Graphical Summaries of Trial Conduct in DMC Reports

Melissa Schultz and Robin Bechhofer
Statistical Data Analysis Center, University of Wisconsin, Department of Biostatistics and Medical Informatics

For many clinical trials, Data Monitoring Committees (DMCs) are charged with monitoring not only the safety and efficacy of an intervention, but also the conduct of the trial itself. A study with low accrual, high dropout, or an unacceptable lag in data collection, adverse event coding or endpoint adjudication may not have information of sufficient quality for monitoring, and may ultimately prove unable to answer the clinical questions of interest.

The **Statistical Data Analysis Center** (SDAC) at the University of Wisconsin–Madison specializes in producing interim reports and analyses for DMCs. Our reports are *graphically* based, allowing DMC members to easily identify differences between treatment groups as well as changes over time, and to review a large amount of information in a short amount of time.

In order to interpret the safety and efficacy data presented in a DMC Report, the DMC must be able to place the information in context and evaluate whether the trial is being conducted in a way that allows them to discharge their responsibilities. We have found that graphical approaches – tailored to answer key questions of interest – make it much easier for DMC members to absorb the data.

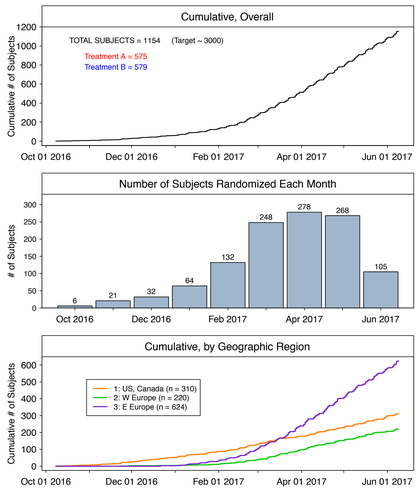
Enrollment of Study Subjects

The following questions are relevant to evaluating **recruitment**:

- Is enrollment meeting projections? What are the enrollment patterns over time in different geographic regions? (Figure ACCR-1)
- Which countries are contributing the most subjects? (Figure ACCR-2) Are a few clinical centers dominating enrollment? (Figure ACCR-3)
- Are stratification factors balanced across treatments? Is the population what was anticipated? (Figure ACCR-4)

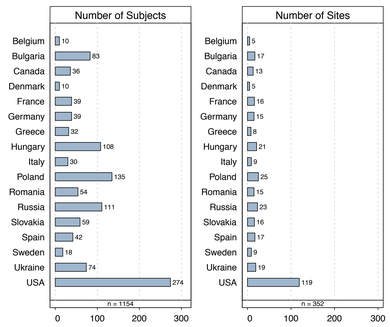
ACCR-1

Subject Accrual over Time



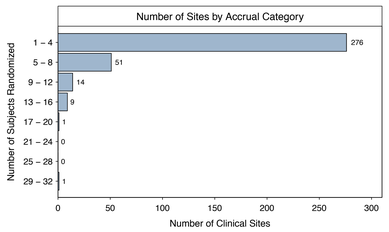
ACCR-2

Geographic Distribution



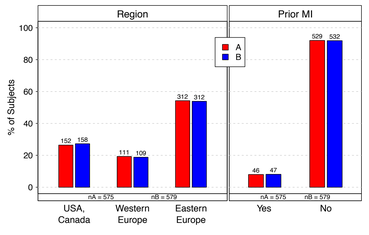
ACCR-3

Distribution of Subjects Across Sites



ACCR-4

Accrual by Stratification Factors



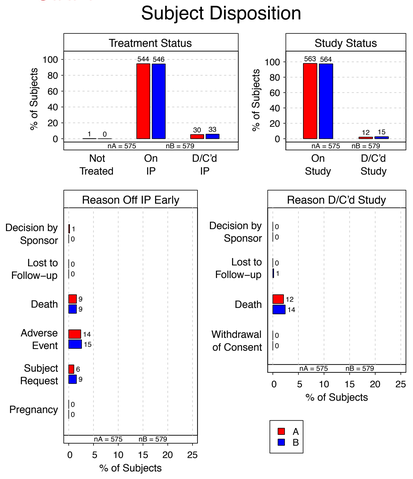
Treatment and Study Status

Questions pertaining to **subject disposition:**

- Are treatment discontinuations clearly distinguished from study terminations? (Figure STAT-1)
- Are subjects adhering to the treatment plan? What are the patterns of treatment termination, by treatment arm? Are there differences in incidence, reasons or timing? (Figures STAT-1 and STAT-2)
- In a multi-phase trial, how many participants are currently in each phase of the study (e.g., double-blind, open-label, safety follow-up)? What is the distribution of time on study in each treatment group? (Figure STAT-3)

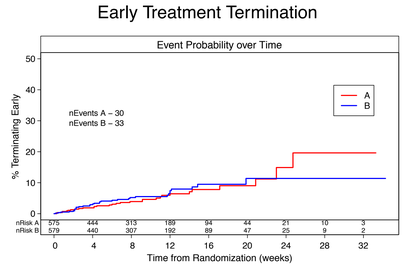
STAT-1

Subject Disposition



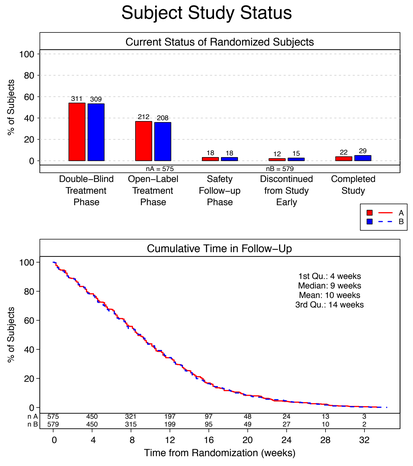
STAT-2

Early Treatment Termination



STAT-3

Subject Study Status



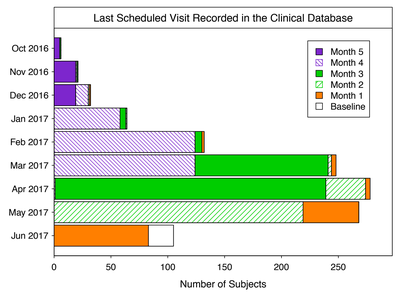
Data Quality and Timeliness

Data quality and quantity are also key components of trial conduct. It is important for members of the DMC to understand how much follow-up information is available, how current the data are, and whether endpoint adjudication is acceptably up to date.

Our DMC reports typically include several figures summarizing both subject data availability (Figures DATA-1 and DATA-2) and adjudication of clinical outcome events (Figures ADJ-1 and ADJ-2). These allow the DMC to easily comprehend not only what they *are* seeing, but also what information is missing and potentially impeding their ability to adequately monitor the trial.

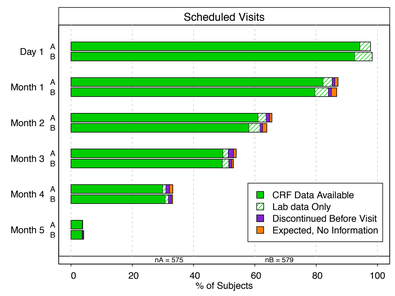
DATA-1

Data Availability by Month of Randomization



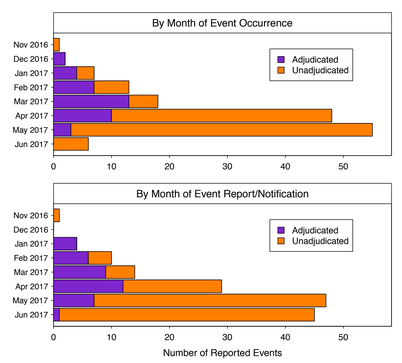
DATA-2

Amount of Visit Data Received



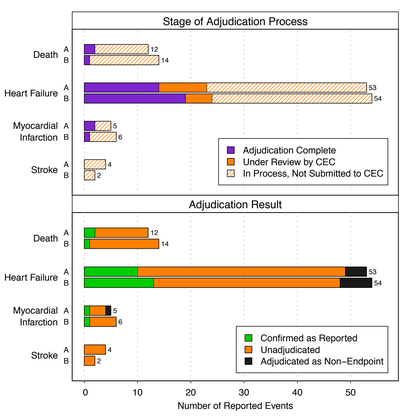
ADJ-1

Adjudication of Potential Endpoints, by Date



ADJ-2

Adjudication by Reported Event Type



For more information about SDAC, including a link to a sample DMC report, please visit our web site:

https://www.biostat.wisc.edu/content/clinical-trials-statistical-data-analysis-center-sdac