



Using Study Metrics to Monitor Several Aspects of Clinical Studies Virtually Real-time

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About Me

- Julio C. Ruiz is a Senior Statistical Programmer III at Rho, Inc.
- Over 12 years of experience using SAS® software in different commercial environments.
- Master in Economics with an emphasis in Econometrics from North Carolina State University.
- Enjoy my role as a programming team lead, but also enjoy developing tools using SAS to make my work and the work of my team members more efficient.

Agenda

- Introduction
- Study Metrics
 - Site Level
 - Subject Level
- Data Sources
- Conclusion
- Questions

Introduction

- Definition of metrics
 - A method of measuring something
- Goal of metrics
 - To guide strategic planning and decision-making
- Benefits of study metrics
 - Evolve toward successful outcomes
 - Promote continuous improvement
 - Enable strategic decision making
- Principal objective of study metrics
 - Promote the quality of study data

Introduction

- Conditions to reach objective
 - Study specific
 - Quickly understood
 - Accepted by various stakeholders
- Which metrics to include?
 - Stakeholders (e.g., Clin Ops, DM, Safety, Biostats)
 - Input from each functional area
- When to implement?
 - At study start-up

Site Level Metrics

- Macro-level view
- Main benefits
 - Easy access
 - Monitor progress
 - Identify trends and potential problems
 - Decision making

Clinical Operations

- Tasked with ensuring proper study planning, conduct, patient safety, and data quality.

Table 1. Site selection, qualification, and monitoring

Metric	Description
1. Site Qualification Visits Completed*	<i>Number of site qualification visits completed to-date</i>
2. Site Initiation Visits Completed*	<i>Number of site initiation visits completed to-date</i>
3. Interim Monitoring Visits Completed*	<i>Number of interim monitoring visits completed by CRA to-date</i>
a) Next Scheduled IMV	<i>The projected date for next IMV</i>
1. Number of pages to be verified at next IMV	<i>Number of pages to be verified by CRA at next IMV</i>
2. Number of days at the site	<i>Number of days CRA spends at the site</i>
b) Projected Last Patient/Last Visit	<i>Project date of last patient/last visit at the site. This date is projected by using the visit windows in the protocol</i>
1. LPLV at "X"	<i>Where X can be a time point of interest from the protocol</i>
4. Close-out Visits Completed*	<i>Number of close-out visits completed to-date</i>

*Note: * indicates that percentages are calculated by dividing by the total expected number of visits for each category*

Clinical Operations

Table 2. Patient enrollment, retention, and management

Metric	Description
1. Patients Randomized	<i>Number of patients randomized to-date</i>
a) Screen Failures	<i>Number screen failures to-date</i>
b) Randomized/Not Dosed	<i>Number patients who were randomized, but not treated</i>
2. Patients Discontinued/Withdrawn	<i>Number of patients who discontinued/withdrew from the study early</i>
a) Reason for Discontinuation	<i>Reasons for discontinuation (as in eCRF) presented in descending order of frequency</i>
b) Time to Discontinuation	<i>Time to discontinuation presented in time intervals (as appropriate for study)</i>
3. Patients in Efficacy Population	<i>Number of patients who have evaluable data for the study end-point (not necessary is efficacy is not being evaluated)</i>
4. Patients Completed All Visits	<i>Number patients who completed all scheduled visits (as mentioned in the protocol)</i>
5. Number of Protocol Deviations (PD)	<i>Total number of PDs recorded to-date. Each PD can be presented in descending order of frequency</i>
6. Number of Patients with PDs	<i>The number of patients with PDs. Each patient can have more than one deviation</i>

Note: eCRF = Electronic Case Report Form

Clinical Operations

- Main benefits to Clinical team:
 - Monitor start up activities and enrollment progress
 - Track progress of Interim Monitoring Visits(IMVs) and Close Out Visits and estimate CRA resources
 - Monitor patient retention rate and identify any potential problems
 - Identify root causes for discontinuations

Data Management

- Tasked with the CRF design, database design, data validation, manual data review and reconciliation, medical coding, and database locking.

Table 3. Data management metrics

Metric	Description
7. CRF Data Entry*	
a) Pages Entered	<i>Number of pages entered</i>
b) Pages Verified	<i>Number of pages verified</i>
c) Pages Ready for Freeze	<i>Number of pages ready for freeze</i>
d) Pages Frozen	<i>Number of pages frozen</i>
e) Pages Signed	<i>Number of pages signed by Principal Investigator</i>
f) Pages Locked	<i>Number of pages locked</i>
8. Total Queries Issued	<i>Number of queries issued to-date</i>
a) Queries Answered, not Closed	<i>Number of queries that have been answered, but not closed</i>
b) Queries Closed	<i>Number of queries closed</i>
c) Queries Open	<i>Number of queries that are still outstanding</i>
9. Duration of Queries Open	<i>The duration of open queries, which can be specified as ranges such as 0-7 Days, 8-14 Days, 15-21 Days, 22+ Days. These ranges can be tailored to fit the study specifics</i>

Note: * captures data entered (to-date) by site staff into the Electronic Data Capture (EDC) system

Data Management

- Main benefits to DM team:
 - Monitor and manage progress of data entry
 - Track status of data queries
 - Track progress of database lock (DBL) activities such as pages verified, signed, locked, etc.

Safety Monitoring

- Ensure that patient safety and compliance with the requirements of the study protocol are always at the forefront by following the established standards in order to protect the rights, safety and well-being of participants.

Table 4. Safety Monitoring

Metric	Description
1. Number of Adverse Events (AEs)	<i>Total number of adverse events reported by the site</i>
a) Mild	<i>Number of mild adverse events</i>
b) Moderate	<i>Number of moderate adverse events</i>
c) Severe	<i>Number of severe adverse events</i>
2. Serious AEs (SAEs) Reported	<i>Number of SAEs reported to-date</i>
3. Pregnancies Reported	<i>Number of pregnancies that occurred while on-study</i>
4. INDs/SUSARs Reported	<i>Number of Investigational New Drug Safety Reports or Suspected Unexpected Serious Adverse Reactions reported by the site</i>

Safety Monitoring

- Main benefits to Safety team:
 - Monitor variability across sites
 - Look at the types of adverse events (AEs) reported
 - Identify any bias in the types of AEs sites are reporting (not reporting)
 - By identifying inconsistencies early in the study, corrective actions can be taken to address the problem.

Biostatistics and Programming

- Metrics of interest
 - Randomized
 - Completed
 - Discontinued
 - Reason for Discontinuation
 - Time to Discontinuation
- Metrics for datasets and displays

Subject Level Metrics

- Provides a micro-level view of the study data and can be used alongside site-level metrics.

Table 5. Subject Level Metrics

Metric	Description
1. Subject Identification	
a) Site	<i>The site Identification number and PI name (e.g., 01- Smith)</i>
b) Subject study Identification	<i>Subject Study ID (as assigned in EDC)</i>
c) Cohort number, if applicable	<i>Cohort number to which subject belongs, if applicable</i>
d) Screen Fail	<i>Identifies whether or not a subject is a screen failure (Yes/No)</i>
2. Subject Status	
a) Current Status	<i>Subject status (e.g., screen failure, randomized, completed, discontinued)</i>
b) Date of Completion or Withdrawal	<i>Date of completion or withdrawal (missing if ongoing)</i>
c) Last Visit/Date	<i>Last completed study visit and date</i>
3. Subject Level Data Management	
a) Pages Expected	<i>Total number of expected pages (based on subject status)</i>
b) Pages Entered	<i>Total number of pages entered by site staff</i>
c) Pages Verified	<i>Total number of pages verified by CRA</i>
d) Pages Requiring Verification	<i>Total number of pages requiring CRA verification</i>
e) Pages Ready for Freeze	<i>Total number of pages ready for freeze</i>
f) Pages Frozen	<i>Total number of pages frozen</i>
g) Pages Locked	<i>Total number of pages locked</i>
h) Open Queries	<i>Number of queries that are still open for the subject</i>

Subject Level Metrics

- Benefits:
 - Easily identify subject records
 - Subject Identification
 - Track subject Status
 - Can help the DM focus on a particular subject when working on DBL.

Data Sources

- Availability data is important
- Main data source
 - Electronic Data Capture (EDC) system
- Other data sources
 - Internal tool for CRA visits
 - Clinical Trial Management System (CTMS)
 - Clinical Data Management System
 - Business Object Report
 - Safety database

Conclusion

- Beneficial to all functional areas
 - Successful outcomes
 - Continuous improvement
 - Decision making
 - Identify potential problems
- Presentation platform
 - Decided by study team
 - Dashboard
 - Excel Report

Questions?



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