

## **How to Write an Oncology Manuscript**

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### **ABSTRACT**

Publications may represent accomplishment in academic medicine, primary documentation of research data, evidence of expertise through writing an authoritative review paper or book chapter or a major determinant in achieving academic promotion and career development.

Editors and reviewers appreciate receiving manuscripts that are easy to read and edit. Much of the information in journals' instructions to authors is designed to accomplish that goal in ways that meet each journal's particular editorial needs.

The CONSolidated Standards of Reporting Trial (CONSORT) statement is an important research tool that takes an evidence-based approach to improve the quality of reports of randomized trials.

The guidance that follows provides a general background and rationale for preparing oncology manuscripts for any journal. Many of these guidelines are based on feedback provided by actual peer reviewers. Even before you start writing, it is good practice to review the typical sections of a manuscript. The text of observational and experimental articles is usually (but not necessarily) divided into sections with the headings Introduction, Methods, Results, and Discussion. This so-called "IMRAD."

The abstract of the manuscript is usually divided into background, purpose, patients and methods, results and conclusion. The section on patients and methods of an oncology manuscript should include the eligibility criteria for the patients, study design, treatment plan, baseline and treatment assessments and statistical analysis. The results include data on patient characteristics, tumor response, time to event measures, toxicity and dose administration. The conclusion must address the primary objective of the study.

Authors will be able to address up front many issues regarding content, organization, presentation, and formatting, thereby increasing the likelihood of successful publication of their papers in peer-reviewed journals.

### **INTRODUCTION**

Authors and editors should have the same goals: the advancement of scientific understanding and improvement in the treatment and

prevention of disease" [1]. Editors and reviewers spend many hours reading manuscripts, and therefore appreciate receiving manuscripts that are easy to read and edit. Much of the information in journals' instructions to authors is designed to accomplish that goal in ways that meet each journal's particular editorial needs. The guidance that follows provides a general background and rationale for preparing oncology manuscripts for any journal.

The text of observational and experimental articles is usually (but not necessarily) divided into sections with the headings Introduction, Methods, Results, and Discussion. This so-called "IMRAD" structure is not simply an arbitrary publication format, but rather a direct reflection of the process of scientific discovery. Long articles may need subheadings within some sections (especially the Results and Discussion sections) to clarify their content. Other types of articles, such as case reports, reviews, and editorials, are likely to need other formats.

The CONSolidated Standards of Reporting Trial (CONSORT) statement is an important research tool that takes an evidence-based approach to improve the quality of reports of randomized trials [2]. The statement is available in several languages and has been endorsed by prominent medical journals such as *The Lancet*, *Annals of Internal Medicine*, and the *Journal of the American Medical Association*. Its critical value to researchers, health care providers, peer reviewers, and journal editors, and health policy makers is the guarantee of integrity in the reported results of research. CONSORT comprises a checklist (Table 1) and flow diagram (Fig. 1) to help improve the quality of reports of randomized controlled trials. It offers a standard way for researchers to report trials.

The checklist includes items, based on evidence, that need to be addressed in the report; the flow diagram provides readers with a clear picture of the progress of all participants in the trial, from the time they are randomized

until the end of their involvement. The intent is to make the experimental process clearer, flawed or not, so that users of the data can more appropriately evaluate its validity for their purposes [3].

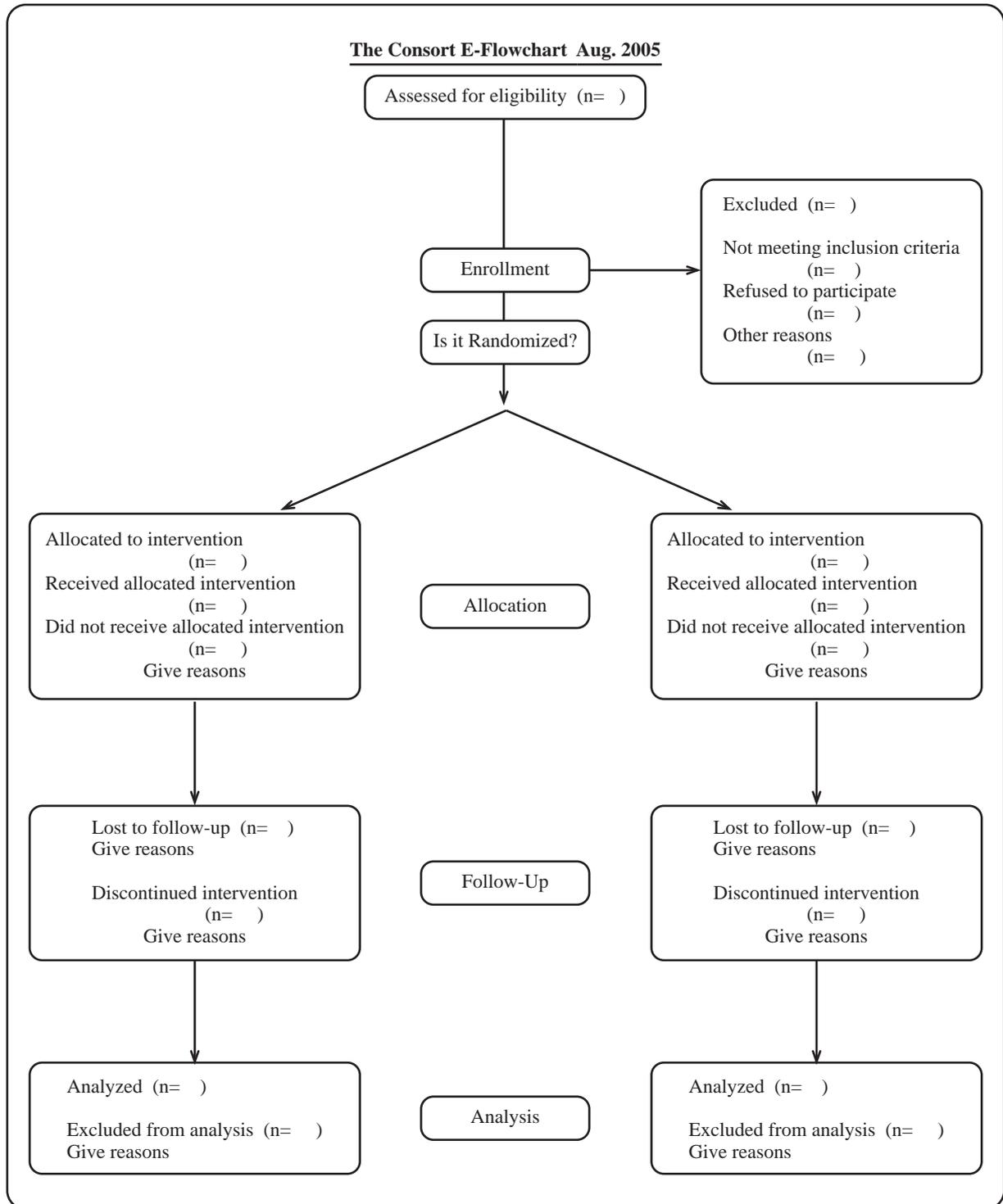


Fig. (1): The CONSORT flow chart, 2005 (3).

Table (1): CONSORT Checklist of items to include when reporting a randomized trial (3).

PAPER SECTION and topic	Item	Description	Reported on Page #
TITLE & ABSTRACT	1	How participants were allocated to interventions (e.g., "random allocation", "randomized", or "randomly assigned").	
INTRODUCTION Background	2	Scientific background and explanation of rationale.	
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	
Objectives	5	Specific objectives and hypotheses.	
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors).	
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (e.g., blocking, stratification)	
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. When relevant, how the success of blinding was evaluated.	
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	
Recruitment	14	Dates defining the periods of recruitment and follow-up.	
Baseline data	15	Baseline demographic and clinical characteristics of each group.	
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (e.g., 10/20, not 50%).	
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (e.g., 95% confidence interval).	
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	
Adverse events	19	All important adverse events or side effects in each intervention group.	
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	
Generalizability	21	Generalizability (external validity) of the trial findings.	
Overall evidence	22	General interpretation of the results in the context of current evidence.	

Even before you start writing, it is good practice to consider the following:

- 1- Spark interest in the results of the study.
- 2- Decide on authorship.
- 3- Select the appropriate journal.
- 4- Review and follow journal guidelines.

#### *Developing an Effective Outline:*

Preparing an outline is the most important step in the process of producing a manuscript for publication in a journal. Its purpose is to divide the writing of the entire paper into a number of smaller tasks.

A good outline will organize the various topics and arguments in logical form. By ordering the topics you will identify, before writing the manuscript, any gaps that might exist.

Remember, at this stage, you are only constructing an outline. You are not writing; you just need to put down some notes to guide your thinking.

- Prepare a central message sentence (20-25 words). If you were asked to summarize your paper in one sentence, what would you say? Everything in the manuscript will be written to support this central message.
- Briefly state the population in which you worked, the sampling method you employed, the materials you used, and most importantly, the methods you used to carry out the study
- Summarize the question(s) and problem(s): What was known before you started the study? What answers were needed to address the problem(s)? List the key points pertaining to the question(s) and problem(s). What did you do to answer the question(s)?

Your central message sentence probably encapsulates the most important findings.

There may be others that you feel ought to be included. List these in note form.

Don't worry about the order or about how many you put down.

- Make brief notes on each of the implications that arise from your study. What are the principal conclusions of your findings? What is new in your work and why does it matter? What are the limitations and the implications of your results? Are there any changes in practice, approaches or techniques that you would recommend?

- List each key point separately. Key points can be arranged chronologically, by order of importance or by some other pattern. The organizing scheme should be clear and well structured. You can use a cluster map, an issue tree, numbering, or some other organizational structure. Identify the important details, describe the principal findings, and provide your analysis and conclusions that contribute to each key point.
- Identify the references that pertain to each key point [4].

#### *Manuscript Sections:*

The original article is like a human body: the brain represents the aim of the study, the heart is considered to be the study design, the body is the materials and methods, the arms and legs are the results, the dress is the references, tables and figures, the I.D. (photograph) is the abstract, while the soul represents the conclusion [5].

#### *Title Page:*

Authors should follow the journal's "Instructions to Authors" for exact requirements, and title page should include the following [6].

- Title of the manuscript.
- Author names and academic degrees, and complete addresses of all corresponding affiliations; be sure to correctly footnote the authors with their institutions.
- Corresponding author with full postal address, telephone, fax, and e-mail.
- Running head (a shortened title); may be optional for some journals.

The title of a manuscript should identify the topic of the paper and should be accurate, complete, specific/informative, concise, and clear. Avoid using abbreviations in titles. In addition to the treatment, the title may include the study type (eg. phase II).

#### *Abstract:*

Depending on the journal's "Instructions to Authors", this section may be called Abstract or Summary.

- Abstract should include: background, purpose, patients and methods, results and conclusions.
- Keep it short but do not exclude key information.

- Briefly state your findings.
- Conclusions must address the primary objective of the study and should be stated in the present tense.
- Place the abstract on a separate page.
- Avoid including references, trademarks, or manufacturers' names and avoid having the same sentences in the abstract and in the body of the paper.
- Define all abbreviations the first time they appear in the abstract.

#### *Introduction:*

Before beginning on the introduction, go through the notes you have made so far in your outline. Read them through and see whether there is a coherent and cohesive story and a unifying theme that runs through the outline.

- The introduction sets up the background for what we are about to learn and why it matters
- Go right to the essence in order to focus the reader's attention
- Use the literature to enhance your introduction, but the introduction is not a literature review
- Define terms used in the title, as needed
- Describe the purpose of your paper clearly and concisely [7].

For a phase I, dose-finding study, the primary objective is usually the determination of the maximum tolerated dose (MTD); secondary objectives typically include the characterization of dose-limiting toxicity (DLT), and may include response and pharmacokinetic assessments. Keep brief (one page if possible).

### **PATIENTS AND METHODS**

The Patients and Methods section in an oncology manuscript typically includes five main components:

- Eligibility Criteria.
- Study Design.
- Treatment Plan.
- Baseline and Treatment Assessments.
- Statistical Analyses.

#### *Eligibility Criteria:*

Authors should describe all patient eligibility criteria and be sure to include any previous therapy and disease stage. An informed consent should be provided.

#### *Study Design:*

Authors should provide enough information for readers to know how a trial was performed, so that they can judge whether the findings are likely to be reliable [2]. They should describe the overall study design (for example, phase II, single-arm, open-label), any special design (for example, multi-stage, sequential), and any statistical considerations for sample size and targeted enrollment.

#### *Treatment Plan:*

- Identify all drugs used including generic name, dose, route of administration, timing of administration (for example, which days per cycle, drug sequence), and cycle length.
- Include the maximum number of cycles planned and reasons for early discontinuation from the study.
- Include guidelines for dose adjustments.
- Describe any other interventions such as surgery, supportive therapy, or post-study chemotherapy or surgery.

#### *Baseline and Treatment Assessments:*

- Describe all pre-study and on-study procedures (plus any important follow-up procedures) and assessments, including the timing of assessments (for example, timing for response and toxicity measures, and median follow-up time for time-to-event measures).
- Specify any formal evaluability criteria for efficacy or toxicity assessments.
- Describe any criteria or identify scales used for response and toxicity assessments (that is, WHO, SWOG, CTC, RTOG criteria, and so on).
- Indicate what response calculations are based on (for example, best response, evaluable, or intent-to-treat patient sample), and how toxicity data are presented (for example, maximum grade, only grade 3/4).
- Include intervals for all time-to-event measures such as duration of response, survival, time to progression, and time to treatment failure. Example: survival was measured from the date of the first dose until the date of death from any cause [6].

#### *Statistical Analyses:*

- Describe all statistical tests or methods used (for example, Kaplan-Meier estimates, log rank test, *t*-test, chi-square test), and include

all relevant statistical output (for example, mean with standard deviation, standard error, or confidence interval, median with range or confidence interval, quartiles,  $p$  values) taking into consideration to specify any computer programs and versions of statistical software used and to provide references for new, or not well established analytical methods.

- Note that the determination of the success or failure of a therapeutic treatment after a phase II trial depends on the quality of the statistical design [8].

## RESULTS

Authors should present their results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first, avoid repeating in the text all the data in the tables or illustrations; and emphasize or summarize only important observations. When data are summarized in the results section, they should give numeric results not only as derivatives (for example, percentages), but also as the absolute numbers from which the derivatives were calculated, and specify the statistical methods used to analyze them. Tables and figures should be restricted to those needed to explain the argument of the paper and to assess its support. The use of graphs as an alternative to tables with many entries may be of help taking in consideration not to duplicate data in graphs and tables. Where scientifically appropriate, analyses of the data by variables such as age and sex should be included [3].

### *Patient Characteristics:*

- Provide dates of the study.
- Include a patient characteristics table with a reference in the text that provides the number of enrolled and evaluable patients, median age plus range, percentage of males and females, and percentage of relevant disease characteristics (such as performance status scores, disease stages, number and types of metastatic sites, previous therapies, and so on).

### *Tumor Response:*

- Indicate the number of evaluable patients and those not assessed and provide reasons why non-evaluable and non assessed cases were excluded from the study (such as insufficient therapy for non-evaluable patients and lack

of a follow-up measurement for non-assessable). Non-assessable patients who meet evaluability criteria should be included in the denominator for calculation of response.

- Use the correct denominator for calculation of response (that is, using an evaluable or intent-to-treat patient sample as specified by the statistical method).
- Provide calculation of overall response with 95% confidence interval, and % of patients with complete and partial response (sum equals overall response), stable disease, and progressive disease. The duration of response should be provided with 95% confidence interval or range [6].

### *Time-to-Event Measures:*

- Give medians plus 95% confidence intervals or ranges for overall survival, and time to progression.
- Include Kaplan-Meier figures for overall survival and other measures if required by statistical methods, also provide median time to follow-up and range for every time to event measure and provide actuarial survival rates.

### *Toxicity:*

- Indicate the number of patients that are evaluable for toxicity and explain reasons for those non-evaluable.
- Summarize the main hematologic and non-hematologic toxicities and clinical consequences (especially bleeding, transfusions required, and neutropenic fever).
- Include a table of toxicities, it is generally sufficient to present just toxicity grades 3/4 in the table and to indicate any toxicity that resulted in death.

### *Dose Administration:*

- Provide the total number of cycles administered, median number of cycles per patient plus range, number of reductions, omissions, and delays, and actual and relative dose intensities.
- Express actual dose intensity as mean or median dose per week.

### *Discussion:*

- Begin with your most important point.
- Do not repeat the introduction.

- Do not present any new data / avoid repeating.
- Second paragraph: describe novelty of your findings or if they parallel previous research
- Third paragraph: describe how study contradicts previous research or established dogmas
- The fourth paragraph: describe study limitations
- Concluding paragraph: summarize potential significance of findings. Avoid overstating conclusions like "a new standard of care has been achieved" unless clearly supported by the data. State conclusions in present tense [7].

#### *Citing References:*

- Be sure that reference numbers in the text, tables, and figure legends correctly match those in the list of references.
- References are usually numbered in the order in which they appear in the manuscript.
- References cited in tables or figure legends but not in the text should be numbered in order from the point at which the table or figure is first cited in the text (as if the tables or figure legends are part of the text).
- Each journal has its own style of references (house-style) explained in "Instructions to Authors". Read the instructions and examine a recent copy of the Journal.
- All references should be written in the same style with the same arrangement.

#### *Tables:*

Tables pick up the content without reading the text and reveal the results at a glance. Each table should be typed with double spacing on a separate sheet of paper and numbered consecutively in the order of their first citation in the text. Statistical measures of variations, such as standard deviation and standard error of the mean should be identified. Each table must be cited in the text (3).

#### *Figures:*

- Check the journal's "Instructions to Authors" and/or other issues of the journal to which you plan to submit to see how many figures are allowed or generally used.
- Figure legends are double-spaced and generally go after the tables and before the figures

on a separate page. All figure legends can appear on a single page.

- Number figures in the order in which they appear in the text; each figure must be on a separate page and be cited in the text.
- Letters, numbers, and symbols (including those on axes) should be clear and of sufficient font and size to be legible when the figure is reduced for publication.
- Usually only black and white figures are necessary, but make sure that different plots are distinctly different (for example, a solid line versus a dashed line); use color in figures only if necessary.

#### *Ethical Considerations:*

- Whatever the results, always publish as you have a responsibility to trial patients, and to ensure the completeness of the evidence base. In general, only publish when you have all patients' data. Always report possible conflicts of interest and obtain informed consent [9].
- Understand the Declaration of Helsinki - particularly with respect to choice of controls [10].

## REFERENCES

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