation Adaptive Design



Patient Enrichment Strategy

- Restricts trial eligibility to patients most likely to benefit from experimental intervention
- Eligibility may be based on:
  - Tumor markers
  - Patient pharmacogenetics
  - Initial response to experimental intervention
- Consistent with personalized medicine
- Easier, but perhaps more restricted drug approval

Randomized Discontinuation Design



Unique Contributions of Research Advocates

- Patient focus
- Holistic perspective
- Passionate
- Sense of urgency
- Out of the box thinkers with successful life experiences

How Research Advocates Influence Clinical Trials

- Setting Priorities
  - Grant reviews
  - Advisory committees
- Helping Designing Trials
  - Cooperative groups
  - SPORES and other research groups
- Reviewing Protocols & Informed Consent
  - IRBs
- Recruiting & Supporting patients
  - Patient friendly information
  - Community outreach
- Public Education
  - Support of research
  - Participation in clinical trials
  - Research results
- …

How Research Advocates Can Improve Clinical Research?

- Ask questions:
  - From a patient perspective
  - With innovation in mind
  - Remember: the only dumb questions are the one not asked
- Become knowledgeable about Bayesian statistics and adaptive designs

Good Luck!