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In the next issue of
EDC Today:

Systems Integration

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eClinical and Metrics

EDC Today is an independent publication on current information and issues in Electronic Clinical Systems (ECS) strategies and technologies for the Biotechnology and Pharmaceutical (biopharma) industry. Each month we examine topics related to ECS theory, technology, practice, or implementation.

Recently we received feedback about the topics covered in EDC Today. Based on that feedback our twentieth issue explores Metrics. In particular, we discuss what they are and why they are important. We also discuss why there is a scarcity of published metrics.

Introduction

In issue 6 of EDC Today, *EDC's Impact on Clinical Data Management: Metrics, Best Practices, and Decision Making*,¹ we began a discussion about metrics. In that issue, we discussed quality and performance issues related to clinical trials and presented some published measurements. In this issue, we want to concentrate more on the what, why, and how of metrics.

Simply stated, a metric is a measurement. It can be a measurement of many different things, but we are most concerned with measurements of performance, quality, and cost. Metrics are similar to report cards. They tell us how we have done. Metrics are a yardstick for us to measure where we are. But a standalone measurement in itself is not meaningful. The only reason that report card letters A, B, C, etc. have meaning is because they have historical context. Over the years our academic institutions have defined A as excellent. But in reality, one's class rank is probably more important, in that all other things equivalent, one can see how one compares to his or her peers.

However, in the biopharma industry, there is a golden aura about metrics. In some sense, metrics are the holy grail of the industry – highly sought after, while at the same time mysterious. Part of this is due to the limited amount of published metrics, and part of it is due to the limited usefulness of these published metrics. But a major reason for their intrigue may be that these values represent comparative and competitive information, and as such, there is no obvious reason for people (or companies) to publish true performance and quality measurements.

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Certainly good quality metrics with a definite tie in to a corrective action plan should prove their worth, but presumably many metrics in the past haven't, and the metric could not be adjusted suitably. It may also be that companies are finding that the collection and utilization of metrics, while they could be very useful in evaluating and improving processes and computer systems, represent an additional cost. Management could view the effort and cost of collecting, programming, and reporting of metrics and any subsequent process adjustments as unnecessary to the bottom line.

In this issue, we start by defining what metrics are in more detail. Then we discuss the purpose of metrics, since the purpose of a metric is instrumental in how we define a specific metric. When one examines the purpose for metrics, it becomes clearer why there are not many published metrics and why those that are published are not very useful. Then we discuss how to collect metrics either automatically or manually. Finally, we discuss how to use the information represented by the metrics.

Defining Metrics

A clinical trial metric is a measurement of performance, cost, or quality, generally expressed as a rate per unit – such as pages of data entered per day or number of data entry errors per page.

Metrics are management tools. From a biopharma management perspective we would want to measure how long it takes to do certain tasks related to the process being managed. Thus, for a clinical trial project manager, it is important to measure how long it takes to enroll a patient, how long it takes to complete an enrollment section of the Case Report Form (CRF), how long it takes to transfer CRF data to the clinical trial database, and many other measurements.

Measurements by themselves are not generally useful. If I say it takes 10 days to enroll a patient, that value by itself is only marginally useful for planning the overall length of a study. To make this value more useful, we need to compare it to a baseline or a benchmark.

Baselines are the same measurement made at some given point in time or in the process. For example, a baseline for enrollment rate per day could be measured in the beginning of a study, perhaps the first week or the first month. Then subsequent measurements would compare how the enrollment rate per day has increased or decreased versus that baseline value.

On the other hand, as with letter grades on report cards, a benchmark can be a standardized comparison value. A benchmark for computer CPU performance could be MFLOPS (a million floating point operations performed in a second).

If a metric is measuring a specific work process or a specific computer system, generally benchmark metrics are obtained from the previously used process or previously deployed computer system. In the specific case of transitioning from paper CRFs to Electronic Data Capture (EDC), the benchmark metrics would be performance and quality values from paper process and computer systems. We would then compare the same metrics using an EDC process and computer applications to these benchmark metrics.

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Purposes for Metrics

A solid definition of a metric is imperative for proper measurement and utilization. However, to solidly define a specific metric, it is imperative to state what purpose the metric serves. How we collect the values for the metric will be determined in a large part by what we hope to accomplish once we have the values.

The main purpose of a metric is to function as a tool for management to more effectively manage projects and processes. Metrics provide information to the management team so that the team can observe what is happening, apply corrections to the process along the way, and keep the project on course for a successful, cost effective, and timely completion.

Certainly a management team can misuse metrics. It is important for the purpose of the metric to be tied directly to the goals of the business, and not to one or more particular individual within the organization. Metrics need to be objective and free of bias and should not be manipulated for any reason.

Metrics must be developed to evaluate each specific portion of the overall process at the granularity that makes sense for a particular level of management to optimally perform its job. As such, there should be a hierarchy of metrics. At the highest level would be general metrics that executive managers use to evaluate the progress of current clinical studies and plan for upcoming studies. At the lowest level, the metrics need to be very specific to a small portion of the process. For example, for the manager of data entry, the appropriate metrics might be how many CRF pages are entered per day per entry operator.

In the case of the executive metrics, the purpose of these metrics should be for use in overall corporate planning, budgeting, and financing. At this level, quality metrics are of interest to the extent that the quality of the clinical trial is sufficient to lead to product marketing approval. See Table 2 for examples of executive level metrics.

In the case of middle level management, planning is often coupled with evaluating different personnel, computer systems, and processes for accomplishing the tasks that need to be done. At this level, metrics may be captured to evaluate the performance and cost effectiveness of various competing methods of achieving the same overall goal. Perhaps it is at this level that metrics are developed to support cost justification of EDC or a portal. Here metrics may be developed and collected that do not provide as much use for day to day planning, but may show where alternative operating procedures could provide greater overall performance. See Table 2 for examples of system comparative metrics.

In the case of lower level management metrics, planning still remains a strong objective, but the planning is on a much more detailed level. At this level, the manager will be more interested in CRF page level measurements, measurements of Data Clarification Form (DCF) turnaround, and specific data quality measurements. In addition, management at this level will be looking for ways to improve the performance of these more specific tasks. As such, specific measurements may be taken at closer time intervals to allow finer process corrections. Many of the metrics given in Table 1 apply to lower level management.

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At the level of the individual clinical trial professional, there may be metrics that individuals can devise to monitor and enhance their own performance. Certainly an individual clinical database programmer could keep track of his or her own performance measurements of how many entry screens or edit checks can be completed in a given day or week or month.

To conclude, most metrics have a purpose that evaluates a specific process or portion of a process in the hope that they allow the appropriate level of management to plan time and personnel resources, proactively correct process problems, and implement process improvements.

Published Metrics

As mentioned above, we detail a number of published metrics in issue 6 of *EDC Today*. In a study published by the *Drug Information Journal*, 14 pharmaceutical companies participated in a telephone survey of production, cost, quality, and performance metrics. Following are some of the survey findings:

- For database development (defined as elapsed time, including edit checks), the mean cycle time was 51.5 days.
- The average time to resolve one query was 8.4 days, with a range of 5 to 49 days. Queries from electronic data capture trials took less time to resolve.
- The mean (i.e., average) time from last subject/last visit to database lock was approximately 36 days, with a range of 20 to 60 days. This metric was based on processing paper CRFs. The one company that reported using EDC exclusively for its clinical studies stated that its cycle time metric was 48 hours.
- The mean cycle time for database lock to primary statistical analysis is 9 days, with a range of 2 to 20 days.
- The mean cycle time from database lock to final statistical tables was 15.4 days, with a range of 2 to 20 days.²

While these numbers are interesting, their usefulness is limited. To begin with, the first metric on database development makes no reference to study type, study complexity, number of pages, number of unique pages, number of edit checks per page, or other critical factors. These comments can be made for the other listed metrics as well.

Even if one does make allowances for the above comments, what can one do with these values? Probably the first thing one would do if they feel their studies are taking longer than these published numbers is to decide that his or her studies are more complex than average studies. However, even if one could prove that, then one is left with a decision – do we make our studies simpler or do we accept the fact that our time to complete them appears “slow”.

Even beyond the shortcomings just presented, one has to question the validity of the values given by the participants in the survey. How accurate are they? Were the values embellished to present a better picture of how well the company(s) surveyed do business? Were the values presented worse than reality because his or her company’s processes frustrated the participant? And finally, were the values presented actual measurements or best guesses?

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Finally, what value is it to a company to publish such metrics? We believe there are no compelling reasons for any company to do so. These metrics are certainly company confidential information and are certainly “competitive advantage” in nature. If a company has developed a good, cost effective process for completing clinical trial studies, why would they want to disclose that fact?

Example Metrics and Metric Collection

In issue 6 of *EDC Today* we presented a partial list of metrics. We reproduce the table below:

Table 1. Common Metrics in the Clinical Trials Process³

Productivity metrics:
<ul style="list-style-type: none"> • Mean number of case report form pages entered per hour per operator • Mean number of data fields or keystrokes entered per hour per operator • Mean number of CRF pages processed to completion, per person hour • Mean cost of processing a data clarification query
Performance metrics:
<ul style="list-style-type: none"> • Mean elapsed time from receipt of last patient’s data until database lock • Mean elapsed time from last patient visit until database lock • Mean elapsed time from receipt of response to last query until database lock • Mean elapsed time from approval of final protocol and CRF until the data management plan is approved • Mean elapsed time from approval of final protocol and CRF until the clinical data management system/operational database is approved as ready to process study data • Mean elapsed time from database lock until key efficacy results are available • Mean elapsed time from database lock until all data displays (listing, tables, figures) are approved for use by study report authors
Data quality metrics:
<ul style="list-style-type: none"> • Estimated error rate of an analysis database in comparison to paper CRFs • Mean number of times per study the database is unlocked due to critical data errors • Mean number of times per study that final tables must be reproduced due to critical programming errors
Data management cost metrics:
<ul style="list-style-type: none"> • Total cost of clinical data management processing through database lock, per CRF page • Total cost of designing, programming, and producing data displays (listings, tables, figures) • Mean number of data clarification queries per CRF page, or per data field

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In addition to the metrics in Table 1, one might also consider the following metrics, depending upon the purpose one may have for a metric and the job and position that one has within their own company.

Table 2. Potential additional metrics

Executive metrics (presented in a dashboard or graphical format):
<ul style="list-style-type: none"> • Percent of patients enrolled in each ongoing study • Percent of data entered into database and cleaned • Percent of Analysis performed • Percent of Submission completed • Overall trial completion time
Comparative performance metrics for different EDC vendor software:
<ul style="list-style-type: none"> • Page turn rate • Time to setup and deploy data entry system • Time to test data entry system • Time spent training users • Time spent in site setup • Reduction in site visits by monitors • Time to implement protocol revisions
System and program quality metrics:
<ul style="list-style-type: none"> • Number of reported bugs in software • Number of bugs fixed versus new bugs reported • Number of reported bugs in deployed data entry system • Amount of system software testing • Amount of data entry system testing • Amount of data entry system update testing
System management cost metrics:
<ul style="list-style-type: none"> • Cost of maintaining system software (frequency of system updates and installation of updates) • Cost of maintaining deployed application (frequency of entry system defects, clinical protocol changes, and time to implement changes) • Annual maintenance and hosting fees

How to go about collecting metric values will depend upon the definition of the specific metric. But in general, our experience has shown that since most metrics are time related, the importance of collecting the date and time of all measured events cannot be overstated. If one wants to collect a metric on patient enrollment rate, one should have the date, and possibly time, when each patient

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enrolled. This information is usually available, as it is typically collected on a CRF and is entered into the clinical trial database. Thus, to obtain that metric, a program can be written to extract the enrollment dates of all enrolled patients and a calculation of rate over time can be applied.

In our experience, most metric information is available in the clinical trial database. Some metric information may be present in a clinical trial management database, such as when monitoring visits occurred, when CRFs were received in house, and when DCFs were sent and received. Additionally, data related to safety metrics are often found in clinical safety databases. Therefore, many metrics can be obtained by programming applications to access the appropriate database systems and harvest the metrics.

There are two areas beyond those mentioned previously that need data collection systems. One area involves personnel performance information related to the length of time it takes to complete individual tasks. The other area involves costs.

A good project management database could provide some information on task completion time requirements (e.g. task start date and time and task stop date and time). Examples of this sort of data would include when a developer starts to develop a data entry screen, when he is finished with the screen development and releases it to testing, when testers start, when testing is finished, and how many iterations of development, testing, re-development, and retesting are performed before final release into production. Clearly other areas such as CRF design can go through similar processes, and task completion time data needs to be captured and perhaps entered into a project management database.

Cost information may be contained in a corporate accounting database. However, it is likely that this cost information may be difficult to access due to the sensitive nature of corporate accounting and contracts with vendors. It may be necessary for accounting system programmers to make certain requested accounting information available to metric programmers. Specific cost information in dollars will often be the most difficult values to obtain.

Cost metrics are often instrumental in deciding which computer systems to purchase and use. However, since true cost is not usually collected at the level of detail required, cost justifications are often incomplete at best, and completely incorrect at worst. Many companies are finding the cost structure with EDC, for example, to be completely different from their cost structure with paper-based CRFs. As a result, companies are often trying to compare apples to oranges. Clearly finer-grained cost metrics would allow a more accurate cost comparison to be made.

Putting Metric Information to Use

Having defined specific metrics for specific purposes, it should follow in a straightforward manner what management can do with the information that is received. For all metrics, the planned use of the metric should be defined when the metric is designed. This proactive thinking is often a difficult step. It may not be clear to those defining the metric precisely what they might be able to do when data indicates a process problem. However, to optimize the benefit of the metric, to the extent possible, a decision tree could be developed to indicate what to investigate, or perhaps simply list what changes one may consider to address the shortcoming revealed by the metric. With the proposed path forward identified with each metric, management is more quickly able to optimize their process(es).

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For example, if enrollment rates are slowing down, a process should be developed to outline steps to take to correct the declining enrollment rates. These steps will vary from company to company. Perhaps a protocol amendment will be investigated to remove some inclusion and exclusion criteria that are no longer deemed critical (within the boundaries of good science, of course). Perhaps additional sites need to be signed up. Perhaps sites do not have a good understanding of who can be enrolled in the study.

As another example, consider the comparison of paper-based CRF processes versus EDC. Each metric could be a decision point in a matrix to determine if EDC should be pursued. Alternatively, each metric could also lead to potential process improvements in either the existing paper CRF process or in the EDC process. A quality metric, like errors per page, is a specific example of such of a metric that could provide for possible process improvements in both cases. For this metric, the potential path forward might be better screen layout or a better CRF paper layout. So both processes may benefit. However, later metrics such as cost of implementing changes or time to deploy changes to the sites may weigh heavily in favor of one data capture technology over the other.

Conclusions

Metrics can be as simple or as complicated as you want to make them. Certainly the more complicated the metric, the more likely the resulting values will be either biased or misused. You should strive for simpler metrics. In either case, the metric's usefulness will depend upon how well they are defined, and the actions that you determine you might take based on the values the metrics present to you.

Searching for published metrics is a start. But it is important to understand the shortcomings of the published values. Published metrics may be more useful as examples of measurements you might consider collecting, as other people believe they are worth collecting.

Understanding your overall process and your management structure will help you to develop a set of metrics. A place to start is to examine each job position and pose hypothetical scenarios along the lines of "If I knew X, I could do Y." That will help you to see what useful information could be collected, and start the definition of the follow-up process that can help lead to action when the measurement values are known.

In addition, existing data should be explored to see how many metrics you might already have with the raw data captured, even if calculations need to be performed. For metrics that require data beyond what you already have, consider adding the required data to your clinical trials, project management, or accounting database.

Finally, metrics should be viewed as tools for helping to manage and improve your clinical process. They are not mystical entities, but instead must be defined in a very specific manner so that the resulting values can be interpreted properly and acted upon to optimize the course of clinical development.



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Who's behind the research?

Our lead researcher, Kirk Mousley, PhD received BS and MS degrees in Electrical Engineering from MIT and a PhD in Computer Science from Lehigh University. He has been the President of Mousley Consulting, Inc. since its founding in 1993 and has directed the company's efforts in the areas of clinical database design, data editing/cleaning, document management, and submissions.

Karl Mousley received his BS in Mechanical Engineering from Rose-Hulman Institute of Technology and a MS in Computer Science from Villanova University. He has been a senior member of the technical staff at Mousley Consulting, Inc. since 1993. Among his significant accomplishments are the investigation, evaluation, and implementation of new computer technologies for clinical data management systems and developing strategic plans for integrating these technologies into current systems. He has extensive experience preparing Standard Operating Procedures (SOPs).



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