

types of studies

primary research

RCTs

- Randomized clinical trials, also referred to as experimental or interventional studies, are the cornerstones of medical evidence.

Advantages:

(i) When participants are randomly allocated to groups, factors other than the variable of interest (e.g., a new therapy for sepsis) that are likely to affect the outcome of interest are usually distributed equally to both groups.

Disadvantages:

- (i) expensive,
- (ii) difficult, and sometimes
- (iii) unethical to conduct
- (iv) many important questions, such as determining the optimal timing of a new therapy or determining the effects of health care practices, cannot practically be studied by RCTs
- (v) do not necessarily reflect the real-world

- The principal alternative approach to the RCT involves observation rather than experimentation.

- (i) case-control,
 - compare a group of patients with a disease or symptom of interest to a selected control group
 - have the advantage of being quick and relatively inexpensive to perform and are often the only feasible study method for very rare disorders, or when the lag time between an exposure and the related disease is very long.
 - They can also be conducted with a relatively small number of patients

types

- (ii) cross-sectional surveys and studies
 - provide a snapshot of a population at one point in time.
 - can also be conducted inexpensively and in a short time.
- (iii) cohort studies.
 - prospectively identify an at-risk group (the inception cohort) and follow them through time, recording exposures and development (or not) of the disease under investigation.
 - Cohort studies have a number of strengths, including the ability to match subjects to controls for some confounders, establish the timing and sequence of events, and standardize eligibility criteria and outcome assessments, and they are easier and less expensive to conduct than RCTs.

observational studies

Advantages:

- (i) Observational outcomes studies are very powerful tools for addressing many questions that RCTs cannot address, including measuring the effect of harmful substances (e.g., smoking and other carcinogens), organizational structures (e.g., payer status, open vs. closed ICUs), or geography (e.g., rural vs. urban access to health care).
- (ii) Observational studies can generate hypotheses about the effectiveness of treatments that can be tested using other research methods.

Disadvantages:

- (i) observational outcomes studies are often performed on large data sets wherein the data were collected for purposes other than research. This can lead to error owing to either a lack of pertinent information or bias in the information recorded.
- (ii) The measured effect size of a variable on outcome (e.g., the effect of the pulmonary artery catheter on mortality rate) can be confounded by the distribution of other known and unknown variables.
- (iii) case-control studies are subject to recall and selection bias, and the selection of an appropriate control group can be difficult.
- (iv) cross-sectional studies can only establish association (at most), not causality, and are also subject to recall bias.
- (v) cohort studies have a number of limitations, including difficulty in finding appropriate controls and difficulty determining whether the exposure being studied is linked to a hidden confounder, and the requirement of large sample size or long follow-up to sufficiently answer a research question can be timely and expensive.

case reports or series

- The last form of primary research is the case report or case series.
- A case is a published account of a single or small number of patients and their response to a particular therapeutic intervention.
- The inability to generalize from a case report makes it the weakest form of clinical evidence available.
- case reports may be the only available or practical information in support of a therapeutic strategy, especially in the case of rare diseases, when the evolution of the therapy predates the common use of randomized study designs in medical practice.

summaries of primary research

critical appraisal

- Determining which studies provide information useful in the care of patients is largely a question of deciding whether a study is valid and, if so, can its results be applied to the patients in question.
- One format for appraising individual studies is the critically appraised topic (CAT) format that has been popularized as part of EBM.
- The purpose of the CAT is to evaluate a given study or set of studies using a standardized approach. Studies that address diagnosis, prognosis, etiology, therapy, and cost-effectiveness all have a separate CAT format.
- The CAT format for studies on therapy asks several questions intended to address the issues of validity and clinical utility.

systematic reviews

- A systematic literature review combines the results of multiple studies through the systematic search, assembly, and appraisal of existing primary research on a given subject.
- Meta-analysis is a type of systematic review that incorporates a quantitative summary of the data, which combines actual data from several small, although high-quality studies.
- All systematic reviews should start with a four-part (three-part when applicable) question, as described previously. Both the search criteria and inclusion and exclusion criteria should be predefined.

Advantages

- (i) by pooling many studies the power to find a true effect is increased.
- (ii) Systematic reviews often represent an exhaustive effort to find all related information in a given area.

Disadvantages

- (i) The disadvantage of systematic reviews is that they are only as good as the studies they include
- (ii) there is considerable variability in the quality and comprehensiveness of systematic reviews that are available. Much of this stems from a lack of commonly accepted methodology for conducting and writing systematic reviews.
- (iii) there is publication bias because popular search techniques to identify studies are inherently limited by the fact that unpublished studies are unaccounted for in any review.

narrative review of multiple studies

Advantages:

- (i) provide a detailed qualitative discussion, usually by an expert with years of experience.

Disadvantages:

- (i) evidence used to support the author's positions is not collected, evaluated, & compared in an organized and reproducible manner. That information is complete or that it is judged in an unbiased manner cannot be assured.
- (ii) review articles and textbook chapters are not generally subject to vigorous review and therefore may be the least reliable sources of information

phases of trials

Phase I clinical trials

- test a new biomedical intervention in a small group of people (e.g., 20-80) for the first time to evaluate safety (e.g., to determine a safe dosage range and to identify side effects).

Phase II clinical trials

- study the intervention in a larger group of people (several hundred) to determine efficacy and to further evaluate its safety.

Phase III studies

- investigate the efficacy of the intervention in large groups of human subjects (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions as well as to monitor adverse effects, and to collect information that will allow the intervention to be used safely.

Phase IV studies

- are conducted after the intervention has been marketed.
- These studies are designed to monitor effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use