Data Visualization for Data Monitoring Committees for Clinical Trial

Adam Hamm, Cytel, Inc., Cambridge, MA, USA

ABSTRACT

The Clinical Trials Transformation Initiative recently published in the journal Clinical Trials an article with recommendations about data monitoring committee (DMC) use, conduct, communication practices, and member preparation and training. This paper focuses on communication practices, specifically in the area of communication of results. Presenting bulky data packages consisting of pages and pages of tables and listings can become tedious and time-wasteful for DMC members tasked with making decisions on efficacy and safety measures. This paper will focus on how data visualization and graphics can best assist in presentations to DMC members to most efficiently present data and make decisions that are in the best interest of the clinical trial. Topics will include graphical presentation of enrollment, subject withdrawal, adverse events, lab parameters, and other safety data of interest to data monitoring in clinical trials.

INTRODUCTION

Data monitoring committees (DMCs) are tasked with the review and interpretation of a diverse set of data from clinical trials. When presented as tabular summaries to committee members, it can become difficult for members who already serve in various demanding roles that leave them little time to perform a full-scale review of data. Executive summaries, or high level reports of the most important data, can often help this cause but do not always tell the entire story.

The goal of this paper is to describe best presentation and report practices for effective communication to data monitoring committees. Focus will be on the graphical presentations that will best suit a meaningful interpretation of the accumulating data. Many of the graphical presentations in this paper are credited to Sanjay Matange in his paper “Clinical Graphs using ODS Graphics” from the 2010 WUSS conference proceedings, Amit, et al. in their paper on the graphical approaches to safety data, and from a sample DMC report from the University of Wisconsin SDAC. Topics discussed will be matters commonly discussed during DMC meetings, such as enrollment rates (projected and actual), disposition, adverse event rates, and lab data. I will discuss these from my own perspective, as one who generally contracts out to sponsor companies or functions as a representative of sponsor companies in presentations to DMCs.

ENROLLMENT AND DISPOSITION

In practice, enrollment rates are generally presented by the sponsor company during an open session with the DMC. Enrollment rates can be presented by linear or non-linear plots over time or with boxplots. Boxplots provide a nice graphical presentation of the cumulative enrollment by treatment group and month as shown in the examples below. Projected enrollment rates could be overlaid on either of these plots.
Disposition information, that is, information on patient populations and discontinuations from treatment and study, are generally presented in tabular format. However, there could be benefits to presenting this information in graphical format with bar charts and shown in the example plot in Figure 2. This could be particularly useful in identifying differential effects of treatment on withdrawal rates. Similarly, time to discontinuation in the form of a Kaplan Meier plot as shown in the example in Figure 3 could be useful in identifying whether subjects discontinued one treatment earlier than another.
ADVERSE EVENTS

Depending on the number of adverse events in a study, review of standard summary tables of adverse events can be tedious, time-consuming, and at times, not very informative. Still, the majority of committees I serve with or on continue to use summary tables of adverse events as the primary source of review. Graphical presentations of adverse event rates, especially if the difference in rates between treatment groups is of interest, can aid committees in making more informed decisions on drug safety. Much like reasons for discontinuation, bar charts can be useful in providing graphical summaries of overall summaries such as the percentage of patients with AEs, related AEs, etc. as shown in Figure 4.
Relative risk, odds ratios and treatment differences can also be presented graphically for system organ classes and/or preferred terms, sorted as the user sees fit. Figure 5 shows an example using trial data that presents point estimates for incidence rates by treatment across system organ classes along with estimates for relative risk with 95% confidence intervals. These plots could be useful for identifying treatment side effects more readily than a standard summary table.

Other plots that could be useful for adverse event summary depending on the focus of safety summaries are cumulative incidence plots (similar to survival plots) for time to first adverse event.
LABORATORY DATA

Laboratory data are commonly presented for final analyses in change from baseline and shift tables, and these displays are usually inserted into DMC summaries as well. Clinicians generally do not have the time to sift through pages upon pages of long tables. Instead, what I have found is that taking a subset of lab parameters of interest in the study and providing a variety of graphical interpretation on those parameters is the most efficient and best use of a committee’s time. My favorite plots are the shift plots, especially for liver function tests and shown in an example in Figure 6 in trellis form.

By color coding the treatment groups, the user can determine if there is a differential treatment effect by examining clusters of outliers or other points of interest.

As with adverse events and treatment discontinuations, bar charts of abnormal lab parameter rates by treatment group over the entire study could be much more useful than bulky shift tables. Plots over time (mean plots and spaghetti plots by subject) could also be useful tools for identifying patients of interest who perhaps had adverse lab effects, and these are the more commonly used plots that I have seen for DMC meetings.

CONCLUSION
This paper presents suggestions for graphical presentations at DMC meetings, primarily for enrollment, disposition, and safety data such as adverse events and labs. It has been my experience that DMC members are very appreciative of any practices that make the conduct of data review for DMC meetings more efficient and graphical presentations can accomplish that. Efficacy data can also be presented graphically in such plots as waterfall or swimmer plots for more efficient review but that discussion is not included as part of this paper.

REFERENCES


3. Amit O, Heiberger RM, and Lane PW. “Graphical Approaches to the Analysis of Safety Data from Clinical Trials.”


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RECOMMENDED READING

http://journals.sagepub.com/eprint/1YE1eTWGd4CdqQraEDHZ/full

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:
Adam Hamm
Cytel, Inc.
Work Phone: 919-817-7159
Email: adam.hamm@cytel.com

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