

ABSTRACT

The University of Wisconsin Statistical Data Analysis Center (SDAC) prepares confidential interim analyses of clinical trial data for Data Monitoring Committees (DMCs). Researchers developing new reports, as well as potential collaborators, may wish to have access to examples of report content and presentation. Confidentiality requires that any given monitoring report be viewed only by the study DMC and the few individuals responsible for preparing the report.

We prepared a sample report based on publicly available data from the Beta-Blocker Heart Attack Trial (BHAT), published in *JAMA* 247:1707-1714, 1982. The report illustrates the organizational structure of a DMC report, and provides specific examples of common data displays and page layouts.

The report includes an introduction that provides a summary of the trial design, an overview of the report and report conventions, as well

ABSTRACT (cont.)

as contact information for key study personnel. Data are displayed graphically in the main body of the report to facilitate the review of large amounts of information in a short period of time. Back-up tables of univariate statistics and frequency counts, cross-referenced to specific graphic displays, are included in a separate section.

Beta-Blocker Heart Attack Trial (BHAT)

- NHLBI-sponsored trial of propranolol following myocardial infarction
- 3,837 patients enrolled from June 1978 through October 1980
- Two treatment arms:
 - A = propranolol hydrochloride
 - B = placebo
- Primary outcome was all-cause mortality
- Trial was stopped early, in 1981, due to observed treatment benefit

Overview of SDAC Report Generation Software

Our system builds on the strengths of SAS, S-PLUS and LaTeX:

- SAS
 - used for restructuring data, basic statistical analysis
 - efficient handling of large datasets
 - industry standard, accepted by industry sponsors and FDA
- S-PLUS
 - used for data presentation, graphical display
 - can build complex graphs from simple elements
 - functions can be easily created to perform repetitive tasks
- LaTeX
 - used to format text, listings and tables, and to compile the report

Features of the SDAC Report Style

- Introduction
 - summary of study procedures, and of report style and content
- Annotated graphical displays
 - primary mode of presentation is graphical, without interpretation
- Supporting tables, cross-referenced to graphical pages
 - tabular backup located in a separate section of report
- Two report versions produced in parallel:
 - Open Session aggregate report
 - Closed Session report by treatment group
- Balance between standardization and flexibility

Report Introduction

- Summary of Study Protocol and Procedures
 - treatment arms, primary and secondary outcomes
 - study procedures and data flow, interim analysis plan
- Overview of Report
 - purpose and structure of report
 - explanation of graphical conventions
 - sources of data (CRFs and associated datasets)
- Notes on Chapter Contents
 - information specific to each section (denominators, timepoints...)
 - derived variables, assumptions used in data handling
- Contact Information for DMC, Steering Committee, SDAC, sponsor

Standard Graphical Displays

- Boxplot
 - summarizes distribution of continuous data
- Bar chart
 - displays one or more dichotomous or categorical variables
- Stacked bar chart
 - presents data falling into nested or ordered categories
- Kaplan-Meier plot
 - illustrates time-to-event data with censoring
- Relative risk graphic
 - shows A/B risk ratio with confidence intervals, overall and within various subgroups

Custom Graphical Displays (not shown)

- Interim monitoring boundary and results of efficacy analyses
- Estimates of conditional power
- Sample size estimation under various design assumptions
- “Stacked” display representing the cross-sectional distribution of patient status within a treatment group, over a time continuum

Text can be added to motivate and summarize any additional analyses included in a report.

Annotations on Graphical Pages

- Number of patients analyzed in each group
 - all randomized, a subset, or patients with non-missing data
 - displays of follow-up data include n 's at each timepoint
 - Kaplan-Meier plots provide the risk set throughout follow-up
- Bars labeled with percent of patients falling into each category
- P-values for treatment comparisons
 - statistical tests vary by type of data and by protocol specification
 - tests are described in page captions or Introduction
- Informative page captions
 - identify source and vintage of data used
 - describe patient set used for denominators

Annotations on Graphical Pages (cont.)

- Informative page captions
 - explain variable derivations, censoring, assumptions made
- Cross-referencing
 - mnemonic figure identifiers appear on every graphic and table
 - each graphical display is linked to its supporting table set
 - all figures, with identifiers, titles and page numbers, are listed at the front of the report
- Supporting tables can be placed on the graphical page if desired

Additional Information

- More information regarding the production process for the SDAC-style report will be available at the following presentation:

Tuesday, May 4, 10:40am - Session IIIA: Potpourri

“Report Production for a Data and Safety Monitoring Board - A Unix-Based System for Report Generation”, Tom Cook

- An Adobe Acrobat version of the SDAC Sample Report, available for downloading, can be found on our Website:

www.biostat.wisc.edu/biostat/sdac/sdacpdf.html