METHODOLOGY 101 Training For Patients and Stakeholders

Training Booklet & Resource Guide

Methodology 101 Training Booklet and Resource Guide

Merit Review and You

This training booklet and resource guide is designed to help you be an active, informed, and successful participant in the Patient-Centered Outcomes Research Institute (PCORI) merit review process for funding applications.

During the merit review process, you and other reviewers will evaluate, rate (score) and discuss the strengths and weaknesses of applications based PCORI's merit review criteria. At the end of this training, you will be ready to apply what you have learned about the research process and PCORI's standards as you contribute your important views and feedback on the applications.

What Will I Learn?

After reading this booklet and resource guide, you will have the knowledge and skills to:

- Identify the main components of a research question
- Understand how research projects are designed and carried out

Reading through this training booklet should take about 45 minutes.

Words that are especially important to understand are highlighted in yellow. There is a glossary of terms at the very end of this guide. You may want to refer to it as you take the course if you find words or concepts that are unfamiliar to you. The glossary is also a tool you can use when you are reviewing applications.

How is This Training Organized?

This booklet is divided into three sections. Each section will give you an overview of topics that are important in the merit review process.

Section 1: An Introduction to PCORI Research

This section focuses on PCORI and basic information on how research questions are written.

Section 2: Study Design and Analysis

This section explains how researchers might make decisions about who to study, what methods of study to use, how to collect and analyze data, and how to determine if findings are significant.

Section 3: Interpreting Study Results

This section describes how researchers understand what the results of a study mean.

Section 1: An Introduction to PCORI Research

What Will I Learn?

This section answers the following questions:

- What is a research study?
- What is a patient-centered outcomes research study?
- What is a comparative effectiveness research study?
- What is a research question?
- What are methods?
- What is the connection between PCOR and methods?
- How do I evaluate a research question?
- What is a hypothesis?
- What are PCORI's Methodology Standards?

After reading this section, you will be able to:

- Understand the importance of methods in Patient-Centered Outcomes Research (PCOR)
- List the four major components of a research question
- Identify a PCOR research hypothesis

This section should take about 20 minutes to complete.

Scientific Research Basics

What is a Research Study?

Research is an organized, planned process of collecting and analyzing information to increase our understanding of something. A research study tries to answer a specific question by collecting and studying information (also called data) using a specific method, or organized approach. Scientific research only uses methods that have been tested to provide trustworthy answers. Sometimes studies are also called trials.

Health and healthcare research focuses on outcomes. Another word for outcome is result. Outcomes research tries to understand what happened as a result of using some type of action (also called an intervention) to improve health, such as taking a medicine or increasing people's exercise. Outcomes research looks at both positive and negative results.

What is a Patient-Centered Outcomes Research study?

PCORI funds a special kind of research called patient-centered outcomes research, or PCOR. Patient-centered outcomes research studies questions and outcomes that are meaningful and important to patients and caregivers. PCOR is based on the belief that patients have unique perspectives that can change and improve the way in which questions about healthcare are asked and answered.

FOR EXAMPLE: Researchers wanting to study ways to treat lung cancer might make the study more patient-centered by looking at the outcomes that matter most to patients and caregivers, such as how each treatment impacts the ability to engage in normal activities like work or taking care of a family.

PCORI funds patient-centered outcomes research that compares two or more different actions to see if there are differences in the outcomes. This is called comparative effectiveness research, or CER. The outcomes that CER focuses on are benefits (how the action causes some type of improvement) or harms (how the action causes a side effect or other problems that do not help a patient). In healthcare, CER might study two or more ways of preventing or slowing down the effect of a condition, diagnosing a condition, treating a condition, or monitoring a condition. CER might also compare ways of delivering healthcare.

What is Patient-Centered Comparative Effectiveness Research?

Like PCOR, patient-centered CER compares actions and outcomes that patients and caregivers need to understand in order to make decisions about what to do to prevent, diagnose, treat, or monitor the condition. Patient-centered CER looks at the benefits and harms that are most important to patients when making clinical decisions.

Clinical Decisions and PCORI

Clinical decisions involve questions that people ask when deciding between two or more available clinical interventions, like choosing between chiropractic manipulation and physical therapy for treatment of lower back pain.

PCORI's founding legislation mandates funding of research that supports comparative effectiveness research so that patients can make informed decisions about their healthcare. PCORI looks to fund studies that will produce information that allows patients to weigh the benefits and harms of each clinical alternative or option.

What is a Research Question?

Creating a research question is the first step in every research study. A research question focuses the information that a research study should provide.

The research question guides researchers to decide on what methods they will need to use to answer the question. Methods tell researchers HOW to gather and make sense of information (data) in order to answer the research question. Analyzed data and the conclusions that are made about it by researchers is called evidence.

There are methods to guide researchers on:

- What types of data to collect
- How to collect the data
- Who to collect data from
- How to make sense of the data that is collected

All research studies should be guided by clear and simple research questions.

Methods help researchers look at data in different ways, understand what it means (or analyze it) and then tell the story of the data as it relates to the research question.

FOR EXAMPLE: This research question:

Compare the effectiveness of pharmacologic and non-pharmacologic treatments in managing behavioral disorders in people with Alzheimer's disease and other dementias in home and institutional settings.

tells researchers that they need methods to:

- Collect data about behavioral disorders in people with Alzheimer's disease and other dementias who live at home as well as in an institution.
- Compare how well medicine or non-medicine therapies help people with Alzheimer's disease who are living at home as well as people living in an institution manage or control their behavioral disorders.

A patient-centered CER question guides studies by identifying:

- The people—the group of people with a specific condition to be studied
- The options—the choices or options that should be compared

The outcomes—the desired information about the results of each option to help people make decisions.

Methods and PCOR: What is the Connection?

Methods are important in PCOR because they explain the approach researchers will take that best ensures that the answer to the research question is valid (or accurate), trustworthy (or credible), and useful.

The methods used in a study should be chosen because they are the best way to answer the research question accurately.

Appropriate methods will lead to research findings that help patients and caregivers make better healthcare decisions, and ultimately to improved patient outcomes. A proposal with a strong plan to engage patients and their caregivers may not be able to provide trustworthy answers if it does not have appropriate methods.

Developing and improving the science and methods of PCOR is a central part of PCORI's work.

Your contribution to the Merit review process will help PCORI fulfill its mission and to fund research that is patient-centered and uses appropriate methods.

How Do I Evaluate a Research Question?

A useful way to decide if a proposed research project will provide new evidence related to a decision that is important to patients and caregivers is to break the research question down into four major categories. This is called the PICO Approach. PICO stands for the first letter in each category.

1. **P**: The **population** of patients/research participants and relevant subgroups of patients
2. **I**: The **intervention(s)** relevant to patients in the target population
3. **C**: The **comparator(s)** relevant to patients in the target population
4. **O**: The **outcomes** that are meaningful to patients in the target population

Descriptions and Examples of PICO Categories

Population (Patient)

The researcher should define the specific patient or population that is being studied. That means that the researcher should be specific about:

- Age
- Race
- Sex
- Health status (overall quality of health at the moment)
- Socioeconomic status (high, middle, or low income)
- Geographic region
- Current medications or treatments
- Setting (for example, a clinic or a nursing home facility)

Intervention (Treatment)

The researcher should describe an intervention (procedure, therapy, medication, or test) that will be given to the population. This intervention will be compared against other interventions. Those other interventions are called **comparators.** Important things to consider about the intervention include:

- Dosage (how much is given
- Frequency (how often it is given)
- Duration (over what period of time it is given, or for how long)
- Mode of delivery (how or in what way it is given)

Comparator

The researcher should describe what actions or interventions are being compared to the first intervention. Comparators may include:

- A different treatment or intervention
- Usual care (care that is widely accepted as standard practice), if the components of the care are well-defined
- No treatment or intervention (doing nothing)

NOTE: Applications submitted to the Improving Methods PFA may not include an intervention or a comparator, as this program's focus is on the methodology of PCOR and not on what is considered "traditional" CER.

Outcomes

The researcher should identify the intended results of the intervention and comparator(s). The outcomes identified in a research question should be:

- Able to be measured
- Meaningful and important to patients and/or healthcare stakeholders
- Include both the benefits and harms of each option examined in the study

FOR EXAMPLE: Here is an example of one study following the PICO approach:	
Population **(Patient)**	Patients who come to an urgent care center with an acute episode of low back pain between the ages of 40-65, who may have had prior episodes of back pain
Intervention	Referral to a chiropractor for spinal manipulation therapy over a 4-week period
Comparator	Patients from the same clinic, matched on key demographics (age, gender, sex) • Group 1: Referral to a physical therapy program consisting of 1-3 visits • Group 2: Usual care, consisting of patient education materials on self-management of back pain
Outcomes	• Self-assessed pain scores, measured 3 times per week for 4 weeks • Ability to return to work • Time until pain completely stops • Short-term aggravation of symptoms that may be related to the treatments

The best clinical effectiveness research questions are ones that lead to a better understanding of the benefits and harms of the different clinical alternatives that are available.

Multiple perspectives—including those of patients, clinicians, researchers, policymakers, and other stakeholders—help shape clinical effectiveness research questions.

What is a Research Hypothesis?

In addition to helping to develop the study's research question, patients and key stakeholders should also play a significant role in creating the research hypotheses.

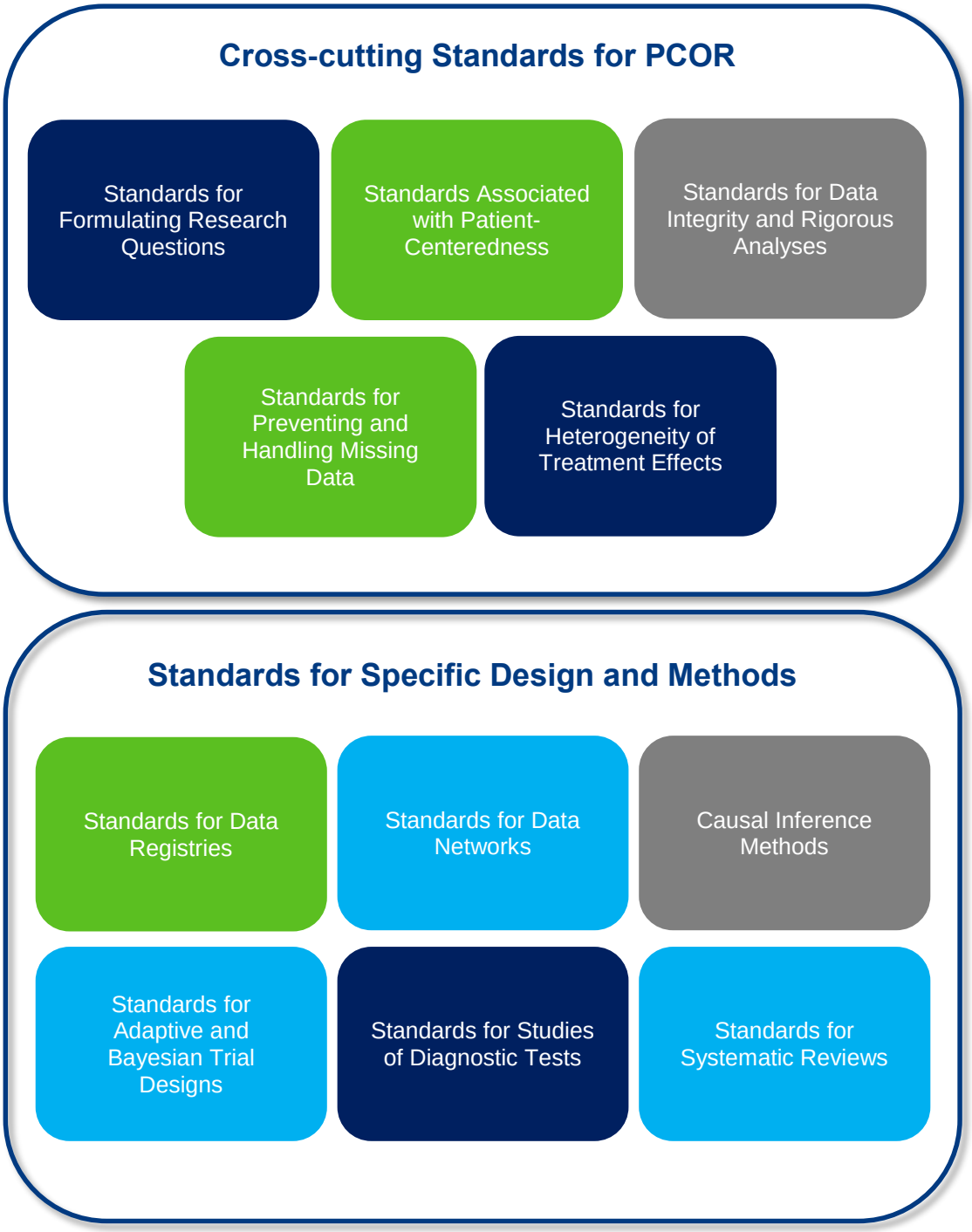
A research hypothesis is an informed best guess about what the study might find. A study will usually have multiple hypotheses. PCOR studies may have a hypothesis that one intervention is superior to the other, or that the benefits and harms are different between two or more treatments.

When formulating research hypotheses, researchers should keep in mind that a PCOR study needs to identify the differences in benefits between two or more clinical alternatives.

What are PCORI Methodology Standards?

PCORI has developed a set of methodology standards that represent best practice recommendations for improving the quality and value of PCOR. The methodology standards were created by the PCORI Methodology Committee, a group of 15 appointed experts in health research, and open to public comment. **While it is important for you to be aware of these standards, keep in mind: Patient and stakeholder reviewers are not responsible for addressing the methodologies in the applications.**

All applicants for funding are required to follow these standards, addressing the 11 areas below:



Key Points to Remember from Section 1

When reviewing applications, make sure that they are in line with PCORI's PCOR values and the suggested PICO approach. To do this, ask yourself these questions:

About PCOR Values

- Will the research question lead to a better understanding of the benefits and harms among available clinical alternatives?
- Does the research question have the characteristics of PCOR?

About the PCOR Approach

- Does the research question cover these elements:
    - Population?
    - Intervention?
    - Comparator?
    - Outcomes?
- Does the research hypothesis include two or more comparators?

Section 2: Study Design and Analysis

What Will I Learn?

This section answers the following questions:

- What are the elements of a research study?
- What is a research methodology?
- What is a sample?
- What is a study design?
- What is an experimental study?
- What is an observational study?
- Why is randomization important to a study's design?
- What is blinding?
- What is data analysis? What are the methods used for data analysis?
- What is power? What is significance?

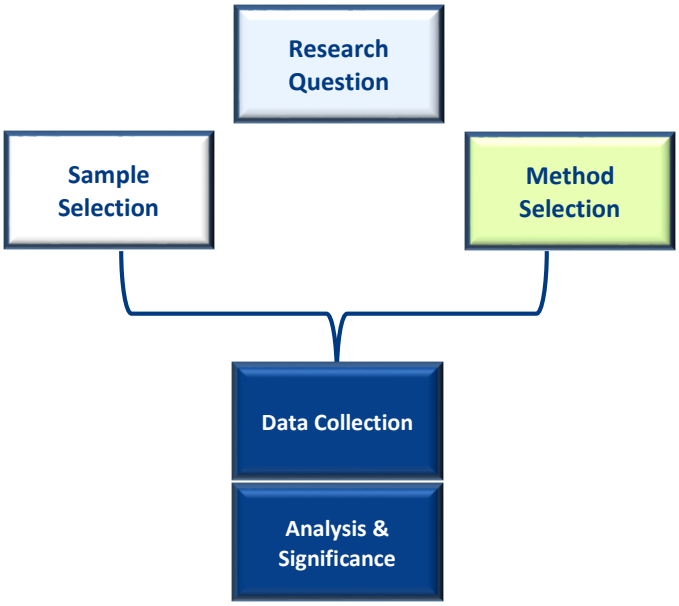
At the end of this section, you should be able to:

- Define study design, sample size, sample selection, and significance
- Explain the differences between experimental and observational studies

This section should take about 15 minutes to complete.

What are the Elements of All Research Studies?

All research studies follow the same process. Each element of the process is shown in the diagram below. Every element of the process is important.



In Section 1, you learned about the study research question, which is needed to make all other decisions about the study. Once the research question has been well-defined, researchers must next decide on where the data they will use to answer the question will come from (this is called sample selection) and the methods they will use to collect and analyze the data (this is called method selection). These two steps are closely related to one another. These two decisions serve as the basic design of the research study and lead to the activities of data collection, analysis, and determining the significance of the results.

Each of these elements will be explained in detail on the following pages.

What is a Research Methodology?

Researchers answer questions by collecting, organizing, and reviewing data in a very specific way. This specific way of gathering and examining information is called the research methodology. Methodologies determine how data should be collected for the study, and also how the data becomes answers to the question.

There are three types of methodologies that researchers use:

- Quantitative Methods focus on the quantity, or amount of things, such as the number of people who choose the same answer on a survey or the number of times an event occurs. Quantitative data are often numbers that are used to measure the amount of something or determine what effect one thing has on another.
- Qualitative Methods focus on the quality of things such as the ways in which people experience something or the way that something occurs naturally. Qualitative data are often are often people's words to describe something or someone's observations about something.
- Mixed Methods use both quantitative and qualitative approaches. Something might be measured with numbers and then described using people's description of their experience.

FOR EXAMPLE: Health researchers wanting understand the effect of a medicine on people with a certain condition using quantitative methods might ask them to complete a survey of their symptoms before and after taking the medicine or measure their symptoms before and after taking the medicine. If researchers wanted to use qualitative methods, they might interview patients and ask them to talk about their experience when taking the medicine.

Researchers may use qualitative, quantitative, or mixed methods to collect data. Here are some examples of quantitative and qualitative methods of data collection:

Qualitative Data Collection Methods	Quantitative Data Collection Methods
• Focus Group • Open-Response Surveys • Interview • Observation • Review Documents for Themes	• Close-response surveys • Review documents for numerical clinical data or categorical data (e.g. Electronic Medical Records)

What is a Study Sample?

A study cannot include absolutely everyone who is affected by the condition that is being researched. Instead, researchers take a smaller group, called a sample, which can represent all the individuals affected by the condition. The number of people enrolled in a study is commonly expressed as "n." For example, n=250 means that there are 250 people enrolled in the study, or the "sample size" is 250 people. A sample must be carefully formed to ensure that it represents the general population.

What is a Study Design?

A study design details the procedure by which studies and experiments will be carried out by researchers to test their hypotheses. The most common types of study designs used in PCOR are Experimental and Observational.

Experimental Study Design
In an experimental study design, researchers control who receives a clinical intervention. There is at least one comparison group that receives a different intervention in this study design. The researchers then compare the outcomes experienced by patients who received one intervention with the outcomes of patients who received a different intervention. In most experimental studies, some participants may be assigned to a “control” group where they do not receive any of the interventions being tested. This is done so that researchers can see if the outcomes of each intervention would be any different than if none of the interventions were chosen.

Often, researchers select the people who will get one intervention or the other one randomly. Random selection is by chance, just like flipping a coin. In “blind” studies, the patients or even the researchers may not know which intervention they are getting or whether they are in the “control” group.

Observational Study Design
This type of study uses data from patients as they are being treated by their doctors rather than through random assignment by researchers. In an observational study, patients with a diagnosed condition receive different treatments selected by them and their providers. Researchers then compare the outcomes experienced by patients who received one treatment with the outcomes of those who received a different treatment.

There are two types of observational studies:

- **Prospective:** In a prospective study, researchers define the research question first and then collect the data over time. For example, a research question might ask if statin drugs to lower cholesterol also helps patients lower their blood pressure. The researcher would track a sample of patients taking a statin to see if their blood pressure changes over time.

- **Retrospective:** In a retrospective study, researchers answer research questions using historical data (e.g. electronic health records, surveys). For example, a researcher might look over the electronic records of a sample of patients who

had taken a statin over the past two years to see if they had any changes to their blood pressure during that time.

When reviewing applications, you may come across the specific types of experimental or observational studies. These are described in the table below.

Design Type	Study	Key Characteristics
Experimental	Randomized Control Trial (RCT)	Participants are chosen randomly to a treatment group or at least one comparison group
	• Cluster RCT	Sites of care or groups of people are chosen randomly rather than individual people
	• Adaptive RCT	Researchers can make changes to an intervention throughout the study
	• Pragmatic RCT	Researchers use real-world settings when creating random assignments of interventions
Observational	Cohort Study	A population of similar individuals (a cohort) is followed prospectively over time

Examples of each of these studies appear on the next pages.

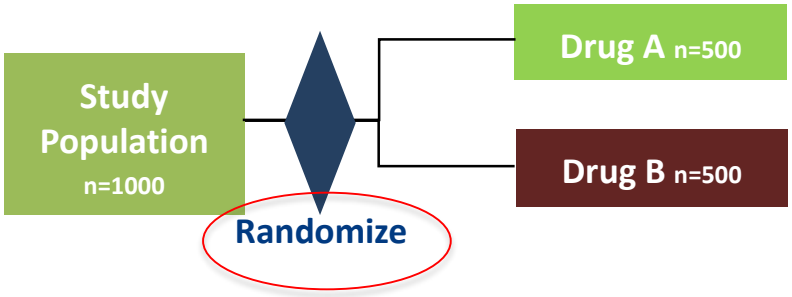
Experimental Studies: Randomized Control Trial (RCT)

Definition: A study in which each individual participant or group of participants is randomly assigned (as if by the flip of a coin) to receive one of two (or more) approaches to treatment.

Types of RCTs include:

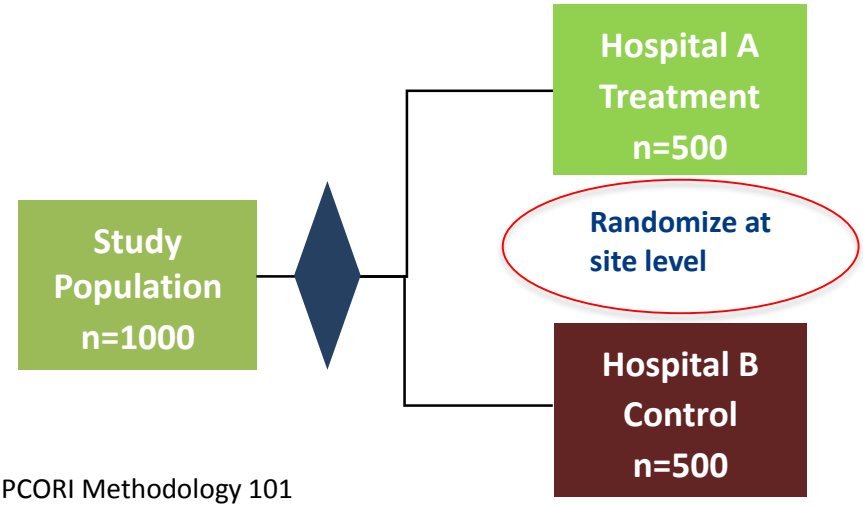
- Randomizing each participant
- Cluster (randomizing a group of participants as a unit)

For example, a patient might be randomly assigned to receive Drug A or Drug B in the case below.



Experimental Studies: Cluster RCTs

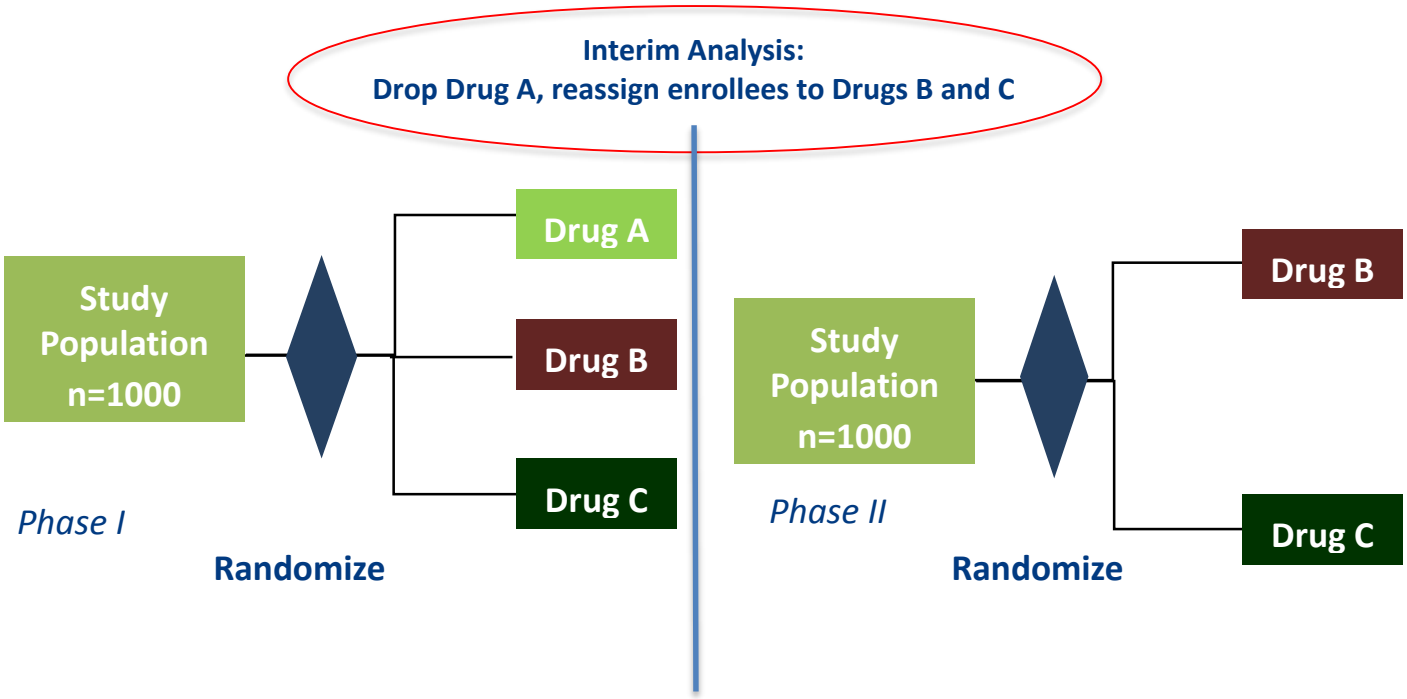
Definition: A study in which an entire group of participants (for example, those who receive care at a particular clinic) is randomly assigned to receive one of two (or more) approaches to treatment rather than randomizing individual patients, as in the case below.



Data analysis can be more challenging with this type of study design.

Experimental Studies: Adaptive Clinical Trial

This type of study is usually an RCT. However, with this design, data is collected as the research is carried out, and the data that is collected can be used to make changes to the study along the way.



Experimental Studies: Pragmatic Clinical Trials (PCTs)

These are studies that test interventions that take place in the real world, instead of in a research setting. The criteria for inclusion and exclusion (who is or is not selected to participate in the study) allow a wider variety of patients and study sites to be involved. There is minimal or little burden imposed on patients, so that the patient experience of study participants in PCTs is similar to the experience of patients who are not enrolled in the study at all.

Why is Randomization Important to a Study's Design?

Choosing randomly which patients get an intervention is important because factors like age, gender or other participant differences that could also influence treatment outcomes are limited by the randomization process. When treatment groups are compared at the end of a trial (or study), researchers are then able to understand the impact of the intervention itself.

Studies where individuals are not chosen randomly for different interventions make it more difficult for researchers to figure out what differences in outcomes were actually caused by the treatment instead of other participant factors like the ones mentioned above.

What is Blinding?

Blinding is when people who are involved in assessing the effects of treatments do not know which treatment was received by the person being evaluated or assessed. For example, patients and interviewers are kept from knowing who received which drug. Blinding is a way to reduce the possibility that researchers made deliberate or unfair choices about who should get which intervention.

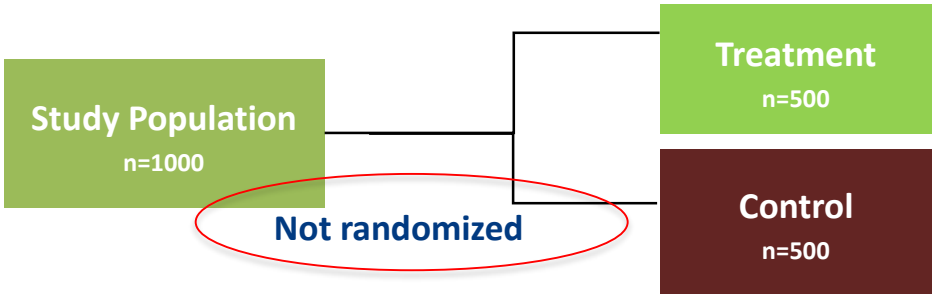
Single-Blind RCT: The researchers are aware of which participants are randomly assigned to each intervention, but the participants are "blind" to this information and do not know which intervention they have received.

Double-Blind RCT: Neither the participants nor researchers know who is assigned to which groups until the study is over. This type of study is considered the gold standard. This approach helps to reduce the chance for bias (giving an unfair advantage to one result over another) because the people providing information do not know which treatment each participant will receive. You will learn more about bias in Module 3.

Open/Unblinded Trial: In this type of trial, participants and researchers know who is assigned to control and treatment groups. Blinding is not possible in some cases. For example, in a study comparing a surgical treatment to a medication.

Observational Studies: Non-Randomized Comparisons of Interventions

An example of an observational study would be one in which infection rates in a hospital that started an infection control program are compared to infection rates in a similar hospital that did not start an infection control program. This type of intervention is shown below.



There are many types of observational studies. However, the most common observational studies for PCOR are case control and cohort.

Observational Study Type	Definition
Case Control	• Population studied retrospectively, meaning after a treatment or intervention occurred ○ Data are limited to what is available in medical records or historical documents
Cohort	• Population followed prospectively over time, meaning patients are observed and provide information in real time

What is Data Analysis?

Researchers also use methods to look at the information collected in a study. This is called data analysis.

There are three approaches to examining data that you may come across during the review process. Each approach has different methods that are used. Definitions of these methods can be found in the glossary.

Approach	Description	Types of Methods That are Used
Causal Inference	The ability to demonstrate that one characteristic in a study directly causes a second (or multiple) characteristics. NOTE: Causality can usually be demonstrated in experimental studies, but not in observational studies.	• Propensity Score Matching • Instrumental Variable Approach
Regression	A statistical analysis approach that examines the relationship between two or more variables.	• Linear • Logistic • Multivariate
Advanced Methods	Often seen in the Improving Methods for Conducting Patient-Centered Outcomes Research PFA.	• Bayesian Methods • Heterogeneity of Treatment Effect

What is Power and Significance?

Power describes a study's ability to detect a statistically significant difference between the outcomes of different interventions. The amount of statistical power is based on the number of people in the study (the sample size) and the amount of outcomes experienced by the people who received an intervention. Many health studies are

designed to have 80% power. This means that the study has a high chance of showing a statistically significant difference between the outcomes of the interventions.

Significance is another concept that PCOR studies use in interpreting study results. Studies may use one or both of these approaches to interpret results.

There are two types of significance: Statistical Significance and Clinical Significance.

Researchers express statistical significance using a "p value."

p <0.05 means less than a 5% likelihood (probability) that study findings are due to chance (and therefore, a greater than 95% likelihood that the interventions are related to the results)

Statistical Significance is used to determine whether the hypothesis has been supported by the data. Statistical significance indicates how much the results of the study are due to the outcomes and how much are due to chance.

Clinical Significance tells whether research findings are of practical use to patients and clinicians.

For example, a study may find small differences in the outcomes between groups. The statistical analysis may show these differences to be statistically significant. However, these differences may not be large enough to be important to patients and clinicians, because the differences seen in the data may not have a big enough impact to be seen or felt by the patients in their daily lives.

It is important that research funded by PCORI is both statistically and clinically significant.

Key Points to Remember from Section 2

When reviewing applications, remember to keep these questions about research elements in mind:

Method Selection:

- Does the study provide an explanation about why the methods were chosen to study the identified outcomes?

Sample Selection:

- Does the study provide a large enough sample size?
- Does the study show the ability to detect a statistically significant difference between the outcomes of different approaches to care?

Significance:

- Does the study include statistical or clinical significance?

Section 3: Interpreting Study Results

What Will I Learn?

This section answers the following questions:

- What makes research findings trustworthy?
- What is bias?
- What is confounding?
- What key questions should I ask—myself and others—during the merit review process?

After reading this section, you will be able to:

- List key factors to consider when interpreting study results
- Understand the importance of bias in research studies

This section should take about 10 minutes to complete.

How do I know if I can trust research findings?

There are two important ways of judging whether or not research findings are credible, or can be trusted: reproducibility and validity.

Reproducibility means the research study findings would be the same—or could be reproduced—if others conducted the research using the same design or collected data.

There are two important parts to validity: internal and external.

Internal validity is related to the way researchers designed and conducted the current study. For results to be valid in this way, they must be free from bias (or leaning) toward any one particular outcome.

External validity is related to the results of a statistical analysis. For results to be valid in this way, they must be applicable or generalizable to other types of data, other cohorts, or other settings beyond the current study. This may also be referred to as generalizability.

Research findings that have high validity and are reproducible are trustworthy. This means that you and others can have confidence in the results that researchers reported.

Bias is an error or mistake in decision-making about the study population, study design, or method of analyzing data. Bias influences research results in a way that makes them less likely to reflect the true outcome or relationship.

Examples of bias include:

- Missing data (when some or all measurements in a study are missing because they were not measured or reported)
- A population group (such as women) is not included in a study that is meant to represent the general population

Applications must assess and control for research bias by addressing the strengths and limitations of their choices of whom and what treatment options to study

What is Confounding?

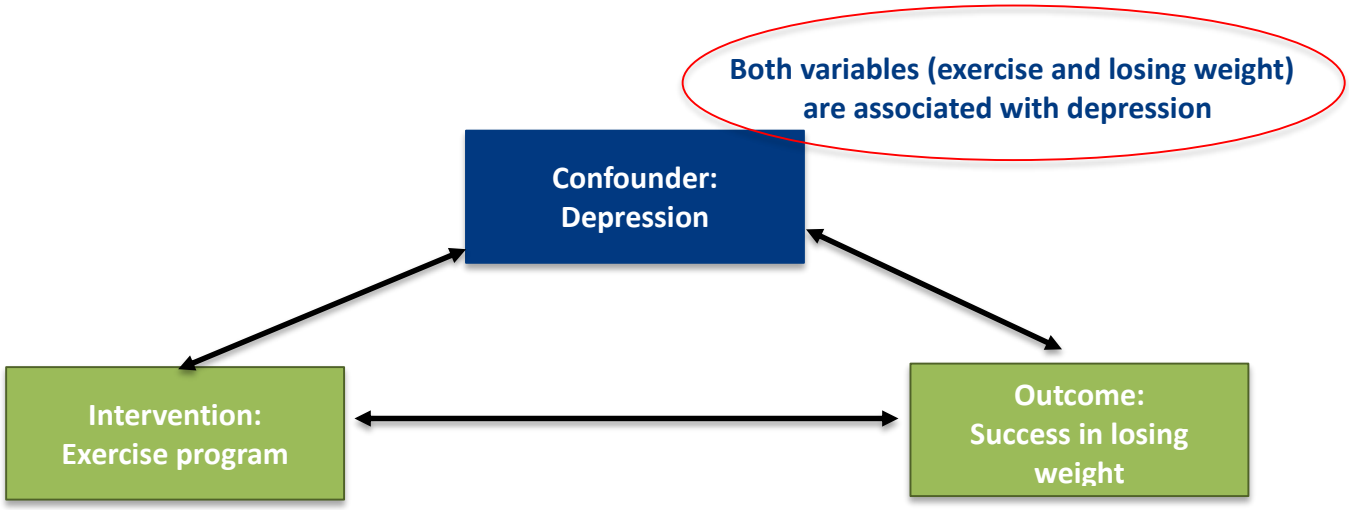
Confounding is a kind of confusion about what is really responsible for the study findings. In some cases, the chosen intervention in a study (or the suspected cause) and the outcome of the study are both affected by some other factor. This other factor is a confounder.

Confounders make it less clear whether the suspected cause would lead to the outcome without this other factor, or confounder.

FOR EXAMPLE:

Researchers may find that exercise (the intervention) is associated with losing weight (the outcomes) but also find, in statistical analysis, that a third factor, depression (the confounder) is associated with both successful weight loss and exercise.

Below is one way researchers might look at how confounding affects a study, like the one described in the example.



Confounding can lead to biased results.

The conclusions of some statistical analyses become less valid when researchers discover that both the suspected cause (or chosen intervention) and the outcome are both dependent on another factor.

Questions to Ask During the Merit Review Process

Here are some questions that will help guide you, when reviewing applications and during the in-person panel review:

Questions to ask yourself:

- Are the study outcomes relevant from your perspective?
- Has the applicant done an adequate job explaining why they chose their methods?

Questions to ask fellow panelists:

- Are any parts of the study question and study design flawed?
- What could be done to strengthen the approach?
- Has the researcher identified a method for dealing with missing data?
- Could the findings for this study be applied in other settings? How will it be disseminated to more patients?

This is the end of Section 3. Congratulations! You have now completed the Methodology 101 training. You should now have a better understanding of how research projects are designed and carried out.

Please keep this Training Booklet and Resource Guide, which includes the Glossary of Selected Terms that follows, for future reference. These materials should be useful to you when reviewing applications and participating in the merit review process.

Please visit PCORI online at www.pcori.org to search for more details about the topics covered in this guide.

METHODOLOGY 101: COMMONLY USED TERMS AND ACRONYMS

This glossary defines terms that are commonly found in PCORI applications, and is supplemental to the Methodology 101 Training. This resource is not meant to include all the terms that might be used in a PCORI application.

Understanding the terms in context

Research can be done in a variety of ways. A methodology describes the ways in which a research question or questions will be answered. To make more sense of these terms, it is helpful to understand the basic categories that make up a research methodology:

1. **General research terms.** These words are used often to describe aspects of research.

Clinical Practice Guideline	A statement or recommendation about appropriate health care for specific clinical circumstances. Clinical practice guidelines are created through a system of examining all the evidence about a test, procedure, or intervention, or the management of specific clinical problems. Clinical practice guidelines help clinicians and patients make decisions. Guidelines may be developed by government agencies, institutions, organizations such as professional societies or governing boards, or by convening expert panels.
Informed Consent	When capable persons agree to participate as research subjects after receiving complete information about the research project and the risks, benefits, and responsibilities of participating.
Institutional Review Board (IRB)	An independent group that reviews research plans to make sure that the interests of research participants are protected throughout the study. Each contractor must obtain IRB approval before beginning research and may need to report to the IRB periodically while conducting each project.

Measures	Statistical tools used to express an outcome by a specific number. The measure may be the number of people who answered a survey question in the same way, or the number of people of a certain age who had the same diagnosis.
Outcomes	The effects of an interventions, or what happens after an intervention is given. For example, survival, reduction in symptoms, quality of life, quality of care. Each study's "primary" outcome is its most important effect. The primary outcome is used to calculate a study's sample size and statistical power.
Protocol	A plan that outlines the procedure for conducting research in detailed steps. Protocols are created before the beginning of a study.
Scientific Evidence	Facts discovered using established and accepted scientific methods. Scientific evidence supports a conclusion about the probability of something occurring. For example, the result of an RCT is scientific evidence that can support a conclusion about a treatment for a condition, whereas the personal stories of a patient or physician about a treatment would not be considered scientific evidence and could not support a conclusion.

These definitions are used to talk about how conditions are counted or reported:

Incidence	Rate at which a condition or event appears in a population. For example,14 new cases of influenza per 100 adults per year.
Prevalence	Percentage of a population that is affected by a condition at any one time. For example, 18% of adults have diabetes at any one time.

2. **The overall method of research, or methodology:** A question might be best answered by collecting, organizing, and reviewing data in a specific way. This "way" of answering the question is called the methodology. Methodologies determine how the study should collect the data, and how the answers should be determined. There are several "standard" research methodologies, and some of them have variations.

Definitions:

Community-Based Participatory Research (CBPR)	A research approach that engages community partners (such as organizations or individuals) in each stage of the research process. CBPR values the unique perspective of community members. Community members and researchers define the central problem to be addressed, conduct the research, and communicate results that can be translated into practice in that community. CBPR differs from PCOR in that it is steeped in community engagement, nurtures partnerships to realize shared outcomes over the long-term, and often occurs outside of the clinical setting. PCOR can use a CBPR approach.
Comparative Effectiveness Research	This research looks at the benefits and risks of two or more alternative methods. The methods address the prevention, diagnosis, treatment, or monitoring of a clinical condition or the improvement of health care delivery.

Some comparative effectiveness research studies use data that has already been collected:

Evidence Synthesis	Quantitative data from different trials are looked at together so that researchers can see effects from all the trials at the same time. Conclusions from evidence synthesis can be used to help people make clinical decisions. An evidence synthesis might look at all the trials on a single treatment option or multiple treatment options for one disease.

Systematic Review	A way to determine what is known about the effectiveness of an approach to care by identifying and summarizing all of the relevant scientific literature based on pre-set rules for including, excluding, and weighting published evidence.
Delphi Approach	A research method that helps researchers find consensus on a set of priorities or other decisions by using a series of surveys with an expert group to brainstorm ideas and prioritize them. A modified Delphi approach may use email or mail to gather input, or may prioritize pre-selected choices that are not generated by the group. The Delphi Approach is not a research methodology, but is often used by researchers to help determine research priorities.
Observational Study	A type of research method that uses data from patients as they are being treated by their doctors rather than through random assignment by researchers. In an observational study, patients with a diagnosed condition receive different treatments selected by them and their providers. Researchers then compare the outcomes experienced by patients who received one treatment with the outcomes of those who received a different treatment. Data can be collected prospectively or retrospectively. • Prospective: A study that answers research questions by defining the research question first and then collecting the data over time after the question is defined. Participants are followed to see how factors may contribute to outcomes. • Retrospective: A study that answers research questions using historical data (e.g. electronic health records, surveys). The data can be used to look back and study factors that may have contributed to observed outcomes.

There are several types of observational study methods. These include:

Quasi-Experimental Study	A study where one group of patients who receive a treatment are compared to a group of patients who received a different treatment. Each group is chosen for a given reason rather than by random. For example, a study might compare the infection rates in a hospital that used an infection control program to the infection rates in a similar hospital that did not.
Conjoint Analysis	A method of research where participants are asked to make choices from available options. This provides valuable insights for researchers on patient preferences or their willingness to accept tradeoffs. For example, patients might be asked if they prefer a medicine that is known to be effective for pain relief, that has notable side effects; or a medicine that that is not as effective for pain relief, but has fewer side effects. Conjoint analysis looks for patterns in the data based on the choices that participants make.

This is PCORI's definition of the research that it funds:

Patient-Centered Outcomes Research (PCOR)	This research approach helps people and their caregivers communicate and make informed healthcare decisions, allowing their voices to be heard in assessing the value of healthcare options. PCOR answers patient-centered questions such as: 1. "Given my personal characteristics, conditions and preferences, what should I expect will happen to me?" 2. "What are my options and what are the potential benefits and harms of those options?" 3. "What can I do to improve the outcomes that are most important to me?" 4. "How can clinicians and the care delivery systems they work in help me make the best decisions about my health and healthcare?"

Many quantitative studies are designed to be randomized controlled trials:

Randomized Controlled Trial (RCT)	Study in which each individual participant is randomly chosen (rather than chosen for a given reason) to receive one of two (or more) approaches to treatment. For example, a patient might be randomly assigned to receive drug A or drug B. Randomization helps to minimize bias.

Some researchers use a variation of a randomized control trial. Some variations include:

Adaptive Trial	Researchers plan to review the data during the course of the study. They might modify the study approach and the research question based on that review. For example, a decision may be made to drop one of the treatments being administered because of the early data that was reviewed.
Cluster-Randomized Controlled Trial	A study in which *groups* of participants (for example, all those who receive care at a particular clinic) are randomly assigned to receive one of two (or more) approaches to treatment. This type of trial is different than a study where individual participants are randomly assigned to receive one of two (or more) approaches to treatment.
Large Simple Trials	A type of trial (or study) that uses simplified methods of participant enrollment, assignment and approaches to data collection. For example, patients that enroll in the study are directly assigned to a control or treatment group without considering other factors such as patient characteristics.

Pragmatic Trials	Pragmatic trials take place in a real-world environment, as opposed to a research setting. They use simple criteria for inclusion and exclusion to enable enrollment of a wider range of patients and study sites. There are fewer burdens imposed on participants so that the patient experience of those enrolled in the study is similar to the experience of patients who are not enrolled in the study.

3. **Specific Research Methods.** There are specific approaches within a general methodology that researchers use to select participants and to collect or analyze data. These terms describe a specific part of a general research methodology or statistical analysis method:

Blinding	Researchers, study participants, or both are not aware of which participants are in which study group. They are "blind" to that information so that it does not influence their conclusions. This is done to reduce bias.
Causal Inference	These methods help researchers find if one variable causes or predicts that another will occur. For example, a study may test the relationship between smoking and mortality. Casual inference methods include propensity score matching, instrumental variables, and regression.
CONSORT	This is an acronym for **Con**solidated **S**tandards **o**f **R**eporting **T**rials, a group that addresses reporting issues of Randomized Control Trials (RCT). This group issues the CONSORT statement, which are a set of evidence-based recommendations for the reporting of RCTs.
Cohort	A group of individuals who share a common exposure, experience, or characteristic. For example, a cohort in one study may be all individuals who were exposed to

	contaminated water.
Covariates	Also known as a predictor, explanatory variable, or independent variable. A covariate is a factor that may predict or otherwise have an effect on an outcome. For example, gender may be covariate when studying heart disease, because it helps explain when people get the condition.
Data Linkage	The process of combining or merging data from two or more data sources that contain information for a particular entity (such as combining survey data with medical records for a patient). This allows researchers to utilize additional information that may be helpful in answering their research question.
Effect Modification	When the effect seen from a treatment or disease exposure is different for different people because of a specific characteristic they have, such as sex, age, or geographic location. For example, children may respond differently to a type of medication than adults who receive that same medication.
Effect Estimate	An estimate of the size or amount of the effect created by a treatment or other variable.
Heterogeneity of Treatment Effect	When individuals with different characteristics respond differently to the same treatment. This variation must be accounted for when performing statistical analysis on how effective a particular therapy is at treating a given condition. For example, the analysis should account for when one medicine works differently for some people than for others.
Missing Data	When some or all measurements in a study are missing because they were not measured or reported. There are

	three types of missing data that may have an effect on a study: Missing at Random (MAR), Missing Completely at Random (MCAR), or Missing Not at Random (MNAR).
Missing at random (MAR)	The missing data are related to measured variables within the patient data that could predict the outcome being studied. For example, people without regular employment (assume this is a measured variable) may have been less likely to report their income (outcome).
Missing Completely at Random (MCAR)	The missing data are not related to measured or unmeasured variables within the patient data. For example, there may have been no characteristic(s) that predicts why some people reported their income and others did not.
Missing not at random (MNAR)	The missing data are related to unmeasured variables within the patient data that predict the outcome being studied. For example, people who make less than the poverty threshold (the unmeasured variable) may have been less likely to report their income (outcome).
Missingness	The type of missing data in a study sample (see above examples: MAR, MCAR, and MNAR).
Placebo	A harmless medicine or procedure given to a study subject as a control so that the outcomes can be measured against those who have the actual medicine or procedure. A placebo makes people believe that they had an intervention when there was no physical effect of the intervention.

4. **Methods of Statistical Analysis.** Within a research study, there may ways that researchers organize, review, and interpret the data they have collected. Statistical analysis methods help researchers determine how they should think about the data they have collected. These terms all relate to the way in which data are analyzed statistically:

Bayesian Methods	A type of statistical analysis that combines other information about a subject (other evidence, common sense, or subjective opinions) with the data that was collected. This type of analysis is different than traditional statistical methods that only analyze the current data at hand. Bayesian statistical analysis helps researchers decide the likelihood that a hypothesis is true. For example, you may discover that a disease you want to study is only present in women. You may change your analysis to limit the cohort to only female participants. If you find halfway through that the disease only occurs in women over 50, you may choose to focus on data only from women in this age group.
Causal Inference	These methods help researchers find if one variable causes or predicts that another will occur. For example, a study may test the relationship between smoking and mortality. Casual inference methods include instrumental variables, propensity score matching, and regression.

Instrumental Variables Method (IV)	An instrumental variable is used in observational research to correct for a confounding variable when it is found. An instrumental variable: 1) is not directly related to the cause of the confounding or the outcome of interest, and 2) directly affects the

	treatment or intervention. If the IV is shown to be valid based on these two criteria, the variable can be used to correct for unmeasured confounding.
Propensity Score	A way to estimate the likelihood that an individual will be assigned to a certain study cohort based on a chosen subset of their characteristics. This process is often utilized in causal inference methods and retrospective studies where a specific control group is not available.
Propensity Score Matching	A way to estimate the likelihood that an individual will be assigned to a certain study cohort based on a chosen subset of their characteristics. This process is often used in causal inference methods and retrospective studies where a specific control group is not available.
Regression Method	A statistical analysis approach that examines the relationship between two or more variables (for example a pain reliever (the treatment being evaluated), and shoulder pain (the outcome being studied).

Regression-Linear	A regression method approach that uses a linear equation to explain the relationship between variables. Simple linear regression predicts or explains an outcome variable using only one independent variable. For example, the outcome variable of lowered blood pressure is explained by the use of a certain medicine (the independent variable).

	Multiple linear regression uses two or more independent variables. For example, the outcome variable of lowered blood pressure is explained by both the use of a medicine (independent variable 1) and increased exercise (independent variable 2). Linear regressions are expressed as a math equation. For example, let's say that the following linear equation best fits (or explains the relationship between) the data you have for x, a predictor, and y, an outcome: Y=2x+2 An example of multiple linear regression: Let's say the following linear equation best fits the data you have for predictors x and z, and outcome y: Y=2x+3z+2
Regression – Logistic	A regression method approach that predicts or explains an outcome variable using one or more dichotomous variables. A dichotomous variable only has two opposite outcomes, such as "yes" or "no."

Mean	This is a statistic of the average across a group of participants – for example, a group of 40 patients may have their blood pressure measured, and an average of all the measures is presented as a single number.

Median	The midpoint of measurements across a group of participants. For example, a group of 40 patients may have their blood pressure measured, and the scores placed in order from highest to lowest. The media would be the "middle" number on that list. Half of the people have higher scores, and half have lower scores.
Meta-Analysis	Data from several studies are combined to draw a general conclusion about an effect across the studies. Meta-analysis is used to gain more precise evidence of a treatment's effects.
Null Hypothesis	The prediction that there is no relationship or difference between two variables. For example, a study on heart disease and depression might have a null hypothesis that predicts there is no relationship between these two conditions.
Odds Ratio	The ratio of the likelihood (odds) that an effect or event will occur. An odds ratio is determined when the likelihood of an effect or event in one studied group is divided by the likelihood (odds) that the same effect or event in a second group. Often, the odds of an effect in the treatment group (a group of people who are given the treatment) are divided by the odds of the effect in a control group (a group of people who are not given the treatment). This measure assists researchers in determining if the effect being seen in the group receiving the treatment is a "genuine" reaction to the treatment and not just a random occurrence.
Power	Study's ability to detect a statistically significant difference between the outcomes of different variables. The amount of statistical power is based on the number of people in the study (the sample size) and the amount of outcomes experienced by the people who received an intervention. Many health studies are designed to have 80% power.

Relative Risk	The ratio of the probability that something will occur (an outcome) for a group of people who have a certain risk factor when compared to people who do not have that risk factor. For example, the relative risk for people with uncontrolled high blood pressure to develop heart disease looks at people with uncontrolled high blood pressure who developed heart disease compared to people without uncontrolled high blood pressure who developed heart disease. Relative risk is also sometimes called risk ratio.
Sample Size	The number of people who provided data in a study, often expressed as "n." For example, n=250 means the data from 250 people were collected in the study.
Statistical Significance	Probability that the results of a study are due to chance, often expressed as a "p value" – e.g., p <0.05 means there is less than a 5% probability that the study findings are due to chance (and, therefore, there is a greater than 95% probability that the study findings are due to the variable being studied).
Surrogate Efficacy Measures	The measure of an effect of a certain treatment or risk factor that may be related to a real clinical outcome, but does not have an absolute relationship to that clinical outcome. A surrogate outcome is measured when the desired outcome cannot be directly measured. For example, high cholesterol levels are a surrogate measure for heart disease, even though there are people with low cholesterol who have heart disease and people with high cholesterol who do not. So a study showing how well a medicine reduces cholesterol is a surrogate measure the more important clinical outcome of death by heart attack or stroke.

Treatment Size	The measured change (of any kind) in the clinical outcomes or symptoms following exposure to a treatment. Also referred to as the effect size.
Variability	How much difference there is in the results of a single set of data. For example, a group of 100 people all taking the same medicine may rate the amount of pain relief they feel. The range of scores among the group would be the variability in the data set.

5. **Qualities of Research Findings**. Some terms describe a certain quality or standard in the way research is conducted that must be met in order for the answers to be useful. These terms describe these qualities of research that a method strives to accomplish or avoid:

Bias	When some decisions about the study population, study design, or method of analyzing the data influence research results, making the results less likely to reflect the true outcome or relationship. Applications must assess and control for research bias by addressing the strengths and limitations of their choices of who and what treatment options to study.
Confounding	The conclusions of some statistical analyses become less valid when researchers discover that both the suspected cause (or chosen intervention) and the outcome are both dependent on another factor. Confounders make it less clear whether the cause (or chosen intervention) would lead to the outcome without this other factor. For example, researchers may find that exercise (the intervention) is associated with losing weight (the outcome), but also find in statistical analysis that a third factor, depression (the confounder), is associated both with both successful weight loss and exercise.

External Validity	The results of a statistical analysis is applicable or generalizable to other types of data, other cohorts, or other settings beyond the current study. This may also be referred to as generalizability.
Internal Validity	The extent to which the researchers have designed and conducted the study so that they are confident that the results will be valid or free from bias toward any one particular outcome.

False Negative	When a clinical test or statistical analysis shows that a result is false (or negative), when the test or analysis should really show the result is true (or positive).
False Positive	When a clinical test or statistical analysis shows that a result is true (or positive), when the test or analysis should really show the result is false (or negative).
Reliability of Measurement	How well a measurement method produces the same value when used to measure the same thing more than once. For example, a scale should show the same weight every time someone gets on it unless the person has lost or gained weight. If a scale said someone was 100 pound one day and 250 pounds the next day, the scale would be unreliable. Research is most likely to produce valuable results if it uses measurement methods that have been tested and shown to be valid and reliable.
Reproducibility	The research study's findings would be the same if any other group conducted the research using the same data or similar data cohort.
Sensitivity	The ability of a test or statistical analysis to determine a "true positive" result consistently. An example of a false positive is when a screening test determines that an individual has a condition, when they do not, in fact, have that condition.

Specificity	The ability of a test or statistical analysis to determine the "true negative" result consistently. An example of a false negative is when a screening test determines someone does not have a condition, when they, in fact, do have it.
Validity of Measurement	How well a measure accurately represents an outcome. Some measures have better validity than others. For example, surveying patients about the severity of their symptoms in the last two weeks may provide more accurate answers than asking them about symptoms a year ago.