

Comparative Effectiveness Research:

Solving surfing techniques

The Role of
Dynamic Predictive
Simulation in
Guiding the
Pragmatic,
Adaptive Trial



Evidence Matters.™

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Questions of Interest

- What are the chances of success (given design choices)?
 - Adaptation
 - Bayesian approach, effect of prior
 - Admissibility (inclusion/exclusion)
 - Duration of follow-up
 - Sample size
 - Response criteria
 - Other
- How much will it cost?
 - Sample size
 - # visits, sites, duration of follow-up
 - Endpoints
- How generalizable?

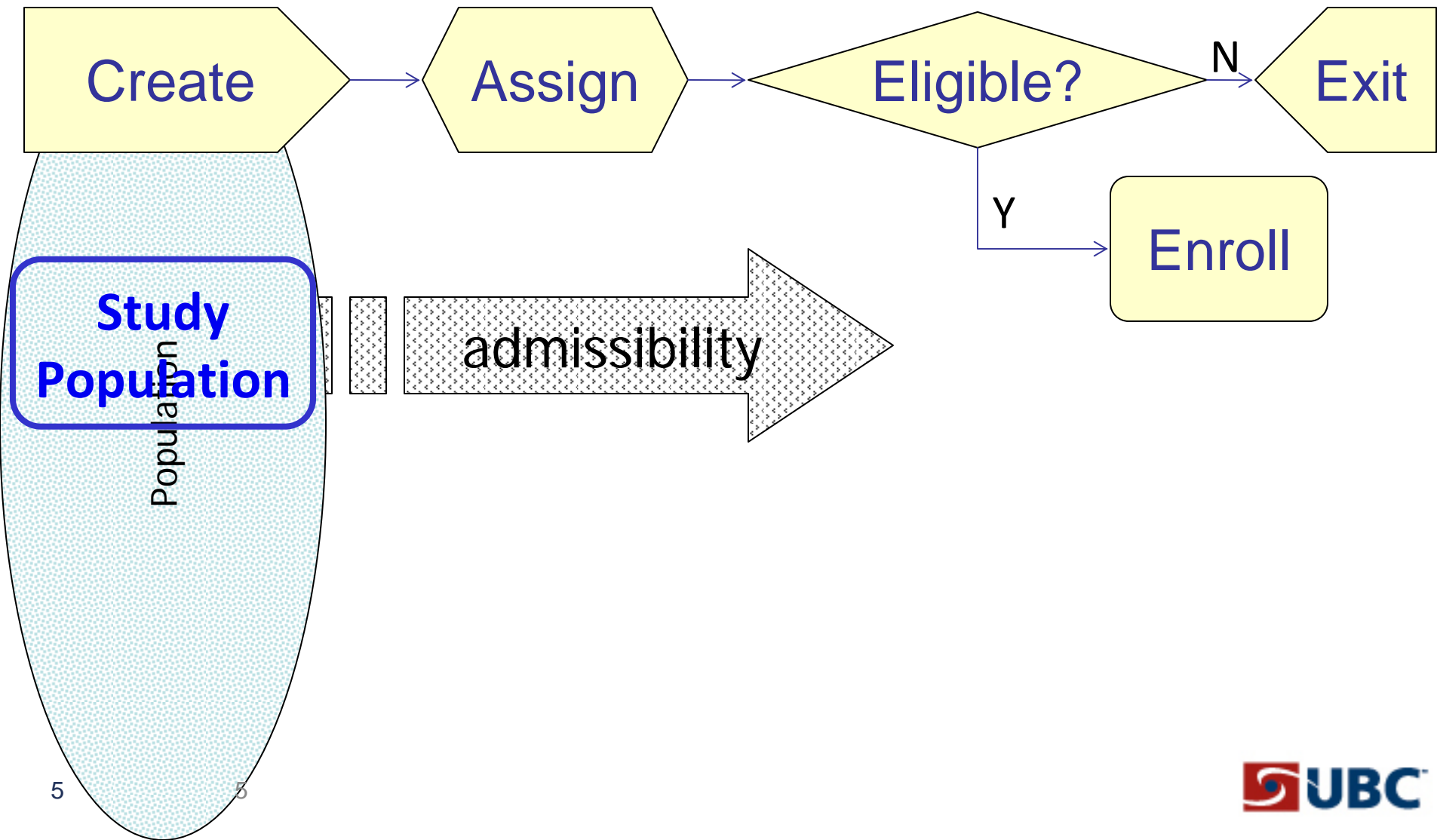
Approaches to CER Trial Design?

- Introspection (“educated guessing”)
 - Clinical Adv Board
 - Internal experts
 - Literature
- Work with the actual system (do a pilot?)
 - Difficult to test all the approaches
 - Generates expensive delays
 - Sample size too small.

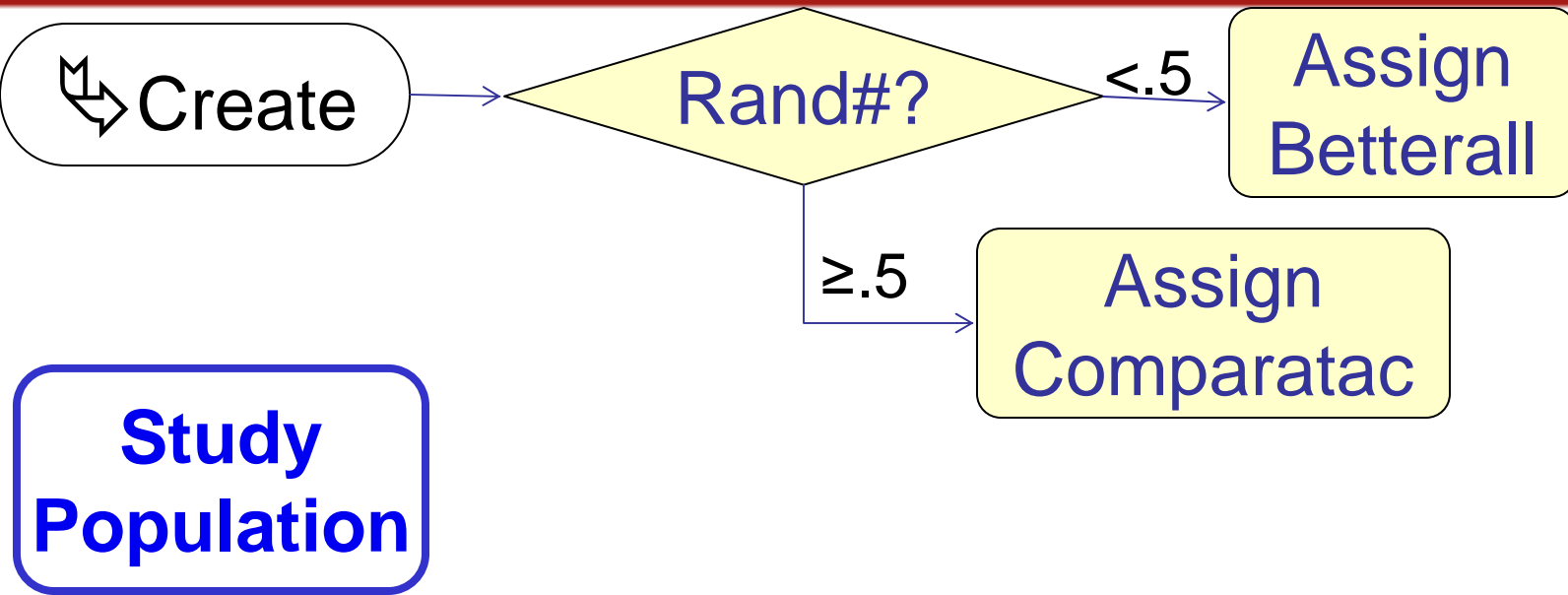
Simulation

- Simulation – set of assumptions/approximations about how the trial might work
- Use the simulation to design trial
 - Much faster, cheaper, safer
 - Can try wide-ranging ideas
 - » Make your mistakes on the computer where they don't count, rather than for real where they do count
 - Often, just building the simulation is instructive – regardless of results.

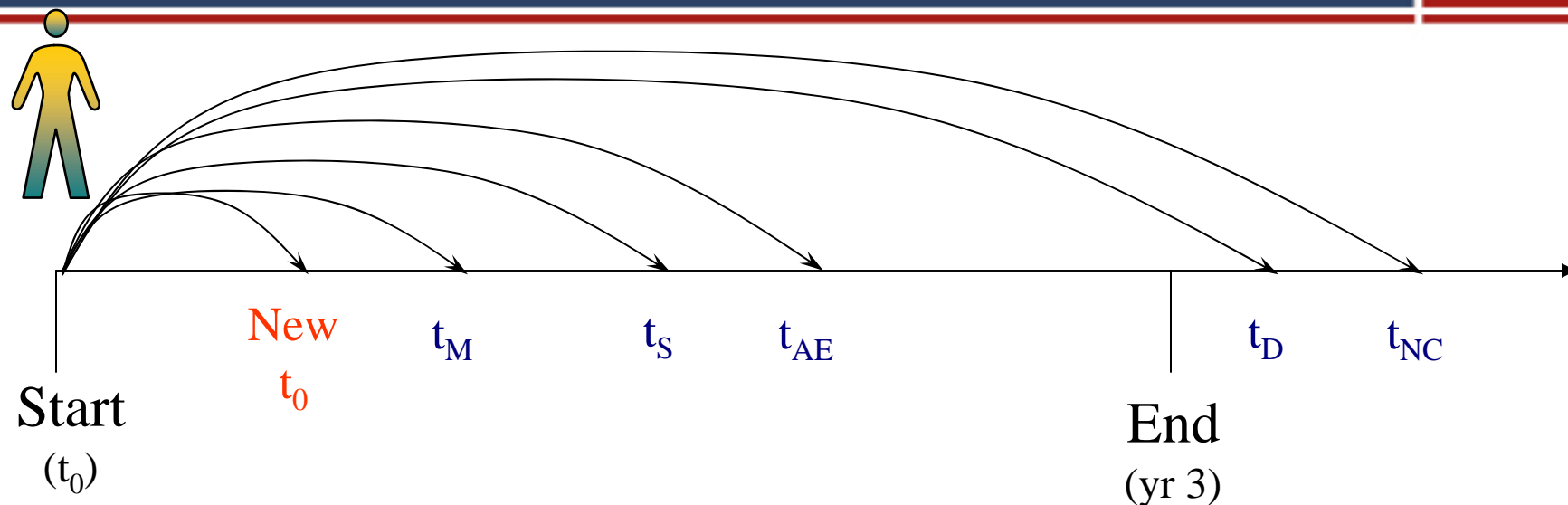
Simulating an RCT



Simulating an RCT



Individual Approach



When are...

- Death (t_D)
- Success (t_S)
 - AE (t_{AE})
- Monitoring (t_M)
 - Visit (t_V)
- Non-compliance (t_{NC}) ?

...predicted for this patient if he continues on treatment x ?

Driving a Trial Simulation

- Direct linking
- Rules
- Stochastic control
 - Prior
 - Can use equations of many types
 - » Regressions (Linear, exponential, weibull, beta, gamma etc.)
 - » Hazard functions, CPH
 - » Piece-meal.