Clinical Trials

Course
World Health Research

Unit X
Research & Cutting-Edge Medical Technology

Essential Question
What is involved in a clinical trial?

TEKS
130.209(c)
4A, 4B, 4C
5A, 5B, 5C, 5D

Prior Student Learning
None

Estimated time
3-10 hours

Rationale
Recognizing how clinical trials are designed, conducted and evaluated is critical to understanding and developing medical research.

Objectives
Upon completion of this lesson, the student will be able to:

- Identify types of clinical trials
- Define and calculate a sample size
- Analyze quantitative methods used to describe clinical trials

Engage
Give each student a handout of clinical trial advertisements. (Additional clinical trials advertisement options can be found at www.clinicaltrials.gov.

Lead students in a discussion of the following information found in ads for Clinical Trials:

1. What is being studied?
2. Who can participate in the trial?
3. If you met the requirements for the trial, would you consider participating? Why or Why not?
4. What might the benefits or risks be from the trial?

Key Points

I. A clinical trial is a research study using human volunteers, aimed at determining the safety and efficacy of a drug, vaccine, medical device, or behavioral intervention.
   A. Before an experimental treatment can be tested in a clinical trial, it must have shown benefit in laboratory testing, animal research, or research in a small group of humans.
   B. Clinical trials are required to follow the same ethical and legal guidelines as all other standards of medical care and interventions to protect patient safety.

II. Every clinical trial in the United States must be approved and monitored by an Institutional Review Board (IRB) to protect patient safety.
   A. Every medical institution that conducts clinical trials has an IRB.
   B. An IRB is a committee of health care professionals and community members that do not have connections to the specific clinical trial.

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C. The IRB is designed to facilitate unbiased decisions about the clinical trial so that patient safety is achieved.

III. Clinical Trials Eligibility
   A. Every clinical trial has guidelines and requirements for who can participate in the study
   B. Variables that determine who can participate in a particular clinical trial include age, gender, race/ethnicity, type and stage of disease, and treatment history
      1. The factors that allow a subject to participate in a clinical trial are called “inclusion criteria”
      2. The factors that disallow a subject to participate in a clinical trial are called “exclusion criteria”
      3. These criteria are used solely to ensure that the research can be objectively studied

IV. Clinical Trial Protocol
   A. A protocol is the clinical trial plan that explains the purpose and process of the study.
   B. A protocol is designed to protect the health of research participants and ensure that research questions are answered in an objective, empirical manner.
   C. A research protocol will include information on:
      1. Who can participant in the study
      2. How many people can participate in the study
      3. The treatment plan (or intervention) which includes procedures, medications and dosages
      4. Type and frequency of tests to be used in the study
      5. How the results will be measured
      6. Reasons why the study can be stopped
      7. Known and expected effects of the study treatment/intervention
      8. Potential benefits of the study

V. Clinical Trial Informed Consent
   A. Informed consent is the process of learning about the clinical trial before deciding to participate.
   B. Informed consent is also a process that continues throughout the entire study – providing participants with information as it may

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change.

C. Before someone can participate in a clinical trial, they must review and sign an informed consent form which will include some of the following information:
   1. Clinical trial process, including tests that may be conducted
   2. Known and expected risks of experimental treatment
   3. Length of clinical trial
   4. Clinical trial contact information

D. Informed consent is not a legal contract; the participant can withdraw from the trial at any time for any reason.

VI. Clinical Trial Process

A. The process for a clinical trial depends on the type of clinical trial being conducted.

B. At the beginning of a trial, the participant's health is checked and the research team provides information to the participant about the study.

C. The participant is then monitored by members of the research team, as determined by the protocol of the study.

D. Follow-up after the study is completed is generally part of the protocol.

VII. Clinical Trials Phases

A. Clinical trials are conducted in phases. Each phase of a clinical trial has a different purpose and approach.
   1. Phase 1 – Researchers test a new drug or treatment in a small group of people for the first time to evaluate its safety, determine a safe dosage range, and identify side effects
   2. Phase 2 – The drug or treatment is given to a larger group of people to see if it is effective and to further evaluate its safety
   3. Phase 3 – The drug or treatment is given to large groups of people to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the drug or treatment to be used safely
   4. Phase 4 – Studies are done after the drug or treatment has been marketed to gather information on the drug's effect in various populations and any side effects associated with long-term use

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VIII. Types of Clinical Trials: There are different types of clinical trials. Deciding which type of investigation to use depends on the type of question the researcher is attempting to answer. In each type of trial, the goal is the same: to safely search for solutions to specific health problems.

A. Interventional or Treatment Trials -- Designed to test/assess experimental treatments, new combinations of drugs, or new approaches to surgery or radiation therapy

B. Prevention Trails
   1. Looks for better ways to prevent disease in people who have never had the disease or to prevent the disease from returning
   2. Typically involves medicines, vaccines, vitamins and/or lifestyle changes

C. Diagnostic Trials -- Designed to find better tests or procedures for diagnosing a particular disease or condition
   1. Screening Trials -- Designed to test the best ways to detect certain diseases or health conditions
   2. Quality of Life Trials -- Designed to find ways to improve the quality of life and comfort for people with chronic conditions

IX. Sample Size and Clinical Trials

A. Sample size is the number of participants in the study and it is one of the first practical steps in designing a clinical trial. If the sample size is too small, the researcher may fail to detect a serious problem with the treatment and if the sample size is too large, money, time and resources are wasted
   1. Determining sample size is usually done in the design phase of the clinical trial, before seeking IRB approval
   2. Researchers typically consult with a biostatistician to determine sample size

B. Sample size calculation is used to find the number of research participants needed to ensure that the treatment/intervention/product is effective.
   1. Determining sample size depends on four key factors:
      a. The specific aim of the study
      b. The study design
      c. The outcomes and predictors of the study
      d. The proposed statistical analysis plan

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X. Methodological Assessment in Clinical Trials Research

Quantitative and qualitative research are two major paradigms in medical research. Although research studies typically use both approaches, the advantages and disadvantages of which one to use are hotly debated in the medical community.

A. Qualitative data is information that is descriptive and cannot be measured by numbers and statistical analysis.
   1. Variables include opinions, experiences, and values
   2. A subjective form of research that is driven by issues or questions that emerge and unfold during in the data collecting process
   3. Data is collected in a text or narrative format on the basis of observation and interactions with research participants
   4. The data is not converted into numerical format and it is not statistically analyzed

B. Quantitative data is information that is absolute and can be measured.
   1. The vast majority of clinical trials are designed to be quantitative studies
   2. Quantitative research is driven by a hypothesis
   3. Its key characteristics are numerical data that permits a range of statistical analysis which is typically carried out with the aid of sophisticated statistical computer packages

C. There are several approaches to quantitative research, including experimental, descriptive, correlational and causal comparison paradigms.
   1. Experimental Studies
      a. an intervention is made under controlled conditions with the exclusive goal of evaluating its effect
      b. the gold standard is the ‘Randomized Controlled Trial” (RTC) which is used to determine if a therapeutic intervention is effective
   2. Descriptive Studies
      a. Collecting data to test a hypothesis
      b. Used largely in epidemiological studies to look at the incidence or distribution of disease, or to assess current health problems or needs
      c. Data is typically collected in the form of questionnaires

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3. Correlational Studies -- used to discover relationships between two variables, such as determining if there is a link between birth weight and gestational diabetes
4. Causal Studies
    a. Usually used in epidemiological research to look at issues associated with cause and effect
    b. It is assumed that if a cause and effect relationship exist between variables, the independence variable cannot be manipulated
    c. The gold standard is a P value which is a statistical concept that means probability; it measures the likelihood that a particular finding or observation is due to chance

XI. Clinical Trials Terminology -- The following terms/concepts are integral to understanding the design, implementation and evaluation of clinical trials.

A. Placebo – an inactive pill, liquid or powder that looks like the experimental treatment but has no effect on the body.

B. Control group – consists of participants who receive experimental treatment or the placebo and serves as a comparison group to measure the effectiveness of the treatment or intervention. Participants are randomly assigned to either a control group or a non-control group.

C. Biostatistics – branch of statistics applied to the analysis of biological phenomena

D. Blind study – a study in which the research participant, the researcher, and anyone assessing the outcome of the study is unaware of the treatment assignments. This is used to reduce the risk of bias.

E. Correlation – the relationship of one variable to another

F. Hypothesis – an educated guess that answers a question or problem

G. Experimental group – research participants exposed to the variable of the control group

H. Mean – the sum of values of all observations or data points divided by the number of observations, a mathematical average

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I. Media – the middle value in a data set so that just as many values are greater than the media and lower than the media

J. Qualitative variable – cannot be measured on a continuum and represented in quantitative relation to a scale (e.g. opinions)

K. Quantitative data – can be measured and documented numerically (e.g. blood pressure)

L. Randomized Controlled Trial –is a specific type of scientific experiment whereby research participants are randomly allocated to receive one or the other of the alternative treatments under study; it is considered the "gold standard" for clinical trials

M. Sample size – the number of subjects in a clinical trial

N. Statistical significance – applies when a hypothesis is rejected

O. Variable – any quantity that varies; any attribute, phenomenon, or event that can have different qualitative or quantitative values; that being measured

Activity

I. Complete the Clinical Trials Vocabulary
II. Complete the Memory Water Investigation.
III. Develop a Clinical Trial – as a team, students access the CyberSurgeon Website:http://www.cybersurgeons.net/resources/?/pbl_dev_clinical_trial/140/ Follow directions and resources to design and present a clinical trial.
IV. Complete the Human Participant Protections Education for Research Teams course which can be found at: http://cme.cancer.gov/clinicaltrials/learning/humanparticipantprotections.asp

Assessment

Evaluation Rubrics
Clinical Trials Peer Assessment

Materials

Handout of clinical trial advertisements
Rubric for Developing a Clinical Trial
Rubric for Writing a Clinical Trial for Pediatric Asthma
Computers
Small cups
Water
Timers

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http://www.clinicaltrials.gov/ct2/about-studies/glossary.

http://www.owlnet.rice.edu/~bioe301/kortum/class/courseinfo/homework.html

https://account.tes.co.uk/LogOn?rtn=http%3a%2f%2fwww.tes.co.uk%2fDownload.aspx%3fstorycode%3d6061109%26type%3dX%26id%3d6093862

Accommodations for Learning Differences
For reinforcement, the student will develop flashcards for vocabulary terms.

For enrichment, the student will research the ethical and legal issues that arise when new medical technologies are tested in developing countries. In what ways can this benefit the population of the developing country? In what ways can the population be harmed? If the researchers are based in the United States, what legal and ethical responsibilities do they have?

National and State Education Standards
National Health Science Cluster Standards
11.1 Health Information Literacy and Skills
11.11 Identify methods and types of data collected in healthcare.
11.12 Use health record data collection tools (such as input screens, document templates).
1.32 Analyze diagrams, charts, graphs, and tables to interpret healthcare results.
5.24 Understand informed consent.
6.11 Differentiate between ethical and legal issues impacting healthcare.
11.1 Health Information Literacy and Skills
11.11 Identify methods and types of data collected in healthcare.
11.2 Privacy and Confidentiality of Health Information
11.21 Apply the fundamentals of privacy and confidentiality policies and procedures.
11.22 Identify legal and regulatory requirements related to the use of personal health information.
11.23 Identify and apply policies and procedures for access and disclosure of personal health information.
11.24 Describe the consequences of inappropriate use of health data in terms of disciplinary action.

TEKS
130.209(c)(4)(A) identify types of clinical trials;
130.209(c)(4)(B) define and calculate a sample size;
130.209(c)(4)(C) analyze quantitative methods used to describe clinical trials.
130.209(c)(5)(A) define informed consent;
130.209(c)(5)(B) explain who can give informed consent;

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130.209(c)(5)(C) identify issues in research that influence the development of ethical principles and legal requirements currently governing research with human subjects; and
130.209(c)(5)(D) explain the ethical guidelines for the conduct of research involving human subjects.

Texas College and Career Readiness Standards
English Language Arts
B.1. Identify new words and concepts acquired through study of their relationships to other words and concepts.
Mathematical Standards
VI.A.1. Plan a study.
VI.B. 1. Determine types of data.
VI.B. 2. Select and apply appropriate visual representations of data.
VI.B. 3. Compute and describe summary statistics of data.
VI.B. 4. Describe patterns and departure from patterns in a set of data.
VI.C. 1. Make predictions and draw inferences using summary statistics.
VI.C. 2. Analyze data sets using graphs and summary statistics.
VI.C. 3. Analyze relationships between paired data using spreadsheets, graphing calculators, or statistical software.
VI.C. 4. Recognize reliability of statistical results.
Science Standards
X.C.1.Recognize variations in population sizes, including human population and extinction, and describe mechanisms and conditions that produce these variations.
Social Studies Standards
IV.B.1. Use established research methodologies.
IV.B.3. Gather, organize, and display the results of data and research.
IV.B.4. Identify and collect sources
Cross Disciplinary Standards
II.D.1. Identify patterns or departures from patterns among data.
II.D.2. Use statistical and probabilistic skills necessary for planning an investigation and collecting, analyzing, and interpreting data.
II.D.3. Present analyzed data and communicate findings in a variety of formats.

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Vocabulary

Placebo	An inactive pill, liquid or powder that looks like the experimental treatment but has no effect on the body.
Control group	Consists of participants who receive experimental treatment or the placebo and serves as a comparison group to measure the effectiveness of the treatment or intervention. Participants are randomly assigned to either a control group or a non-control group.
Biostatistics	Branch of statistics applied to the analysis of biological phenomena
Blind study	A study in which the research participant, the researcher, and anyone assessing the outcome of the study is unaware of the treatment assignments. This is used to reduce the risk of bias.
Correlation	The relationship of one variable to another
Hypothesis	An educated guess that answers a question or problem
Experimental group	Research participants exposed to the variable of the control group
Mean	The sum of values of all observations or data points divided by the number of observations, a mathematical average
Media	The middle value in a data set so that just as many values are greater than the media and lower than the media
Qualitative variable	Cannot be measured on a continuum and represented in quantitative relation to a scale (e.g. opinions)
Quantitative data	Can be measured and documented numerically (e.g. blood pressure)
Randomized Controlled Trial	Is a specific type of scientific experiment whereby research participants are randomly allocated to receive one or the other of the alternative treatments under study; it is considered the “gold standard” for clinical trials
Sample size	The number of subjects in a clinical trial
Statistical significance	Applies when a hypothesis is rejected
Variable	Any quantity that varies; any attribute, phenomenon, or event that can have different qualitative or quantitative values; that being measured

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Vocabulary

Placebo	
Control group	
Biostatistics	
Blind study	
Correlation	
Hypothesis	
Experimental group	
Mean	
Media	
Qualitative variable	
Quantitative data	
Randomized Controlled Trial	
Sample size	
Statistical significance	
Variable	

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Memory Water Investigation
Teacher Guidelines

The Memory Water Company claims that they have developed a water that actually improves your memory. You will conduct an investigation to test this theory.

1. Use either tap water or bottled water. Pour water in cups labelled A. Pour water in cups labelled B.
2. Students are in teams of two; one is the participant and the other the scientist.
3. The scientist collects one memory square with numbers, a blank grid, and a cup of water making a note of the letter (A or B) they received.
4. The participant has 3 minutes to memorize the numbers and then has to write them into the blank grid. The scientist records how many they got right.
5. The participant then drinks the water. Half the class should get A, and the other half B.
6. The pairs wait for 5 minutes.
7. They then repeat step 4 but using a different number grid.
8. The scientists record the results.
9. The students answer the questions.

Note: *Informing the students that neither water is actually Memory Water is optional!*

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Memory Grids

A

6	8	2
6	3	5
7	0	5
8	0	4
1	1	1
2	9	0
2	7	2

B

5	5	3
2	2	6
7	1	4
9	0	1
2	2	0
3	2	2
4	4	1

C

4	3	6
7	7	4
1	1	1
0	9	0
3	5	5
6	0	8
1	4	8

D

8	8	8
9	3	6
1	0	1
2	1	5
3	3	2
6	8	3
5	4	6

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Memory Water Investigation

Purpose:
In this investigation, the student will explore clinical trials.

Materials:
Cup of water
Number Grid
Blank Grid
Timer

Procedure:
1. One of you is the participant and the other the scientist.
2. The scientist collects one memory square with numbers, a blank grid, and a cup of water making a note of the letter (A or B) they received.
3. The participant has 3 minutes to memorize the numbers and then has to write them into the blank grid. The scientist records how many they got right.
4. The participant then drinks the water.
5. The pairs wait for 5 minutes.
6. They then repeat step 3 but using a different number grid.
7. The scientists record the results.

Data:
Record results on tables.

Team Results

Letter	
Number Correct 1st Attempt	
Number Correct after drinking water	
How many more numbers remembered correctly after drinking water	

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Class Results

Water	Number Correct 1st Attempt Class Average	Number Correct after drinking water Class Average	How many more numbers remembered correctly after drinking water
A			
B			

Conclusion:

1. One cup of water was a placebo. What does this mean? Why is it important to use a placebo?

2. This trial was a double-blind trial. What does this mean? Why is it important to run the trial in this way?

3. Water B was the Memory Water. (Water A was tap water). Has this investigation proved that it improves memory? Explain your answer.

Adapted from:
https://account.tes.co.uk/LogOn?rtn=http%3a%2f%2fwww.tes.co.uk%2fDownload.aspx%3fstorycode%3d6061109%26type%3dX%26id%3d6093862

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Clinical Trial Rubric

Student: _____ Date: _____

Scoring criteria	5 Excellent	4 Good	3 Needs Some Improvement	2 Needs Much Improvement	1 N/A
Identifies, summarizes and understands the investigative work.					
Considers the material and makes appropriate assumptions.					
Presents, assesses, and analyzes appropriate supporting data/evidence.					
Identifies and assesses conclusions, implications, and consequences.					
Communicates effectively.					
No spelling, grammatical or punctuation errors.					
The student actively listens to and values the opinion of others in the group					

Comments:

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Clinical Trial Advertisements

Do you exercise? This study will examine the effects of exercise on pain management.

Looking for participants who exercise regularly. Must be at least 35 years old. Benefits if you qualify:

- Study-related health assessments
- Potential compensation for your time

Do you have asthma or allergies?

You may qualify for a free pulmonary function test.

Must be at least 18 years old. If you qualify and complete the study you may qualify for up to $500 in reimbursement.

Contact research assistant for more information.

Do you suffer from acne?

Male and female subjects with acne between the ages of 18-25 are needed for a clinical research study for a new acne gel.

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study.

Arthritis Study

Need extra cash? Participate in our clinical trial and help yourself and others.

- Male or female
- Age 30 or older
- Free medical exam
- Financial compensation

Call Medical Center at 123-456-7890 to qualify.

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