Working with authors to develop high-quality, ethical clinical manuscripts: Guidance for the professional medical writer

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Abstract

One measure of career success for clinical researchers is reporting their findings in a peer-reviewed journal. Writing a clinical manuscript that has impact and relevance to their intended audience is crucial for publication success. However, clinicians and scientists whose native language is not English may find it challenging to effectively communicate the clinical relevance of their research and they may seek help from a professional medical writer. In this article, we focus on what makes a high-quality clinical manuscript and some of the ethical issues that must be considered. Professional medical writers will benefit from understanding and applying these concepts as they assist authors in preparing a well-structured, ethically sound, and highly readable manuscript that clearly expresses the clinical relevance of their findings. Using these approaches, medical writers and their clients can be confident that the final manuscript meets the quality expectations and ethical standards of international English-language journals.

Keywords: Clinical relevance, Manuscript structure, Medical writing

Introduction

A critical aspect of a career in medicine involves sharing clinical experiences and research findings with the broader medical community. From single-patient case reports to large multi-centre clinical trials, reporting clinical research findings in peer-reviewed journals is an important way to disseminate new medical knowledge and improve clinical practice both regionally and internationally.

For clinical researchers with little experience in academic publishing, or whose native language is not English, the task of communicating their data clearly and effectively can be daunting. Many seek out professional medical writers to assist them in the preparation of manuscripts for submission to peer-reviewed journals. Consequently, the role of a medical writer is to not only assist with language issues but also advise authors on the best way to present their results.

Thus, to achieve the goal of publication, the clinical researcher (the author of the planned article) and the medical writer must work as a team, and it is important that both parties understand what journal editors are looking for when they evaluate submitted manuscripts. Because the goal of a journal editor is to increase the status of their journal in their field, they are interested in high-quality research that is novel and has high clinical relevance. They are looking for manuscripts that will be interesting to their readers and highly cited. They also want manuscripts that are written in clear and concise English. This does not simply mean good spelling and grammar but rather that the manuscript clearly and effectively communicates the ideas and findings of the authors. Finally, all journals must follow a set of publication policies and ethical standards to ensure that the research they publish is of the highest quality. In this paper, we expand on each of these topics to provide professional medical writers with advice on how to help researchers prepare high-quality clinical

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manuscripts for publication in English-language journals.

Elements of a good clinical manuscript

Clinical significance

Although there are journals that will accept articles simply based on well-executed research, other journals (especially those with a higher impact factor) will place a greater emphasis on the significance of the findings presented. Thus, authors should perform an honest and objective evaluation of the significance of their research findings when choosing a journal. But what does this 'significance' actually encompass? Broadly, it is an indication of the importance of an article's findings and can be divided into three components: novelty, relevance, and appeal.

Writers should ensure that the novelty of the presented findings is clearly communicated, particularly if they represent a conceptual advance in the field. Because authors will often overestimate the novelty of their results, medical writers need to be aware of the general state of the field of an author's work and have a keen eye for results that might have wide-reaching implications. Identifying novel aspects of the presented findings, such as new mechanisms of disease or improved safety of a new medicine, will help the writer to focus the manuscript on the most important results and interpretations of their data. Even if the findings represent only a small or incremental advance in the field, the focus of the manuscript might be a discussion on how the results will help improve current practice or suggest subsequent steps in a research path.

With respect to the relevance of research findings, it is important to consider whether the results have implications for only a restricted geographical location or ethnic group, or whether there are potential implications for broader areas and populations. Authors may want to emphasise regional findings locally to maximise immediate practical use of their findings; however, the broader the relevance of the findings, the greater the significance and impact worldwide. Medical writers need to consider the authors' goals and target audience when approaching how to discuss the relevance of results in a manuscript, and tailor the discussion accordingly.

It is important to remember that journal editors want to publish research that will be widely read and highly cited. Research that has a high level of popular appeal will likely achieve greater numbers of citations simply because more people will be made aware of the publication. Therefore, it is important for medical writers to work with authors to identify important research questions raised by their work and emphasise the potential clinical applications of the research in the manuscript.

While all three components of significance – novelty, relevance, and appeal – are clearly interrelated, each should be considered independently and emphasised in the manuscript to ensure that

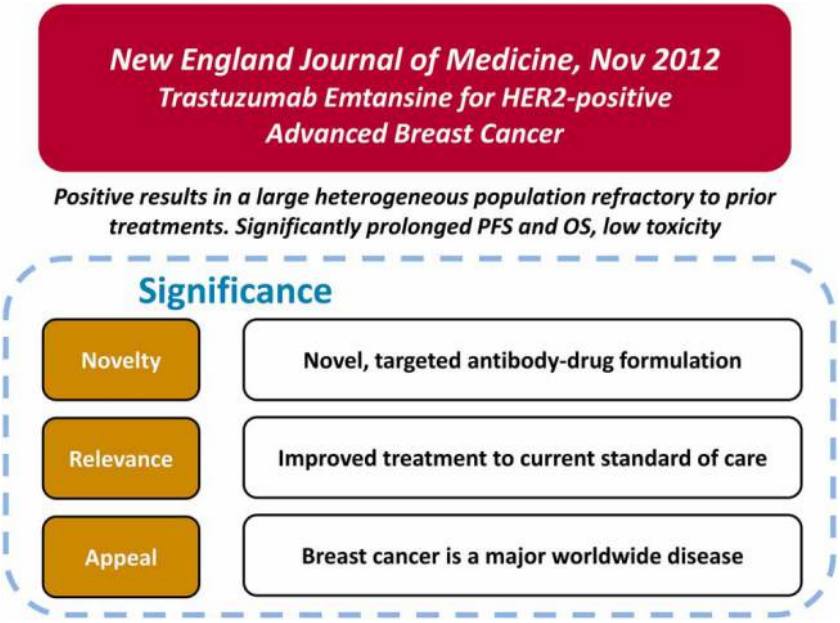

Figure 1: Novelty, relevance, and appeal in a good-quality oncology manuscript. The selected article[1] was among the journal's 'most viewed' in the month of publication. The reason for this, we believe, is that it contained all of the components of significance (novelty, relevance, and appeal) and these were clearly communicated in the manuscript text. PFS, progression-free survival; OS, overall survival.

Table 1: Qualities of a good medical oncology paper

Feature	Example
Accurate, objective reporting of methodology and results	Enough information in methods to replicate; clear rationale; calculation of statistical power; limited interpretation of results in the Results section
Concise illustrations and descriptions	Figures showing key outcomes such as progression-free survival, overall survival, and response rates; table listing adverse events
Insightful and objective discussion	Findings put in context of what is known; limited speculation, but statements are supported by evidence
Full disclosure and registered trial	Registry and registration number provided
Full ethical compliance	Details of institutional review board approval and informed consent provided
Multiple, complementary, well-controlled experiments	Combination of imaging, pathology, and clinical work-up to tell a more convincing story
Mechanistic findings to complement clinical findings	Cellular/biochemical-level findings to support descriptions of clinical effects
Clear description of clinical implications and how the findings might influence clinical practice	What the results mean for patients and how clinical decisions might be improved on the basis of the presented findings

the significance of the article is clearly communicated. Figure 1 illustrates how this was done in a highly viewed article in a top-tier journal.[1] As well as presenting findings that are clearly of great significance, the article outlined in Figure 1 contains many of the important qualities that editors and readers look for in a medical oncology paper (Table 1). Indeed, regardless of the research topic or target journal, medical writers working on clinical manuscripts should aim to include all of the items listed in the table somewhere within the manuscript and emphasise the importance of these inclusions to authors. Combining these elements together will produce a high-quality clinical manuscript containing information that influences clinical practice based on the most appropriate methods for the research question.[2,3]

Clear writing

Good science alone, however, is not enough to make a good manuscript. Effective writing is also needed to clearly communicate a researcher's ideas and findings. If these are not expressed clearly, even experts in the field may not understand what was done and why, thereby limiting the clinical applicability of the findings.

The key goal for any kind of writing, including medical writing in clinical research papers, is readability. This refers to the logical presentation of ideas and organisation of material in places where readers expect to find it. It is crucial to remember that the manuscript is written for the reader; the purpose of a manuscript is to share research findings with others, not simply create a personal record of the author's work.

Without realising it, readers expect certain information to appear in certain places within a text. By considering these reader expectations, the readability of a manuscript can be greatly enhanced, making it as easy as possible for readers to find the information they are looking for. Gopen and Swan proposed a methodological approach for constructing ideas within a manuscript that would provide the reader with important clues and cues to properly interpret an author's meaning.[4] The key concepts they outlined included logically connecting ideas together by using topic sentences and referencing back to previous ideas, emphasising shorter sentences, and keeping subjects and verbs close together. They also encouraged good use of elements known as the topic position (beginning) and stress position (end) of a sentence to introduce the reader to the next concept and emphasise the important message, respectively.

However, a well-constructed paragraph can still have poor readability if the language being used is not taken into consideration. Many authors and writers think that complicated language makes their writing appear more sophisticated. Unfortunately, use of unnecessarily long words and technical jargon can actually make the work harder to understand and may introduce ambiguity. Because many of their readers may not be native English speakers, editors want articles with good accessibility and clarity. Therefore, to maximise the accessibility of the research findings and ideas, it is important to use simple, unambiguous language and short sentences that can be easily understood.

Manuscript structure and flow

While clear writing to effectively communicate ideas and results is important, so is logical presentation of the ideas. The sections and order of a research paper allow readers to logically move from an overview of the research (Abstract), to the rationale for the study (Introduction), the experiments conducted (Methods), the findings obtained (Results), and finally, the significance of the findings and their

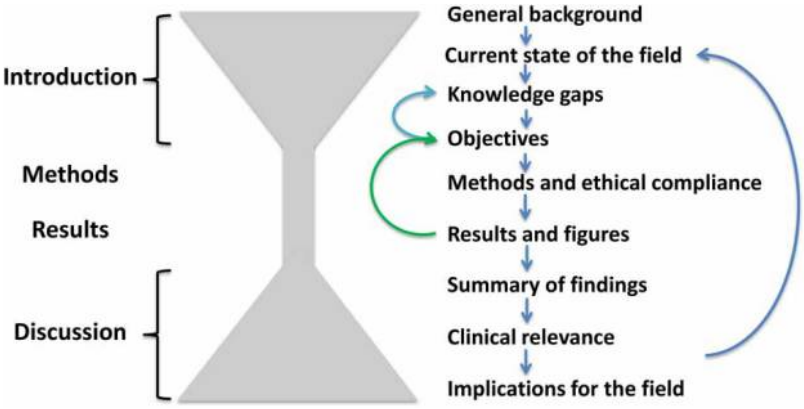

Figure 2: Manuscript structure and flow. Logically presenting research findings and showing how they fit into the context of current knowledge leads to a highly readable and well-organised clinical manuscript. This figure illustrates how to arrange ideas from a broad Introduction (upper triangle) down to the specifics of the paper's Objectives and Methods (narrow centre), and finally back to the broader clinical relevance of the research findings in the Discussion (bottom triangle), producing an hourglass-type shape. To the left, the corresponding sections of the manuscript are noted. Curved arrows indicate the important areas where ideas should be linked back to each other to create flow and strengthen the logical presentation of the research.

implications for the field (Discussion). Figure 2 illustrates this basic structure of a manuscript and how these sections relate to one another.

The Introduction should concisely present the topic being investigated and the related problem currently being faced by clinicians (Figure 2) to put the study into context. Authors need to be made aware of the importance of setting the scene for their study, as discussing previous work, both supportive and opposing, will help identify the research gap that led them to conduct the work. For example, if the research being reported evaluated the efficacy of a treatment for triple-negative breast cancer (TNBC) liver metastasis, the Introduction would briefly describe TNBC, the incidence of metastasis, and the efficacy of current treatments. It would then highlight the important problem in the field that the author's research attempted to address; in this example, perhaps the limited treatment options for TNBC that has metastasised to the liver. The clinical significance of a manuscript will not be effectively communicated to readers without a properly structured Introduction, and this is an area of the manuscript where medical writers can provide considerable guidance to authors on how to best highlight the importance and rationale of their work.

Moving to the Results, one challenge for medical writers working with authors to develop a manuscript can arise from the level of detail an author wants to include. Some authors may be reluctant to include data that weaken their results, while others may want to incorporate all of their data, even those that are not relevant to the specific focus of the manuscript. Medical writers must therefore be able to help authors structure their manuscript in such a way that all of the necessary data (i.e. data that a peer reviewer would expect to see) are included. Thus, it is helpful to think like a peer reviewer during the outlining stages of manuscript development and ask the sorts of questions that a reviewer would ask *before* the final content has been decided.

Once it has been decided exactly which results will be included, it is important to present them in a logical manner. If the manuscript is reporting results from a randomised clinical trial (RCT), inclusion of a flowchart illustrating the flow of patients through the trial, such as that provided by CONSORT (Consolidated Standards of Reporting Trials),[5] is helpful for making an informed analysis of the treatment course. This flowchart can also serve as a helpful resource, aiding good communication between author and writer. For case reports, the patient background, medical history, and other key details for understanding the choice of treatment should be discussed. Keeping the aims of the study and the manuscript in mind, medical writers can help guide authors on what information will be essential to their narrative while also providing the objectivity necessary to present an honest description of the findings. Guidance on the statistics (e.g. *P* values, confidence intervals, and odds ratios) that would support their argument is also something that writers may need to provide.

One of the biggest challenges for many authors is writing a good Discussion. Readers will often look ahead to the Discussion to obtain a summary of the findings, their relevance for the field, and their

clinical implications; thus, the Discussion should be both concise and objective. Many authors are reluctant to discuss the limitations of their work in the Discussion for fear that they imply weaknesses in their results. However, in this situation, it is useful to ask the questions that a peer reviewer would, to identify possible weaknesses in the study. Acknowledging these in the Discussion can pre-empt questions from peer reviewers by providing reasons why certain better approaches were not possible, potentially saving time and effort in the post-submission stages. Conversely, authors may wish to emphasise a conclusion that is somewhat speculative or overemphasises the significance of their results. Medical writers need to ensure that they discuss with authors the overall relevance and implications of the results and make sure the conclusion presented is based on the initial objectives stated in the Introduction, thus tying the entire manuscript together from beginning to end (Figure 2).

Finally, medical writers should ensure that articles comply with the target journal's instructions for authors, which can vary considerably. Ideally, the target journal is decided during the outlining stages and the drafts are developed with these instructions in mind; however, this is not always possible. Even if a draft has been developed with journal requirements in mind, instructions may be revised and updated. Thus, medical writers should perform final checks for compliance with journal instructions prior to submission. It is also a good idea at this stage to thoroughly check the consistency of the presented data among figures, tables, and text, and to cross-check the values against the source data provided because errors may have been introduced during multiple rounds of revision. Writers should ensure that the final documents are submission-ready and completely free of errors.

Ethical considerations

In addition to the structural components of a manuscript, adherence to research and publication ethics is crucial to publication success. To ensure that the author is preparing a high-quality clinical research manuscript in accordance with the most up-to-date ethical guidelines, there are three primary resources worth keeping on hand: the International Committee of Medical Journal Editors (ICMJE) industry-standard guidelines for publication ethics;[6] the Good Publication Practices (or GPP2) document,[7] which provides recommendations for authors working on company-sponsored research; and the Committee on Publication Ethics (or COPE) forum,[8] which provides resources and case examples for ethical publication issues. Many authors may be unaware of the ethical issues surrounding authorship, sponsorship, and potential conflicts of interest in publishing their research in medical journals, or the recent controversies regarding ghostwriting and guest authoring of sponsored clinical study findings. Therefore, medical writers have a responsibility to inform authors on these ethical issues, and to adopt a strong ethical stance in the face of resistance from either party.

Authorship and acknowledgement

The ICMJE recommendations include four criteria for authorship of a medical journal article (Table 2).[6] ICMJE recommendations state that 'all individuals who meet the first criterion should have the opportunity to participate in the review, drafting, and final approval of the manuscript'. Thus, those individuals who qualify for authorship under criterion 1 cannot be omitted from an author list simply because they were denied the opportunity to meet criteria 2 and 3. In addition, many medical writers may not yet be familiar with criterion 4, which was introduced in a 2013 revision. Criterion 4 makes all authors accountable for the work as a whole (not only their own contributions). As such, authorship on a paper indicates more than just credit for the work, but also responsibility for its integrity. This means that any disagreements among authors with respect to the data or the opinions presented in the manuscript must be resolved before submission. It also means that all authors have a responsibility to resolve any post-publication queries regarding the accuracy or integrity of the work. Medical writers need to clearly communicate this responsibility to the authors on the articles they prepare.

Professional medical writers who help authors prepare articles for publication in the peer-reviewed

Table 2: ICMJE criteria for authorship[6]

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
2. Drafting the work or revising it critically for important intellectual content; AND
3. Final approval of the version to be published; AND
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

literature usually do not meet the ICMJE criteria, and are thus appropriately absent from the author list. However, the ICMJE does recommend that medical writers who contribute to the preparation of a manuscript should be acknowledged, usually in the Acknowledgements section of the article. Many peer-reviewed medical journals have adopted the ICMJE criteria and incorporated them into their publication policies. It is therefore essential that medical writers discuss with authors the importance of understanding and following the ICMJE recommendations and other ethical guidelines for publication of medical research, not only to maintain transparency and protect against accusations of ghostwriting but also to ensure compliance with journal policies.

Following GPP2

The International Society of Medical Publication Professionals (ISMPP) developed GPP2, a set of practices to help authors, research sponsors, and medical writers meet the ethical publication standards set forth by various groups, including the ICMJE.[7] The ISMPP acknowledges that publication of medical research is a team effort, involving researchers, statisticians, and medical writers, and states that all parties must be aware of the ethical standards for publishing research findings in the medical literature. GPP2 recommends that a written publication plan should be developed that outlines the responsibilities of the sponsors, authors, and other contributors, and describes the processes in place to ensure compliance with all ethical guidelines.

To ensure that ICMJE authorship criteria are met, GPP2 recommends that the authors of a paper and any professional medical writers work in close collaboration, with at least the lead author reviewing each step of the writing process, from development of the outline to preparation of various working drafts and approval of the final paper (Figure 3). Achieving this requires clear lines of communication and tools for maintaining version control, which can be as simple as agreeing on a file naming system that incorporates dates and initials or the use of cloud computing or secure file transfer systems to share files and maintain a centralised archive of drafts.

CONSORT and STROBE

Many journals ask clinical authors to submit a checklist from CONSORT[5] or STROBE (Strengthening the Reporting of Observational Studies in Epidemiology)[9] upon submission of their manuscript. CONSORT is used for reporting results from RCTs, while STROBE is used for observational studies. These checklists cover the essential points needed by journal editors and readers to properly assess the study results and ethical compliance throughout the course of the study. Even if a journal does not require submission of a CONSORT or STROBE checklist, both are highly useful resources during manuscript preparation and can help writers anticipate questions that reviewers might ask. How patients were chosen to participate in the study and what consideration was given to participants who might be particularly susceptible to harm are issues of concern regardless of the type of study. Therefore, working in

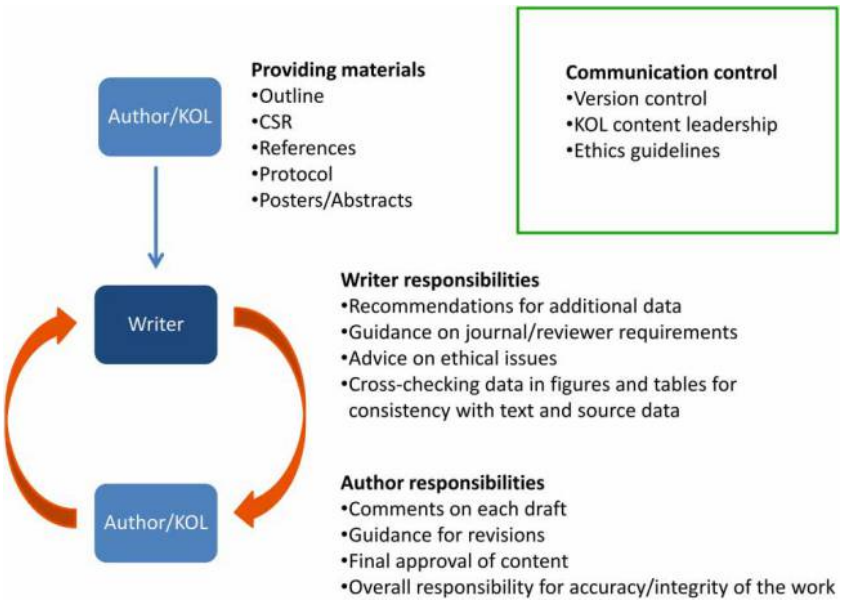

Figure 3: Recommended procedure for medical writers working together with the researchers who will be authors on developed articles, and the responsibilities of each party. CSR, clinical study report; KOL, key opinion leader.

accordance with these checklists will demonstrate that the author has followed good clinical practice for working with human subjects.

Clinical trial registration

For authors involved in clinical trials, trial registration is required as a condition of publication in many journals. The ICMJE defines a clinical trial as 'any research project that prospectively assigns human subjects to intervention and comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome', which is supported by the World Health Organization as the world standard.[10,11] Trial registration has become the standard practice in clinical research as it allows open sharing of potentially critical data with researchers, clinicians, and patients, and helps reduce the issue of selective reporting. The implementation of registration requirements means that all Phase 2 and 3 trials that started enrolling patients on or after 1 July 2005, and all Phase 1 studies started on or after 1 July 2008, should be prospectively registered before publication.[10,12]

Clinical trial registration needs to be done in a public database such as Clinicaltrials.gov (http://clinicaltrials.gov/). Most medical journals follow the ICMJE guidelines, and are thus very strict about only accepting trials for publication that have been prospectively registered.[13] However, many still accept retrospective registration in certain cases. Therefore, if an author's trial is not registered at the time of manuscript preparation, it is worth enquiring whether the target journal will accept retrospective registration and whether a rationale for the delay is required.[14]

Plagiarism

Finally, with the strong increase in recent years in the numbers of rejections and retractions for plagiarism,[15] close analysis of the use of references and the author's previously published work is a necessary part of manuscript preparation. Copying any previously published material – even if it is the author's own work or was done unintentionally – is considered unethical, and with more journals using plagiarism detection software such as iThenticate (CrossCheck), it is more likely that plagiarism will be noticed and the paper rejected by the journal. Medical writers have a responsibility to identify potential plagiarism in the manuscript resulting from additions made by one or more of the authors. Medical writers should help authors determine the best approach for including previously published information, whether by citation, paraphrasing, or obtaining permissions to reprint display items, to ensure the authors' ideas are retained without violating any ethical standards.

Conclusion

The primary goal of manuscript publication in the peer-reviewed medical literature is to share clinical research findings with an international audience. To do so effectively, authors and the professional medical writers who work with them need to be aware of the structural and content requirements for their manuscript, as well as the ethical guidelines underlying how research is done and how it is shared. Active involvement and awareness of the publishing process by medical writers will ensure that authors end up with a well-written and ethically sound manuscript that has a greater chance of acceptance.

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