Reading medical articles critically

What they do not teach you in medical school

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ABSTRACT

The article aims to distinguish between the various types of research published in medical journals; illustrate the anatomy of a scientific article in primary research and provide a guideline on how to read journal articles critically in order to maximize the readers understanding of the medical literature. Additionally, it provides a framework for things to consider when reading articles in various fields of research. It also enables non-experts at all levels to recognize strengths and weaknesses of different epidemiologic study designs. To achieve these goals, the hierarchy of medical journals is explained and highlighted, the various research designs used in the medical literature are identified and examined; the basic structure of a scientific paper is illustrated and reviewed; guidelines for reading medical articles in general are presented; and things to consider when reading articles published in the various fields of research are summarized.

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Despite the overwhelming widespread of modes for continuing education in the medical field in recent years (for example seminars, workshops, conferences, symposiums and so forth), reading the medical literature remains the most widely used method for continuing education in the medical profession at all levels. The reasons behind this wide popularity include convenient, economy and suitability to one's busy and hectic work schedule. Readers can proceed at any time and at any pace desired. For the reader, the main uses of the medical literature are 1) to answer focused clinical questions; 2) to acquire or maintain knowledge in a specific area; and 3) to acquire or maintain general knowledge. It is estimated that over 10 million medical articles exist on library shelves, about a third of which are indexed in the huge Medline database compiled by the National Library of Medicine of the United States.[1] The internet represents a great potential for making journal articles even more popular and more convenient way for continuing education through the venue of a huge number of scientific journals covering almost each specialty area. Debate continues as to whether scientific evidence alone is sufficient to guide medical decision-making, but few practitioners would dispute that finding and understanding relevant research based evidence is increasingly necessary in clinical practice. This article aims to distinguish between the various types of research published in journal articles; illustrate the anatomy of a scientific article in a primary research and provide a guideline on how to read journal articles critically in order to maximize the readers understanding of the medical literature. It also enables non-experts at all levels to recognize strengths and weaknesses of different epidemiologic study designs. To achieve these goals, the hierarchy of medical journals is explained and highlighted, the various research designs used in the medical

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literature are identified and examined; the basic structure of a scientific paper is illustrated and reviewed; guidelines for reading medical articles in general are presented; and things to consider in reading articles published in the various fields of research are summarized.

The hierarchy of medical journals. To invest your time and money wisely in reading medical journals as a method for continuing education, you have to choose carefully the articles you decide to read. To select the best medical articles for reading, one must first select the journal in which the article is published. In order to select the most authoritative journal(s) in your filed, you must get familiar with the hierarchy of medical journals. In each specialty area of medicine, a hierarchy of scientific journals has developed over time. For instance, the most prestigious and selective medical journal is the New England Journal of Medicine (NEJM), which is published since 1812 by the Massachusetts Medical Society. Through the years, the NEJM has adopted a strict peer review process.[2] Articles submitted for the NEJM's editors are first subjected to a thorough review. These editors insist on pertinent references supporting views the authors present. Authors must also disclose their sources of financial support. The editors then send articles passing their initial screening process to anonymous reviewers, who are usually experts in the field covered by the articles to be considered for publication. One of the referees evaluating the article is usually a statistician who must peruse and agree with the testing of the data. These highly responsible referees must either reject, accept with recommended revision, or rarely accept without revision all articles that clear the editors' primary review. Only one out of 10 articles submitted survives the NEJM strict peer review process.

A close second to the NEJM is the Journal of the American Medical Association (JAMA). The American Medical Association has published JAMA since 1883. The JAMA also accepts about one in 10 articles submitted. For the fields of general medicine, these 2 journals have attained the first tier status in the hierarchy of medical journal reporting. The second tier medical journals subject articles submitted for publication to similar peer review process but tend to accept and publish articles that meet with lower standards of quality review. The third and the lowest tiered journals have the least degree of peer review and accordingly may accept and publish nearly all articles submitted. Akin to the third tiered journals are unpublished Internet articles. Without any peer review process to scrutinize materials, methods, and statistical evaluation, one needs to be more wary about the quality of conclusions tabulated in unpublished Internet articles. The informed reader should be highly suspicious with articles published in the lowest tiered medical journals and unpublished Internet studies or findings. High quality peer reviewed articles, however, cannot be accepted fully, even if the data appear to be statistically valid. Many sources of unrecognized biases can still escape the safeguards of the strict peer review process utilized by high quality medical journals.[3-5] In addition, many papers published in medical journals have potentially serious methodological flaws.[6] Further, while a single published article has some truth in its content, it does not necessarily have all the truth. Thus, only multiple articles reporting different studies, all statistically valid, and each concluding similar findings can inform and guide judicious medical decision-making.

Distinguishing the different types of research. After this introduction that should help you in deciding on the journal and the article that you would like to review, you need to distinguish the type of research materials or studies published in scientific journals. Research materials included in papers published in scientific journals can be classified into 2 general categories: 1) primary research; and 2) secondary research. Each category can be classified into subcategories each containing different research methodologies or study designs. **Table 1** summarizes the major research types in the medical field and their classification. The following sections describe these different types of research and the various general categories and research methodologies or design that can be classified under each type. This is not meant to be an article on how to conduct the different types of research described below, if you wish to read about that, you should look elsewhere.[7-10]

Table 1 - Classification of research types in the medical field.

Research types	Classification	Study types
Primary research	Descriptive	Correlational studies Case reports and case series Cross-sectional surveys
	Observational/analytic	Case-control studies Cohort studies
	Interventional/ experimental	Randomized clinical trials Non-randomized clinical trials
Secondary research	Unsystematic reviews	Review articles
	Systematic reviews	Meta-analysis Clinical practice guidelines Decision analyses Economic analyses

Primary research. Primary researches are original papers written by the scientist(s) who actually conducted the study. Primary studies, which are the most published research in medical journals, usually fall into one of 3 general categories: descriptive studies, observational or analytic studies, and intervention or experimental studies. The following is a description of these subcategories and the types of research methodologies or designs that can be classified under each subcategory.

Descriptive studies. Descriptive studies documents patterns of disease occurrence in relation to variables such as person, place, and time.[7] They use information from such diverse resources as census data, vital statistics records, employment health examinations, clinical records from hospitals, as well as national figures on consumption of food, medications, or other products. Since this information is often routinely collected and readily available, descriptive studies are generally far less expensive and time-consuming than analytic and experimental studies. While features inherent in their design usually preclude the ability to test epidemiologic hypotheses, descriptive studies are very useful to describe patterns of disease occurrence as well as to formulate new research questions and hypotheses. There are 3 main types of descriptive studies: correlational studies, which consider patterns of disease among populations; case reports or case series; and cross-sectional surveys of individuals. Each of these descriptive study designs provides information on various characteristics of person, place, or time, and each has unique strengths and limitations, which will be illustrated, in the following section:

In correlational studies, measures that represent characteristics of entire populations are used to describe disease in relation to some factors of interest such as age, calendar time, utilization of health services or consumption of medications and other medical products. The correlation coefficient, denoted by r with value that can vary from (+1) to (-1), is the descriptive measure in correlational studies. This coefficient quantifies the extent to which there is a linear relationship between exposure and disease, that is, whether for every unit of change in the level of exposure, the disease frequency increases or deceases proportionally. A famous example of correlational studies is the study conducted in 1960 when mortality rates from coronary heart disease collected from 44 US states were correlated with per capita cigarette sales.[11] Results indicated that death rates were highest in states with the most cigarette sales, lowest in those with the least sale, and intermediate in the remainder. A chief strength of correlational studies, which contributes to their frequent use as a first step in investigating a possible exposure-disease relationship, is that they can be carried out quickly and inexpensively, often using already available information. The chief limitation of correlational studies is their inability to link exposure with disease in a particular individual. A second major limitation is the inability to control for the effects of potential confounding factors that may explain the correlation between the exposure and the disease.

In contrast to correlational studies, which consider whole populations, case reports and case series studies describe the experience of a single patient or a group of patients with a similar diagnosis. Case reports document unusual medical occurrences and can represent the first clues in the identification of new diseases or adverse effects of exposures. Case reports are among the most common types of studies published in medical journals, accounting for over a third of all articles in one systematic review.[12] In recent years case reports have raised the question of new health hazards related to a number of currently popular diseases. For example, it was a single case report that led to the formulation of the hypothesis that the use of oral contraceptives increases risk of venous thromboembolism.[13]

Case series are basically collections of individual case reports, which may occur within a fairly short period of time. The collection of a case series rather than reliance on a single case report can mean the difference between formulating a useful hypothesis and merely documenting an interesting medical oddity. Case series studies have a historical importance in epidemiology, as they often used as an early means to identify the beginning or the presence of an epidemic. The usefulness of case series in the recognition of new diseases and the formulation of new hypotheses concerning possible risk factors can be illustrated by the early epidemiology of acquired immunodeficiency syndrome (AIDS). Between October 1980 and May 1981, 5 cases of Pneumocystis carinii pneumonia were reported among young, previously healthy, homosexual men in Los Angeles.[14] This case series was unusual in that this type of pneumonia had previously occurred only in older cancer patients whose immune systems were suppressed, usually due to chemotherapy. Similarly, in early 1981, an unprecedented number of cases of Kaposi's sarcoma were diagnosed in young homosexual men.[15] As a result of these case series the Centers for Disease Control and Prevention immediately initiated a surveillance program to quantify the magnitude of this problem and develop diagnostic criteria for what became a new disease. More recent examples of case series studies are those conducted in Hong Kong and Toronto, Canada and led to the identification of the coronavirus, which caused the severe acute respiratory syndrome or SARS.[16,17] While case reports and case series are very useful in

the identification of new disease and hypotheses formulation, they cannot be used to test for the presence of valid statistical association. One fundamental limitation of a case report is that it is based on the experience of only a single person. Although case series are frequently sufficiently large to permit quantification of frequency of exposure, the interpretability of such information is severely limited by the lack of an appropriate comparison group. This deficiency can either obscure a relationship or suggest an association where none actually exist.

The third type of descriptive studies is the cross-sectional survey or the prevalence survey, in which exposure and disease measures are obtained and assessed simultaneously at the level of the individual in a well-defined population.[8] A cross-sectional survey starts selecting a sample of subjects and then determining the distribution of exposure and disease. The majority of data are collected for the first time primarily for the purpose of the study, although they may be supplemented with secondary data such as medical records. The primary utility of cross-sectional surveys is to provide quantitative estimates of the magnitude of a problem. To do this, 2 basic approaches are used: collect data on each member of the population (namely a census data), or take a sample of the population and draw inferences to the remainder. The latter approach is the more common because it can be accomplished in a shorter period of time, less expensive and one could derive reasonable estimates of the extent of a health problem through a survey on a subset of the population. Since exposure and disease status are assessed at a single point in time, in many cases, it is not possible to determine whether the exposure preceded or resulted from the disease. This type of "chicken or egg" dilemma is common to virtually all cross-sectional data. In most cases, therefore, cross-sectional studies cannot be used to test epidemiologic hypotheses. The one special case where a cross-sectional survey can be considered as a type of analytic study and can be used to test epidemiologic hypotheses is when the current values of exposure variables are unalterable over time. Such variables include factors present at birth, such as blood group or eye colors whose values are present at the initiation of the disease.

Observational and analytic studies. Since descriptive studies provide data on populations rather than individuals (correlational studies), lack an adequate comparison group (case reports and case series), or cannot usually discern the temporal relationship between an exposure and disease (cross-sectional surveys), they generally cannot be used to test etiologic hypotheses. To do this, it requires utilization of analytic design strategies, such as case-control studies and cohort studies to be described.

Historically, case-control studies began in developed countries in the twentieth century, in part as a response to needs that accompanied the shift from acute to chronic disease as a major public health problem.[18] Case-control studies are generally concerned with the etiology of a disease rather than its treatment and they are especially useful in the early stages of the development of knowledge on a particular disease or outcome of interest. In a case-control study, subjects are selected based on whether they do have a particular disease (cases) or do not have the disease under study (controls). Data are collected by searching back through the 2 groups' medical records or by asking them to recall their own history on past exposure in order to find a possible causal agent for the disease. The 2 groups are then compared with respect to the proportion having a history of an exposure or characteristic of interest. Because such design look backward from the outcome to ascertain the possible cause, some investigators use the term retrospective studies as a synonymous with case-control studies. The major potential problem in case-control studies relate to the fact that both the exposure and the disease have already occurred at the time the participants enter to the study. Therefore, this design is particularly susceptible to bias from the differential selection of either the cases or controls into the study based on their exposure or disease status. Additionally, similar to cross-sectional survey, case-control studies cannot show causality since both exposure and disease have already occurred at the time of conducting the study. Nonetheless, case-control studies offer a number of advantages for evaluating the association between exposure and disease. Specifically, the case-control design offered a solution to the difficulties of studying diseases with very long latency period, since investigators could identify affected and unaffected individuals and then look backward in time to assess their antecedent exposures rather than having to wait a number of years for the disease to develop. Thus, case-control studies are particularly efficient in terms of both time and cost relative to other analytic designs. Moreover, since case-control studies select participants based on their disease status, this design allows the researcher to identify adequate number of cases and controls. Consequently, case-control studies are well suited to the evaluation of rare disease, which would otherwise need to follow a tremendously large numbers of individuals in order to accumulate a sufficient number of cases.

The second major type of observational analytic studies is the cohort or the follow-up study in which 2 or more groups of people are selected on the basis of differences in their exposure to a particular agent, such as a vaccine, a drug or an environmental hazard and followed-up to see how many in each group develop a particular disease or other health

outcome.[9] Depending on the temporal relationship between the initiation of the study and the occurrence of the disease, cohort studies can be classified as either prospective or retrospective. The feature that distinguishes a prospective from a retrospective cohort is simply and solely whether the outcome of interest has occurred at the time the researcher initiates the study. By definition, both prospective and retrospective cohort studies classify participants based on the presence or absence of exposure. In retrospective cohort studies, however, all the relevant events (both the exposure and the outcome of interest) have already occurred when the study is initiated. Therefore, retrospective cohort studies can usually be conducted much more quickly and cheaply than their prospective counterparts and they are particularly efficient for investigating disease with long latency periods requiring many years to accrue sufficient end points. In prospective cohort studies, the relevant exposure may or may not have occurred at the time the study is initiated, but the outcomes have certainly not yet occurred. As a consequence of this design, prospective cohort studies can clearly establish the temporal sequence between exposure and the disease. However, the follow-up period in prospective cohort studies is generally measured in years and sometimes in decades since it takes this long for some diseases to develop. Since prospective cohort studies often involve following large numbers of individuals for many years, they are generally very time-consuming and expensive.

The world's most famous prospective cohort study, which won its 2 original authors a knighthood, was conducted by Sir Austin Bradford Hill and Sir Richard Doll.[19] Beginning in 1950, Hill and Doll followed up 40,000 British physicians who were divided into 4 cohorts: non-smokers, light smokers, moderate smokers, and heavy smokers. Mortality from lung cancer among those who never smoke was then compared with that among all smokers as well as with the experience of those who smoked differing numbers of cigarettes (namely the light, the moderate and the heavy smokers). Publication of their 10 year interim results in 1964 showed increased death rates from lung cancer among those who smoked compared with those who did not, as well as marked and steady rises in lung cancer mortality with increasing levels of cigarette smoking. The 20 year and 40 year results of this momentous prospective cohort study, which achieved an impressive 94% follow-up of those recruited at the beginning of the study and not known to have died, illustrate both the link between smoking and ill health and the strength of evidence that can be obtained from a properly conducted prospective cohort study.[20,21]

Intervention and experimental studies. An intervention study or clinical trial is a planned experiment designed to assess the efficacy of a prevention strategy or a treatment in humans by comparing the outcomes in a group of individuals or patients treated with the test intervention with those observed in a comparable group of individuals or patients receiving no intervention or receiving a control treatment (placebo).[8-9] Clinical trials can generally be considered either therapeutic or preventive. Therapeutic trials are conducted among patients with a particular disease to determine the ability of an agent or procedure to diminish symptoms, prevent recurrence, or decrease risk of death from that disease. Preventative trials involve the evaluation of whether an agent or procedure reduces the risk of developing a certain disease among those who are free from the condition at enrollment. Thus, preventative trials can be conducted among healthy individuals at usual risk or those already recognized to be at a high risk of developing a disease. In clinical trials, investigators start by determining eligibility of potential subjects. Eligibility rules must be carefully defined and rigidly enforced. Criteria for inclusion or exclusion will vary by the type and nature of the proposed intervention. Once eligible subjects agree to participate, they are allocated to either an intervention group or a control group. Both groups are then followed for a specified period of time and analyzed in terms of outcomes defined at the outset (for example recovery, death, and so forth). When the assignment of participants to the 2 groups is carried out randomly, the trial is called randomized. In many cases, however, random assignment may be impossible, impractical or unethical.

As apposed to the several varieties of analytic studies where the investigator is merely a passive observer, clinical trials provide the greatest control over the study situation. The investigator has the ability to control the amount of exposure (for example drug, dosage), the timing and frequency of the exposure, and the period of observation for end points. However, clinical trials have several limitations. Ethical considerations preclude the evaluation of many treatments or procedures in a clinical trial. On one hand, there must be sufficient doubt about the particular treatment to be tested to allow withholding it from half the subjects. On the other hand, there must be sufficient belief in the treatments potential to justify exposing the remaining half of all willing and eligible participants. In addition, the widespread adoption of measures by either the medical community or the general public can cause insurmountable problems of feasibility. It may become difficult to find a sufficiently large population of individuals willing to forego treatment or practice believed to be beneficial for the duration of the trial, even if there is no sound evidence to support this view. In addition to the unique ethical and feasibility

problems, there is also the question of cost. Clinical trials of primary prevention have generally cost on the order of $3,000-$15,000 per randomized participant.[7] Nevertheless, when issues of ethics, feasibility, and cost are addressed satisfactorily, the randomized clinical trial represents the gold standard for scientific decision-making in the clinical field.

Secondary research. Secondary or integrative researches are papers that summarize and draw conclusions from the original work of others. In other words, secondary research is based on information from primary studies. Although, secondary researches are often written by individuals other than those who actually did the original research, it is possible for authors to summarize their own previously published primary research, in which case, these later summary descriptions can still be considered secondary research. Secondary research can be classified into either unsystematic reviews or systematic reviews.

Unsystematic reviews represent the traditional approach to research integration. Using this method, a reviewer provides a narrative, chronological discourse on previous finding reported in primary research. A good example of an unsystematic review is the summary of literature in the introduction section of each scientific paper published in a journal. The most popular form of unsystematic review is the narrative review article. Generally, a review article summarizes or synthesizes what is currently known about a topic. Some review articles also provide a critical analysis of the research methods and the quality of the research published on a certain topic. Review articles usually are qualitative or narrative in form. Some peer-reviewed journals that concentrate on original or primary research papers will periodically publish a review article. In many fields, there are also journals, such as the Epidemiological Review, that publish only review articles. But even review articles need be read critically. There is a growing literature on criteria for evaluating the quality of review articles for researchers, practitioners, and science writers.[22-25] In addition, checklists have been developed for what constitutes an acceptable review in health sciences.[26]

Despite their popularity, review articles suffer from some problems. First, they are unable to deal with a large number of studies on a topic. When numerous investigators study important issues, the resulting amount of information on a given topic is often overwhelming and not amenable to summary. Therefore, reviewers often focus on a small subset of studies without even describing how the subset was selected. Second, preparing reviews is a complex process entailing many subjective judgments throughout the process and prone to bias and error.[27] In addition, reviewers sometimes cite the conclusions of previous studies without examining those studies critically. Further, authors of review articles are usually active and prominent in the field under review. Therefore, they might not be inclined to give full weight to evidence that is contrary to their own positions. Thus, it is hardly surprising that reviewers using unsystematic methods often reach opposite conclusions.[28] Selective inclusion of studies that support the author's view is common in the medical field. For example, the citation of clinical trials is related to their outcome, with studies in line with the prevailing opinion being quoted more frequently than unsupportive studies.[29,30] Moreover, clinical medicine is riddled with controversies, with reviews being commissioned to end an argument. However, in controversial areas the conclusions drawn from a given body of evidence may be associated more with the specialty of the reviewer than with available data.[28] Such problems could lead to misleading reviews. To avoid faulty narrative reviews, it is important to synthesize primary researches systematically, which is the aim of systematic reviews. A systematic review is a type of secondary researches that summarizes results found in primary research studies according to a rigorous and predefined methodology. Another term used to describe systematic reviews is tertiary research. Although the term tertiary research has not been standardized, the generation and availability of tertiary research materials has evolved over the past 25 years. Although, there is no universally agreed upon system for conducting systematic research, different methodologies for coping with the information explosion in the medical field have been developed. Four examples of these methodologies are described in the following section.

Meta-analysis. A meta-analysis consists of a critical evaluation of research studies that statistically combines the results of comparable studies or clinical trials on a specific topic. It is simply a tool that can be used to quantitatively synthesize the findings of different studies. Some researchers traces the origin of the statistical basis for meta-analysis back to the 17 century when, in astronomy, intuition and experience suggested that combinations of data might be better than attempts to select amongst them.[31] Others consider the distinguished statistician Karl Pearson to be the first medical researcher to use formal techniques to combine data from different studies[32] in his 1904 account on the preventive effect of serum inoculations against enteric fever.[33] However, the American Psychologist Gene Glass was the first researcher to use the term "meta-analysis" in 1976 first in his presidential address to the American Educational Research Association and then in a paper entitled "Primary, Secondary and

Meta-analysis of Research".[34,35] Since that time, meta-analysis has become a widely accepted research tool, encompassing a family of procedures used in a variety of disciplines.

Meta-analysis typically follows the same steps as primary research. The meta-analyst first defines the review's purpose. Second, sample selection consists of applying specified procedures for locating studies that meet specified criteria for inclusion. Third, data are collected from studies in 2 ways: 1) study features are coded according to the objectives of the review and as checks on threats to validity; and 2) study outcomes are transformed to a common metric so they can be compared. A typical metric in medical research is the effect size, the standardized difference between treatment and control group means. Finally, statistical procedures are used to investigate relations among study characteristics and findings.

Meta-analysis studies respond to several problems in medical research. First, meta-analyses tend to be more narrowly focused than unsystematic reviews. They usually examine a single research question that may relate to treatment, causation, or the accuracy of diagnostic test. Second, they have a strong quantitative component as they attempt to pool the quantitative results of several studies to give a more precise estimate of effect than would the results of any of the individual studies included in the analysis. In addition, practitioners can now make decisions as to the use of therapies or diagnostic procedures based on a single article that synthesizes the findings of tens or hundreds clinical studies. Further, a meta-analysis of series small clinical trials of a new therapy often yields a finding on the basis of which practitioners can confidently begin using it without waiting long years for a large clinical trial to be conducted.

Clinical practice guidelines. Clinical practice guidelines, generated largely by the Americans, were defined in 1992 by the Institute of Medicine as "systematically developed statements to assist practitioners and patient decisions about appropriate health care for specific clinical circumstances".[36] They represent an attempt to distill a large body of medical knowledge into a convenient, readily useable format. The first Practice Guideline was commissioned in 1993 and funded by the Agency for Health Care Policy and Research (AHCPR), a federal granting agency created by the US Congress in 1989. Since that time, the AHCPR commissioned and published practice guidelines on many topics including acute pain management, depression in primary care, HIV infection, otitis media with effusion in children, and post-stroke rehabilitation. Like meta-analyses, clinical practice guidelines collect, appraise, and combine evidence published in the medical literature. Practice guidelines however, go beyond most reviews in attempting to address all the issues relevant to a clinical decision and all the values that may sway a clinical recommendation. They differ from meta-analyses in relying more on qualitative reasoning and in emphasizing a particular clinical context. Thus, they reflect value judgments about the relative importance of various health and economic outcomes in specific clinical situations. In addition, clinical practice guidelines make explicit recommendations, usually on behalf of sponsoring health organizations, with a definite intent to influence medical practices in specific clinical situations. As a result, they should be required to pass unique tests about how matters of opinion, in addition to matters of science, are conciliated

Decision analyses. Another example of systematic review methodologies encountered with less frequency in the medical literature is decision analyses. A decision analysis is the application of explicit, quantitative methods to analyze decisions under conditions of uncertainty.[37] It is used in the medical field to compare the expected consequences of pursuing different clinical strategies, such as deciding whether or not to screen for prostate cancer, choosing a testing strategy or selecting a treatment option. Clinical decision analyses can help by refining questions and exploring the trade-offs between competing benefits and harm. Decision analysis can also be applied to more global questions of health care policy, analyzed from the prospective of society or a national health authority. Most clinical decision analyses are structured as decision trees, and decision analyses studies will usually include one or more diagrams showing the structure of the decision tree used in the analysis. The reader must review such diagrams to understand the model being considered and then make a judgment whether the model fits the clinical problem well enough to be valid.

Economic analyses. An economic analysis, or cost-benefit analysis, is a systematic study that uses a set of formal, quantitative analytical techniques to compare alternative strategies with respect to their resource utilization and their expected outcomes.[38] As with other integrative systematic reviews, economic analyses use estimates of costs and effectiveness from summaries of several original researches of therapy, diagnosis, and prognosis. The main distinction between an economic analysis and other studies is the explicit measurement and evaluation of health resources consumption and their costs. Primary studies such as randomized clinical trials usually generate data on the efficacy of therapies, but sometimes investigators may gather data about the cost involved in providing these therapies. The economic analyst then integrates these cost data to compare alternative treatment strategies with respect to resource allocation and its expected outcomes. However, the integration of cost

data often involves placing values on the health outcomes so that they can be compared to the costs of alternative treatment strategies. The results of cost-benefit analyses are usually expressed as a composite index, such as the quality-adjusted life year (QALY).[39] This composite index involves placing a lower value on time spent with impaired physical and emotional function than time spent in full health. Quality-adjusted life year is calculated by multiplying the preference value of a certain state of health with the time the patient is likely to remain in that state.

As stated previously, one of the main uses of the medical literature is to answer focused clinical questions. Therefore, after briefly reviewing the most common types of research designs used in the medical literature, the question is what is the most appropriate type of research or study to be used in answering focused clinical questions faced by practitioners? The answer to this question will depend on the field of research addressed by the study. Most research studies in medicine are concerned with one or more of the following broad fields: diagnosis, screening, causation, therapy, and prognosis. **Table 2** illustrates the major fields of research, their focuses and the recommended research designs appropriate for each field. It also specifies the appropriate secondary research study when the research field is either filled with complex literature presenting conflicting results or similar results.

Anatomy of a medical article. After specifying the research field of interest and selecting the appropriate article to review, it is time to get acquainted with the basic structure or anatomy of a typical medical article. Most articles now appearing in medical journals are presented more or less in standard format or structure. By knowing this structure, you can easily locate different parts of the research study. This structure is typically divided into 8 sections: an abstract, an introduction, methods, results, discussion, conclusion, a list of references and an acknowledgment. It is important to mention, however, that journal articles published in health related journals may not always include all these sections or be described in the same order described here; there may also be other sections and subsections not included in the following discussion.

Title/Authorship section. It consists of the title of the article and name and affiliations of the author(s) who conducted the research and wrote the paper. The one thing that you should pay attention in this section is the order of the authorship. This order is very important in most scientific journals, with the first author being the person who had the

Table 2 - Summary of research fields and recommended study designs.

Research fields	Research focus	Recommended study design
Diagnosis	Determining whether a new diagnostic test is valid and reliable.	Cross-sectional survey
Screening	Demonstrating the value of tests which can be applied to large populations and which pick up the disease at a pre-symptomatic stage.	Cohort study
Causation/etiology	Determining whether a putative harmful agent, such as environmental pollutant is related to the development of illness.	Depending on how rare the disease, cohort or case-control study. Case reports may also provide crucial information.
Therapy/prevention	Testing the efficacy of drug treatments, surgical procedures, alternative methods of service delivery, or other interventions.	Randomized controlled trial
Harmful effects	Investigating or reporting harmful consequences to patients either due to medical intervention or environmental agents.	Randomized controlled trial is the best choice but are not used because it not ethical to expose subjects to a putative casual agent. Alternatively, cohort studies, case-control studies are recommended.
Prognosis	Identifying the presence of and determine the increased risk associated with a prognostic factor.	Cohort studies. Case-control studies are useful when the outcome is rare or the required duration of follow-up is long.
Review of complex literature with conflicting results	The availability of multiple studies which test the same hypothesis and come up with contradictory findings.	Systematic reviews such meta-analysis, practice guidelines, decision analyses, and economic analyses.
Review of literature with similar results	The availability of multiple studies which test the same hypothesis and come up with similar findings.	Review articles

most responsibility for the research study. In some fields, however, the most senior scientist is listed last in order of authorship. This is often the person who provided the research monitorship, the laboratory, or the grant support for the research being reported; however, he or she may not have taken the primary responsibility for the study being published. Knowledge of the field itself is needed to determine whether this protocol is followed in the peer-reviewed journals in a particular field or specialty.

Abstract section. It is an abbreviated description of the study described in the paper. Abstracts are often restricted in length and format, for example, no more than 250 to 500 words and usually without citations of previous studies or articles. They usually do not include enough information about the research methods to permit the reviewer to make a judgment about the scientific merit of the study. Therefore, reading the abstract section of a journal article will only gives you a hint of the paper's content. Summarizing the abstract sections of journal articles does not in any way constitute a review of the literature because there are not enough details in this abbreviated description to allow you to understand how the research was carried out or how to interpret the results.

Introduction section. Generally, the introduction section of a scientific paper includes 4 major parts: 1) A brief summary of the author's own review of previous literature on the topic in question; 2) the motivation of the paper, that is, why the author(s) decided to conduct the research or the gap in the current state of knowledge which the research is trying to fill; 3) an overview of the scientific theory or conceptual models on which the current research was based (if there is one), and; 4) the purpose of the research study described in this paper. Depending on the journal or author, the purpose of a study can be in the form of a statement, a research question, or a hypothesis. If the purpose of the research is stated in the form of a hypothesis, it is usually presented in the negative such as "treatment X will not improve or control condition Y", which is known as a null hypothesis. The authors of the study, however, rarely believe that their null hypothesis to be true when they conduct their research. In the contrary, they have usually embarked on their research to falsify, rather than confirm, their null hypothesis, that is, "treatment X will improve or control condition Y". In fact, setting up falsifiable hypotheses that researchers then proceed to test is the very essence of the scientific method.

Methods section. It consists of a description of the procedures used to carry out the research study. Although this section may sometimes be the shortest section of the entire paper, it is the one that demands the most knowledge and skills to judge the quality and validity of the research described in the paper. This section should be complete enough to permit other researchers to replicate the study without the need to contact the authors. The methods section of a typical scientific paper includes information on the following 5 subsections: the study design, subjects, data sources, data collection methods, and statistical and analytic procedures. It is important to know, however, that the choice and order of the subsections in the methods section described here depend on factors, such as the field, the content, the type of the study, and the choices made by the journal editors or by the individual author. In the study design, the authors describes how the research was structured, including the use of pretests and/or posttests; the use of one or more groups of subjects, that is, experimental and control groups; and how subjects were assigned to these groups. For example, the researcher may use random assignment of subjects to the experimental and control groups or apply self-selection into groups by subjects of the study. This section should also include a description and operational definitions of each of the major variables in the study, including the independent and dependent variables and the covariate. Under the subjects heading, the author describes how the subjects of the study were chosen- the inclusion and exclusion criteria, sampling design, the number of subjects included in the study and their demographic characteristics such as age, gender, income or disease status. This section also include a description of how many individuals were initially selected; the number who actually participated in the study; and differences between those chosen, those who agreed to participate, those who dropped out, and those who participated at each stage of the research project.

In the data source(s) subsection, the researcher gives an explanation of whether the information collected on the study's subjects is based on primary source data or secondary data. Primary source data are gathered by the researchers who are reporting the study using various data collection methods such as questionnaires, surveys, interviews or direct measurement through diagnosis and laboratory testing of specimens collected from or about the study's subjects. Secondary source, on the other hand, is gathered by others such as information abstracted from medical records. Some studies will include both primary and secondary source, for example, information from a survey of the subjects by the researchers, which the same researchers then combined with clinical data obtained from the medical records that were recorded by the treating physicians. Secondary source data described here should not be confused with secondary research that is described at the beginning of this paper. If secondary data are used, then the authors should

include a description of the characteristics of the database, the original reason the data were gathered, and the dates during which the data were gathered.

In the data collection segment of a journal article, a description of all the procedures used in collecting primary data from or about the subjects in the study is provided. Any questionnaire, survey, interviews protocol, or other data collection instrument will be described along with either the results or validity and reliability analyses of the data collection instrument or references to previous studies that include such information. Under the statistical and analytic procedures subheading, the author describes how the data were analyzed or manipulated. As a minimum, this section includes a description of what specific statistical tests or analytical procedures were used (for example descriptive statistics such as percentages or means, a bivariate analysis such as chi-square or t test, or multivariate techniques such as analysis of variance or regression analysis and so forth). If applicable, the authors also describe the assumptions underlying the use of these statistical procedures and evidence indicating the fulfillment of these assumptions.

Results section. This section is devoted to describe the findings of the study, and in so doing answer the research question(s). It verifies or refutes the hypothesis, or addresses the purposes of the study that should have been stated clearly in the introduction section. Depending on the research in question, this section could be either the longest section of the entire paper where details may be presented in several tables or figures or the shortest section in which details may be presented concisely in one or 2 tables or figures. The results section may also require the most intensive reading in order to fully understand the study findings. Some journals limit this section only for the presentation of the results; others, however, allow authors to discuss their interpretation of the findings in this section. In the later case, the reader must be sure to distinguish the actual results from the author's interpretations or opinions.

Discussion section. It usually addresses 3 topics or areas that may be included in this section of the paper. They are: 1) interpretation and discussion of the study findings and what these findings mean; 2) a description of the strengths and weaknesses of this particular study in comparison with previous research on the topic; and 3) a statement about the significance of the research study and its contribution to the current state of knowledge in the field.

Conclusion section. A research paper is usually concluded with a brief summary of the research study as it relates to the purpose or research question or hypothesis described in the introduction section and a discussion of future research or remaining gaps in the current state of knowledge to be addressed by future studies. Because our knowledge is accumulative and no single studies can answer all questions, often results of one study suggest additional research questions and the process goes on.

List of references. It contains a listing of all papers or other sources cited by the authors in describing previous or related research.

Acknowledgment section. It includes a description of how the research study was funded and the names of the granting agencies or foundations. It also includes the names of individuals who assisted in the research or review.

Guidelines for reading medical articles. The information presented thus far helps the reader to distinguish the various types of research found in the medical literature, the appropriate research methodology to be used in answering clinical questions faced by practitioners, and the standard format or structure used to present information in a medical article. The remaining of this paper will be devoted to provide the reader with guidelines on how to read medical articles in general and things to consider to critically evaluate and use articles on the various fields of research addressed by the study (namely diagnosis, therapy or prevention, harmful effects and prognosis).

Guidelines for reading medical articles in general. The best start for reading a journal article is to ask yourself what the purpose of the study was and why the authors did it. In another word, what was their hypothesis or research question? It is important to distinguish between what they said their purpose was in the introduction section and what they actually addressed or answered in the results section. A sign of a poor quality journal article is the failure of its authors to state specifically and clearly the purpose of the study in the introduction section.

In reviewing the methodology section, consider how the authors conducted the study through examining the methodological design. In the medical sciences, the major designs will include one of the previously discussed primary and secondary research designs (namely descriptive designs, analytical designs and experimental designs). Determine whether the study design is appropriate for the purpose of the study stated by the authors. Continue your review by specifying the independent and dependent variables and how these variables were operationally defined in this particular study. Describe the procedures or treatment applied to one or more of the groups of subjects, usually to the intervention group, including the timing of the procedures with respect to data collection. Depending on the purpose of the study, some research may not include an actual intervention. Alternatively, the intervention may be some external

event, such as an environmental risk factor. In these kinds of research, the author is expected to give a clear description of the external event or there should be at least a reference to other document or source materials that describe such event.

Another essential information provided in the methods section is related to features of the subjects of the research study. When reviewing the information about the study subject, the first question to answer is what was the unit of analysis? Typically, the unit of analysis will be an individual person. However, the unit of analysis may be a group or an organization or a social artifact which has been defined in the literature as the products of social beings or their behavior[40] such as a practice guideline, a health care policy or law or a single study as it is the case in meta-analyses studies. For instance, in some studies the unit of analysis can be a surgical team (a group) or a health care provider such as a hospital or medical department (an organization). If a unit of analysis other than the individual is used, then it is important to determine how the authors operationally defined that unit. For example, if the unit of analysis in a particular study is a hospital, then the authors should describe what they meant by a hospital in terms of bed size, specialty, geographic location and type of ownership. The number of subjects in a study is often abbreviated as (N) in tables of result. This number is a fundamental piece of information that authors usually failed to provide. Therefore, you might need to figure out the total number of subjects in the study. It is also important to determine what was the total number of subjects the researchers began with and compare it to the number of subjects who left the study (drop-outs), and the final number of subjects who completed the study. A mark of a poor research quality paper is the absence of these enumerations in the methods section and such omission raises concerns about the possibility of bias in the study. It is also difficult to find information about differences between people who remained in the study and those who either refused to participate in the study in the first place or left before the conclusion of the study.

Read the article carefully to determine how subjects were selected to participate in the study. If the researchers select the subject conveniently or the subject volunteered for the study, then there was no random selection. This is a very important point to examine since the generalization of results from the study sample to a population will technically depend on the selection method of the study participants. The generalizability of the study results is usually not possible without random selection. If there is more than one group of subjects (an intervention group and a control group), then pay attention to the number for each group and determine how the subject characteristics in each group such as age, gender, race, geographic location, socio-economic status are similar or different. Another important question to answer about the study subject is how the subjects were assigned to the intervention and control group. If the assignment was randomly arrange, then "random assignment" was used. If subjects could choose for themselves which group to be enrolled in, or if they were already in-groups to begin with (namely healthy or sick, smokers or nonsmokers), then random assignment was not used. Under the subject topic, you should also note the inclusion and exclusion criteria used to select subjects. An example of inclusion/exclusion criteria might be age range and the admission during a specified dates: only people between the ages of 18 and 65 and who were admitted during the period June 2001 to May 2003 qualified for the study. Thus, people who were below 18 or above 65 and/or those admitted prior to June 2001 or after May 2003 were excluded from the study.

Under the data collection method section, it is important to identify the data sources of the study. As described previously, primary research consists of data and information collected directly by the researchers who conducted the study from subjects in that study. Alternatively, the researchers may use secondary data that has been gathered by others or for purposes other than the original study. If primary data were used find out what specific data collection methods or instruments (namely survey, questionnaire, and telephone or in-person interviews) were used in the study. If such methods or instruments were used, note whether or not the authors provide results of validity and reliability testing of these instruments. If no information was given about validity and reliability, the authors should at least provide a reference for a data source where such information can be found. Also, determine when the data were collected (namely the number of pre-testing and post-testing used); whether the data were collected prospectively or retrospectively; and whether the data collected at multiple points in time (cohort study) or at a single point in time (cross-sectional study). If secondary data were collected, examine why the data were collected initially and what sources of bias could affect their quality. If relevant to the area of the published research or study, determine the setting in which data were gathered, for example, urban or rural hospital, a nursing home or a health insurance provider.

For most readers, reading the data analysis section is often the most difficult part in a journal article simply because it requires an adequate statistical background which they usually lack. For instance, the reader must be familiar with specific statistical tests and other analytic procedures commonly used in the medical literature such as bivariate analysis (chi-square or t test) or

multivariate techniques (linear regression, logistic regression, analysis of variance, factor analysis and path analysis). Readers must be also familiar with statistical assumptions underlying the application of these techniques in order to render a valid judgment about either the fulfillment or violation of these assumptions. Such knowledge is sometimes lacking even in the most experience readers which explains why one of the referees evaluating the article for publication is usually a statistician who must peruse and agree with the testing of the data. It is worthy to note here that one of the most common reasons articles are rejected by peer reviewed journals is either the inappropriateness or incorrectness of data analysis.[1] Although we believe that an adequate statistical background is a prerequisite for critical reading of medical articles, statistical tests and analytic procedures commonly used in the medical literature are sufficiently complex that they are beyond the scope of this article. Therefore, readers should refer to the "Basics Statistics for Clinicians" series in the Canadian Medical Association Journal[41-44] or "Statistics for the non-statistician" series in the British Medical Journal,[45,46] or consult a basic medical statistics textbook[47] to be acquainted with some of the background materials required for comprehending the data analysis section of a typical medical article. If an important medical decision would be made based on the results provided by a scientific article, it is recommended to seek the assistance of a statistician to judge the quality of the data analysis section. You should not let statistical significance alone dictates the decision you are about to make.

In analyzing the results section, the most important thing to consider is whether the authors answered the research question or hypothesis they posed in the introduction section of the article. It should be apparent by now whether it was the right question to ask in the first place. Another things to consider are differences between initial and later research questions. Sometimes, researchers provide answers to research question(s) they did not initially ask which is not a problem in itself as long as these questions are supported by the data analysis. It becomes a problem only when such additional research questions either inappropriate to the study or not supported by the data analysis.

When reading the discussion and conclusion sections, it is important to distinguish between the results of the study, which are facts, from the author's opinion or interpretations of the results and their significance. Your existing knowledge about the subject matter and the critical reading of the previous sections should help you to decide whether the author's interpretations are logical and valid based on the findings of the study. You can also decide whether or not the results of this study are consistent with the findings of other studies on the same topic. The discussion and conclusion sections are usually the place for authors to point out the strengths and weaknesses of their study. Issues addressed in this topic include the possibility of generalizing the study results to other populations and settings, problems with the methodological design that the authors were aware of but could not have been remedied, sample size inadequacy, or problem in sample selection. It is part of human nature that authors of journal articles are usually quick and pleased to describe the strengths of their study; yet they may be reluctant to point out and discuss the weaknesses which most of the time will be an assignment that is left for the critical reader. However, authors who do not point out the weaknesses of their studies make themselves vulnerable to criticisms from others. When reading the conclusion section, make sure that conclusions do not exceed the evidence that is presented in the article and that any recommendations made by the authors are linked to the strength of such evidence.

Things to consider in reading articles in the various fields of research. The previous section provides general guidelines to critically read articles commonly published in medical journals. While these guidelines may be applied to help the reader understand the basic structure of most research articles, not all research articles published in medical or health related journals will include every subsections discussed in the method section of a typical medical article. The content of information and the choice and order of presenting such information in the methods section of a medical article depend on the field of research (namely diagnosis, therapy, prognosis and so forth), the study design, and even the choices made by the individual author or the editors.

Since it would be unwise to suggest a uniform guideline that is applicable to every article published in medical journals, it is helpful to provide the reader with things to consider and pay attention to when reading articles that deal with the various fields of research. **Table 3** suggests a framework that can be used to critically evaluate articles dealing with the most common research fields and studies in the medical literature.

Conclusion remarks. In their day-to-day clinical practice, practitioners have to make major decisions. These decisions must be supported by reliable clinical information that is obtained from 2 principal sources: the individual patient and previous scientific research. To provide effective care, both types of information are needed. The information about the individual patient is elicited through a careful history taking, complete physical examination, and the results of investigative tests and procedures. The information from scientific research is usually gained through several venues of continuous education, such as seminars, workshops,

Table 3 - A framework for critically evaluating studies in various fields of research.*

Research fields	Primary considerations	Secondary considerations
Diagnostic tests/procedures	A study sample that includes an appropriate spectrum of patients.	Whether the results of the test being evaluated influence the decision to perform the standard reference.
	Independent and blind comparison with a standard reference (for example biopsy, autopsy or surgery)	Full and detailed description of methods for performing the test/procedures to permit replication.
Therapy/prevention	Random assignment of subjects to treatments.	Blinding of both subjects and study personnel.
	Low or minimal dropout rate.	Similarity of subjects at the start of the trial.
	Sufficient and complete follow-up. Assessment of unwanted side effects.	Equal treatment of the study groups aside from the intervention.
Harmful effects	The availability of a comparison group that is similar with respect to important determinants other than the one being investigated by the study.	Whether exposure to the harmful effect precede the adverse outcome (namely correct temporal relationship).
	Similar measurements of the exposures and outcomes in the groups being compared.	The existence of a dose-response gradient (namely the adverse outcome increases as the duration or quality of exposure increases).
	Sufficient and complete follow-up.	
Prognosis	A well-defined study sample of patients at a similar point in the course of the disease.	Use of objective and unbiased outcome criteria.
	Sufficient and complete follow-up.	Adjustment of the analysis for important prognostic factors, such as age and gender.
Meta-analyses	Addressing a single, focus clinical question.	Whether important relevant previous studies are missed or excluded.
	Whether the criteria used to select articles for inclusion are objective and appropriate.	Whether the validity of the included studies is appraised.
		Whether assessments of studies are reproducible.
		Whether results are similar from study to study.
Practice guidelines	Specification of all important options and outcomes.	Whether an explicit and sensible process is used to consider the relative value of different outcomes.
	Whether an explicit and sensible process is used to identify, select, and combine evidence.	The likelihood that the guideline accounts for important recent development.
		Whether the guideline has been subjected to peer review and testing.
Decision analyses	The inclusion of all important strategies and outcomes.	Whether the utilities are obtained in an explicit and sensible way from credible sources.
	Whether an explicit and sensible process is used to identify, select, and combine evidence into probabilities.	Determination of the potential impact of any uncertainty in the evidence.
Economic analyses	Provision of full economic comparison of alternative health strategies.	Whether appropriate allowance is made for uncertainties in the analysis.
	Proper measurement and evaluation of costs.	Whether estimates of costs and outcomes related to the baseline risk in the treatment population.
	Whether all direct, indirect, and intangible costs and benefits have been included.	

*adopted with modifications from the "Users' Guides to the Medical Literature" series published in JAMA.[48-63]

conferences, symposiums and reading the medical literature available in medical textbooks, the internet and medical journals. Clinical information provided through such venues is of no less importance to the quality of care than information elicited directly from patients.

From the perspective of the busy practitioners who want to provide effective medical care but are sharply restricted in time for attending conferences, workshops and seminars, reading the medical literature is highly efficient way for keeping up with current developments in the medical field. However, sources of the medical literature vary in terms of the currency and the quality of clinical information provided. For example, a medical textbook is only as up-to-date as its most recent reference; all are at least partly out-of-date before they are published. And with all the traditional safeguards provided by peer review are lost when enthusiastic researchers report their latest findings over the convenient computer network, internet reporting becomes a great potential for transmission of medical misinformation. Excluding these sources leaves the burden for transmitting current and responsible scientific information falls into the venue of peer reviewed medical journals. In order for published research to enhance our understanding and be able to transfer its valid findings in day-to-day clinical practice and provide patients with care that is based on the best evidence currently available, it is important that practitioners at all levels acquire the skills of reading medical articles critically. Thus, knowing how to use and evaluate the medical literature is a prerequisite for ensuring that we are providing optimal patient care.

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