Guidelines for Statistical Reporting in Medical Journals

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ABSTRACT

Statistical methods are essential in medical research. They are used for data analysis and drawing appropriate conclusions. Clarity and accuracy of statistical reporting in medical journals can enhance readers' understanding of the research conducted and the results obtained. In this manuscript, we provide guidelines for statistical reporting in medical journals for authors to consider, with a focus on the *Journal of Thoracic Oncology*.

Keywords: Statistical results; Reporting; Presenting; *p* value; Medical journals

Introduction

High-quality reporting of statistical methods and results is essential for reviewers and readers to evaluate the quality and credibility of evidence presented in a manuscript. To help authors adhere to best practices, many journals[1-4] now provide detailed guidelines. Specific guidelines are also available, such as the CONSORT statement[5] for randomized clinical trials, the Strengthening the Reporting of Observational Studies in Epidemiology statement[6] for observational studies, the STARD initiative[7] for diagnostic accuracy studies, and Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement for meta-analyses[8] (see the Enhancing the Quality and Transparency of Health Research Network[9] for a comprehensive listing of study type–specific reporting guidelines). These guidelines aim to improve the clarity of presented methods and results and standardize statistical reporting to enhance comparability with similar research. Here, we present guidelines for authors to consider when drafting manuscripts for the *Journal of Thoracic Oncology*.

Guidelines on Statistical Reporting

In the Methods Section

The principle of writing the methods section is that it should "describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to judge its appropriateness for the study and to verify the reported results."[10]

To achieve this goal, the statistical design of the study should be described, including the objectives of the study and patient population or patient selection. Clinical trial design parameters, such as type I error (including the choice of a one-sided or two-sided test), study power, primary end point, effect size, and assumed accrual rate, are needed for readers to judge the validity of the sample size and the number of events required. Additional details on the randomization scheme, planned interim analyses, primary end point, and analysis method (including population definitions) are also necessary. For an observational study, one should mention whether the study is designed for hypothesis testing or hypothesis generation. Good practice dictates that the statistical analysis plan should be determined before conducting the analysis. This plan should include

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the level of significance that will be used in the study, which means the threshold below which a p value would indicate statistical significance. In addition, the plan should specify whether there will be p value adjustment for multiple comparisons and the rationale for the decision.

The method(s) for handling missing data should also be specified. If a data-driven variable selection was conducted, the methods employed should be described and accompanied by sufficient details of the steps taken in the process (e.g., variables initially used in the variable selection process, the threshold p value in a stepwise selection, or tuning parameter selection in a machine learning method). For Bayesian analyses or more complex statistical analyses, sufficient details should be provided in an appendix so that interested readers can fully understand the methods used for the study.

Finally, the analysis software and version should be included because they may use different optimization and numerical routines, which produce slightly different results. For a clinical trial, the clinical trial number should be listed accompanied by the trial protocol, if required by the journal.

In the Results Section

Patient Characteristics Table. The first table in the results section usually summarizes the baseline characteristics of the study population. If there is only one group of patients in the study, this table only has a single column of summarized data. However, if the main objective is to compare across identified groups, each group should have its own column. Baseline variables measured on each patient are listed as rows. This table should include all key baseline variables that define the study population in terms of demographics, comorbidities and history, and disease characteristics along with prognostic variables associated with the primary outcome. Continuous variables should be summarized with mean and SD. If the distribution of value is skewed, it is recommended that the median and range (minimum and maximum values) or the interquartile range (lower quartile and upper quartile values) should be included. Categorical values should be reported as the count and percentages for each level of the variable. If there are missing observations, the number of patients with missing data should be recorded for both continuous and categorical variables. When the number of missing values is negligible, then the percentage of missing category do not need to be calculated, and the denominator for percentage calculations should not include missing values.

If patients were randomized to the groups being compared, the p value should not be included in the patient characteristics table for the comparison across groups because any differences observed between the groups is random. However, if the study is an observational study, a p value comparing the value of a specific variable across the groups (using an appropriate statistical test) should be included for each variable in the table. For data that are for a subset of randomized patients, such as quality of life or biomarker substudies that contain only patients who consented to the substudy, the randomization no longer holds, and it cannot be assumed that differences between the groups are because of chance. If the subset contains less than 90% of the originally randomized patients, it is recommended that p values be provided in the patient characteristic table.

***p* Value.** The p value is the probability of obtaining a result at least as extreme as what was observed when the null hypothesis is true.[11] A small p value usually means that the difference found in a study is unlikely because of chance alone.[12] When results are reported, the magnitude of the difference between groups should be reported along with the p value. Differences between groups should be estimated with a point estimate (e.g., absolute differences in means or proportions, ORs, or hazard ratios, whichever is the most appropriate for the outcomes) and confidence interval (CI). The precise p value should be reported rather than stating that it is less than the level of significance or that it is not significant. Generally, it is acceptable to report p values to two decimal places (round to the nearest 100th) when greater than 0.01; three decimal places (round to the nearest 1000th) when less than 0.01. If a p value is quite small, then it is acceptable to report it as a p value less than 0.001. The p values arising from genome-wide association studies or other high-dimensional data analyses should follow guidelines specific for those methods.[13] Two-sided p values should be reported except when study designs explicitly assume a one-sided p value. Recently, the American Statistical Association[14] and other groups of the scientific community called for less emphasis on p values. As a result, we recommend reporting p values only when proper type I error controls are in place and strongly discourage p values for secondary and subgroup analyses in which point estimates and CIs are preferred. Finally, if there is a prespecified level of significance, a result is either statistically significant or not. The word *trend* should only be used in a statistical test for trends in the data and not to describe a p value that is close to the prespecified level of significance.

Reporting of Categorical Outcomes. Categorical outcomes such as response to treatment and occurrence of adverse events are common in clinical studies.

Categorical outcomes are summarized by frequencies and percentages. CIs should be reported along with the point estimates. It is important to clearly state the denominator used for estimation. When the denominator is the same for all categorical outcomes being reported, it is sufficient to state the denominator once and clarify that it is used for all subsequent outcomes; otherwise, it is important to specify the denominator used in computing the estimate for each outcome. When reporting comparisons of categorical outcomes among groups of patients, specify the statistical test used—for example, the chi-square test, Fisher's exact test, or the Z-test with or without continuity correction. It is good practice to include the same number of decimal places for all percentages. We recommend reporting the percentage with one decimal place (e.g., 12.3%) when the denominator is larger than 200.[2]

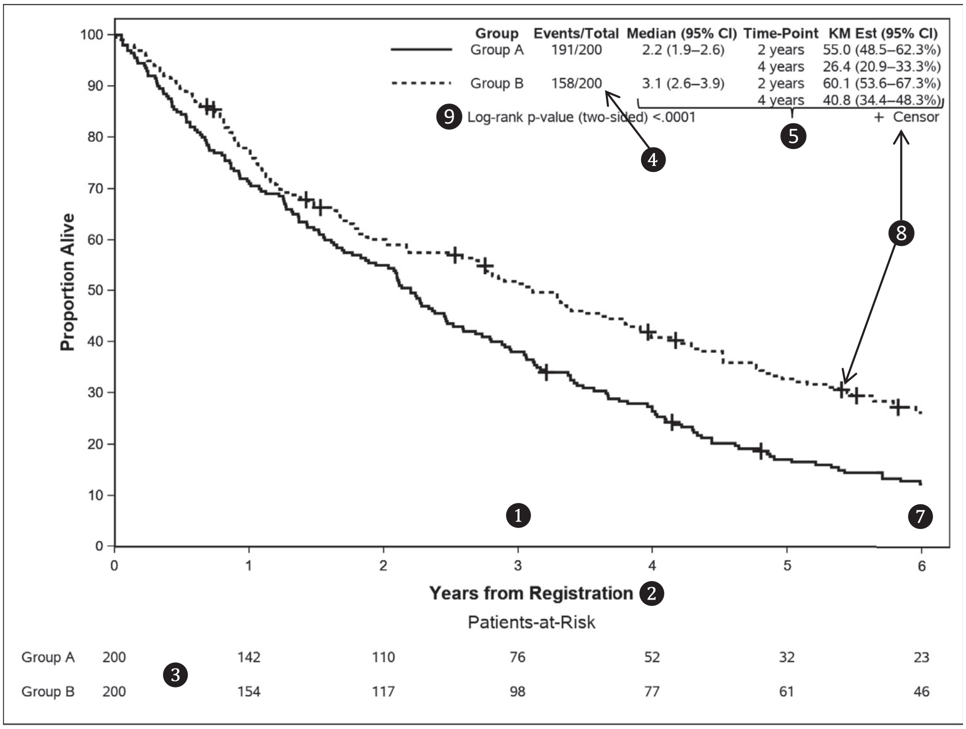
Forest Plots Are a Good Way to Present Subgroup Analysis. Forest plot is a common graphical method of illustrating treatment effects across all subgroups of interest at one glance.[15] It is meant as a visual aid rather than an inferential tool. An informative forest plot should include point estimates, CIs, and the sample sizes (including the number of events when applicable) for each subgroup so the readers can judge the precision of the estimated effects. Including subgroup *p* values in forest plots are strongly discouraged when trials are not powered to detect the treatment effect in subgroups. If hypothesis tests for specific subgroups are prespecified, the trial design should be appropriately powered and should account for the number of hypothesis tests considered in the trial.

Another strongly discouraged practice is to include *p* values for interaction tests in forest plots for subgroup analysis.[4] It is important to distinguish between subgroup analyses and interaction tests. An interaction test is a formal statistical test to evaluate whether the treatment effect is influenced by other patient characteristics (factor of interest). The test is conducted by a regression model that includes the treatment, the factor of interest, and an interaction term between the two variables using the full patient set. This is in contrast with subgroup analysis in which the treatment effect is evaluated separately for each subgroup of patients, one at a time, making it impossible to formally compare the treatment effects among subgroups of patients.

Survival Analysis. Overall survival (OS) is a common outcome used in clinical studies to judge the effectiveness of a new treatment or the prognostic effect of a baseline factor. OS data consist of two components that need to be clearly defined. The first component is the time interval starting from the time of origin (the time from which OS is being measured) to the time of death or of the last follow-up. The second component is an indicator of whether the patient died or was alive at that last time point. OS data can be summarized in multiple ways. Kaplan-Meier curves[16] are the most common visual summary for survival data, and Table 1 includes some suggestions to consider when plotting Kaplan-Meier curves with an example in Figure 1. Another quantity that is often reported with survival data is the median time that patients were followed in the study. The median follow-up time should be estimated using the Kaplan-Meier estimator with the event, and the

Table 1. Good Practices to Consider When Plotting Kaplan-Meier Curves

Domain	Recommendations
Horizontal axis	• The horizontal axis should be labeled with the time unit corresponding to the tick marks along the axis (see ❶ in Fig. 1). • If possible, specify the time of origin in the label. For example, "Months from starting treatment" (see ❷ in Fig. 1). • The numbers of patients at risk at various time points should be included at the bottom of the plot along the horizontal axis (see ❸ in Fig. 1).
Summary statistics	• Include the number of events out of the total number of patients at risk at the time of origin for each group, which are represented by a curve in the plot (see ❹ in Fig. 1). • The median survival time and survival probability at a clinically meaningful time point for each group could be included (see ❺ in Fig. 1). • If there is interest in illustrating the survival probabilities at multiple time points, this information can be included in a separate table to avoid overcrowding the plot (see ❻ in Fig. 1).
Others	• It is good practice to consider truncating the plot when the number of at risk is small, unless all patients are followed up until the end of the protocol-specified follow-up duration (see ❼ in Fig. 1). • Censored observations could be indicated in the plot with a special symbol (see ❽ in Fig. 1). • Be judicious with including *p* values in the plot. If reporting results from a randomized trial comparing survival between treatment arms using the log-rank test, it is okay to include the log-rank *p* value in the plot. If the survival comparison is based on other tests such as comparison of the survival probabilities at a fixed time point, or a comparison based on the Cox model adjusting for other covariates (as often is the case with observational studies), clearly state the statistical test used to obtain the *p* value; or better yet, do not include a *p* value in the plot. If a *p* value is included, denote whether it is one-sided or two-sided (see ❾ in Fig. 1).



❻	Event/Total	Median (95% CI)[a]	Survival Estimates (95% CI)[a]
Group			
Group A	155/200	2.2 (1.9–2.6)	2 years: 55.0 (48.3–62.6%) 4 years: 25.7 (19.7–33.5%)
Group B	118/200	3.3 (2.5–4.5)	2 years: 59.3 (52.5–67.0%) 4 years: 42.2 (35.0–51.0%)

Figure 1. A Kaplan-Meier plot of OS for two groups of patients. Refer to Table 1 for details about ❶ to ❾. A SAS macro is available to generate the Kaplan-Meier plot revealed (please refer to https://communities.sas.com/t5/SAS-Communities-Library/Kaplan-Meier-Survival-Plotting-Macro-NEWSURV/ta-p/479747). [a]Kaplan-Meier method. CI, confidence interval; KM, Kaplan-Meier; OS, overall survival.

censoring indicator reversed.[17] This method provides a more appropriate estimate of the median follow-up time than the crude median follow-up time of survivors. Additional guidelines on time-to-event analysis will be discussed in another manuscript in this special series.

Prognostic and Predictive Biomarkers in Oncology Studies. In studies that evaluate treatment impact, the goals may include discovering prognostic or predictive biomarkers. Prognostic biomarkers identify patients who have better outcomes regardless of treatment, whereas predictive biomarkers identify patients who benefit from treatment (versus those who do not). Illustrating that there is a statistically significant association between the biomarker and the outcome is sufficient to declare a biomarker as prognostic. In contrast, to declare a biomarker as predictive, it must be illustrated that the biomarker status and treatment interaction term is statistically significant.[18,19] Because the interaction between the biomarker status and treatment is required for modeling, a single-arm trial or a trial with biomarker-selected patients is inappropriate for the evaluation of predictive biomarkers.

In the Conclusion Section and the Interpretation of Statistical Results

***p* Value Greater Than 0.05 Does Not Mean Equivalence.** Care must be taken to ensure that conclusions are supported by the results of the study. If a p value is not statistically significant, it can only be concluded that no difference between the groups was observed. A nonstatistically significant p value does not support the conclusion that the two groups are similar; this can only be concluded if the study were designed to evaluate equivalence (please refer to the article on clinical versus statistical significance in this special series).[20]

Observational Study: Discuss Potential Bias and Unmeasured Confounder. Care is needed when making conclusions from observational studies. A single observational study is not sufficient to establish causation or to state that a variable impacts (influences) the outcome when the *p* value for the association is statistically significant. The *p* value only measures the likelihood that the differences are because of chance, assuming that the groups are the same on all other factors. If there are imbalances between the groups owing to biases and unmeasured confounders, this could impact the *p* value; for example, the *p* value may be statistically significant because of differences between the groups that are associated with the potential confounders, even though the group itself is not associated with the outcome. Hence, for observational study designs, an observed association or difference between groups that are statistically significant could reflect the following: (1) a true difference or association, (2) underlying biases and unmeasured confounding, or (3) a combination of (1) and (2). The study conclusions need to properly reflect this.

Conclusions

In this manuscript, we provide guidelines for authors to consider when reporting statistical results in medical manuscripts. These guidelines are not exhaustive, but they cover many common outcomes and statistical methods used in clinical studies. We strongly encourage authors who submit manuscripts to the *Journal of Thoracic Oncology* to use these guidelines to improve the clarity of their reported methods and results.

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