# **EVIDENCE BASED PRACTICE**

## Abstract

Evidence-based medicines involves providing healthcare using the best available research evidence for assisting clinical decision making. Evidence-based medicines fundamental components consists of the following:

- 1. Draft clinical query.
- 2. Gathering the most significant data.
- 3. Analyzing the validity of the gathered data.
- 4. Implementing the evidence in practice while considering professional expertise and the patient's preferential treatment as factors.

A precise assessment of the clinical question is the first step towards identifying the optimal response. The four PICO elements should be taken into account while designing questions about an intervention's efficacy. Three levels of complexity exist for summaries of the evidence is: Primary research, Systematic reviews, Summaries and Guidelines. The research question will establish the best research study design. Practicians ought to have the abilities required to assess research publications critically that are pertinent to their field of expertise. Critical evaluation abilities improve autonomy and expertise in medical practise. Evaluating both external validity is the main goal of critical appraisal. As implementing EBM adequately, a workable plan for modifying clinical conduct according to requirements should be included. Information access is one of the many requirements for this implementation.

**Keywords:** The four PICO elements should be taken into account while designing questions about an intervention's efficacy.

# Authors

## Dr Kiron SS, MPharm

PhD Professor Department of Pharmacy Practice College of Pharmaceutical Sciences Government Medical College Kannur, India. drkironss@gmail.com

## Ms. Theertha S, Pharm D

Pharm D (Intern) Department of Pharmacy Practice College of Pharmaceutical Sciences Government Medical College Kannur, India. theerthakannan2000@gmail.com

#### Ms. Krishna D S, Pharm D

Pharm D (Intern) Department of Pharmacy Practice College of Pharmaceutical Sciences Government Medical College Kannur, India. krishnads466@gmail.com

## Ms. Megha S, Pharm D

Pharm D (Intern) Department of Pharmacy Practice College of Pharmaceutical Sciences Government Medical College Kannur, India. meghasomanath24@gmail.com

## I. INTRODUCTION

The definition of Evidence-Based Medicine states that it integrates clinical knowledge, patient values, and the best available evidence when making decisions about a patient's medical care. Evidence based medicine (EBM) is the conscientious, explicit, judicious and reasonable use of modern, best evidence in making decisions about the care of individual patients. EBM integrates clinical experience and patient values with the best available research information. Care for one's own patients necessitates the need for clinically essential knowledge regarding diagnosis, prognosis, therapy, and other clinical and medical difficulties. Evidence-based medicine is an ongoing, self-directed learning process [1].

EBM recommends focusing on reading topics linked to particular patient problems rather than routinely scanning the contents of hundreds of journals for intriguing papers. To stay up to date with the literature, it may be more efficient to develop clinical queries before examining current databases. Evidence-based medicine "transfigure the academic practice of reading and evaluating literature into the practical practice of applying it to help specific patients, while simultaneously improving the physician's knowledge [1]. With philosophical roots dating back to mid-1800s Paris and beyond, evidence-based medicine continues to be a hot topic for physicians, public health professionals, buyers, designers and the public. Meta analysis and systematic reviews has helped get better evidence for the research by critically sorted and later summarized [2]. Computerized decision support tools for clinicians make it easy to combine individual patient data with the best available research data [3].



Figure 1: Flowchart of Evidence Based Practice

The practice of EBM involves five essential steps; which includes converting information needs into answerable questions. To seek out the best evidence to be able to answer those questions, the evidence is assessed critically for its probativeness and usefulness and the results of the examination are applied to clinical practice. Converting a clinical problem into an answered question could be one of the trickiest parts of using EBM. Many questions may come up when we encounter a patient with a specific issue, and we would like answers. These inquiries are typically complicated and poorly organised, and they may not even be clear to us. A well-crafted clinical query should be the first step in the EBM process. As a result, we should practice turning our informational wants into questions that can be answered [4]. A good clinical question should have four (or sometimes three) essential components: the patient or problem in question; the intervention, test, or exposure of interest; comparison interventions (if relevant); the outcome, or outcomes, of interest [4].

Applying the standard of PICO criteria, where 'P' denotes 'population' or 'patients', 'I' 'intervention' or 'exposure', 'C' 'comparison', and 'O' 'outcome'. After creating a clinical questionnaire, it is important to confirm its category in order to understand the kind of data the question will need. Diagnosis, prognosis, therapy, and risk (factors) are frequent categories of inquiries, and the category determines the type of study required to provide an answer. A cross-sectional study or a case-control study is the best research strategy to address a clinical topic if it falls under the diagnosis category. Cohort studies are useful for clinical questions in the field of prognosis. A randomized controlled study or a thorough literature analysis of randomized controlled studies is required if the category is therapy. A case-control study, cohort study, or randomized controlled trial is required if a clinical topic falls under the category [5].

Patient Population: In order to get an adequate informed clinical decision, the trial group can be either defined broadly or narrow that would affect the results. Specific number of individuals are required for an inclusive study. Intervention: It is important to define the metric under consideration. A similar approach is used to assess questions related to diagnosis or prognosis. Comparison: In randomized treatment trials the group's effect can be controlled [6].

Outcomes: Patient's outcome whether positive or negative should be considered. Outcome must be defined and any changes must be noted [6].

| PICO                       | Description             | Example               |
|----------------------------|-------------------------|-----------------------|
| P: Patients or populations | What details do I seek  | Patients undergoing   |
|                            | regarding then subjects | sedation therapy      |
|                            | groups?                 |                       |
| I: Intervention or         | Which treatment results | Combination therapy   |
| exposure                   | do I need?              | within propofol and   |
| _                          |                         | others sedative       |
| C: Comparison or control   | What is an evaluation   | Propofol mono therapy |
|                            | alternative where an    |                       |

## Table 1: Shows an example of PICO-SD specified for a question established by the Propofol Task Force Team

|            | intervention is not<br>carried out or a different<br>intervention technique is<br>utilized? |                         |
|------------|---|-------------------------|
| O: Outcome | What is the impact?   | Risk of adverse effects |

PICO-SD example (Table 1)

## **II. EVIDENCE SOURCE**

Despite the ease with which medical information is currently available, quick research skills are still essential. Depending on the purpose of the information search, several methodologies are applied. A key component of EBM is the ability to quickly and accurately respond to a specific clinical query. To master this method, most physicians do not require complex technical knowledge. It would be challenging and simply impossible for an individual physician to address all crucial clinical questions by reading, evaluating, and summarizing the evidence. Entrusting the task to reliable sources is vital [6]. Many sources are available online for this purpose, through an online survey an attempt was made to determine the frequency of usage of Wikipedia among medical students. Students often engage with them instead of more established authoritative resources since they have simple user interfaces [7].

Traditional patient care practitioners use data from all the four phases of the healthcare research process. Those who employ the concepts of EBP, however rely on information collected during the clinical research stage, to guide their clinical judgement. Development of EBP is crucial because practitioners who utilize EBP use information from the literature base than just clinical experience and pathophysiology. The reports of primary research trials and investigations as well as secondary reports that synthesize, analyse and present data from numerous research studies are both included. Systematic review articles, meta-analysis, economic assessments and clinical practice recommendations are few examples of secondary reports [8].

A choice is made between a database, which comprises of articles and references; these include Cochrane library, MEDLINE, EMBASE. A navigation portal with a build in search engine such as PubMed are included [6]. In MEDLINE, search techniques can find legitimate studies with a significant level of specificity and sensitivity. Combing MeSH terms and text words while trying to find articles that match methodological criteria enhances the sensitivity of methodological search terms in MEDLINE [9]. The Cochrane Library, which was created by the Cochrane Collaboration, is a more reliable source of data on clinical research. The collaboration is a global volunteer organization and network of medical professionals, patients and the members of the general public who are committed to gathering references to reports of clinical research for therapy studies, developing broadened abstracts for meta-analysis and systematic reviews, and there authoring and periodic updating [8].

Characteristics of reliable data for clinical research includes; readily accessible data for therapeutic decision making. Data should be directed to particular clinical question. Portal and focused on the most recent information [6]. Multiple databases may be accessible

through a single access gateway. Access portals might also offer tools to coordinate citations and creating citation maps. Citation maps are database of citation acquaintances between different data. These might be either incoming including more recent reports citing the index piece, outgoing including publications cited in a certain paper's bibliography. Analysing citation maps is an ethical way of literature search, yielding unforeseen and beneficial discoveries [6].

The COSI (Core, Standard, Ideal) model, which is provided by the US NLM, serves as the framework for the literature review. The phase Core refers to the essential components of a literature review, or the bare- borne database needed in a matter of minutes to identify the best outcome. A manual search of core journals as well as searches of databases that are not "core" are included in the term "Standard". It refers to the customary scope of the literature review. Ongoing trials, unpublished research data, grey literature make up the "Ideal" portion [10]



# Figure 2: Cosi Model

Pre-defined search phrases created for a particular purpose are called search filters. These are specific to both database and portals. The filters are platform specific which meant that for seemingly equivalent searches, the results could be substantially distinct [6]. In order to understand hierarchies of evidence, we have set out, in order to discover the best evidence, you need to be able to detect high level of information and the virtues of starting a data search with more extensive processing [11].

## **III.EVIDENCE BASED RESOURCES**



Figure 3: Resources

- 1. Original Research (Primary): Data from individual or groups of subjects with welldefined physicians and geography or other variables are collected for primary research. When conducting primary research, the sequence of evidence is considered to lessen the likelihood of bias. The research question will determine the most effective study design. Most effective method being Randomized Control Trial for determining the benefits and risks of an intervention. Prospective cohort are effective method for determining the risk factors for disease and prognosis [6].
- 2. Systematic Review and Meta analysis: The most effective evaluation is those that follow a systematic process. Compared to typical reviews, they are more scientifically organized and translucent. To eliminate publication bias, reviews take special attention to include all compelling data [12]. The most sophisticated types of documents are summaries and guidelines. Guidelines should ideally be a synthesis of original research, clinical experience, systematic reviews and patient preferences. The greatest summaries

and recommendations are a thorough synthesis of the best available data. The quality of the published guidelines varies greatly. There are several instances of guidelines on the same subject providing contradicting advice [6,13].

Grades of Recommendation, Assessment, Development and Evaluation (GRADE) system offers guidelines for ranking evidence quality and grading recommendation strength in the sector of health care [14]. Strong and weak recommendations can be distinguished by GRADE. Strong recommendations eliminate the need for a thorough evaluation of the evidence with each patient since they symbolize a clear preference for one alternative and should be applicable to virtually all patients [13].

#### **IV. VALIDITY OF THE EVIDENCE**

Clinicians need to be capable of analyzing research publications that are crucial to their field. Skills in thoughtful assessment help physicians gain autonomy and expertise. Critical thinking abilities can also aid physicians in making more informed decisions on the sources of information they implement, opting for those that provide clear guidelines for evaluating the strength of the evidence. Through the facilitation of focused attention on exceptional articles and omission of weak ones, these abilities can also increase the effectiveness of casual reading [6].

There are a variety of suggestions that outline requirements for carrying outline reporting various types of studies. According to the type of study, the set of criteria endorsed by the International Committee of Medical Journal Editors (ICMJE) can help with the evaluation of specific studies critically [6]. The PRISMA Statement was developed to help authors publish systematic reviews and meta-analyses more effectively. PRISMA can be used as a foundation for publishing systematic reviews of various kinds of research, notably evaluations of therapies, it has been mostly applied to randomized trials. PRISMA may also be beneficial for evaluation [15].

To enhance the reporting of randomized controlled trials, the Consolidated Standards of Reporting Trials (CONSORT) Statement is applied globally [16]. The SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) suggestions can be widely used to help with protocol design, materials, and implementation, trial registration, appraisal and potency and ultimately, transparency for patient care [17]. The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) initiative, which aims to improve the reporting of observational studies in epidemiology, has produced guidelines on what information should be included in an observational study's accurate and comprehensive report [18]. The STARD (Standards for Reporting of Diagnostic Accuracy) initiative's goal is to raise the standard of diagnostic study reporting. Authors may utilize the items on the checklist and the flowchart to describe key aspects of the study's design and conduct, test execution and outcomes [19]. The TRIPOD (Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis) Statement intends to enhance the reporting of research creating, validating, or updating a prediction model, whether it is used for prognostic or diagnostic reasons. Regardless of the research techniques employed, the TRIPOD statement strives to increase the transparency of publishing a prediction model study [20].



Figure 4 : Evaluating both Internal and External validity is the main goal of critical evaluation

- 1. Internal Validity: An analysis of a study's internal validity determines if the methods used in its determines if the methods used in its planning, execution and analysis provide reliable responses to the research objectives. Internal validity isn't a number that can be calculated; it is a subjective concept. The presence of systematic error is investigated by looking at internal validity. Such systematic inaccuracy may be caused by selection bias, performance bias, detection bias or attrition bias [21].
- 2. BIAS: Any systematic mistake that can give a false impression of the genuine effect is considered biased. With the intention of decreasing prejudice, randomized trials are done and well conducted studies typically have a minimal risk of bias. Clinical trial conduct errors, however have the potential to skew the outcomes. Chance, which is a random error that exists in every observation. By examining a large number of patients, the possibility of chance providing inaccurate results can be reduced. P-value are sometimes misconstrued as the like hood that the results are the result of chance. Instead, p-values

indicate the likelihood that the study would uncover a difference if the null hypothesis were true [6].

- **3.** External Validity: Examining a study's external validity reveals its finding may be applied to different context. Studies are based on samples and if the sampling was random and representative of the population, findings can be correctly generalization of the study's findings to that group. However, results might not apply to different groups. Therefore, research that limit concurrent treatment and exclude very ill and suicidal individuals, patients with personality disorders, substance abuse and other medical comorbidities, have a poor external validity. Low levels of external validity are also present in short term studies of patients who require months to years of treatment. Both internal and external validity are based on judgment [21].
- **4. Indirect Evidence:** practitioners may be predisposed to dismiss the evidence when a study includes a group that is somewhat different from the one that the EBM practitioner is interested in. in fact, when there is lack of direct data, this kind of indirect evidence can aid in informing medical decisions. However, there is typically less confidence in the projected conclusions than there would be if there were clear evidence.
- **5. Subgroup Analyses:** One tactic is to use subgroup analyses, which compare results based on various patient characteristics, when the study does not focus on the particular patient population of interest. To prevent making erroneous inferences, care should be used while evaluating the results of subgroup analysis. Potential issues comprise of: Reporting Bias, Multiple comparisons, Lower statistical power [6].

EBM practitioners should ask the following questions to reduce the possibility of obtaining inaccurate inferences from subgroup analysis:

- Can the apparent subgroup effect be explained by chance?
- Is the effect consistent across studies?
- Was the subgroup hypothesis one of a few developed beforehand with a clear direction?
- Is there strong evidence preexisting biological support?
- Is the evidence for the effect based on within or between study comparisons?
- Did the subgroup analysis have a plan before the information was gathered?
- How did each subgroup fare?
- Is the distinction between the groupings statistically tested? [22,23].

In particular, failing to specify subgroup analyses a priori and failing to test for effect modification, subgroup differences reported in randomized controlled trials frequently have shortcomings, few are corroborated in subsequent meta-analysis or randomized controlled trials [24].

## V. APPLYING EVIDENCE

We must determine if a piece of evidence may be applied to a specific patient or demographic once we have determined following critical appraisal that it is legitimate and significant. We must consider the patient's own values and circumstances when making this choice. To enable the patient or parents, or both, to make an informed choice, the evidence addressing both efficacy and hazards should be thoroughly reviewed. This method enables the development of a "therapeutic alliance" with the patient and the parents and is in line with the core tenet of EBM: the integration of solid evidence with clinical know-how and patient values [4].

Patients differ in terms of their values, interests, expectations, and circumstances because no two people are the same. Patients are frequently found in circumstances that are distinct from those that have been searched for and assessed. As a result, it might not be suitable to treat patients using the ideal evidence that was gathered and examined. Decisions in this situation should take into account the patient's situation as well as the accumulated evidence. Additionally, doctors with various levels of training, experience, and specialization may favour various therapy modalities. As a result, the retrieved data can be at odds with the preferred treatment strategy chosen by each practitioner. In such situations, conflicts could arise. In these situations, EBM might aid the patient in selecting an intervention or course of treatment [5].

The "know-do gap" is a discrepancy between the strongest evidence and actual practice occurs at regular intervals. There are many sources for the gap, including confusion about how results from large studies apply to specific patients, ignorance or distortion of the evidence, and inability to structure treatment in a way that advocates the use of evidence [25]. Lack of knowledge is the cause of inability to act in accordance with the best available evidence. But information by itself rarely modifies conduct [6]. Variations in initial risk- as indicated, ambiguity about whether the findings of large studies apply to a particular patient may restrict the use of evidence in practice. The response of patients in clinical trials often does not follow a predictable pattern; rather the outcome of treatment varies among patient. Treatment effect heterogeneity is synonym for this. In general, only meta-analysis of numerous trials or single trials that prospectively evaluate for distinctions in treatment effect across designated subgroups examine treatment effect heterogeneity [26]. Asymmetric distributions of treatment or side effects are also possible based on baseline risk, though less so than for treatment advantages. Regardless of baseline risk, all patients generally experience the same costs and hassles of treatment. Patients with low baseline risk for important outcomes can therefore have more negative side effects than positive side effect from treatments [27].

| Advantages                             | Disadvantages                             |
|--|---|
| Clinicians update knowledge base       | Time consuming                            |
| routinely                              |   |
| Improved understanding of research     | Informed overload                         |
| methods                                |   |
| Physician becomes more critical in use | Time needed for team conferencing,        |
| of data                                | planning and review                       |
| Increased confidence in management     | Requires financial sources to establish   |
| decisions                              | resource infrastructure- library, office, |
|  | computers etc                             |
| Better reading habits                  | May increase cost of care due to internet |

Table 2: Advantages and Disadvantages of EBM

|                                      | cost, subscription costs- online and paper |
|--------------------------------------|--|
|                                      | resources                                  |
| Provides framework for group         | Requires programs, software                |
| problem solving, team generated      | information, CD-ROMS                       |
| practice                             |  |
| Transforms weakness or paucity of    | Exposes gaps in the evidence, may          |
| knowledge in positive change         | expose current practice as obsolete or     |
|                                      | dangerous                                  |
| Can be learned by non-clinicians and | Requires computer skills (but can be       |
| other health care workers            | done with minimal computer literacy and    |
|                                      | skill)                                     |

## **VI. EVALUATION**

After applying the evidence, the data, intervention and the EBM process are evaluated. The evaluation takes into account the importance of the quantity and quality of available evidence, the difficulty of obtaining evidence and results, the cost of the application, the rate of patient response and compliance and the difficulty of treatment. Application, clinical outcomes, impact of actual application and experienced changes in physician thinking and skills. There should be a feedback mechanism for the knowledge gained during the actual implementation process of the evidence so that others can perform the process well and the EBM implementation strategy can be improved. Additionally, doctors with various levels of training, experience, and specialization may favor various therapy modalities. As a result, the retrieved data can be at odds with the preferred treatment strategy chosen by each practitioner. In such situations, conflicts could arise. In these situations, EBM might aid the patient in selecting an intervention or course of treatment [28]. In order to determine whether an evidence-based practice has improved it is necessary to determine why some patient's responses were different from those anticipated and make any necessary changes [29].

Current application of EBM:

- 1. EBM is currently widely used by lawmakers, policymakers, and payers in the United States in a number of different contexts.
- 2. EBM frequently plays a significant role in performance bonuses that pay doctors for meeting preset goals.
- 3. The design of Health plan benefit is another area where EBM is becoming more significant. Health plans, both public and private, use evidence-based guidelines to determine which clinical procedures, treatments, medical devices and drugs are covered.
- 4. The creation of continuing medical education (CME) content benefits from the use of EBM [30]



Figure 5: The steps that are required to be taken from the creation of evidence to its implementation

## VII. CONCLUSION

EBM is a set of principles, tools and methods designed to ensure that medical decisions, guidelines and practices are, to the greatest extent possible, based on and consistent with good evidence of effectiveness and serve better patient care. Limitations of EBM includes; Lack of evidence (shortage of studies). Difficulty in applying evidence to care of a particular patient. Barriers to the practice of high-quality medicine. Lack of time to learn and practice EBM (Promotes lifelong learning through better focus). Lack of physician resources for instant access to evidence (EBM has worldwide applicability). Language barriers and lack of skills. Physician attitude can be the greatest limitation. Interpreting and understanding evidence syntheses, systematic reviews, and other analytical literature is a complex task. It is important that pain physicians understand the goals, principles, and processes of EBM in order to improve its applications.

#### REFERENCE

- [1] Masic I, Miokovic M, Muhamedagic B. Evidence based medicine new approaches and challenges. Acta Inform Med [Internet]. 2008 [cited 2023 Jul 10];16(4):219–25. Available from: http://dx.doi.org/10.5455/aim.2008.16.219-225
- [2] Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. BMJ [Internet]. 1996 [cited 2023 Jul 24];312(7023):71–2. Available from: http://dx.doi.org/10.1136/bmj.312.7023.71
- [3] Masic I, Miokovic M, Muhamedagic B. Evidence based medicine new approaches and challenges. Acta Inform Med [Internet]. 2008 [cited 2023 Jul 24];16(4):219–25. Available from: http://dx.doi.org/10.5455/aim.2008.16.219-225
- [4] Akobeng AK. Principles of evidence based medicine. Arch Dis Child [Internet]. 2005;90(8):837–40. Available from: http://dx.doi.org/10.1136/adc.2005.07176
- [5] Kang H. How to understand and conduct evidence-based medicine. Korean J Anesthesiol [Internet]. 2016 [cited 2023 Jul 23];69(5):435–45. Available from: http://dx.doi.org/10.4097/kjae.2016.69.5.435
- [6] Arthur T Evans, MD, MPH, Gregory Mints, MD, FACP. Evidence based practice [Internet]. Uptodate.com. 2023 [cited 2023 Jul 19]. Available from: https://www.uptodate.com/contents/evidencebased-medicine

- [7] Allahwala UK, Nadkarni A, Sebaratnam DF. Wikipedia use amongst medical students new insights into the digital revolution. Med Teach [Internet]. 2013 [cited 2023 Jul 19];35(4):337. Available from: https://pubmed.ncbi.nlm.nih.gov/23137251/
- [8] McKibbon KA. Evidence-based practice. Bull Med Libr Assoc [Internet]. 1998 [cited 2023 Jul 24];86(3):396–401. Available from: https://pubmed.ncbi.nlm.nih.gov/9681176/
- [9] Haynes RB, Wilczynski N, McKibbon KA, Walker CJ, Sinclair JC. Developing optimal search strategies for detecting clinically sound studies in MEDLINE. J Am Med Inform Assoc [Internet]. 1994 [cited 2023 Jul 19];1(6):447–58. Available from: http://dx.doi.org/10.1136/jamia.1994.95153434
- [10] Kang H. How to understand and conduct evidence-based medicine. Korean J Anesthesiol [Internet]. 2016 [cited 2023 Jul 20];69(5):435–45. Available from: http://dx.doi.org/10.4097/kjae.2016.69.5.435
- [11] Kamath S, Guyatt G. Importance of evidence-based medicine on research and practice. Indian J Anaesth [Internet]. 2016 [cited 2023 Jul 21];60(9):622–5. Available from: http://dx.doi.org/10.4103/0019-5049.190615
- [12] Ethan Balk, MD, MPH Peter A L Bonis. Systematic review and Meta analysis [Internet]. Uptodate.com. 2021 [cited 2023 Jul 21]. Available from: https://www.uptodate.com/contents/systematic-review-andmeta-analysis
- [13] Neumann I, Santesso N, Akl EA, Rind DM, Vandvik PO, Alonso-Coello P, et al. A guide for health professionals to interpret and use recommendations in guidelines developed with the GRADE approach. J Clin Epidemiol [Internet]. 2016 [cited 2023 Jul 21];72:45–55. Available from: https://pubmed.ncbi.nlm.nih.gov/26772609/
- [14] Gordon H Guyatt, Andrew D Oxman, Holger J Schünemann, Peter Tugwell, Andre Knottnerus. GRADE guidelines: A new series of articles in the Journal of Clinical Epidemiology [Internet]. Jclinepi.com. 2010 [cited 2023 Jul 21]. Available from: https://www.jclinepi.com/article/S0895-4356(10)00329-X/fulltext
- [15] Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med [Internet]. 2009 [cited 2023 Jul 21];6(7):e1000097. Available from: http://dx.doi.org/10.1371/journal.pmed.1000097
- [16] Schulz KF. CONSORT 2010 statement: Updated guidelines for reporting parallel group randomized trials. Ann Intern Med [Internet]. 2010;152(11):726. Available from: http://dx.doi.org/10.7326/0003-4819-152-11-201006010-00232
- [17] Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med [Internet]. 2013 [cited 2023 Jul 22];158(3):200–7. Available from: http://dx.doi.org/10.7326/0003-4819-158-3-201302050-00583
- [18] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ [Internet]. 2007 [cited 2023 Jul 22];335(7624):806–8. Available from: http://dx.doi.org/10.1136/bmj.39335.541782.AD
- [19] Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Standards for Reporting of Diagnostic Accuracy. Clin Chem [Internet]. 2003 [cited 2023 Jul 22];49(1):1–6. Available from: https://academic.oup.com/clinchem/article/49/1/1/5638966
- [20] Moons KGM, Altman DG, Reitsma JB, Ioannidis JPA, Macaskill P, Steyerberg EW, et al. Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD): Explanation and Elaboration. Ann Intern Med [Internet]. 2015;162(1):W1–73. Available from: http://dx.doi.org/10.7326/m14-0698
- [21] Andrade C. Internal, external, and ecological validity in research design, conduct, and evaluation. Indian J Psychol Med [Internet]. 2018 [cited 2023 Jul 23];40(5):498–9. Available from: http://dx.doi.org/10.4103/IJPSYM\_J34\_18
- [22] Sun X, Ioannidis JPA, Agoritsas T, Alba AC, Guyatt G. How to use a subgroup analysis: users' guide to the medical literature: Users' guide to the medical literature. JAMA [Internet]. 2014 [cited 2023 Jul 23];311(4):405–11. Available from: https://pubmed.ncbi.nlm.nih.gov/24449319/
- [23] Fletcher J. Subgroup analyses: how to avoid being misled. BMJ [Internet]. 2007 [cited 2023 Jul 23];335(7610):96–7. Available from: http://dx.doi.org/10.1136/bmj.39265.596262.AD
- [24] Wallach JD, Sullivan PG, Trepanowski JF, Sainani KL, Steyerberg EW, Ioannidis JPA. Evaluation of evidence of statistical support and corroboration of subgroup claims in randomized clinical trials. JAMA Intern Med [Internet]. 2017 [cited 2023 Jul 23];177(4):554–60. Available from: http://dx.doi.org/10.1001/jamainternmed.2016.9125

- [25] Haynes B, Haines A. Getting research findings into practice: Barriers and bridges to evidence based clinical practice. BMJ [Internet]. 1998 [cited 2023 Aug 13];317(7153):273–6. Available from: http://dx.doi.org/10.1136/bmj.317.7153.273
- [26] Kent DM, Trikalinos TA, Hill MD. Are unadjusted analyses of clinical trials inappropriately biased toward the null? Stroke [Internet]. 2009 [cited 2023 Aug 14];40(3):672–3. Available from: http://dx.doi.org/10.1161/strokeaha.108.532051
- [27] Vickers AJ, Kent DM. The lake Wobegon effect: Why most patients are at below-average risk. Ann Intern Med [Internet]. 2015 [cited 2023 Aug 14];162(12):866–7. Available from: http://dx.doi.org/10.7326/m14-2767
- [28] McColl A, Smith H, White P, Field J. General practitioner's perceptions of the route to evidence based medicine: a questionnaire survey. BMJ [Internet]. 1998;316(7128):361–5. Available from: http://dx.doi.org/10.1136/bmj.316.7128.361
- [29] Evidence-Based Medicine Working Group. Evidence-based medicine. A new approach to teaching the practice of medicine. JAMA [Internet]. 1992 [cited 2023 Jul 24];268(17):2420–5. Available from: https://pubmed.ncbi.nlm.nih.gov/1404801/
- [30] Swanson JA, Schmitz D, Chung KC. How to practice evidence-based medicine. Plast Reconstr Surg [Internet]. 2010 [cited 2023 Jul 24];126(1):286–94. Available from: http://dx.doi.org/10.1097/PRS.0b013e3181dc54ee.