



Simplifying the concept of level of evidence in lay language for all aspects of learners: In brief review



Abdullah Al Noman^a, Onusree Sarkar^{a,*}, Tanzia Mohsin Mita^a, Khadiza Siddika^a, Fahmida Afrose^b

^a School of Pharmacy, Brac University, 66 Mohakhali, Dhaka, 1212, Bangladesh

^b Department of Pharmacy, Varendra University, Rajshahi, 6204, Bangladesh

HIGHLIGHTS

- The evidence pyramid stratifies study designs based on their susceptibility to bias, with systematic reviews and meta-analyses providing the highest quality evidence.
- Randomized controlled trials establish causality but can be expensive, unethical, or infeasible.
- Observational studies like cohort and case-control analyses establish correlations but lack experimental rigor.
- Case reports and expert opinion offer lower quality evidence but generate hypotheses.
- There is no rigid hierarchy, as the appropriateness of evidence depends on the clinical context. Clinicians must synthesize the most rigorous evidence tailored to the scenario.

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ABSTRACT

The level of evidence is a fundamental structure for assessing the excellence of evidence while making healthcare choices. It assesses medical research according to its structure, credibility, and relevance. The different degrees of proof are frequently represented as a triangle shape, with the most powerful proof on the highest point. The pyramid is divided into two primary parts: refined data (systematic reviews, meta-analyses) that combines information from multiple studies, and raw data (randomized trials, cohort studies, case series) that consists of original research. Systematic evaluations condense results from various investigations on a subject using thorough, replicable approaches. Meta-analyses mathematically integrate information from similar research studies. Case studies provide information about a specific patient. Case-control studies examine the occurrences in separate groups of people who have a particular illness and those who do not. Randomly assigned intervention and control groups are compared in randomized controlled experiments to observe the differences in their outcomes. Cohort studies track groups over a period to investigate connections between factors and results. The upper levels of the pyramid are typically seen as more trustworthy proof because of thorough combination or research structure. However, every level provides valuable information. Recognizing the positive aspects of various research methods enables individuals to assess the credibility of information when making choices related to healthcare.

* Corresponding author.

E-mail address: onusree.sarkar@g.bracu.ac.bd (O. Sarkar).



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1. Introduction

The level of evidence is a basic diagram that aims to explain how to analyze different levels of evidence while making decisions about one's health. It helps to evaluate the results of each study design based on the relative strengths and shortcomings of each design.¹ (see Fig. 3)

Levels of evidence commonly referred to as the hierarchy of evidence, is a system for ranking medical studies. It is determined by the design's quality assessment, validity, and applicability, also known as generalizability, to broader clinical groups.²

The levels of evidence can be represented visually by a pyramid model. Each level of the pyramid, from bottom to top, shows the quality and quantity of available evidence. Stronger evidence is presented at a higher position on the pyramid. Every level uses information and analysis that was initially made in the lower layers. This pyramid (Fig. 1) typically has two or three sections. The top level contains the filtering and consolidation of information. The conclusions or suggestions of these products are typically the most trustworthy. This section consists of systematic reviews, meta-analyses and critical appraisal of all relevant RCTs (randomized controlled trial). The next level includes unfiltered or raw data from well-designed studies, randomized controlled trials, cohort studies, case-controlled studies, case series, and case reports. A well-constructed study can provide a statistically and clinically significant result and eliminate potential bias. These could be examined collectively for a meta-analysis or systematic review (see Fig. 2).

In some models there is an additional segment at the bottom of the pyramid for background information and expert opinion. It is the most basic type of evidence that does not include data. But, information from authority opinions or expert committee reports may still provide vital insight into concerns.³ The purpose of this research is to offer a brief but complete summary of the different levels of proof and how they are used to assess the excellence of published research. This will help healthcare experts make knowledgeable clinical choices that are based on solid evidence.

2. Filtered vs unfiltered information

As we mentioned, from the top to the base of the pyramid, it consists of 7 sections stacked on top of each other. Based on their sources all of them fall under 2 types of evidence based information called filtered and unfiltered information. In the pyramid top 3 sections; Section 1, Section 2, Section 3 fall under filtered Information. The next 3 sections from fourth through sixth are under unfiltered Information. The base of the pyramid which contains background information and expert opinion is not a filtered or unfiltered resource.⁴

Filtered resources are also known as secondary information which derives from the selective screening of the primary sources. The section only includes synthesized evidence from higher level information. They assess the quality of studies and thus help to make informed decisions and recommendations for practice in patient care.⁵ For instance: the main

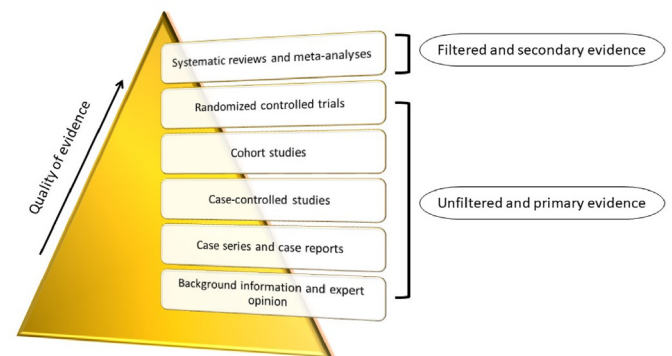


Fig. 1. Levels of evidence pyramid.

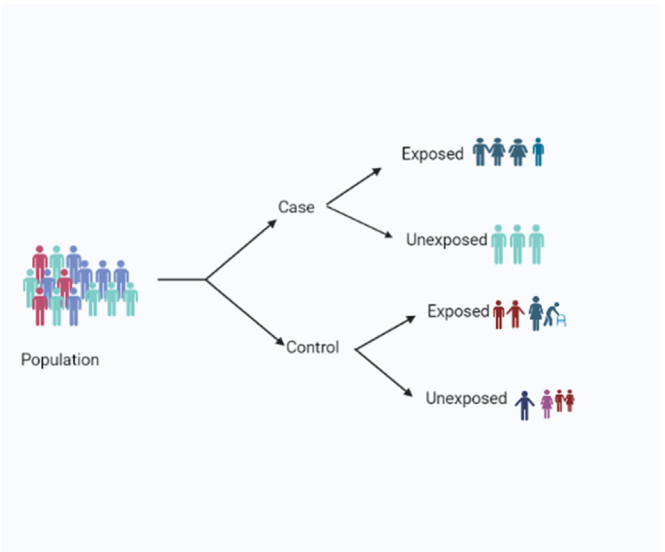


Fig. 2. Case control study-quantitative study design.

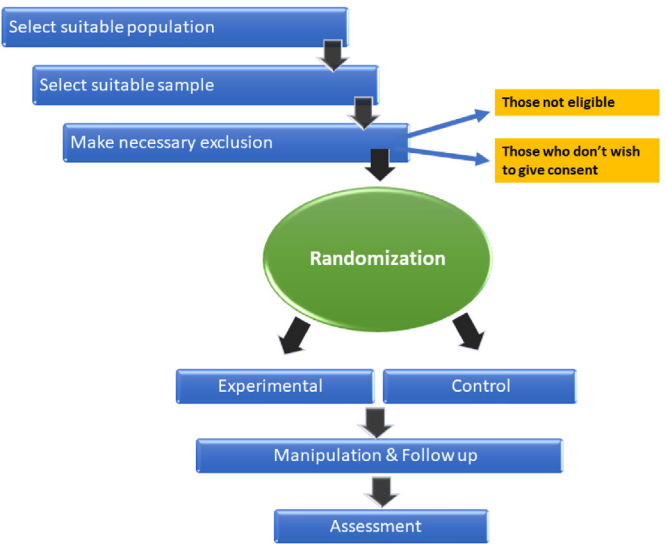


Fig. 3. Designing the randomized controlled trail.

types of filtered databases are:critically-appraised individual articles, critically-appraised topics and systematic reviews. All of them can be used as the strongest level of evidence. So, practitioners do not need to analyze the quality of the article to use it as the evidence.

Unfiltered literature, sometimes when working with our topic we may not get available information in the filtered literature. In these circumstances we have to look for the primary or unfiltered database. As unfiltered resources have a huge database having most current as well as a large number of articles, while using them the validity and reliability must be made sure to find the best knowledge.¹ For instance: for practice in specific patient care, when no filtered information is available or fit in our case we need to search for individual studies and journal articles. As most of the current journal articles are not evaluated, the practitioner has to analyze the quality of the article to use it as the evidence.

3. Systematic review and meta-analysis

A systematic review is an overview of clinical research that uses repeatable techniques to comprehensively explore, analyze, and summarize a topic.⁶ It summarizes various basic research that are related by

minimizing preconceptions and arbitrary errors. For this reason, systematic reviews can produce a statistical synthesis called meta-analysis if the studies are comparable enough. Overviews are a common name for systematic reviews. Systematic reviews might also highlight areas of misunderstanding. The results can then be utilized to direct additional research. Clinical testing (diagnostic, screening, and prognostic), public health initiatives, adverse (damage to a person) impacts, economics (expense) assessments, as well as why treatments are effective are typically the subjects of systematic reviews.⁷ The Cochrane Database of Systematic Reviews is the most widely used resource of systematic reviews. Participants of the Cochrane Collaboration, a worldwide not-for-profit organization that aims to assist individuals in making well-informed medical choices by planning, establishing, and helping to promote the connectivity of systematic reviews of the impacts of treatment options.⁸

The purpose of a meta-analysis is to establish a single assessment, for example the effect of a risk factor or treatment, by combining data from several research papers on the same subject. It refers to the data evaluation of a large number of studies and discoveries from various investigations with the intention of integrating the results. In general usage, the term “meta-analysis” refers to the complete spectrum of quantitative approaches applied in the field of literature. Assessments of studies are known as meta-analyses.⁹ The justification for meta-primary analysis is that it reduces the amount of information by collecting data from several sources, enhances future research design, and provides basic guidelines. In addition, it assures generalizability, helps ensure linkages are regular, identify the reasons abnormalities, assesses the data, and aids in the correct application of current data. Utilizing specialized techniques improves the precision of risk assessment.⁸

So, systematic review will apply to the full procedure of gathering, analyzing, and summarizing all relevant information, whereas meta-analysis may apply to the quantitative tool used to remove and combine data in order to arrive at a conclusive conclusion.⁸

4. Case series and reports

Compared to the more effective case-control study or randomised controlled trial, case series often contain a significantly smaller number of patients (RCT). In this strategy, patients who have received a treatment and whose exposure is known are followed prospectively to find new diseases or side effects. Retrospective case series are also possible; in this case, medical records are searched to find a connection between an exposure and a disease.¹⁰ A case series is a collection of linked case studies or case reports. A case study, which is sometimes called a case report, is a detailed look at a single person or group.¹⁰ Using a case study or case report is appropriate in the following situations:

When a new sickness or condition is treated and aberrant or deviant behavior develops or there is an unexpected side effect.

5. Case-control study

According to National Cancer Institute,¹¹ “A study that compares two groups of people: those with the disease or condition under study (cases) and a very similar group of people who do not have the disease or condition (controls). Researchers study the medical and lifestyle histories of the people in each group to learn what factors may be associated with the disease or condition. For example, one group may have been exposed to a particular substance that the other was not. Also called retrospective study”.

When compared to other types of studies, case-control studies have some advantages. They are quick, cheap, and easy compared to other things.¹² They are especially good for looking into outbreaks and studying rare diseases or results.^{12, 13} A study of endophthalmitis after surgery on the eye would be an example of this. When a disease is spreading, answers need to be found quickly. An example would be a study of risk variables for uveal melanoma or ocular ulcers. Since

case-control studies begin with people who already have the result, it is possible to recruit enough patients with a rare condition to participate.¹² Case-control studies have some flaws, but the fact that they can give quick answers or look into rare events may make up for them.¹⁴ Due to how quickly they can be done, they may also be the best way to start looking into a possible risk factor for a common condition.^{15, 16} The results can then be used to justify a more expensive and time-consuming longitudinal study.

6. Randomized controlled trials

Randomized controlled trials (RTC) is one of the experimental or intervention studies. It is an approach where study is carried out are under the direct controlled of the investigation. RCTs are quantitative, comparative, controlled experiments in which investigators study two or more interventions in a series of individuals who receive them in random order. The RCT is one of the simplest and most powerful tools in clinical research.¹⁷ Because it considered.¹⁸

- Many sources of bias as possible are removed from the process.
- Previous scientific errors have taught where can go wrong, drawing false conclusions from the research.
- It can eliminate major errors
- New and unknown therapies, it is the best way to evaluate

Basic steps of conducting Randomized controlled trails are given below.¹⁸

1. Drawing up a protocol,
2. Selecting references and experimental population,
3. Randomization,
4. Manipulation or intervention,
5. Follow-up,
6. Assessment of outcome

For instance, in a randomized controlled trial conducted at the diabetes care clinic of the Capital hospital Islamabad in Pakistan, the effects of a 6-month pharmacist-led educational intervention on glycemic control, diabetes self-care practices, and disease awareness were compared between 80 adult T2DM patients (age >30 years) with poorly controlled T2DM (HbA1c > 7 %). After doing the trials, it's clear that T2DM patients need to do the best self-care activities to control their blood sugar. The goal of this study is to help people with T2DM who don't take good care of themselves and are at a higher risk of late complications from the disease.¹⁹

7. Cohort study

Cohort studies are an example of observational studies, which means that there is no intervention among the subjects.²⁰ It is also a kind of longitudinal study in which study participants are monitored over time.²¹ Both prospective and retrospective cohort studies can employ previously acquired data or medical records. Prospective cohort studies collect fresh data throughout time. This kind of study evaluates whether a group of individuals who share a trait or exposure produce an interest-related result. A study that determines which participants smoke and then examines the risk of lung cancer in both smokers and non-smokers several years later is an illustration of a prospective cohort study.¹⁹

8. Conclusion

To sum up, the levels of evidence play a crucial role in assessing the reliability of published information for guiding clinical decisions. This evidence pyramid categorizes research design methodologies that have different levels of vulnerability to bias. Systematic reviews and meta-analyses are at the top, combining results from various strict

randomized controlled trials to generate summarized data with limited prejudice. Random trials prove a cause-and-effect relationship between interventions and results, but they can encounter challenges in terms of practicality, morality, cost, and standard. Lower tiers consist of unregulated clinical information and professional viewpoints with growing probabilities of prejudice, nevertheless, they present more economical, prompt, provisional methodologies to steer forthcoming investigations. Instead of a strict chain of command, this complex pyramid involves subtle maneuvering to choose appropriate information that is customized for the clinical situation. The perfect medical professional combines the best quality information to make careful, fact-based choices that enhance patient treatment. A simplified comprehension of this pyramid can give healthcare experts the ability to avoid excessive dependence on less reliable information or personal judgments. Given the scarcity of reliable evidence for clinical inquiries, this framework offers a guide for healthcare professionals to navigate the vast field of biomedical research. It helps clinicians utilize the currently accessible data effectively to enhance patient outcomes.

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Data availability

This review article did not generate or analyze any primary data. The findings are based solely on the authors' expert analysis and synthesis of secondary data from previously published literature available in the public domain. The referenced works constituting the evidence base for this review are properly cited within the manuscript text. Any additional information required to support the conclusions of this review is available from the corresponding author upon reasonable request.

CRedit authorship contribution statement

Abdullah Al Noman: Conceptualization, Formal analysis, Supervision. **Onusree Sarkar:** Methodology. **Tanzia Mohsin Mita:** Validation, Writing – review & editing. **Khadiza Siddika:** Project administration, Writing – review & editing. **Fahmida Afrose:** Investigation, Project administration, Resources, Software.

Declaration of competing interest

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References

1. Bares J. Stimson library LibGuides: evidence-based practice: evidence pyramid [cited 2023 Oct 31]; Available from: <https://amedd.libguides.com/c.php?g=476751&p=3259492>.
2. Murad MH, Asl N, Alsawas M, Alahdab F. New evidence pyramid. *Evid based med* [cited 2023 Oct 31];21(4):125–7. Available from: <https://pubmed.ncbi.nlm.nih.gov/27339128/>; 2016.
3. Levels of evidence in medical research [Internet]. [cited 2023 Oct 31]. Available from <https://openmd.com/guide/levels-of-evidence>.
4. James J. Academic guides: evidence-based research: levels of evidence pyramid [cited 2023 Oct 31]; Available from: <https://academicguides.waldenu.edu/library/healththevidence/evidencepyramid>.
5. Grimes David A, Schulz Kenneth F. *An Overview of Clinical Research: The Lay of the Land* [cited 2023 Oct 31]. 2002. [https://doi.org/10.1016/S0140-6736\(02\)07283-5](https://doi.org/10.1016/S0140-6736(02)07283-5).
6. Aromataris E, Pearson A. The systematic review: an overview [cited 2023 Oct 31]; 114(3):53–8. Available from: *Am J Nurs*; 2014. https://journals.lww.com/ajnonline/fulltext/2014/03000/the_systematic_review_an_overview.28.aspx.
7. Elliott JH, Synnot A, Turner T, et al. Living systematic review: 1. Introduction-the why, what, when, and how [cited 2023 Oct 31];91:23–30. Available from: *J Clin Epidemiol*; 2017. <https://research.monash.edu/en/publications/living-systematic-review-1-introduction-the-why-what-when-and-how>.
8. Gopalakrishnan S, Ganeshkumar P. Systematic reviews and meta-analysis: understanding the best evidence in primary healthcare, 2(1):9–14. Available from *J Fam Med Prim Care*; 2013. <https://pubmed.ncbi.nlm.nih.gov/24479036>.
9. Lee YH. *An Overview of Meta-Analysis for Clinicians* [cited 2023 Oct 31];33(2):277–83. Available from: *Korean J Intern Med*; 2017. <https://typeset.io/papers/an-overview-of-meta-analysis-for-clinicians-2ahk2urwii>.
10. RLO. Case series and cross-sectional studies [Internet]. [cited 2023 Oct 31]. Available from: https://www.nottingham.ac.uk/helmopen/rlos/ebp/case_studies/page_one.html.
11. Definition of case-control study - NCI dictionary of cancer terms - NCI [Internet]. [cited 2023 Oct 31]. Available from <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/case-control-study>.
12. Seddon JM, Gragoudas ES, Glynn RJ, Egan KM, Albert DM, Blitzer PH. Host factors, UV radiation, and risk of uveal melanoma. A case-control study. *A M A Archives of Ophthalmology*. 1990;108(9):1274–1280.
13. Lischko AM, Seddon JM, Gragoudas ES, Egan KM, Glynn RJ. Evaluation of prior primary malignancy as a determinant of uveal melanoma: a case-control study. *Ophthalmology*. 1989;96(12):1716–1721.
14. Lewallen S, Courtright P. *Epidemiology in Practice: Case-Control Studies* [cited 2023 Oct 31];11(28):57. Available from: <https://pmc/articles/PMC1706071/>. 1998.
15. Rees AM, Austin MP, Owen C, Parker G. *LibGuides: Quantitative Study Designs: Case Control* [cited 2023 Oct 31];166(2–3):254–9. Available from; 2009. <https://deakin.libguides.com/quantitative-study-designs/casecontrol>.
16. Rees AM, Austin MP, Owen C, Parker G. Omega-3 deficiency associated with perinatal depression: case control study. *Psychiatry Res*. 2009;166(2–3):254–259.
17. Randomized clinical trials | definition of Randomized clinical trials by Medical dictionary [Internet]. [cited 2023 Oct 31]. Available from <https://medical-dictionary.thefreedictionary.com/Randomized+clinical+trials>.
18. Randomized controlled trials | PPT [Internet]. [cited 2023 Oct 31]. Available from <https://www.slideshare.net/NabeelaBasha/randomized-controlled-trials-68651612>.
19. Hariton E, Locascio JJ. *Randomised Controlled Trials – the Gold Standard for Effectiveness Research* [cited 2023 Oct 31];125(13):1716–1716. Available from; 2018. <https://onlinelibrary.wiley.com/doi/full/10.1111/1471-0528.15199>.
20. Grimes DA, Schulz KF. *Cohort Studies: Marching towards Outcomes* [cited 2023 Oct 31];359(9303):341–5. Available from; 2002. <https://pubmed.ncbi.nlm.nih.gov/11830217/>.
21. Belbasis L, Bellou V. Introduction to epidemiological studies [cited 2023 Oct 31]; 1793:1–6. Available from: *Methods Mol Biol*; 2018. <https://pubmed.ncbi.nlm.nih.gov/29876887/>.