

Insight brief

Risk-Based Monitoring Improves Site Performance and Investigator Satisfaction



By reading this insight brief, you'll learn how RBM:

- Leads to earlier insights that improve trial quality
- Influences trial planning and design to improve patient safety
- Changes trial monitoring practices and roles to provide superior delivery
- Helps sites improve safety, efficiency and outcomes
- Improves investigator satisfaction and results

Executive summary

This paper explores the growing body of data that supports the broad acceptance of risk-based monitoring (RBM) strategies across the biopharma world. RBM is increasingly seen as an appropriate methodology to improve patient safety and study quality, while lowering study risks.

Sponsors initially expressed concerns about the potential impact of RBM processes and procedures on investigators and site performance. Studies by biopharma services provider Quintiles and ongoing site surveys by investigator site management teams suggest the opposite. Far from impeding site performance, RBM is improving data entry speed and accuracy, reducing source document verification, and aged queries improving investigator satisfaction, and enhancing communications compared to traditional study management techniques.

Table of contents

| | |
|--|---|
| Use Risk-Based Monitoring to Improve Clinical Trial Efficiency | 3 |
| Uncover Actionable Insights to Drive Trial Execution | 3 |
| Improve Quality while Enhancing Investigator Satisfaction | 4 |
| Uncover Actionable Insights to Enhance Execution Effectiveness | 5 |
| Drive Execution Efficiency for Stronger Outcomes | 5 |
| Contact Us | 6 |



UBM ADVANSTAR

UBM



Use Risk-Based Monitoring to Improve Clinical Trial Efficiency

Clinical development is at a crossroads. Clinical trial times and costs continue to rise, forcing the industry to search for novel approaches to reduce time and costs in moving new products through clinical trials toward approval and market launch.

It can be difficult to reduce the time needed to observe and evaluate the therapeutic effects and adverse events seen during clinical trials. But the costs associated with planning and conducting clinical trials may be more flexible. While there are multiple cost categories associated with clinical trials, monitoring and investigator site management costs account for a significant portion of total study spending.

Risk-based monitoring offers the prospect of optimizing monitoring, management and execution at the site level and the global trial level by facilitating faster and more informed decisions, improving patient safety, increasing study quality and enhancing the efficiency of trial management while reducing overall spending.

Regulators and industry are both moving toward risk-based strategies and methodologies throughout the clinical trial processes.

The standard RBM approach begins with an upfront assessment of risk and a planned reduction in source document verification based on a combination of on-site monitoring and remote monitoring to reduce in-person visits by site monitors. The primary goal is to improve quality and efficiency, while following guidance from regulatory agencies to enhance the research and development of innovative new therapies.

Enhanced RBM approaches start with a similar upfront risk assessment, then adds structured data surveillance and predictive analytics to reduce the burden of in-person site visits by trial monitors while enhancing data quality and overall safety. One result of the move toward RBM is an evolution of contract research organization roles and activities.

Uncover Actionable Insights to Drive Trial Execution

Quintiles expanded the typical RBM approach with their Data-driven Trial Execution approach that creates and operationalizes predictive analytics that are unique to each trial. These predictive analytics allow for the preemptive identification and resolution of multiple issues at the site and patient level. The goal is to move as quickly as possible from data to actionable insights by combining technology and centralized data surveillance.

Quintiles' approach uses innovative technology that integrates multi-source data in near real-time for safe, efficient and high quality trial management. The approach balances dynamic ongoing site monitoring, remote monitoring and centralized monitoring to help managers focus on the sites, data, patients and events that most need attention. The system tracks global performance and facilitates the recognition of early trends and soft signals to foster the rapid initiation of triggers and alerts to resolve issues proactively. Quintiles' approach to RBM can provide more timely site communication, improved compliance and faster, better-informed decision making.

A combined team of multifunctional experts, including project managers, data managers, biostatisticians, medics and therapeutic experts from the CRO and sponsor start with an index risk assessment to create a risk assessment and mitigation plan. The plan focuses on the most critical data points to guide the allocation of study resources to the higher risk areas. The targeted allocation of resources and attention mitigates risk by improving both data quality and the data review process.

Ongoing data surveillance, which includes patient level reviews by clinically trained staff, is used to optimize and adapt monitoring throughout the trial. Data surveillance triggers reassessment of risk as appropriate, corrective actions as needed and communication with investigator sites as necessary.

The traditional approach to site management relies on 100 percent source document verification (SDV).

RBM is evolving to replace rote SDV with a balanced approach using various monitoring approaches: on-site, remote and centralized. The use of advanced and predictive analytics tailored to address the unique risk profiles inherent in every site and study can improve data quality and patient safety while it lowers overall risks.

The team also handles typical management activities such as vendor support, centralized labs, clinical supplies and investigator batch payments. At the same time, it provides management support to clinical research associates (CRAs) responsible for site monitoring and oversight.

CRAs typically visit each site as part of the site selection process. While on-site, they discuss RBM methodology in detail to help manage investigator and site staff expectations. Most monitoring is accomplished remotely, which greatly reduces the need for subsequent site visits. Most site visits are scheduled in response to triggers generated by data surveillance that either cannot be resolved remotely or are better resolved through an in-person monitoring visit. The total monitoring load is not appreciably different from the investigator and staff perspective.

Site support includes unified monitoring by the same CRA for both remote and on-site visits. Each CRA and site also have a dedicated clinical analyst on the central team. The combination of centralized operations with a single CRA and single clinical analyst for each study site builds consistency of knowledge and understanding about that site, its operations, challenges and personnel throughout the life of the study.

Centralized support encourages both timely response to alerts and site requests and appropriate follow through for timely closure. Centralized support automates tasks such as trigger trending that might indicate the need for closer review of a specific site or a particular portion of site operations and the creation of support materials for site visits.

Improve Quality while Enhancing Investigator Satisfaction

Many sponsors are moving toward some form of RBM, but acceptance is not universal. Surveys of Quintiles customers in both 2014 and 2015 found that site-related concerns topped the list of implementation barriers cited by RBM users. Sponsors wondered about the impact of reduced in-person face time between investigators and the CRA, the ongoing investigator compliance if they are not visited on a regular basis, the potential for missing data if the CRA was not on-site on a regular basis, and the impact of CRA visits based on data triggers rather than at fixed intervals.

Recent surveys of Quintiles RBM studies found those concerns to be misplaced. Across the company's entire portfolio of studies, RBM resulted in a 4x lower error rate in critical data in a head to head comparison to traditional 100 percent SDV from 2014 to 2015. In 2015, RBM studies showed a 45% reduction in the number of missing pages versus traditional studies. RBM studies showed a 47% higher action item closure versus non-RBM in 2015. Five times as many RBM study sites enter data within 7 days compared to traditional study sites (46% vs. 8%) in 2015. Also, developed RBM solutions can bring as much as 25% cost reduction over traditional trial execution approaches.

In 2015, RBM studies scored consistently higher on every investigator performance measure compared to traditional studies. RBM investigators scored three percent higher on effective communication and three percent higher on good working relationships. Overall loyalty scores were three percent higher for RBM sites. RBM investigators also scored higher for efficient SSU process, efficient CTA process, effective trainings, study materials on time, timely issue resolution, efficient investigator payments, protocol knowledge, therapeutic knowledge, quality support and GCP adherence.

A separate site outreach survey found that 85 percent of investigators said they were satisfied with their level of interaction with their CRA and that 89 percent of CRAs have the appropriate level of training and skills. Only four percent of investigators reported that they made any changes in their standard operating procedures or processes on site due to Quintiles' RBM approach.

The traditional CRO approach collects and verifies data.

RBM shifts that role to data interpretation and insight into the performance of each site across multiple parameters. The result is an enhanced focus on the most critical elements of the trial and drives a more site centric and patient centric approach to the design and conduct of clinical trials.



The goal is to move as quickly as possible from data to actionable insights by combining technology and centralized data surveillance.

Uncover Actionable Insights to Enhance Execution Effectiveness

An integrated network of trial sites across North Carolina, South Carolina, Tennessee and Illinois conducted a survey of site coordinators in 2016. Respondents gave positive scores to the Quintiles RBM model and reported centralized support of monitoring practices as being received by sites. How well RBM is received by investigators and site staff depends largely on the quality and success of site training on the risk-based approach and its impact on staff and operations.

Site staff envision remote monitoring might add to their already-heavy administrative burden. They can rest assured that, with a targeted training program, RBM does not require any additional document handling because remote monitoring is accomplished using data surveillance techniques, not by sending source documents to monitors. And once an RBM-based trial is under way, investigators and site staff quickly see the advantages of centralized support for monitoring practices.

Drive Execution Efficiency for Stronger Outcomes

RBM holds the potential to transform clinical development as it enhances site effectiveness. Risk-based monitoring enhances site communication and drives patient focus. It can also reduce costs and risks inherent in clinical trials by assessing risks up front, and throughout the study, which encourages a more efficient allocation of resources to monitor and mitigate higher-risk areas.

Such collaboration between site and CRO helps to enhance the effective and efficient operation of each site. The focus on data and quality that is enabled by centralized clinical operations also shifts the focus of quality control to the site level. Enhanced data surveillance and predictive analytics allow real-time data acquisition at the site level, near real-time analysis of operations, and immediate intervention as needed.

In summary, RBM approaches are evolving. They have come to add data surveillance and predictive analytics that help reduce the burden of in-person site visits by trial monitors while enhancing data quality and overall safety. One result of the move toward RBM is an evolution of contract research organization roles and activities. The traditional CRO simply collects and verifies data. RBM shifts that role to data interpretation and insight into the performance of each site across multiple parameters. The result is an enhanced focus on the most critical elements of the trial and driving a more site-centric and patient-centric approach to the design and conduct of clinical trials. RBM is improving data entry speed and accuracy, reducing source document verification, and aged queries improving investigator satisfaction, and enhancing communications compared to traditional study management techniques.



RBM holds the potential to transform clinical development as it enhances site effectiveness.



Enhanced data surveillance and predictive analytics allow real-time data acquisition at the site level, near real-time analysis of operations, and immediate intervention as needed.

ANSTAR



UBM ADVANSTAR

Co-authored by

**APPLIED
CLINICAL TRIALS**



Contact us

U.S. Toll Free: 1.866.267.4479

U.S. Direct: 1.973.850.7571

Europe and other areas: +44.203.564.4649

Asia Pacific: +65 6602 1245

www.quintiles.com

clinical@quintiles.com