

# Clinical Trials

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**Outcome**  
(Disease)

+

-

**Exposure**  
(Risk Factor)

+

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***BEHOLD!***

# **CLINICAL TRIALS**

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## Objectives:

**Review Fundamentals of Clinical Trials**

**Design and Analyze a Study**

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## Experimental Trial:

A trial is a type of cohort study, in that we follow a group that has yet to develop the outcome of interest.

**Key Point** ⇒ In a trial the investigators assign the “exposure” (i.e., the treatment).

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## Experimental Trial:

**Contrast with standard cohort study:**

- 1. Randomized assignment of exposure (usually a treatment)**
- 2. Outcome is typically (not always) a cure rather than disease.**

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**Randomized, Blinded Trial**  
**(The Gold Standard)**

**Main Purpose:**

**Compare Treatments**

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It all comes down to . . .

Obtaining groups that are comparable for *everything except* the treatment . . .

.

So that differences in outcome can fairly be ascribed to the the only difference between the groups (i.e., to the treatment).

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## Randomized, Blinded Trial

1. Assemble Cohort
2. Check baseline variables
3. Randomize
4. Treat (“Double Blind”)
5. Measure Results

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## 1. Assemble Cohort

Inclusion Criteria

Exclusion Criteria



Representativeness

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Generalizability

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## 1. Assemble Cohort

**Limiting to persons at high risk  
increases study power . . .**

**. . .at the cost of generalizability to  
low-risk populations.**

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## 1. Assemble Cohort

**Exclude based on:**

- 1. Unacceptable risk for Rx or placebo**
- 2. Treatment unlikely to be effective**
- 3. Unlikely to adhere to protocol**
- 4. Unlikely to complete follow-up**
- 5. Unable to give informed consent**

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## 1. Assemble Cohort

**For ethical reasons, you must plan for an adequate sample size (i.e., providing sufficient power to test your hypothesis).**

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## 2. Check Baseline Variables

Document absence of study outcome (which in this case is cure of a condition). In other words, we only keep them in the trial if they are still ill with the condition of interest.

Other baseline characteristics (e.g. age, sex, etc.)

Establish banks of material (blood, etc.) if feasible.

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## 3. RANDOMIZE

**“Assures” Comparability**

**Prevent biases**

**Tamper-proof**

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## 4. Treat

**Double-blind  
(if possible)**

**Dosage, etc. as per standard practice**

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**Ethical Issues:**

**“Informed Consent”**

**Is (nearly always) A Must**

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## 5. Follow Cohort for Outcome

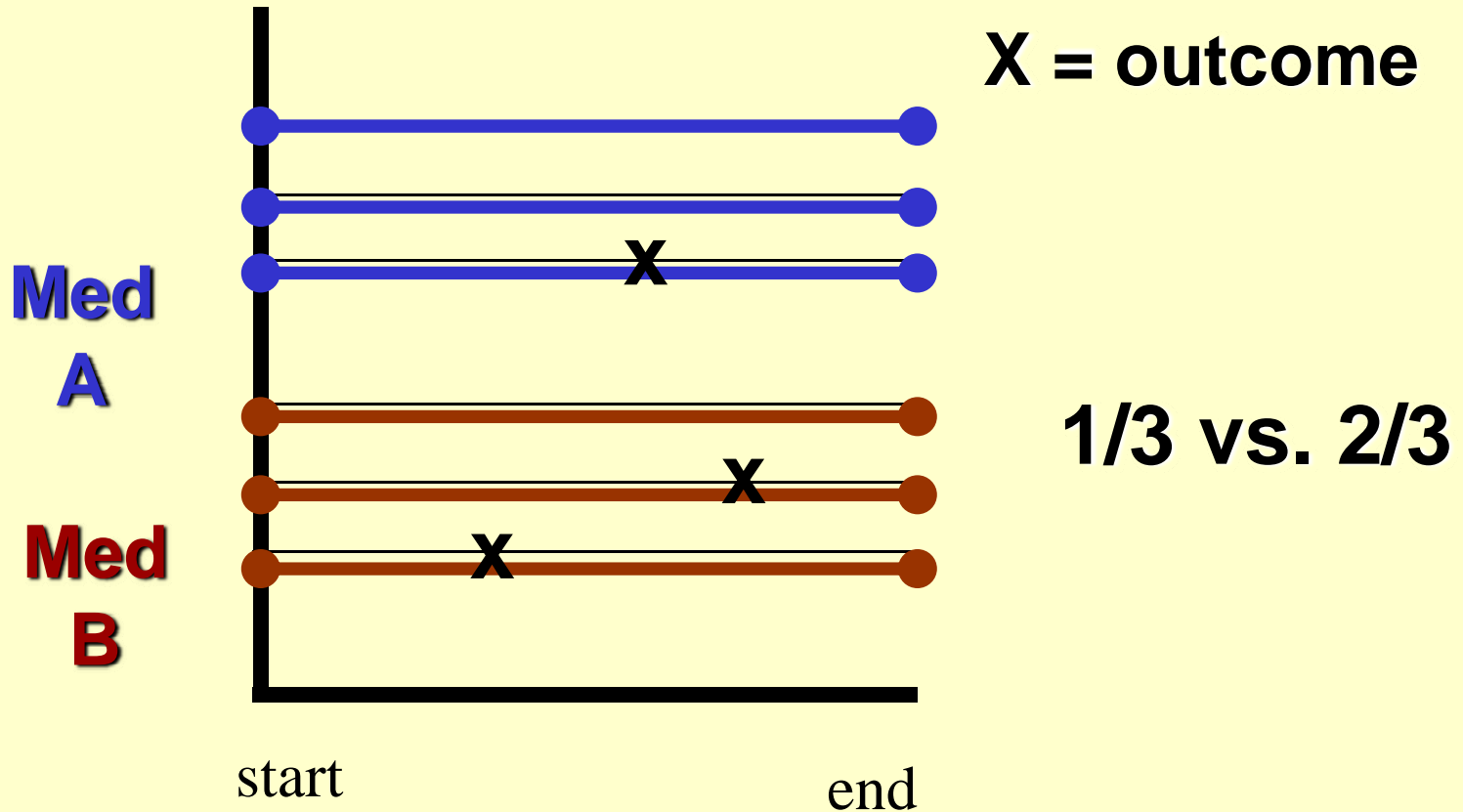
**“Fixed Cohort”**

**vs.**

**“Dynamic Cohort”**

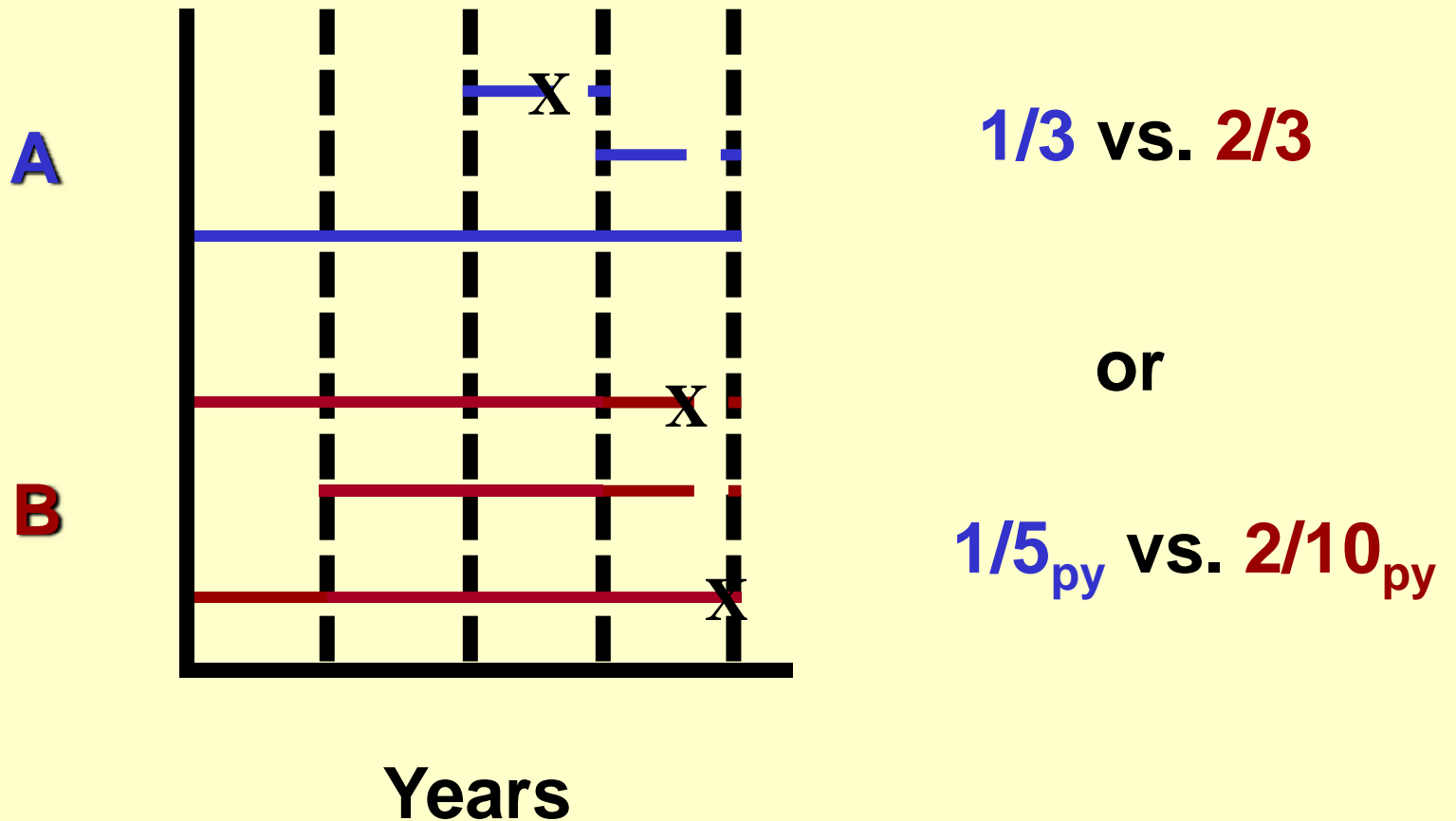
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## FIXED COHORT



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## DYNAMIC COHORT



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## Fixed Cohort

Short term outcomes (e.g., cure of infection)

## Dynamic Cohort

Long term outcomes (e.g., heart disease)

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What about drop-outs?

Analyze by

“Treatment Received”

or

“Intention to Treat”

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## Treatment Received

**Shows effect of treatment for those able to complete it**

**Fails to address dropout (which may be due to difficult treatment regime)**

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## Intention to Treat

Lumps those who did not complete treatment in with those who did (thereby addressing drop out)

**Maintains group comparability achieved by randomization**

**Most conservative (and recommended) analysis**

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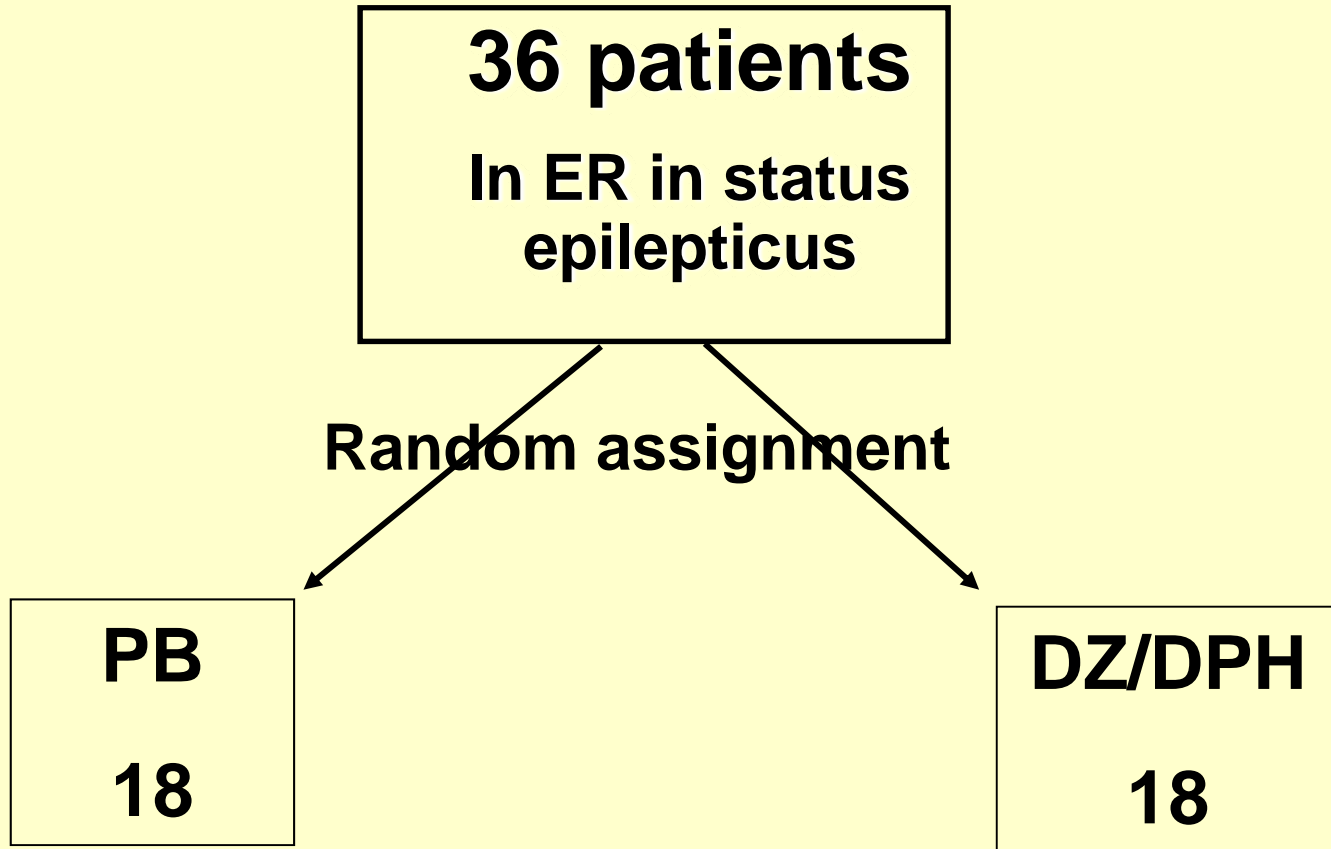
**Status Epilepticus is life - threatening**

**Two common treatments**

**(PB vs. DZ/DPH) have not been  
compared.**

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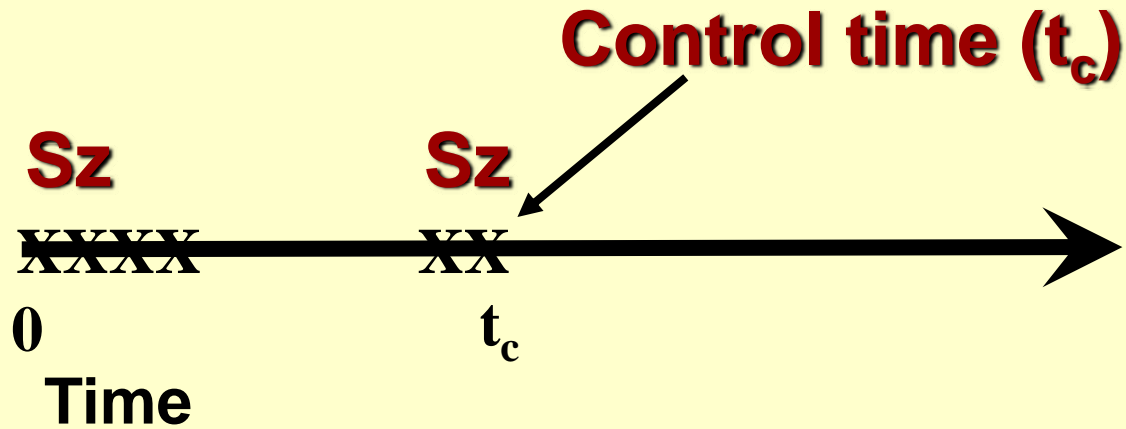
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Measured outcome: control time



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## Patient Characteristics

	<b>PB</b>	<b>DZ/DPH</b>
<b>N</b>	<b>18</b>	<b>18</b>
<b>Age (Mean <math>\pm</math> SD)</b>	<b>56 <math>\pm</math> 19</b>	<b>43.8 <math>\pm</math> 16</b>
<b>Prior Sz HX</b>	<b>11</b>	<b>14</b>
<b>Sex (F:M)</b>	<b>5:13</b>	<b>9:9</b>



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## Strengths:

**Strong evidence for cause and effect.**

## Limitations:

**May be costly**

**Potential ethical problems**

**May be difficult to standardize treatments.**