Experimental Design and Statistical Analysis Seminar

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1

Quick review of the last week

2

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR

Beginner Session (9-12 Weeks):

1: Introduction to Study Design (2 Weeks)
2: Basic Principles in Experimental Design (2 Weeks)
3: Definitions And Descriptive Statistics (2 Week)
4: Normal Curve And Derived Scores (1 Week)
5: Data Screening (2 Weeks)
6: Inferential Procedures (2 Weeks)

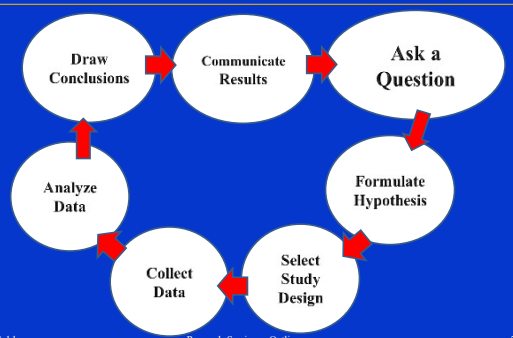
3

Why Learn about statistics and why these selected topics?

- **Research:** Research is the empirical investigation of the relationship between or among several variables.
- There are three basic goals in any research:
  1. To collect data that are free of bias.
  2. To draw valid conclusions concerning the effects of an independent variable.
  3. To make valid generalizations to populations and settings of interest.

4

Research Process



5

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR: OBJECTIVES

The main emphasis of this seminar is on understanding statistical procedures rather than memorization or calculation. We will discuss:

- Basic statistical concepts (i.e., randomization, hypothesis testing)
- Basic principles in Experimental Design
- Variety of Experimental Designs, their strengths and weaknesses

6

PUZZLER: The Temperature Flip

I was driving in the early morning on highway 5 south. It was a drizzly, foggy and cold morning for San Diego. One of the local bank sign was showing current Temperature. The temperature comes up in Fahrenheit, and a few seconds later it comes up in centigrade.

I saw something very interesting. The digits were exactly reversed. For example, it might have read 31 degrees "F", and when it showed the centigrade reading it said 13.

It turns out to be a enjoyable and nice warm, sunny day. on my way home, I came to the same intersection in the afternoon and I saw the temperature again. They were again two digits reversed!

What was the temperature in the morning, and the evening?

7

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR:
STUDY DESIGNS

1. Classification of Study Designs
2. Essential Design Features of a Controlled Clinical Trial
3. Quality Assurance
4. Computer Facility
5. Data Security Precautions
6. Preparation of Analysis Files
7. Broader classifications of study designs
8. Randomization
9. Activities By Stage Of Clinical Trial

8

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR:
STUDY DESIGNS

Study Type:
- I. Observational studies
- II. Experimental studies
- III. Practice-Based Research

Main Objectives:
- I. Feasibility
- II. Efficacy
- III. Effectiveness

9

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR:
STUDY DESIGNS

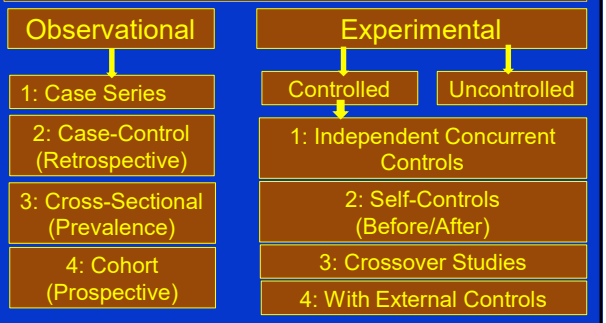
I: Observational studies: one or more groups of subjects are observed, and characteristics about the subjects are recorded for analysis.

II: Experimental studies: involve an intervention such as a drug, a procedure, or a treatment, and the interest lies in the effect the intervention has on the study subjects.

III. Practice-Based Research (PBR): is a real-world clinical research that uses data from daily, "messy" practice settings rather than controlled laboratories to evaluate and improve patient care.

10

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR:
STUDY DESIGNS: Study Type



11

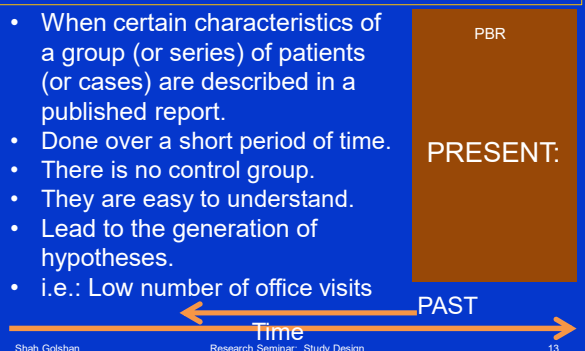
EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR:
STUDY DESIGNS

1. Feasibility studies are focused on the viability of an idea with an emphasis on identifying potential problems. (Experimental)
2. Efficacy studies are focused on the ability of a drug/treatment/intervention to achieve the desired effect. (Experimental)
3. Effectiveness studies are focused at how much benefit "actual" patients gain from "real-life" therapy. (Observational)

12

OBSERVATIONAL STUDIES:
1: Case Series Studies

- When certain characteristics of a group (or series) of patients (or cases) are described in a published report.
- Done over a short period of time.
- There is no control group.
- They are easy to understand.
- Lead to the generation of hypotheses.
- i.e.: Low number of office visits



13

I: OBSERVATIONAL STUDIES:

1. Case Series
2. **Case-Control** (Retrospective Studies)

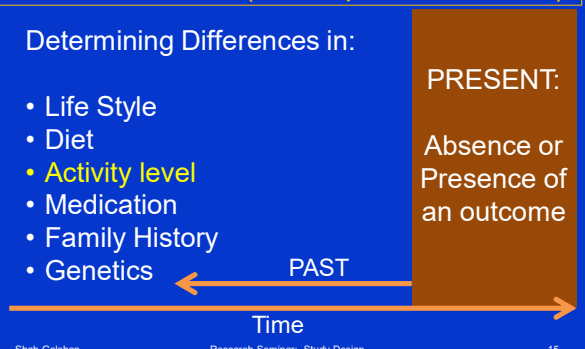
- It begins with the absence or presence of an outcome and then look backward in time.
- They try to detect possible causes or risk factors that may have been suggested in a case-series report.
- Individuals are selected on the basis of some disease or outcome
- The controls are individuals without the disease or outcome.
- Identify a characteristic or risk factor present in the cases' histories but not in the controls' histories.
- Longitudinal
- Matching method can be used

14

OBSERVATIONAL STUDIES:
2: Case Control (Retrospective Studies)

Determining Differences in:

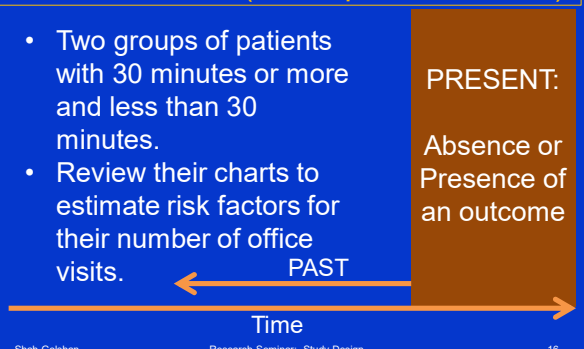
- Life Style
- Diet
- Activity level
- Medication
- Family History
- Genetics



15

OBSERVATIONAL STUDIES:
2: Case Control (Retrospective Studies)

- Two groups of patients with 30 minutes or more and less than 30 minutes.
- Review their charts to estimate risk factors for their number of office visits.



16

I: OBSERVATIONAL STUDIES:

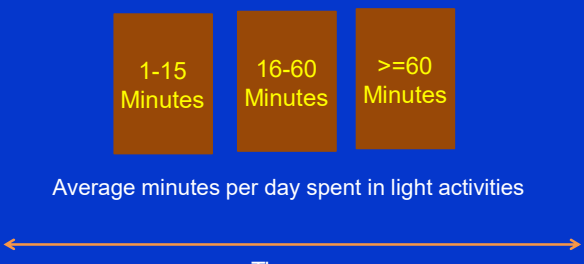
1. Case Series
2. Case-Control (Retrospective Studies)
3. **Cross-Sectional** (Prevalence Studies)

- Data is collected on a group of subjects at one time in a short period of time.
- They are designed to learn "what is happening?" right now.
- Surveys and polls are generally cross-sectional.
- Cross-sectional studies may be designed to address research questions raised by a case series, or they may be done without a previous descriptive study

17

OBSERVATIONAL STUDIES:
3: Cross-Sectional (Prevalence Studies)

Question: "what is happening?" right now.



18

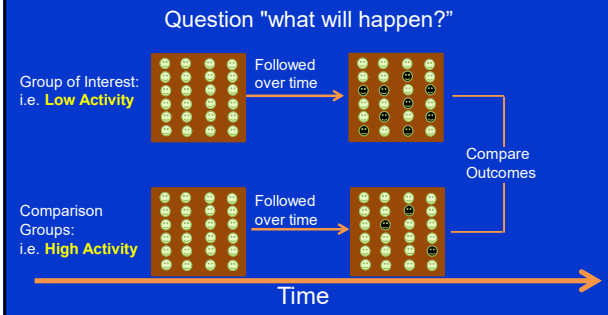
I: OBSERVATIONAL STUDIES:

1. Case Series
2. Case-Control (Retrospective Studies)
3. Cross-Sectional (Prevalence Studies)
4. **Cohort** (Prospective Studies)

- A cohort is a group of people who have something in common and who remain part of a group over an extended period of time.
- Subjects are selected by some risk factor for a disease or health effect.
- Cohort studies ask the question "what will happen?".
- The subjects, both exposed and unexposed, are followed over a certain period of time in order to observe the effect of these defining characteristics.

19

OBSERVATIONAL STUDIES: 4: Cohort (Prospective Studies)



20

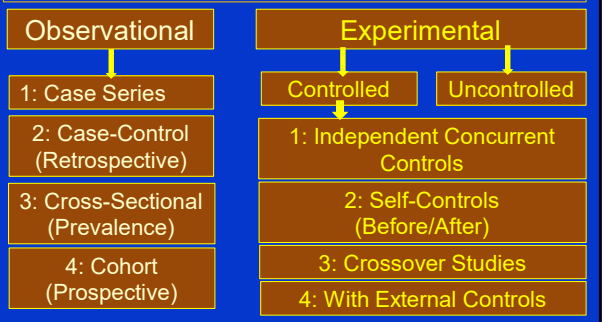
I: OBSERVATIONAL STUDIES:

1. **Case Series**
2. **Case-Control** (Retrospective Studies)
3. **Cross-Sectional** (Prevalence Studies)
4. **Cohort** (Prospective Studies)

The easiest way to distinguish between case-series and cohort studies is to determine whether there is a group of unexposed subjects or controls; if so, the study is a cohort. If the study describes only cases (exposed subjects) instead, it is likely to be a case-series.

21

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR: STUDY DESIGNS: Study Type



22

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR: STUDY DESIGNS

Studies can be divided into whether the subjects were merely observed or whether some intervention was performed.

I: Observational studies: one or more groups of subjects are observed and characteristics about the subjects are recorded for analysis.

II: Experimental studies: involve an intervention such as drug, a procedure, or a treatment, and interest lies in the effect the intervention has on the study subjects

23

II: EXPERIMENTAL STUDIES:

- Involves an intervention.
- Interest lies in the effect the intervention has on subjects.
- **Clinical Trials:** Experimental studies involving humans.
- A clinical trial is a planned experiment designed to assess the efficacy of a treatment.
- This is done by comparing the outcomes in a treatment group with those in a control treatment.
- Patients in both groups are enrolled, treated, and followed over the same time period and under the same situation.
- The groups are established through randomization.
- The period of observation may be short or long depending on the outcome measure.

24

II: EXPERIMENTAL STUDIES:

- Avivenna in his book, "Canon of Medicine" **(1025)**, discussed seven rules to evaluate the effect of drugs on diseases:
  1. should be used in its natural state
  2. with uncomplicated disease
  3. in two "contrary types of disease"
  4. the time of action and reproducibility of the treatment effect should be studied
- Lady Mary Wortley-Montague and Maitland did the **first planned experiment** without a formal comparison group by in **1721**.
  - The subjects were six convicted felons whose sentences were commuted by King George I.
  - The prisoners were inoculated by engrafting smallpox matter from a patient with the natural disease onto both arms and the right leg.
- The importance of **a control treatment as a means of identifying placebo effects** was recognized by Haygarth in his **1799** study of Perkins' Tractors - metallic rods used to stroke the body of an ailing person. He used imitation tractors made of wood on five patients affected with chronic rheumatism.

25

II: EXPERIMENTAL STUDIES:

- In **1865**, Sir William Gull in collaboration with Henry Sutton, demonstrated the importance of placebo treatment.
- In **1923**, the concept of randomization as a device for treatment assignment was introduced by Fisher.
- In **1938**, the double-blinded, placebo-controlled trial was used in treatment of the common cold.
- Multi-sites did not emerge until the late 1930s and early **1940**s.
- In **1962** amendments to the U. S. Food, Drug and Cosmetic Act of 1938 a series of legal requirements which had to be satisfied before a drug could be approved by the Food and Drug Administration was established.

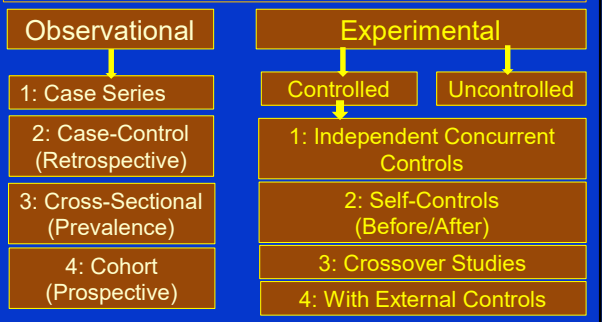
26

II: EXPERIMENTAL STUDIES:

- 1025: Book: "Canon of Medicine"
- 1721: Planned experiment w/o a formal comparison group.
- 1799: Control treatment.
- 1865: Placebo treatment.
- 1923: Randomization
- 1938: Double-blinded, placebo-controlled trial
- 1940: Multi-sites
- 1962: Amendments to the U. S. Food, Drug and Cosmetic Act of 1938 a series of legal requirements which had to be satisfied before a drug could be approved by the Food and Drug Administration was established.
- **Research is about the evolution of knowledge and it is a slow march of accumulating evidence.**

27

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR:
STUDY DESIGNS: Study Type



28

II: EXPERIMENTAL STUDIES:

The clinical trials fall into two major categories:

- **Uncontrolled trials**: The treatment is not compared with another treatment.
- **Controlled trials:** The experimental treatment is compared with another treatment or placebo.
- Controlled studies have greater validity in medicine than uncontrolled studies.

29

II: EXPERIMENTAL STUDIES:

Types of Control Studies:

1. **Studies With Independent Concurrent Controls**
2. **Studies with Self-Controls**
3. **Crossover Studies**
4. **Studies with External Controls**

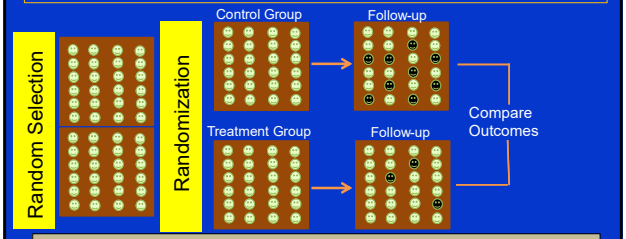
30

Control Studies:

1. **Trials With Independent Concurrent Controls:**
   - Two groups of subjects, one receiving the experimental and the other receiving the placebo or standard procedure.
   - Both groups for the same time period in the same study. In this way, the study achieves **concurrent control**.
   - It involves a masking method for study execution
   - The best method of group assignment is random assignment.
   - The studies that do not use randomized assignment are generally referred to as **nonrandomized trials** or simply as clinical trials or comparative studies, with no mention of randomization.

31

CONTROLLED INTERVENTIONAL STUDIES:
1: Studies with Independent Concurrent Controls



Study of Acupuncture to Treat Osteoarthritis Knee Pain:
- Control Group: Sham Treatment.
- Treatment Group: Acupuncture Treatment.
- Outcome: Group differences on their Pain level at the of study

32

Control Studies:

1. **Trials With Independent Concurrent Controls:**
   - Stratification is done to reduce or eliminate variation in the outcome measure due to the stratification variables
   - It involves the placement of patients into defined strata for randomization.
   - It takes place in conjunction with randomization.

33

Control Studies:

1. **Trials With Independent Concurrent Controls:**

Stratification:

1. It is unreasonable to expect that all baseline variation can be controlled.
2. It is impractical to control for more than two or three variable.
3. It has minimal benefit for trials with sufficient number of subjects per treatment group ≥ 50.
4. It's efficiency depends on the relationship of that variable to outcome measure.
5. It complicates the randomization process.

34

Control Studies:

1. **Trials With Independent Concurrent Controls:**

Stratification:

6. Only variables that are observed and recorded before randomization may be used.
7. Stratification Variables should be easy to observe and reasonably free of measurement error.
8. Variables that are subject to major sources of error due to differing interpretations should not be used for stratification.
9. Use of a large number of allocation strata may allow for fairly large chance departures from the desired allocation ration if there are only a small number of patients per stratum.

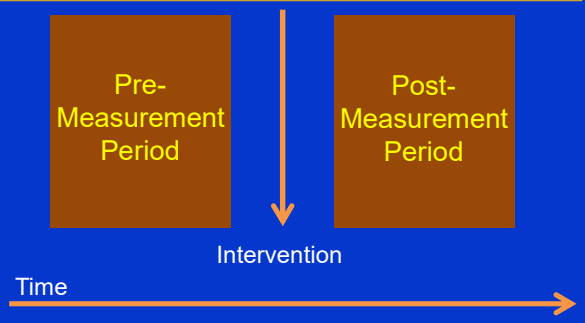
35

Control Studies:

1. **Trials With Independent Concurrent Controls.**
2. **Trials with Self-Controls:**
   - Using the same group of subjects for both experimental and control options.
   - Subjects are evaluated at the onset of the study and the baseline data are collected.
   - At the end of the study, subjects were re-evaluated to determine any changes versus the baseline data.

36

CONTROLLED INTERVENTIONAL STUDIES:
2: Studies with Self-Controls (Before/After)



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37

Control Studies:
1. Trials With Independent Concurrent Controls.
2. Trials with Self-Controls.
3. **Crossover Studies:**

- One group is assigned to the experimental treatment, and the second group is assigned to the placebo or control treatment.
- After a period of time, the experimental treatment and placebo are withdrawn from the groups for a washout period with no treatment.
- The groups are then given the alternative treatment.

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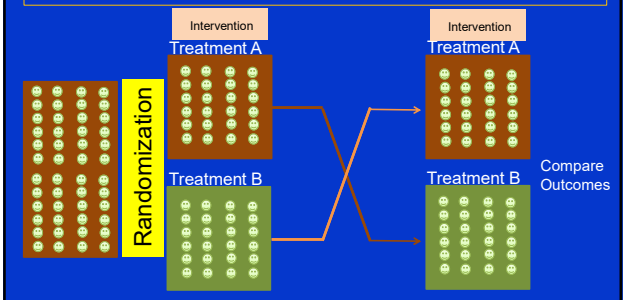
38

CONTROLLED INTERVENTIONAL STUDIES:
3: Crossover Studies



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39

Control Studies:
1. Trials With Independent Concurrent Controls.
2. Trials with Self-Controls.
3. Crossover Studies.
4. **Trials with External Controls:**

- This method uses controls external to the study.
- Sometimes, the result of another investigator's research is used as a comparison.
- Or patients previously treated in another manner is used **(Historical Controls)**.
- In these studies, researchers should evaluate whether other factors may have changed since the time the historical controls were treated; if so, any differences may be due to these other factors and not the treatment.

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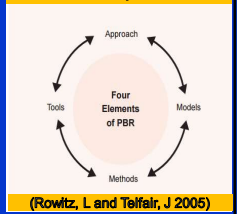
40

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR:
STUDY DESIGNS

Study Type:
I. Observational studies
II. Experimental studies
III. Practice-Based Research (PBR)

PBR is an original investigation undertaken to gain new knowledge, partly by means of Practice and the outcomes of that Practice.

Four Elements of Research within any PBR:



(Rowitz, L and Telfair, J 2005)

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41

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR:
STUDY DESIGNS

Study Type:
I. Observational studies
II. Experimental studies
III. Practice-Based Research

Main Objectives:
I. Feasibility
II. Efficacy
III. Effectiveness

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42

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR:
STUDY DESIGNS

1. Feasibility studies are focused at the viability of an idea with an emphasis on identifying potential problems and attempts to answer one main question: Will the idea work and should you proceed with it?
2. Efficacy studies are focused on the ability of a drug/treatment/intervention to achieve the desired effect.
3. Effectiveness studies are focused at how much benefit "actual" patients gain from "real-life" therapy.

43

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR:
Feasibility Study

1. These are Pilot studies that are used to ensure that the theories or methods behind the research idea are sound, as well as to "work out the kinks".
2. They should not be used to test hypothesis.
3. They should not be used to estimate sample size or power computations
4. The standard error of the estimate of the effect size in these studies are so large, that the study will be aborted or will be underpowered.

44

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR:
Efficacy Study

1. Are focused on the ability of a treatment to achieve the desired effect.
2. Are focused on the degree to which an intervention accomplishes the projected outcomes.
3. Popular method and trusted by researchers.
4. Are highly controlled and methodologically developed (RCT).
5. Are time-consuming and expensive.

45

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR:
Effectiveness Study

1. They look at how much benefit "actual" subjects gain from "real-life" therapy.
2. Subjects who have already begun (and possibly completed) treatment are surveyed.
3. They are asked detailed questions about their treatment and its effectiveness.
4. They reflect the full spectrum of disease, comorbidities, variable compliance rates, and use of other medications
5. Most effectiveness studies are essentially surveys.
6. They are much less time-consuming and less expensive to perform.

46

Efficacy Studies	Effectiveness Studies
• Done usually in research facilities or in tertiary care settings.	• Settings usually reflect the initial care facilities available to a diverse population with the condition of interest.
• Surrogate outcomes (i.e. scores, laboratory data) are frequently used.	• Primary outcome should capture the net effect on a health outcomes, using objective scales to measure their impact on health.
• Study duration is often limited.	• Study duration is often long to reflect the clinical setting.
• Sample size are usually based on effect size.	• Large sample size to detect at least a minimally important difference on a health-related QOL scale.
• They usually exclude protocol violators.	• They are always done on an intent-to-treat basis.

47

EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR:
STUDY DESIGNS

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6. Preparation of Analysis Files
7. Broader classifications of study designs
8. Randomization
9. Activities By Stage Of Clinical Trial

48