Introduction to Clinical Trials - Day 2

Session 1 - Introduction

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Goals of Clinical Trial Design

Clinical trials

- Experimentation in human volunteers
- Investigation of a new treatment or preventive agent
 - Safety : Are there adverse effects that clearly outweigh any potential benefit?
 - Efficacy : Can the treatment alter the disease process in a beneficial way?
 - Effectiveness : Would adoption of the treatment as a standard effect morbidity in the population?

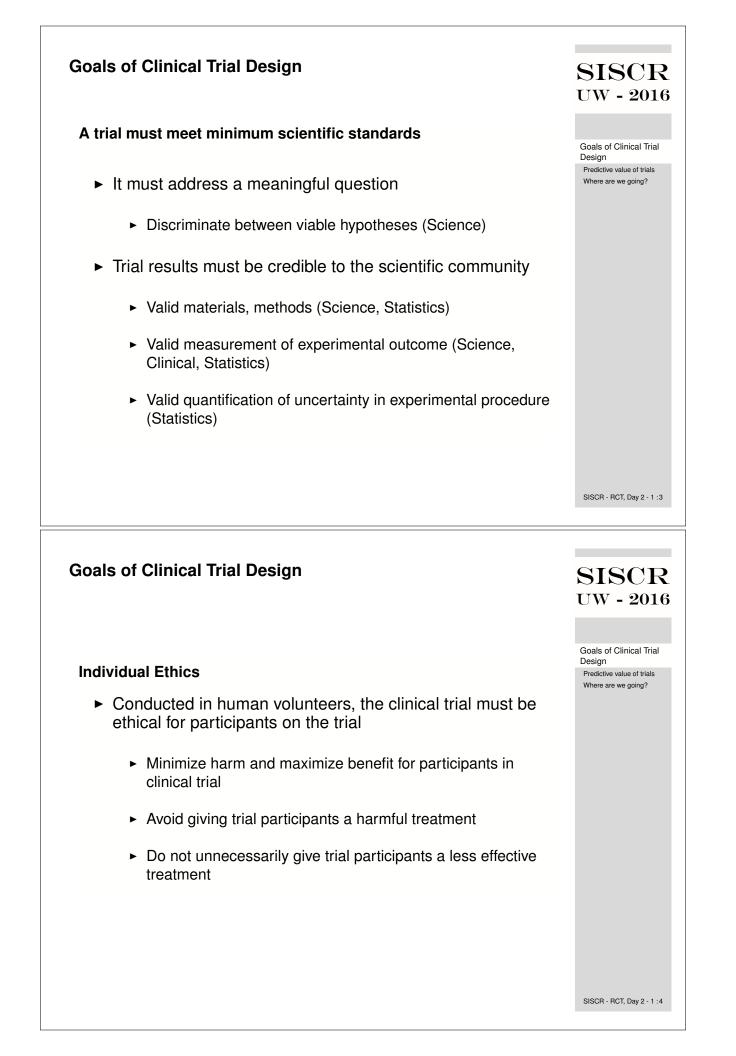
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Goals of Clinical Trial Design Predictive value of trials Where are we going?

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Group Ethics

- The clinical trial must ethically address the needs of the greater population of potential recipients of the treatment
 - Approve new beneficial treatments as rapidly as possible
 - Avoid approving ineffective or (even worse) harmful treatments
 - Do not unnecessarily delay the new treatment discovery process

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Design

Goals of Clinical Trial Design

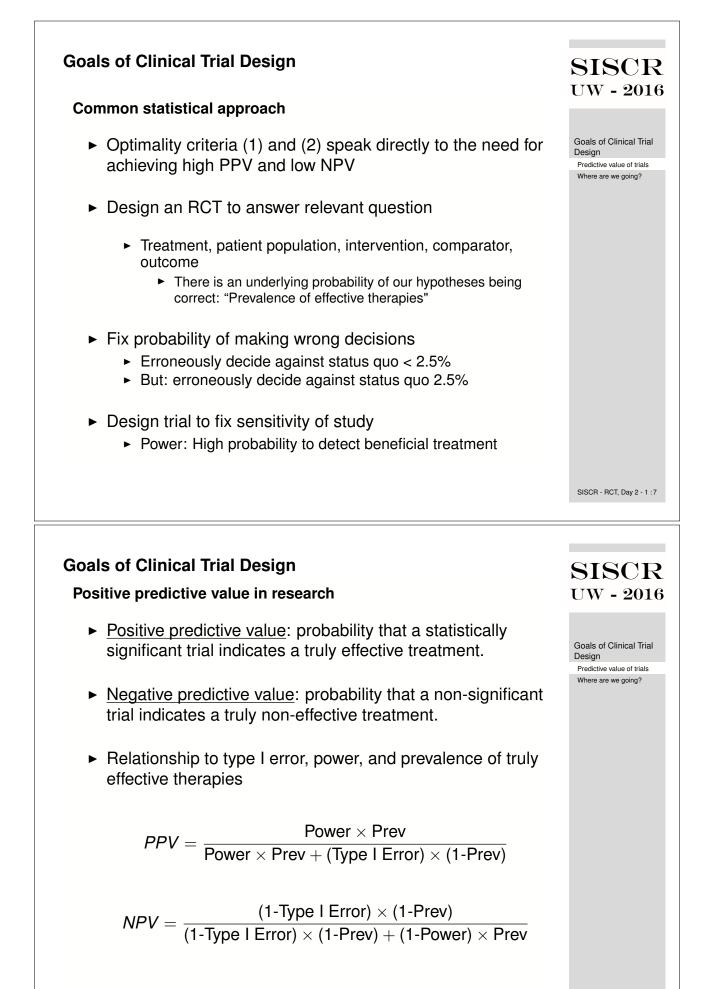
Optimality criteria

- A good procedure will
 - 1. Minimize "false positives"
 - Any treatment recommended for adoption will have a high probability of being a truly effective therapy
 - 2. Minimize "false negatives"
 - Any truly effective therapy will have a high probability of being recommended for adoption
 - 3. Be highly safe and ethical
 - Minimize the number of patients exposed to inferior treatments while investigations proceed
 - 4. Be efficient
 - Minimize costs (patients, calendar time, money)

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Goals of Clinical Trial Design Predictive value of statistically significant result depends on 1. Probability hypothesis is true to begin with (start with "good ideas") • Fixed when hypothesis is formulated 2. Type I error (Specificity) • Fixed by level of significance 3. Power (Sensitivity) • Statistical power made as high as possible by design	SISCR UW - 2016 Goals of Clinical Trial Design Predictive value of trials Where are we going?
Goals of Clinical Trial Design	SISCR - RCT, Day 2 - 1 :9 SISCR - RCT, Day 2 - 1 :9
 The later two elements are improved by 1. Minimizing bias Remove confounding and account for effect modification Decreasing variability of measurements Homogeneity of population, appropriate endpoints, appropriate sampling strategy, more precise measuring device 	Goals of Clinical Trial Design Predictive value of trials Where are we going?

Goals of Clinical Trial Design

Common pitfalls of studies

- Common pitfalls of experimentation are:
 - ► Data driven hypotheses (↑ Type I error)
 - Multiple comparisons (
 Type I error)
 - ► Poor selection of subjects (↓ Power)
 - ► Over-fitting of data (↑ Type I error, (↓ Power)
 - ► Poor selection of subjects, outcomes (↓ Power)
 - Noncomparability of treatment groups (
 Type I error)
- Each of these pitfalls leads to increases in variability and/or bias in clinical trials...

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Course roadmap

Where are we going?

- ▶ Module 1: Design
 - Background
 - Phases of clinical trials
 - Interplay between science and statistics
 - Ethics and varying roles of oversight committees
 - Role screening studies in trial design
 - Fundamental design elements
 - Variability and bias
 - Identification of target population
 - Definition of intervention(s)
 - Choice of outcomes
 - Choice of comparison groups
 - Blinding
 - Brief introduction to randomization
 - Statistical tasks in trial design
 - Refinement of hypotheses
 - Probability models and summary measures
 - Determination of sample size
 - Focus on elements of a clinical trial protocol

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Where are we going?

