

Experimental Design and Statistical Analysis Seminar

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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

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EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR: 9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
2. Protocol Development Stage
3. Subject Recruitment Stage
4. Treatment and Follow-up Stage
5. Subject Close-out Stage
6. Termination Stage
7. Post-Trial Follow-up Stage (optional)

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EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR: 9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
 - A: Design specification
 - B: Organizational Structure
 - C: Subject recruitment, treatment, and data collection
 - D: Data processing and analysis

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1. Initial Design Stage:

A: Design specification

1. Purpose and rationale of trial
2. Population from which patients are to be selected
3. Number and type of test treatments
4. Number and type of control treatments
5. Level and method of blinding (masking)
6. Primary and secondary outcomes
7. Type and frequency of observations
8. Estimated sample size
9. Inclusion and exclusion criteria
10. Stratification variables to be used in randomization
11. Subject safeguard procedures
12. Projected timetable for trial
13. Approach to the close-out phase (fixed date versus fixed follow-up interval)

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9: Activities By Stage Of Clinical Trial

1. Initial Design Stage:

B: Organizational Structure

1. Develop general guidelines for Key staff
2. Outline responsibilities
3. Establish key elements of the overall organizational structure
4. Outline meeting schedule
5. Specify functions/duties of the staff
6. Outline general plans for paper writing

C: Recruitment, treatment, and data collection

1. Outline methods for recruitment and procedures for randomization
2. Outline data collection procedures
3. Outline timetable for testing and finalization of data collection forms
4. Determine specifications for drugs to be evaluated
5. Outline the main elements of the treatment protocol

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1. Initial Design Stage:

D: Data processing and analysis:

- 1) Outline data processing and database management procedures.
- 2) Develop a timetable for implementation of database management procedures.
- 3) Outline general **data analysis plan**.
- 4) Outline plans for quality control of data collection and processing activities.

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EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR: 9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
2. Protocol Development Stage
3. Recruitment Stage
4. Treatment and Follow-up Stage
5. Close-out Stage
6. Termination Stage
7. Post-Trial Follow-up Stage (optional)

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EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR: 9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
2. Protocol Development Stage
 - A: Subject recruitment and care
 - B: Data processing and analysis
 - C: Training and communication
 - D: Quality assurance
 - E: Treatment monitoring
 - F: Authorship
 - G: Management

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9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
 2. Protocol Development Stage
- ### A: Recruitment and Care
1. Write treatment **protocol (SOP)**
 2. Develop detailed **inclusion and exclusion** criteria
 3. Identify the source of subjects
 4. Determine **recruitment goals**
 5. Establish procedures for **monitoring subjects**
 6. Develop **consent** procedures
 7. Generate the treatment allocation schedule

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9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
 2. Protocol Development Stage
- ### B. Data processing and analysis
- 1) Develop procedures for data interface between clinic and the data center
 - 2) Specify contents of **data collection forms**
 - 3) Draft and **test** data collection forms
 - 4) Submit forms to appropriate study body for review and approval (**IRB**)
 - 5) **Develop plan** for data management systems
 - 6) Initiate development of data system and test computer programs

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Activities	Wk - 2	Wk 0	Wk 2	Wk 5	Wk 8	Wk 12
Informed Consent, 1:1 Meeting with RD	X	X	X	X	X	X
Usual Diet (Day -14 to Day -1)	X					
Modified ITIS Diet (Pre-defined Menu)		X	X			X
Modified IT IS Diet (Independent Menu)				X	X	X
Fatigue Assessment Survey	X	X	X	X	X	X
Pittsburg Sleep Quality Index	X	X	X	X	X	X
Beck Depression Index	X	X	X	X	X	X
PROMIS 8A Anxiety From	X	X	X	X	X	X
Montreal Cognitive Assessment	X		X			X
Plasma Inflammatory Markers	X	X	X			X
Stool Collection for future microbiome/metabolomics	X	X	X			X
Study satisfaction survey						X

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Table 4. Assessments and Timeline					
Domain	Measure	Baseline	Midway	Post-ix	3-month Fu
Diagnostic assessment					
Diagnosis	SCID or MINI	X			
Deficit Syndrome	Schedule for the Deficit Syndrome	X			
Symptoms					
Negative symptoms (primary outcome)	Clinical Assessment Interview for Negative Symptoms (CAINS)	X	X	X	X
Positive symptoms	Positive and Negative Syndrome Scale (PANSS) positive subscale	X	X	X	X
Depressive symptoms	Calgary Depression Scale for Schizophrenia (CDSS)	X	X	X	X
Functioning					
Performance-based functional capacity	UCSD Performance-Based Skills Assessment – Brief (UPSA-B)	X	X	X	X
Performance-based social competence	Maryland Assessment of Social Competence (MASC)	X	X	X	X
Rehabilitation goals (work, education, financial, residence)	Psychosocial Rehabilitation (PSR) Toolkit	X	X	X	X
Self-reported real-world independent living skills	Specific Levels of Functioning Scale (SLOF)	X	X	X	X
Cognition	MATRICS Consensus Cognitive Battery	X	X	X	X
CBST-CCT Content Knowledge	Comprehensive Modules Test (CMT)	X	X	X	X
Defeatist Performance Attitudes	Defeatist Performance Attitudes Scale (DPAS)	X	X	X	X
Effort Allocation					
Pupil response to digit span recall	6 th -digit dilation amplitude	X	X	X	X
Pupil response to Span of Apprehension task	10-letter army dilation amplitude	X	X	X	X
Fidelity to CBST-CCT	Cognitive Therapy Rating scale for Psychosis, Social Skills Training Fidelity scale, CCT fidelity scale		monthly		

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9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
2. Protocol Development Stage
- B. Data processing and analysis
- 7) Write study SOP:
 - a) Informed consent procedure
 - b) Recruitment and randomization procedures
 - c) Patient follow-up procedure
 - d) Procedures for data collection and processing
 - e) Study organization structure
- 8) Outline procedures for **monitoring** the **randomization** process
- 9) Review **data storage, backup, and security** procedures

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9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
2. Protocol Development Stage
- C: Training and communication
 1. Develop and implement training for key study staff:
 - I. Design and methods of the trial
 - II. Importance of integrity in data collection
 - III. Need for data security
 - IV. Study organization
 - V. Performance and treatment monitoring procedures
 2. Initiate **regularly** scheduled **meetings** of:
 - I. Study investigative group
 - II. Steering committee
 3. Consider distribution of **newsletters** at periodic intervals
 4. Develop procedures for dealing with requests for **study information** originating outside the study

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1. Initial Design Stage
2. Protocol Development Stage
- D: Quality assurance

Develop procedures for monitoring, reviewing and reporting **performance of staff** concerning data collection and data quality
- E: Treatment monitoring (Fidelity)
 1. Outline content of treatment effects monitoring reports
 2. Establish timetable for treatment monitoring and reports
- F: Authorship

Establish authorship policies for study papers
- G: Management
 1. Outline study policy
 2. Develop guidelines and procedures required to decide **when to terminate a treatment** due to adverse effects

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EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR: 9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
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7. Post-Trial Follow-up Stage (optional)

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EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS SEMINAR: 9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
2. Protocol Development Stage
3. Subject Recruitment Stage
- A: Treatment and subject care
- B: Data processing and analysis
- C: Training and communication
- D: Quality assurance

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9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
2. Protocol Development Stage

3. Subject Recruitment Stage:

A: Treatment and subject care

1. Establish channels for **subject referral**
2. Review **progress** in subject recruitment
3. Project **time requirements** for completion of subject recruitment based on recruitment performance

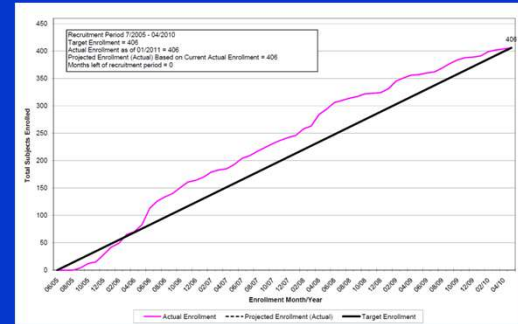
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9: Activities By Stage Of Clinical Trial



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9: Activities By Stage Of Clinical Trial

3. Subject Recruitment Stage:

B: Data processing and analysis

- 1) **Initiate** and maintain procedures for collecting and processing study data and related materials.
- 2) Verify that **incoming baseline** data forms document subject eligibility for the trial.
- 3) Initiate **data editing** procedures.
- 4) Establish and maintain monitoring procedures to **identify deficiencies in data collection and data processing**.
- 5) Define the responsibilities of clinical staff and of the data center for locating **subjects lost** to follow-up.
- 6) Outline quality control procedures for data analyses.
- 7) Complete final editing of recruitment and entry data.

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9: Activities By Stage Of Clinical Trial

3. Subject Recruitment Stage:

C: Training and communication

1. Maintain staff training and certification procedures
2. Continue to hold regularly scheduled meetings

D: Quality assurance

1. Review the adequacy of the **randomization** procedure
2. Review **documentation** standards and monitor adequacy of documentation for:
 - I. treatment procedures,
 - II. modification of data collection forms,
 - III. modification of the study protocol,
 - IV. data management and data analysis procedures

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9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
2. Protocol Development Stage.
3. Subject Recruitment Stage.

4. Treatment and Follow-up Stage:

A: Treatment and subject care

1. Monitor and report **adverse treatment effects**
2. Review procedures for monitoring and evaluating the clinical management of individual patients

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9: Activities By Stage Of Clinical Trial

4. Treatment and Follow-up Stage:

B: Data processing and analysis

- 1) Continue procedures for maintaining **adherence** to follow-up visit schedule, particularly for patients classified as **inactive or lost to follow-up**.
- 2) Expand data edit procedures to provide checks for **consistency within and across forms**, including forms used for pre-randomization visits.
- 3) Revise data collection forms as necessary.
- 4) Develop and test data collection **forms** and data management systems required for the patient **close-out** stage.

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9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
2. Protocol Development Stage.
3. Subject Recruitment Stage.
4. Treatment and Follow-up Stage.

5. Subject Close-out Stage:

A: Treatment and subject care

1. Initiate procedure for **unmasking** treatment
2. Monitor for **adverse effects**
3. Inform subjects and **their primary care** physicians of study results
4. Transfer of subject care responsibilities to appropriate sources, if needed

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9: Activities By Stage Of Clinical Trial

1. Subject Close-out Stage:

B: Data processing and analysis

- 1) Perform **final edit** of accumulated study data.
- 2) Identify items that need review or corrections.
- 3) Initiate special search procedures to **locate subjects** classified as lost to follow-up for final data analysis.
- 4) Develop and **carry out data analyses** that summarize study findings.

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9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
2. Protocol Development Stage.
3. Subject Recruitment Stage.
4. Treatment and Follow-up Stage.
5. Subjects Close-out Stage.

6. Termination Stage:

A: Treatment and subject care

Verify that all subject have complied with close-out procedures.

B: Data processing and analysis

- 1) Complete final edit procedures.
- 2) Create final data file.
- 3) Prepare data listings.
- 4) Update backup tapes of data files

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1. Initial Design Stage
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5. Subject Close-out Stage.
6. Termination Stage.

7. Post-Trial Follow-up

A: Preparatory steps

1. Assemble **roster** of subjects to be **followed**
2. Outline approach to be used in the follow-up, and the **amount of data** to be collected
3. Initiate mechanisms to establish **subject contact**
4. Assemble data collected from the post-trial follow-up

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9: Activities By Stage Of Clinical Trial

1. Initial Design Stage
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4. Treatment and Follow-up Stage.
5. Subject Close-out Stage.
6. Termination Stage.

7. Post-Trial Follow-up

B: Data Analysis

- 1) Link added follow-up data with existing files.
- 2) Carry out analyses to summarize post-trial follow-up results.
- 3) Prepare a **manuscript** summarizing results.
- 4) Store updated subject identifying and location information for **future follow-up**.

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