How to write a scientific manuscript for publication

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Introduction

The origins and development of the scientific and technical press can be traced back to 1665 when the first "modern" scientific papers appeared and were characterized by non standardised form and style[1]. Subsequently, nearly 300 years ago[2], in an attempt to ensure that articles met the journal's standards of quality and scientific validity, the peer-reviewed process for scientific manuscripts was born in England and France. Since then, there has been an enormous proliferation of scientific journals and manuscripts so that, at present, the numbers of biomedical papers published annually by over 20,000 journals, at a rate of 5,500 new papers per day, far exceeds 2,000,000[1,2].

Published scientific papers and professional meetings are really essential to disseminate relevant information and research findings. However, most of the abstracts of presentations given at scientific meetings are usually available only in conference proceedings although they have the potential to be subsequently published as articles in peer-reviewed journals.

A recently published Cochrane review showed that only 44.5% of almost 30,000 scientific meeting abstracts were published as articles[3]. No association between full publication and authors' country of origin was detected. Factors associated with full publication included acceptance *vs* rejection of abstracts for oral or poster presentations, acceptance for oral presentations rather than poster sessions, "positive" results, using the report authors' definition of "positive", randomised trial study design and basic rather than clinical research.

Possible reasons for failed publication include lack of time, research still underway, problems with co-authors and negative results[4]. Undoubtedly, lack of the necessary skills and experience in the process of writing and publishing is another possible contributing factor also in the field of Transfusion Medicine although the specialists in this discipline are currently adopting the principles and research methodologies that support evidence-based medicine[5], and high-level research is actually being carried out at the same rate as in all medical specialties.

There are three broad groups of manuscripts: original scientific articles, reviews and case reports. Although case reports are part of the evidence hierarchy in evidence-based practice, albeit at a lower level, and case series are incorporated in a significant proportion of health technology assessments[6], this article will address the multiple steps required in writing original articles and reviews with the aim of providing the reader with the necessary tools to prepare, submit and successfully publish a manuscript.

The anatomy of a paper: from origin to current format

The history of scientific journals dates from 1665, when the French "Journal des sçavans" and the English "Philosophical Transactions of the Royal Society" first began systematically publishing research results[7]. From then on, the initial structure of scientific papers evolved gradually from letters (usually by a single author, with a polite style and contemporarily addressing multiple subjects) and experimental reports (essentially descriptive and presenting experiences and effects in chronological order) to a better structured and more fluent form characterised by an embryonic description of methods and interpretation of results. This evolved way of reporting experiments gradually replaced the letter form.

It was not, however, until the second half of the 19th century that the method description became fully developed and a comprehensive organisation of the manuscripts known as "theory-experiment-discussion" emerged[1]. At the beginning of the last century a gradual decrease of the use of the literary style coincided with a growing standardisation of the editorial rules that paved the way for the formal established Introduction, Methods, Results, and Discussion (IMRAD) structure of scientific papers, which was adopted in the 1980s.

At present, IMRAD is the format encouraged for the text of observational (i.e. retrospective/descriptive) and experimental (i.e. randomised controlled) studies by the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" which have become the most important and widely accepted (by over 500

biomedical journals) guide to writing, publishing, and editing in international biomedical publications[8]. The Uniform Requirements are released by the International Committee of Medical Journal Editors (ICMJE), an evolution of the initial group of Journal Editors who met for the first time in Vancouver in 1978 and subsequently issued a number of editorial policy statements and guidelines for manuscript submission.

According to the ICMJE, "this so-called IMRAD structure is not an arbitrary publication format but rather a direct reflection of the process of scientific discovery"[9]. In addition it facilitates modular reading and locating of specific information, which is normally found in pre-established sections of an article[7].

"Long articles may need subheadings within some sections (especially Results and Discussion) to clarify their content. Other types of articles, such as case reports, reviews and editorials, probably need to be formatted differently"[9].

This format does not comprise other important and integral parts of the article, such as the Title Page, Abstract, Acknowledgements, Figures and Tables (comprising their legends) and References[8].

There are often slight variations from one journal's format to another but every journal has instructions to authors available on their website and it is crucial that authors download and comply with them.

The latest edition of the Uniform Requirements was updated in April 2010; it is available at the ICMJE website and is an essential guideline for all authors writing a biomedical manuscript[9].

Consolidated standards of reporting trials

Medical science depends entirely on the transparent reporting of clinical trials[10].

Unfortunately, several reviews have documented deficiencies in reports of clinical trials[11-15].

In 1996, a group of scientists and editors developed the CONsolidated Standards Of Reporting Trials (CONSORT) statement which is intended to improve the reporting of a randomised, controlled trial (RCT), enabling readers to understand the design of a trial, its conduct, analysis and interpretation and to assess the validity of its results[16]. It emphasises that this can only be achieved through complete transparency from authors.

The CONSORT statement was updated in 2001 and after the 2007 meeting the statement was further revised and published as CONSORT 2010 which is the most up-to-date version and can be freely viewed and downloaded through one of the several link to Journals available at the CONSORT website under the section "CONSORT Statement - Downloads"[17]. The statement facilitates critical appraisal and interpretation of RCT and many leading medical journals and major international editorial groups have endorsed it.

The statement consists of a checklist (25 items) and a flow diagram that authors can use for reporting a RCT. The checklist items pertain to the content of the Title, Abstract, Introduction, Methods, Results, Discussion and Other information. The flow diagram is intended to depict the passage of participants through a RCT (enrolment, intervention allocation, follow-up and analysis). It is strongly recommended that the CONSORT Statement be used in conjunction with the CONSORT Explanation and Elaboration Document which is available at the CONSORT website under the above mentioned section[17].

Another major point to consider is the obligation to register clinical trials[9].

In September 2004 the ICMJE changed their policy and decided they would consider trials for publication only if they had been registered before the enrolment of the first participant. The ICMJE accepts registration in the international registries listed in Table I.

Table I - International trial registries acceptable to the International Committee of Medical Journal Editors and relevant websites.

Registry	Website
Australian New Zealand Clinical Trials Registry (ANZCTR)	www.anzctr.org.au
ClinicalTrials.gov	www.clinicaltrials.gov
International Standard Randomised Controlled Trial Number Register (ISRCTN)	www.ISRCTN.org
University Hospital Medical Information Network Clinical Trial Registry (UMIN-CTR)	www.umin.ac.jp/ctr/index/htm
Netherlands Trial Register	www.trialregister.nl/
European Union Drug Regulating Authorities Clinical Trials (EudraCT) Database	https://eudract.ema.europa.eu/
Any of the primary registries that participate in the WHO International Clinical Trials Registry Platform (ICTRP)	http://www.who.int/ictrp/network/primary/en/index.html

Strengthening the reporting of observational studies in epidemiology

The reporting of observational studies frequently lacks details and is not clear enough[18,19]. Consequently the quality is poor although many questions in medical research are investigated in observational studies and overwhelming evidence is also extrapolated from them[20]. In fact, observational studies are more suitable for the detection of rare or late adverse effects of treatments, and are more likely to provide an indication of what is achieved in daily medical practice[21].

To improve the reporting of observational studies (cohort, case-control or cross-sectional studies) a group of methodologists, researchers and editors developed a useful checklist of 22 items: the StrengThening the Reporting of OBservational studies in Epidemiology (STROBE) Statement[21]. The checklist items pertain to the content of the Title, Abstract, Introduction, Methods, Results, Discussion and Other information sections of articles. The STROBE checklists can be freely viewed and downloaded at the STROBE website under the section "Available checklists"[22]. They also include a draft checklist for conference abstracts (items to be included when reporting observational studies in a conference abstract) pertaining to the content of the following sections: Title, Authors, Study design, Objective, Methods, Results and Conclusion.

The STROBE Statement provides guidance to authors on how to improve the reporting of observational studies, it facilitates critical appraisal and interpretation of studies and is widely supported by reviewers, a growing number of biomedical journal editors and readers.

The STROBE checklist is best used in conjunction with an explanation and elaboration article which discusses each of the 22 checklist items, gives methodological background, publishes examples of transparent reporting and is freely available at the STROBE Statement website under the above mentioned section through the link with the Journals in which the document has been published (PLoS Medicine, Annals of Internal Medicine and Epidemiology)[22].

Reviews

As review articles comprehensively cover a specific biomedical topic and justify future research directions, they require that the author extensively review and master the literature and then develop some general statements and conclusions with practical implications for patients' care[23,24]. In addition, they should provide an updated reference for those readers interested in broadening their knowledge of critical issues. Review articles are, therefore, important not only for younger physicians early in their career but also for senior academic staff as they represent a tool for intellectual enrichment and enhancement of the standards of research. Writing a review requires knowledge and continuous improvement of qualifications in line with the accumulation of better and updated scientific literature evidence. For this reason, journals often invite experts on a specific topic to write a review article. However, authors can also ask Editors if they would be interested in publishing a review article on a particular, topical, relevant and debated issue.

As reviews are the most accessed among the various types of articles and contribute substantially to the impact factor of journals, obviously they are welcomed and encouraged by many journals and have become an inseparable part of the writing scientific culture.

The three basic types of literature reviews are narrative reviews (which include editorials, commentaries and narrative overviews or non-systematic narrative reviews), qualitative systematic reviews and quantitative systematic reviews (meta-analyses) (Table II)[25].

Table II - Summary of the types of literature reviews.

- Narrative reviews:
Editorials
Commentaries
Narrative overviews or non-systematic narrative reviews
- Qualitative systematic reviews
- Quantitative systematic reviews (meta-analyses)

Editorials

Editorials, typically written by the editor of the journal or an invited guest, may be a narrative review if the author retrieves and summarises information about a particular topic for the reader[25]. Usually, these types of narrative reviews are based upon a short, select and narrowly focused review of only a few papers. However, editorials may be no more than the editor's comments regarding a current issue of the journal or a current event in health care and do not, therefore, automatically qualify as narrative reviews.

Commentaries

Commentaries may also be written as a narrative review; however, they are typically written with a particular opinion being expressed[25]. Research methodology is not usually presented in these articles which reflect the author's biased synthesis of other articles. Commentaries are usually shorter than a full-length review article and the author should be an expert in the content area of the commentary. Usually, the purpose of a commentary is to stimulate academic debate between the journal's readers.

Narrative reviews

Non-systematic narrative reviews are comprehensive narrative syntheses of previously published information[26]. This type of literature review reports the author's findings in a condensed format that typically summarises the contents of each article. Authors of narrative overviews are often acknowledged experts in the field and have conducted research themselves. Editors sometimes solicit narrative overviews from specific authors in order to bring certain issues to light. Although the bibliographic research methodology is an obligatory section in systematic reviews and

meta-analyses, it is also becoming an inseparable part of narrative literature reviews. Providing information on the databases accessed, terms, inclusion and exclusion criteria and time limits adds objectivity to the main messages and conclusions. It is advisable to use only credible databases (at least two or three) which only select high-quality publications that contain the most up-to-date information (see Table III)[24]. The best way to organise the analysis of the sources in the main text of a narrative biomedical review is to transform information from the retrieved publications into bibliographic cards with a short description of the main results, level of evidence, strengths and limitations of each study and relevance to each section of the manuscript. Furthermore, the readability of a review can be improved by including a few self-explanatory tables, boxes, and figures synthesising essential information and conveying original messages[24]. We also suggest the use of software packages for reference management, which saves time during the multiple revisions.

In conclusion, a successful narrative review should have the following characteristics: be well-structured, synthesise the available evidence pertaining to the topic, convey a clear message and draw conclusions supported by data analysis.

Table III - Main online libraries, catalogues and databases.

MEDLINE/PubMed
Excerpta Medica/EMBASE
Scopus
Thomson Reuters' Web of Science
Cochrane Library
Database of Abstracts and Reviews of Effectiveness (DARE)
Cumulative Index to Nursing and Allied Health Literature (CINAHL)
Google Scholar

Qualitative systematic reviews

Qualitative systematic reviews are a type of literature review that employ detailed, rigorous and explicit methods and are, therefore, a more powerful evidence-based source to garner clinical information than narrative reviews, case reports, case series, and poorly conducted cohort studies. A detailed bibliographic research based upon a focused question or purpose is the peculiar characteristic of a systematic review[27]. These reviews are called qualitative because the process by which the individual studies are integrated includes a summary and critique of the findings derived from systematic methods, but does not statistically combine the results of all of the studies reviewed.

Quantitative systematic reviews

A quantitative systematic review or meta-analysis critically evaluates each paper and statistically combines the results of the studies[28]. The authors of a meta-analysis employ all of the rigorous methodology of qualitative systematic reviews and, in addition, gather the original patients' data from each of the studies under review, pool it all together in a database and produce the appropriate statistics on this larger sample. While this process leads to a more powerful and generalizable conclusion, which is the strength of the meta-analysis, on the other hand it can pool together studies that are very heterogeneous which is the main drawback of a quantitative systematic review. Nevertheless, well-executed quantitative systematic reviews constitute the highest level of evidence for medical decision making[28].

The recently published Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement aims to help improve reporting, focusing on systematic reviews of RCT. The Statement consists of a checklist of 27 essential items for transparent reporting and a flow diagram for the phases of study selection and is accompanied by the PRISMA Explanation and Elaboration Document, which, among other things, provides examples of good reporting for the various review sections[29].

A further guidance on the reporting of systematic reviews has been published by the Cochrane Collaboration, an international organisation that prepares, updates and publishes systematic reviews of the effects of health-care interventions following a standardised format[30].

Preparing to write a manuscript

Background information

The question or hypothesis formulated by the investigator is the common starting point to search the relevant published literature for an answer[31]. Gathering the background information through an extensive literature search relevant to the topic of interest is the subsequent essential step. Peer reviewers are often experts and not citing important articles poses the manuscript at risk of rejection. It is advisable to consult at least two or three credible databases (see Table III) to identify the crucial relevant articles and to track down "landmark" articles. In addition, avoid using papers published more than 10 years ago and do not rely on just the abstracts but obtain full-text articles. Articles relevant to the research topic and published in the journal in which the paper is to be submitted should be reviewed and cited[32].

Last but not least, the bibliographical search should also aim at finding recently published articles similar to the one the author intends to submit. In fact, a journal can be less interested in publishing such a manuscript unless the results reflect new or different findings.

Target journal

It can be worth thinking about this issue before starting to write as a proper choice of the journal can affect not only the writing style but also the ease of publication and the prompt dissemination of research. Ideally, the target journal should be the one in which similar work has been published[32].

Electronic and open-access journals are the latest resources for publishing and data dissemination available on the scientific journal horizon.

It is also worth considering an appropriate level of impact factor or journal quality. The impact factor of a journal is a measure reflecting the average number of citations to recent articles published in science and social science journals. It is determined by the ratio of the number of citations of papers from that journal in the whole of the biomedical literature over a 2-year period. It is frequently used as a proxy for the relative importance of a journal within its field, with journals with higher impact factors deemed to be more important than those with lower ones.

It is also extremely important to read the instructions to authors section of the selected journal carefully. In fact, although there is a general style for most biomedical journals as agreed by the ICMJE in the Uniform Requirements[9], individual journals may differ slightly in detail.

Authorship

It is always best to sort out authorship before writing a manuscript as authorship order can be a source of problems once the paper has been written[23].

Several guidelines relating to authorship are available and this issue has been extensively addressed in a recently published review article by Elizabeth Wager[33]. Most guidelines on the authorship of scientific articles are focused more on creative and intellectual aspects of research than on routine or technical contributions.

Alhough not universally accepted, the authorship criteria suggested by the ICMJE are the ones most widely promoted by medical journals[9]. According to these criteria, co-authors should: (i) substantially contribute to conception and design of the study, acquisition of data, or analysis and interpretation of data; (ii) draft the article or revise it critically for important intellectual content; and (iii) approve the final version.

The authors are listed in decreasing order of their contribution and the senior author, or mentor, should be the last but this convention has never been codified[33].

It is advisable to provide accurate affiliations and contacts as they will be published on PubMed as well as in the journal but it is also important to agree on the corresponding author who should have full access to the study data and through the provided e-mail address will be the link with the scientific community for the future[1].

Ethical issues

In addition to the authorship discussed above, there are several ethical issues involved in writing a paper. These include fabrication of data, duplicate publication, plagiarism, misuse of statistics, manipulation of images and inadequate or obviously false citations[31].

A must-read for all those who are involved in any editorial activity are the guidelines released by the Committee on Publication Ethics (COPE) which is a forum for editors and publishers of peer-reviewed journals to discuss all aspects of publication ethics[34]. COPE provides advice to editors and publishers on all aspects of publication ethics and, in particular, how to handle cases of research and publication misconduct.

Writing the manuscript

Several models for the initial draft exist. A useful algorithm for writing a scientific manuscript is the one recently published by O'Connor and Holmquist[35]. According to these authors, the writing should start with making figures and tables, and then proceed with summary statements (the conclusions summarising the major contributions of the manuscript to the scientific community), identification of the audience, materials and methods, results, discussion, references, introduction, title and conclusion. The aim of this algorithm is to give the structural backbone to the manuscript and is designed to overcome writer's block and to assist scientists who are not native English speakers.

A further and more general strategy to increase productivity during the early phases of manuscript writing is to ignore at the outset all the details that can be approached later such as structure, grammar and spelling.

The sequence of writing should address the following core sections of the paper in the order from first to last: methods, results, discussion and introduction[31,36,37].

"Like every well-written story, a scientific manuscript should have a beginning (Introduction), middle (Materials and Methods), and an end (Results). The Discussion (the moral of the story) puts the study in perspective. The Abstract is an opening summary of the story and the Title gives the story a name"[38]. However, as correctly pointed out by Michael McKay, "writing is not necessarily in the temporal order of the final document (i.e. the IMRAD format)"[39].

The take-home messages are, therefore: (i) a clear understanding of the essential components of each of these sections is critical to the successful composition of a scientific manuscript; (ii) the proper order of writing greatly facilitates the ease of writing; (iii) the approach to writing can be customised by authors on the basis both of the subject they are dealing with and their personal experience; (iv) the CONSORT[16,17], STROBE[21,22]

or PRISMA[29] statement must be used as a guidance document for the appropriate reporting of the type of study the authors are dealing with[31,32,38].

In the following part of this paper the different sections of a manuscript will be dealt with in the order they are presented in the final document.

Title, keywords and abstract

The title is determinant for the indexing process of the article and greatly contributes to the visibility of the paper. It should reflect the essence of the article, its novelty and its relevance to the biomedical field it deals with[24]. It should be clear, brief, specific, not include jargon or non-standard and unexplained abbreviations, reflect the purpose of the study and state the issue(s) addressed rather than the conclusions[38]. Indicative titles are, therefore, better than declarative ones. Obviously, the title and abstract should correlate with each other.

Available evidence suggests that the presence of a colon in the title positively correlates with the number of citations[40]. In other words, the more specific and accurate the description of the content is, the more chance the manuscript has of being cited[38].

The title of systematic reviews should ideally follow the participants, interventions, comparisons, outcomes, and study design (PICOS) approach, and include the terms "systematic review", "meta-analysis", or both[41].

The keywords enable the database searching of the article and should be provided in compliance with the instructions to authors. A careful choice from the Medical Subject Headings (MeSH) in the National Library of Medicine (NLM) controlled vocabulary thesaurus used for indexing articles in PubMed greatly increases the chances the paper is retrieved and cited by other authors[42].

The abstract is the last section to be written but it is the most important part of a paper because it is usually the first to be read and readers use the information contained in it to decide whether to read the whole article or not. It should be a concise summary of the manuscript and no longer than specified in the instructions to authors. Usually, abstracts do not contain references and abbreviations and acronyms are not always allowed. If required, it has to be structured in a specific way. For example, original articles submitted to Blood Transfusion, require an abstract of no more than 2,000 characters (including spaces), structured as follows: Background, Materials and methods, Results, Discussion[43].

A good abstract should be easy to understand and broadly appealing, informative but not too detailed. It can start with a sentence or two outlining the work; then the disease and/or system studied must be introduced and what was previously unknown has to be stated in order to provide a brief overview of the current state-of-the art knowledge on the issue. The methods must be summarised without too many details; the major findings must be clearly indicated and followed by a sentence or two showing the major implications of the paper that must be consistent with the study conclusions without overestimating their possible relevance[44]. In the abstract the present tense should be used to refer to facts already established in the field, while the findings from the current study should be dealt with in the past tense.

Introduction

The aim of the introduction is to introduce the topic to the readers in a straightforward way, avoiding excessive wordiness[42]. For this reason it should be short and focused, comprising approximately three paragraphs in one page[37].

The first paragraph should mention the questions or issues that outline the background of the study and establish, using the present tense, the context, relevance, or nature of the problem, question, or purpose (what is known)[23,37].

The second paragraph may include the importance of the problem and unclear issues (what is unknown).

The last paragraph should state the rationale, hypothesis, main objective, or purpose thus clearly identifying the hypothesis to be treated and the questions addressed in the manuscript (why the study was done).

One of the most common mistakes is the failure to make a clear statement of purpose. This is because many research projects, especially retrospective clinical studies, do not start at the beginning (with the identification of a specific question, followed by methods and data collection) but begin by collecting data without first identifying a specific question to be addressed that must in any case be established before beginning to write[38]. Data or conclusions from the study should not be presented or anticipated in the introduction section.

Writing the introduction at the end of the process prevents any block and it is easier after the methods, results and discussion have been completed.

Materials and methods

The methods section is one of the most important parts of a scientific manuscript and its aim is to give the reader all the necessary details to replicate the study.

CONSORT[16,17], STROBE[21,22] and PRISMA[29] statements provide a guideline relevant to the particular type of study[2,42].

The two essential elements of this section are a clear presentation of the study design and the identification and description of the measurement parameters used to evaluate the purpose of the study.

It is, therefore, necessary to provide a thorough explanation of the research methodology, including the study design, data collection, analysis principles and rationale. Special attention should be paid to the sample selection, including inclusion and exclusion criteria and to any relevant ethical considerations. A description of the randomisation or other group assignment methods used should be included, as should be the pre-specified primary and secondary outcome(s) and other variables.

According to the Uniform Requirements[9], in the case of experimental/clinical reports involving patients or volunteers, the authors must provide information about institutional, regulatory and ethical Committee authorisation, informed consent from patients and volunteers and the observance of the latest release of the Helsinki Declaration[45].

When reporting experiments on animals, authors should state which institutional authority granted approval for the animal experiments[9].

Finally, in addition to describing and identifying all the measurement parameters used, it is also important to describe any unusual statistical methodology applied, how subjects were recruited and compensated and how compliance was measured (if applicable).

Results

The results section consists of the organised presentation of the collected data. All measurements that the authors described in the materials and methods section must be reported in the results section and be presented in the same order as they were in that section[35]. The past tense should be used as results were obtained in the past. Author(s) must ensure that they use proper words when describing the relationship between data or variables. These "data relation words" should be turned into "cause/effect logic and mechanistic words" in the discussion section. A clear example of the use of this appropriate language can be found in the article by O'Connor[35].

This section should include only data, including negative findings, and not background or methods or results of measurements that were not described in the methods section[2]. The interpretation of presented data must not be included in this section.

Results for primary and secondary outcomes can be reported using tables and figures for additional clarity. The rationale for end-point selection and the reason for the non-collection of information on important non-measured variables must be explained[35].

Figures and tables should be simple, expand text information rather than repeat it, be consistent with reported data and summarise them[23]. In addition, they should be comprehensible on their own, that is, with only title, footnotes, abbreviations and comments.

References in this section should be limited to methods developed in the manuscript or to similar methods reported in the literature.

Patients' anonymity is essential unless consent for publication is obtained.

Discussion

The main objective of the discussion is to explain the meaning of the results.

This section should be structured as if it were a natural flow of ideas and should start with a simple statement of the key findings and whether they are consistent with the study objectives enunciated in the last paragraph of the introduction. The strengths and the limitations of the research and what the study adds to current knowledge should then be addressed[42].

Through logical arguments, the authors should convert the relations of the variables stated in the results section into mechanistic interpretations of cause and effect using the present tense as these relations do exist at present[35]. In addition, they should describe how the results are consistent or not with similar studies and discuss any confounding factors and their impact.

They should avoid excessive wordiness and other commonly made errors such as[38]: (i) including information unrelated to the stated purpose of the article; (ii) repeating detailed data previously presented in the Results section; (iii) not interpreting and not critically analysing results of other studies reviewed and cited but rather just repeating their findings; (iv) presenting new data or new details about techniques and enrolment criteria, and (v) overstating the interpretation of the results.

Another common mistake is to forget to criticise the research described in the manuscript by highlighting the limitations of the study. The value of a scientific article is enhanced not only by showing the strengths but also the weak points of the evidence reported in the paper.

Conclusion

The conclusion is a separate, last paragraph that should present a concise and clear "take home" message avoiding repetition of concepts already expressed[32]. The authors should also avoid excessive generalizations of the implications of the study and remember that except for RCT there can only be testable hypotheses and observed associations, rather than rigorous proof of cause and effect[42]. Possible implications for current clinical practice or recommendations should be addressed only if appropriate.

Finally, the areas for possible improvement with future studies should be addressed avoiding ambiguous comments such as "there is a need for further research"

and if there is a real need for further studies on the topic it is strongly advisable to be specific about the type of research suggested.

Acknowledgements

All contributors who do not meet the criteria for authorship should be listed in an Acknowledgements section[9]. The authors should, therefore, add a statement on the type of assistance, if any, received from the sponsor or the sponsor's representative and include the names of any person who provided technical help, writing assistance, editorial support or any type of participation in writing the manuscript.

In addition, "when submitting a manuscript authored by a group, the corresponding author should clearly indicate the preferred citation and identify all individual authors as well as the group name. Journals generally list other members of the group in the Acknowledgments. The NLM indexes the group name and the names of individuals the group has identified as being directly responsible for the manuscript; it also lists the names of collaborators if they are listed in Acknowledgments"[9].

References

The first suggestion is to follow the journal's policies and formatting instructions, including those for books and web-based references. Other general considerations related to references, including the following ones, can be found in the Uniform Requirements[9].

References to review articles are an efficient way to guide readers to a body of literature but they do not always reflect original work accurately. Papers accepted but not yet published should be designated as "in press" or "forthcoming" and information from manuscripts submitted but not accepted should be cited in the text as "unpublished observations".

Avoid using abstracts as references and citing a "personal communication" unless it provides essential information not available from a public source. In this case the name of the person and date of communication should be cited in parentheses in the text. Do not include manuscripts "in submission"

In addition it is important to remember that "authors are responsible for checking that none of the references cite retracted articles except in the context of referring to the retraction. Authors can identify retracted articles in MEDLINE by using the following search term, where pt in square brackets stands for publication type: Retracted publication [pt] in PubMed"[9]. Last but not least, remember that if a reviewer does not have access to any references he or she can ask the author for a full (pdf) copy of the relevant works.

Tips for successful revision of a manuscript

Most papers are accepted after some degree of revision. In some cases, a manuscript may be rejected after internal and editorial review only.

The process of revising a manuscript and successfully responding to the comments of reviewers and Editor can be challenging. Little has been published addressing the issue of effectively revising a manuscript according to the (minor or major) comments of reviewers. This topic was recently extensively and pragmatically covered by James M. Provenzale[46]. The ten principles for revising a manuscript suggested by the author are reported in Table IV.

Table IV - Ten principles for revising a manuscript suggested by James M. Provenzale[46].

1.	Decide whether to resubmit the manuscript to the same journal
2.	Contact the editor regarding unresolved issues
3.	Prioritise the reviewers' comments
4.	Approach the reviewer as a consultant rather than an adversary
5.	Deal with reviewers' comments with which one does not agree
6.	Disagree without being disagreeable
7.	Devise a strategy for responding to divergent comments
8.	Put in the work and show all that you have done
9.	If requested, shorten the manuscript
10.	Review the medical literature before resubmission

Conclusion

Many manuscripts are not published simply because the authors have not followed the few simple rules needed to write a good article. We hope that this paper provides the reader with the basic steps to build a draft manuscript and an outline of the process needed for publishing a manuscript. However, in Table V we summarise the ten principles we strongly recommend to comply with in order to improve the likelihood of publication of a scientific manuscript[47].

Table V - Ten principles to improve the likelihood of publication of a scientific manuscript, suggested by James M. Provenzale[47].

1.	Organise the manuscript properly
2.	State the study question and study rationale clearly
3.	Explain the materials and methods in a systematic manner
4.	Structure the materials and methods and results sections in a similar manner
5.	Make the discussion section concise
6.	Explain if -and why- your study results are important
7.	Avoid overinterpretation of the results
8.	Explain the limitations of the study
9.	Account for unexpected results
10.	Fully incorporate reviewers' suggestions into a revised manuscript

Keywords: medical manuscript, publication, journal article, review, authorship.

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