

TEACHING ARTICLE**PEER REVIEW, CRITICAL REVIEW AND WRITING OF MANUSCRIPTS**Rawleigh C. Howe, MD, PhD^{1*}

Peer Review is generally considered as a necessary and essential component of the process of research output dissemination, yet one which is far from being efficiently, or sometimes even fairly implemented on a consistent uniform basis. Many have stressed the need to improve the process, yet there is still no consensus on how it should be modified (1-3). Although online guidelines are now available (4-5), in most cases peer reviewers have never received formalized training. It is generally assumed that researchers, once attaining a certain level of expertise in proposing, conducting and writing up their research for publication, basically “know how to do it”.

One of the purposes of the present article is to address some of the “how to” of peer review. At the same time, it must be acknowledged that the skills developed for this task really do overlap extensively with proper manuscript writing and critical review of manuscripts for one’s research purposes. This teaching article will be oriented towards those areas of overlap. Therefore, we will begin by discussing some of the key features of a well written manuscript, pointing out common errors by inexperienced writers and researchers. We will then discuss some additional issues needed from the researcher’s perspective while critically reviewing the literature. Finally, we will return to the topic of peer review and discuss some aspects of this process. We do not extensively review each of these topics; the reader is referred to recent excellent online sources for more information (4-11).

Manuscript writing:

The **Abstract** is a brief synopsis of the paper; that is a statement of the problem, objectives, methods, key findings and conclusions. Depending on the study, the abstract may have many if not all the key details of the study, but often there are many very important points about the paper which are not possible to infer from the abstract, and hence critical review of papers can never simply end with reading the abstract. From the author’s perspective, despite its location at the beginning of a manuscript, when it comes to writing the abstract, it is often recommended to compose the abstract as the very last step in writing, because it is usually only then that the structure of the manuscript, the key objectives, findings and arguments have crystallized.

The **Introduction** has several critical elements. It must describe the importance of the general problem area and define enough of the relevant literature in the appropriate field(s) to equip the reader with sufficient background to understand the paper. It must explain why the authors have chosen the study, i.e. define a research gap or question which is important to advance the field. Finally, it must concisely state the specific objectives or hypothesis of the study. A common error among beginners is to indulge in excess background information which has only questionable relevance to the study. Part of the goal of the introduction again is mainly to help the reader understand the research study, not to provide a treatise on the field; that is reserved for review articles. The introduction should begin broadly and progressively narrow in focus to the study objectives; significant space restrictions of most journals encourage this.

The introduction and ultimately the statement of hypothesis or aims ideally should be oriented or pitched towards the results which are ultimately obtained and basically pose the question which the results and discussion must answer. Though this seems obvious, it is not uncommon for the stated objectives or hypotheses in the introduction to be at odds with the results obtained and/or their interpretation. This can sometimes happen when intended objectives are altered due to time or financial constraints during the study execution or if unexpected results are obtained. Thus, like the abstract, the introduction may require modification towards the end of the writing period after the results and discussion have taken form.

Implicit in the introduction, rationale and statement of objectives should be a sense of the originality of the work, i.e. that the authors are not merely repeating what others have done, and that answering the question or executing the objectives will advance the field. There are many aspects of originality: it can be an entirely novel hypothesis, a new approach to the same problem, or it may be simply a repeat of a previous study design but with a novel results and/or interpretation which are particularly applicable to the population setting. The latter is particularly relevant in the setting of resource limited countries, because often the starting point for research is repetition of a study approach common elsewhere, but not yet done in the host country. While many studies begin with repetition of some key approach, ultimately novelty is the extent

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to which such a starting point is extended into new ground. As an example, consider a study exploring the use of the complete blood count in a remote rural setting. If the study identifies an unexpectedly high prevalence of anemia, possibly of rare etiology, then the study indeed has high novelty. If there was a high index of suspicion and supportive evidence to suggest that anemia was quite high in the population, and the result of the study in fact indicated the contrary, the study may still have considerable novelty at least for members of that community. If the study provides a normal prevalence of anemia without necessarily stating any underlying suspicion for that, then arguably the study as reported has little novelty. At the same time, no one would dispute the value of having such testing capacity for remote areas. From a research perspective, the novelty component could rather be developed differently, namely to define the barriers and solutions towards implementing and maintaining such a service, which may have considerable novelty value and be of interest to multiple- albeit different- stakeholders.

The **Materials and Methods** contain the important details on how the study was executed. Ideally, this section should present sufficient detail so that anyone can reproduce the findings. Practically speaking however, journals must restrict space, so that there is seldom sufficient space to provide all the adequate details. This is particularly true of laboratory based methods. It is therefore customary to provide brief summaries of methodologies sufficient to adequately understand and critically review the paper, citing descriptions in the literature where appropriate. In addition, online journals give the option of publishing supplementary information which can provide more extensive detail. In research settings where sample size calculations are critical to the study design, power statements should be included providing estimates of expected differences and variance to attain a given level of power or confidence in addressing the hypothesis. All relevant details of the subject or sample population must be provided. Statistical approaches used should be stated in enough detail so that readers are well informed and can understand the approach. Ethical considerations should be addressed.

The **Results** section should be presented in a logical and coherent fashion to state all aspects of the study. Many support the view, particularly in clinical studies, that all key information should be simultaneously present in both the textual results section as well as in the figures and tables. Others state the preference for tables and figures to contain all key details, with the results phrased in more general terms, summarizing the key findings, particularly when large numbers of variables are present. Still others show preferences for textual results, and provision for figures and tables only when such information cannot be conveyed in the results in text form. To some extent this may reflect journal and author preferences. Arguably, the principal point is to have both clarity and conciseness. Regarding any aspect of the study, be it a unique experiment or a single or set of variables within a larger design, the key points which need to be addressed include: describing what the results were, for which sample or population, reference to relevant statistics including measures of mean or median, spread and statistical inference, and where appropriate some brief general conclusions about what the experiment or study aspect showed. Adequate inclusion of control subjects or samples, or control experimental details should be clearly apparent in the text and/or figures and tables. Figures and tables need to be laid out in a manner to optimize clarity. Sufficient detail should be present so that the results can be independently interpretable by the reader. In general, the content of the results section should be restricted to the findings obtained, and not overlap appreciably with points made in the introduction, materials and methods or discussion. There are times, however, when it may be appropriate to restate why or how a particular aspect of the study was done (with more detail provided in the materials and methods if needed). This may be more important for topic areas the audience is not likely to be familiar with, hence providing additional clarification or emphasis. Extensive interpretive discussion of the data should be reserved for the discussion portion of the paper.

There is considerable attention to detail on the part of the author which goes into the creation of the results section, figures and tables. Similarly, reading the manuscript requires the same of three additional personnel: the peer reviewer, ultimately the editorial staff of the journal, and as well the discerning future reader. Data present should be logically consistent throughout. In cases where variables are repeatedly depicted in multiple results sections, figures or tables, then their associated values should be contextually consistent, not for example, high in value in one figure and low in the next. Such disparity are cues to the discerning reader that there may be much greater variability in variable outcomes than the author is maintaining, or that author errors were made during data analysis or presentation. Numbers of subjects included in any given analysis should ideally be cited for each result, particularly if differing from that described in the materials and methods. Given the tedium needed to ensure adequate detail in the results section, it is often tempting for the beginner or the busy author, peer reviewer, editorial reviewer, or discerning future reader to slack off or even avoid the process altogether. Yet errors in the fine details have significant consequences, from simply creating an unfavorable impression about the work or the journal, to misleading inferences with ethical consequences which could ultimately lead to manuscript retraction.

The **Discussion** is a critical portion of the manuscript, often underemphasized, particularly- it seems- in resource limited countries, but is especially vital along with quality data and originality for acceptance into journals with very high international reputation and impact. Ideally the discussion is oriented back to the question(s) posed by the introduction. Whereas

the introduction can be viewed as starting with the bird's eye view of the landscape and gradually focusing in on the trees and bushes far below which represent the specific study research questions, the discussion can be thought of as the reverse process, whereby the trees and bushes-now the results-are viewed and discussed while simultaneously re-elevating the reader back to the bird's eye view of the landscape. The discussion is ideally a synthesis, it responds to the hypothesis and places the results in context of the field in general. Research studies which answer a question, create new questions. Hence, the discussion represents both the finishing point of the current study and the seeds for future studies. From this perspective, the skills acquired in writing a proper synthesis in a discussion overlap extensively with the skills required to write a truly novel, original research proposal.

A commonly used approach is to begin the discussion by restating the aims and approach, and then summarizing the key experimental findings. Each of the key points is then discussed, one after the other in the ensuing paragraphs. The goals of the discussion of each key finding are to 1) discuss the results in relation to the current knowledge base of the field, 2) infer the implications of the findings, 3) identify, where appropriate, caveats into the study conclusions and inferred implications, and 4) suggestion of future studies.

Placing the results into broader context is not merely re-stating the results and whether they are the same or different from other studies, a very common and arguably suboptimal practice, but answering the question of how this knowledge advances the field, how it explains previously unexplainable findings or mechanisms. This is critical because it helps the reader (and potential peer reviewer of the manuscript) better appreciate the novelty of the study. By necessity it requires a deep understanding and critical review on the part of the author of the relevant literature. The implications of the findings are an opportunity to speculate on the logical consequences and predictions of the findings; i.e., if this is true, then could that be true? The caveats represent a counterpoint or caution to both the immediate conclusions of the key finding as well as speculation of the implications, and serve as an important cue to the audience (and the reviewer) that the author has thoroughly thought through the question, approach and findings. Suggestion of future studies provide insights as to how to resolve the implications and caveats. What might be the next step? These are components of a genuine synthesis. Although ideally all these components should be addressed in the discussion, they do not all necessarily need to be addressed or organized in association with each key finding. For example, it is common in clinical journals to have a special "Study Limitations" section, which pertains to the caveat components of the study findings in general. Moreover, perhaps related to competitiveness of the field, some authors may not want to reveal all their ideas or plans. Nonetheless, a true synthesis contains these (and potentially other) elements and complements the importance of the research findings in stimulating interest among the readers. It helps the discerning reader answer the question "Can I really believe this?", and "How much weight should I place on the study findings and interpretations?", thereby cementing the importance of the study.

Manuscripts should have some **conclusion** or summary sets of statements. This may either appear in a specialized section following the discussion or at the end of the discussion itself, and basically should be the "Take home message". Ideally, it should be oriented towards the general audience, and should be stated in very general terms; experienced readers whether they are simply glancing at the study or reviewing in detail will often refer to the concluding statement because it should put the study into brief perspective. It may also include brief recommendation(s) for future studies or policy changes.

References must conform to journal standards. This is also an area requiring detailed attention and often neglected at many levels. It can be very frustrating if the reader wants to find a cited reference only to find that it doesn't exist- presumably because of either omissions or mistakes made- or that its real content has nothing to do with the implied content in its cited context.

The reference list need not be extensive, and many journals restrict number. However, the references must be relevant and appropriate for the paper. Often, the higher the journal ranking, the more attention by the review process to which references were cited. It can be a cue to the especially critical reviewer of how well informed the author really is on the topic area. It is preferable to include references for the key and seminal advances in the field, and not overload with references of relatively low impact. Omission of key references related to important advances in the field is also interpreted negatively, and claims of novelty by the author when similar studies appear in the literature is a common mistake and an easy excuse to reject a paper.

As a final point it is relevant to bring up the topic of plagiarism. A major impediment to learning how to write a proper manuscript in general is plagiarism, which in this context means not using your own words to craft the manuscript. It is now possible to detect plagiarism relatively easily using online software, and it is apparent that it is more common than previously suspected. A well-constructed and written manuscript can really be considered as unique as a fingerprint. If a study is truly novel, it is unlikely that an optimal introduction, including rationale, aims, and the pitch-posing the right question in the right context to be answered by the discussion- could ever be done by copy and paste approaches using

other sources. One can make an even stronger case for the discussion, as the answer to the question and synthesis of the results in the context of the literature, because it is highly unlikely that two truly novel studies will ever attain identical results and coincidentally have the same discussion. It follows, then, that apart from the fact that it is unlawful, copying and pasting can never provide the solution towards writing a truly quality and original paper.

Learning how to write a quality manuscript does not come naturally to most in research, in part because it ultimately entails more than simply writing, but all skills needed to plan, conduct and interpret research. It may take years of practice and struggle-particularly with proper discussion sections- before it can be done quickly and naturally. It is really a rite of passage in research, and students and other inexperienced professionals should receive as many opportunities as well as constant encouragement to develop this skill as best as possible.

Critical Review of Manuscripts:

We now turn from the perspective of the idealized manuscript, to the manuscript review process, and we will begin not with peer review, but more with the day to day critical review which researchers are more familiar with. Researcher's critical review may range from a brief survey of the paper, to a much more in depth and rigorous poring over the details. We will start with the quick review. The abstract is a convenient starting place, and when article access is limited, often the only source for a given journal. Yet we have argued above that although it is a quick and useful synopsis, there is far more material to gain from accessing the entire manuscript.

The first priority is to get a reasonable sense of the study objectives, approaches and findings. As alluded to earlier, high yield locations to focus on in an article, in addition to the abstract, include the end of the introduction, which often outlines the aims of the study. The beginning of the discussion, which may summarize the key findings of the paper, often provides a somewhat different perspective on the overall study than the abstract, since it is not constrained by journal specific formatting or space. Finally, the last paragraph of the discussion or the conclusion section, if present, may provide key take home messages.

The second priority is to briefly get a sense of the overall quality of the paper. Is the focus and hypothesis of the study relevant, both in a general sense, and from the researcher's specific perspective? Is the design reasonable, are the needed controls present? Are the laboratory or subject recruitment methods or approach suitable? Has ethical consideration been given due emphasis? Is the author trying to address too difficult a question with the approach, or conversely, is the methodology excessive for the objectives? Are the data believable, quality wise, are the findings sufficiently robust, statistically significant, to be convincingly reliable? Are the authors' interpretations and conclusions of that data reasonable? Are there alternative explanations for the data? Did the authors under-interpret their data, i.e. miss an important implication the inclusion of which would increase the impact of the paper? Conversely, did the authors over-interpret the data, that is, read too much into their data?

If the paper is close to the researcher's range of expertise, s/he may already know the critical types of experiments and data and quickly scan through the various figures and tables to locate key experiments most likely to influence his/her opinion about the paper. For example, if his/her research focus is on plasma biomarkers and s/he has a good idea what the limits of sensitivity are of most tests, s/he might quickly jump to the figure to see the actual levels measured and already get a sense of the test reliability. Or if s/he is a researcher on HIV disease s/he may quickly scan for the typical demographics table to look at the range of CD4 counts among participants to get an impression of the disease severity of the patient cohort which may have a large impact on the study outcomes. These are among many approaches useful to quickly probe the paper to decide whether to stop, or continue to read it in much greater detail.

If one elects to do a more detailed critical review, one must commit to poring over many of the paper's fine details. This proceeds naturally if the paper overlaps considerably with the researcher's own research experience and this makes careful and critical review of the paper easier. Did the authors get the same kind of results that s/he got with the same approach? If not, how does their methodology and patient and study setting differ from his/hers, etc.

Review of papers outside one's expertise requires more discipline, more time and can be significantly more challenging because of difficulties understanding many of the details. Simply understanding the paper's main points may require considerable independent review of the topic or methods. Yet at the same time the benefit can be very high; approaches used in unrelated fields often provide the seeds for ideas of novel research applied in one's own area. For training purpose, one of the most valuable means of learning such skills is the journal club. While journal clubs have many formats, the typical approach is that a single researcher selects a paper-ideally a novel, particularly interesting one -which s/he distributes in advance, then presents and leads a group discussion of the paper. The time taken to prepare for the journal club may de-

pend on the complexity of the study as well as the level of expertise of the presenter, and may range from several hours to several days, particularly if the presenter is not very familiar with the topic area. During the presentation, the presenter as well as the audience is expected to critique the paper, and is encouraged to consider alternate explanations of the data, and challenge the interpretations and conclusions of the study. One of the most common experiences of those participating in such journal clubs, for students and senior faculty alike, is that however exciting and convincing the paper initially seems, often the consensus after discussion is that the paper was not nearly as impressive as originally thought. This reinforces the importance of in depth critical review of papers and not to rely exclusively on quick abstract reading.

As much as it is important to learn critical thinking and review skills, and to understand idealized experimental design, it is equally important to understand the context and stage of maturation of a given topic area, along with the practical aspects, feasibility and limitations of any given approach. As an example, a double-blinded randomized prospective interventional clinical trial may be the highest research standard and evidence upon which medical policies are based, yet it is also expensive and time consuming. Less weight is usually given to cross-sectional studies, chart reviews and anecdotal experiences of medical care providers, yet such studies are much cheaper to perform, and while ultimately of less specificity they often provide the data and rationale upon which randomized prospective studies are based. In fact, both approaches are necessary for the progress of the field; there is a time when the chart review is more likely to be fruitful, and another when the randomized trial should be done. This example is given to underscore the importance, as part of the critical review process, of understanding the context, the stage of maturation of a given research topic area, in which a given hypothesis or set of study objectives is undertaken. This is a skill the responsible reader and critical reviewer should ideally have, but it is equally important that the author convey this context, so that the reader can better appreciate the usefulness and importance of the study.

Peer review of manuscripts for journals:

We shall now touch upon the topic of peer review for journals. We have discussed above two types of review process which researchers commonly employ for their own means: the quick review to get the basics of the article and for a sense of the overall quality, and the more detailed review, more likely done when the topic area is close to one's own research field, but also seen in other contexts, for example in the academic journal club.

The peer review requires both skills to critically assess the relevance, originality and quality of the paper. Often, these skills of the referee or reviewer will have been honed over years of experience. Likely, the reviewer will have been selected by the editor because the paper topic overlaps with his/her area of expertise, though some elements of the paper may be unfamiliar. Time constraints also contribute to the review. It is not surprising then, that it is sometimes recommended to use two steps (5), a brief review phase, in which major flaws may be quickly identified, and a longer phase of review whereby the paper is scrutinized very carefully using all the approaches mentioned above to evaluate relevance, hypothesis, methods, data quality, interpretations and conclusions from the data, and the adequacy of the reference list.

The review undertaken by the peer reviewer, however, has two additional components which distinguish it from the standard critical review. First, if the referee deems the paper potentially worthy of publication, s/he has the responsibility to suggest ways to significantly improve the paper. Nearly all papers which initially get accepted for publication require either minor or major changes. From a scientific perspective this can include pointing out data inconsistencies which need clarification, figures or tables which need additional information, sentences or entire paragraphs or even sections which need to be re-written to improve readability, to address study limitations, or to become more concise to meet journal length restrictions. From an editing perspective, though journals should have an editorial screening mechanism which returns papers prior to review which conflict with journal standards of formatting, language, length or figure or table limits, it is also the responsibility of the referee to indicate to the editor and author that major revisions regarding spelling, grammar, English usage and references are needed.

A second distinctive aspect of the peer review is the report to the Editor. Although there is variation of formats required by different journals, in general this should consist of 2-3 sections. The first section should be a concise summary in a paragraph or less in general terms, stating briefly the objectives, methodology and key findings. This serves to give an informed summary to the Editor and author, and as an opportunity to relate the positive aspects of the paper. The next two sections should consist of the reviewer's critical comments and suggestions for modifications of a general and specific nature, respectively. General comments may often relate to textual concerns such as conciseness, need to shorten or expand certain sections. For example: "Although the results section and figure legends are appropriate and clear, the discussion is too long (the article itself exceeds the journals standards) and is rambling in spots (particularly paragraph 3 and 4 of the discussion). It is recommended to reduce their discussion to a more concise form". Specific comments should be numbered in sequence and address specific issues with specific page and line references. For example, "Item 3. Figure 5 (page

17) needs to be improved. The y axis units are not given, and in the legend, it is stated $p=10.1$, obviously an incorrect value, presumably a typo.” The itemization provides a convenient reference for editor and author alike to address and correct all the issues.

Peer review, critical review and manuscript writing represent complex sets of skills which overlap extensively in biomedical research. There are aspects of each which are unique and can be learned independently (4-11), but the purpose of presenting them collectively here is to reinforce the idea that improvement in any one supports improvement in all three. They are each part and parcel of what it means to do quality original research. Thus, the ability of the reviewer to perform a good peer review for a journal, apart from many editorial technicalities, is heavily dependent on his/her skill level to critically review or write a manuscript in his/her own research.

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