

Types of clinical studies and their components

Clinical studies are important in advancing medical knowledge, improving people's health, and developing new treatments and therapies. These studies are designed to investigate various aspects of human health, ranging from understanding disease mechanisms to assessing the effectiveness, acceptability, cost-effectiveness and safety of medical interventions.

Types of clinical study

There are several different methodologies for conducting clinical studies; each having different strengths, weaknesses, and ethical considerations. Some of these are outlined below (Institute for Quality and Efficiency in Health Care 2016).

1. **Observational Studies:** Observational studies are designed to observe and analyse individuals in their natural settings without any intervention by the researchers. They aim to identify associations between certain variables, such as risk factors and health outcomes. Observational studies can be categorized into three main types:
 - a) **Cohort Studies:** Cohort studies follow a group of people over a specific period, tracking their exposure to risk factors and monitoring their health outcomes. These studies help identify potential causes or risk factors for diseases.
 - b) **Case-Control Studies:** In case-control studies, researchers compare individuals with a particular outcome (cases) to those without it (controls). By analysing past exposures or characteristics, researchers can determine potential associations between risk factors and diseases.
 - c) **Cross-sectional Studies:** Cross-sectional studies collect data at a specific point in time to assess the prevalence or frequency of a condition or exposure in a population. They provide a snapshot of the population and help generate hypotheses for further investigation.
 - d) **Case series:** Case series studies are a type of observational research design that provides valuable insights into rare or novel medical conditions, treatments, or interventions. In these studies, researchers collect and analyse data from a group of patients who share similar characteristics or have been exposed to a particular treatment. Unlike randomised controlled trials, case series studies lack a control group, making them less rigorous in establishing causality but highly informative in generating hypotheses for further investigation. Medical professionals often employ case series studies to explore the presentation of new diseases, adverse reactions to medications, or the outcomes of innovative treatments when randomised trials may not be feasible or ethical. (Mathes and Pieper 2017)
2. **Experimental Studies:** Experimental studies involve intentional manipulation of variables to assess the effects of interventions or treatments. These studies are often used to evaluate the efficacy and safety of medical interventions. Experimental studies can be further divided into two main categories:
 - a) **Randomized Controlled Trials (RCTs):** RCTs are considered the gold standard in clinical research. Participants are randomly assigned to different groups: an intervention group receiving the treatment under investigation and a control group receiving either a placebo or standard care. Ideally this is done on a "double blind" basis; where neither the participants nor the treating clinicians know whether an individual is in the intervention group or the control group. RCTs allow researchers to establish causal relationships between interventions and outcomes.

- b) **Non-Randomized Controlled Trials:** In some cases, randomisation may not be feasible or ethical. Non-randomized controlled trials assign participants to different groups based on other criteria, such as their location, age or clinical characteristics. While these studies have limitations, they can still provide valuable insights when randomised designs are not possible.
3. **Interventional Studies:** Interventional studies focus on assessing the effects of specific interventions or treatments on participants' health outcomes. These studies aim to investigate the potential benefits, risks, and optimal dosage or administration of interventions. They can be conducted as both experimental and non-experimental studies, including clinical trials and other controlled investigations. Healthcare service evaluations may also be interventional studies.
 4. **Descriptive Studies:** Descriptive studies aim to describe the characteristics, patterns, and distribution of diseases or health-related events in populations. They often involve collecting data from medical records, surveys, or registries. Descriptive studies provide valuable information about the burden of diseases, risk factors, and potential public health interventions. They may also highlight areas for further study.
 5. **Healthcare service evaluation:** Healthcare service evaluation studies play an important role in assessing and improving the quality and effectiveness of healthcare services. These studies are designed to analyse the various aspects of healthcare delivery, ranging from the accessibility and affordability of services to the satisfaction of patients and overall health outcomes. Researchers use a combination of quantitative and qualitative methods to gather data, often involving surveys, interviews, and clinical assessments. By scrutinising these findings, healthcare professionals and policymakers can identify strengths, weaknesses, and areas for enhancement in healthcare. (Moore, et al. 2015)
 6. **Literature-based studies:** Literature-based studies are studies where scientific research that has been published in academic journals is analysed together so overall conclusions can be drawn. They are powerful methods of evidence synthesis in medical research that aim to summarise and evaluate the findings of multiple individual studies on a specific topic (Bello, et al. 2015).
 - a) **Systematic reviews:** Systematic reviews involve a comprehensive and systematic search of the literature to identify all relevant studies meeting predefined inclusion criteria. Once selected, these studies are critically appraised for their quality, and their results are synthesised to provide a comprehensive overview of the evidence available.
 - b) **Meta-analyses:** Meta-analyses take the process one step further by statistically combining the results of the included studies, providing a more precise estimate of the treatment effect or association between variables.

By pooling data from multiple sources, systematic reviews and meta-analyses increase the statistical power and generalisability of the findings, enabling researchers and healthcare professionals to draw more robust conclusions and make evidence-based decisions.

Components of clinical studies

The analysis above explores the different approaches to clinical study design, but there are common components or concepts that may be necessary regardless of the type of study. These include (Evans 2010):

- **A study protocol:** This is a written document that describes the purpose of the study, the study design, the methods that will be used, and the safety and ethical considerations.

- **Inclusion and exclusion criteria:** These are the criteria that participants must meet in order to be eligible to participate in the study. This can relate to a given illness or exposure to a given hazard, to the person's wider characteristics like age or gender, or to other characteristics that may impinge on potential risk or benefit.
- **Informed consent:** This is a process that explains the study and any risks, benefits and rights to potential participants. Participants must sign an informed consent form before they can participate in the study.
- **Data collection:** This is the process of collecting information about the participants, such as their medical history, their responses to the treatment, and any side effects they may experience.
- **Data analysis:** This is the process of analysing the data that was collected to determine the safety and effectiveness of the treatment.

The study protocol

The study protocol is the blueprint for the study and ensures that all aspects of the study are conducted in a consistent and ethical manner. A study protocol should include the following information:

- The purpose of the study
- The study design
- The methods that will be used
- The safety and ethical considerations
- The inclusion and exclusion criteria
- The informed consent process
- The data collection methods
- The data analysis plan

Ethical considerations in clinical studies

In any clinical study, there are key ethical considerations (Muthuswamy 2010). These include:

1. **Informed Consent:** As alluded to above, one of the fundamental ethical principles in clinical studies is obtaining informed consent from study participants. Informed consent ensures that individuals fully understand the nature, purpose, risks, and benefits of the study before deciding to participate. Researchers have a responsibility to provide clear and comprehensive information to participants, allowing them to make autonomous decisions. Informed consent must be voluntary, without any coercion, and participants should have the freedom to withdraw from the study at any time without penalty.
2. **Beneficence and Non-Maleficence:** The principles of beneficence and non-maleficence emphasise the obligation of researchers to maximize benefits and minimize harm to study participants. Researchers must carefully design studies to maximise potential benefits while minimising risks and adverse effects. Ethical considerations include selecting appropriate control groups, ensuring the validity and reliability of data collection, and monitoring participant safety throughout the study. If potential risks outweigh the expected benefits or

if harm occurs during the study, researchers have an ethical obligation to halt the study and prioritise participant well-being.

3. **Privacy and Confidentiality:** Respecting privacy and maintaining confidentiality are crucial ethical considerations in clinical studies. Participants' personal information, medical records, and study data must be kept confidential to protect their privacy and maintain trust. Researchers must adhere to strict data protection protocols, use anonymised data whenever possible, and ensure that only authorised individuals have access to participants' personal information. Safeguarding privacy is not only a legal requirement but also an ethical imperative that promotes respect for individuals and upholds their dignity.
4. **Equitable Participant Selection:** Equity in participant selection is essential to avoid biases and ensure fair representation in clinical studies. Researchers should strive to include diverse populations, including individuals of different ages, genders, races, and socioeconomic backgrounds, to ensure the generalisability of study findings. Exclusion criteria must be scientifically justified and not based on discriminatory factors. Ethical considerations also involve addressing any potential power imbalances between researchers and participants and promoting inclusivity in the research process.
5. **Risk-Benefit Assessment:** Clinical studies must undergo rigorous risk-benefit assessment before initiation. Researchers must carefully evaluate the potential risks and benefits associated with the study and weigh them against alternative approaches. The risks should be minimised to the greatest extent possible, and the potential benefits should outweigh the potential harm. Ethical considerations include regular monitoring of participant safety during the study and prompt reporting of any adverse events to relevant authorities.

Ethical considerations in clinical studies are essential to protect the rights, safety, and well-being of study participants. For this reason, most studies will need to undergo ethical scrutiny from an external body, either an institutional ethics committee or a national or regional one.

The importance of sample size in clinical studies

Sample size determination is crucial for ensuring adequate statistical power in a clinical study. Statistical power refers to the probability of detecting a true effect when it exists. By including an adequate number of participants, researchers increase the power of their study, enabling them to detect smaller, yet clinically meaningful, differences between treatment groups. A small sample size may result in insufficient power, leading to a higher likelihood of false-negative results and missed opportunities for identifying effective interventions. Therefore, a larger sample size enhances the ability to detect significant treatment effects accurately (Evans 2010).

The generalisability of study findings, or external validity, is contingent on an appropriate sample size. In clinical research, it is essential to ensure that the sample is representative of the target population to generalize the results to a larger group of individuals. A small sample size may not adequately capture the heterogeneity present in the population, leading to limited external validity. By increasing the sample size, researchers can enhance the representativeness of the sample, increasing the generalisability of the study findings and their applicability to a broader population. For this reason, a study with a smaller sample size is usually less influential scientifically than a similar study with a larger sample size.

Sample size also influences the precision of statistical tests and the width of confidence intervals. Statistical significance is determined by the p-value, which measures the probability of obtaining the observed results by chance alone. A larger sample size increases the precision of estimates, reducing the standard error and leading to narrower confidence intervals. Consequently, it becomes easier to

determine whether the observed results are statistically significant or due to random variation. A small sample size can result in wider confidence intervals and decreased precision, which may lead to inconclusive findings or overestimation of treatment effects.

Several factors influence the determination of an appropriate sample size. These factors include the research question, study design, desired effect size, expected variability, statistical power, and available resources. Researchers must carefully consider these factors to strike a balance between practicality and statistical robustness. Consulting statisticians and utilising power calculations can aid in sample size estimation and ensure that the study has sufficient power to detect clinically meaningful effects.

Generally speaking, cohort studies or studies that contain a control group need to be larger than things like case series or healthcare evaluation studies (Mathes and Pieper 2017), so it is not always practicable to conduct an RCT. This can be a particular issue with smaller effect sizes, rarer conditions or smaller populations.

References

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