Clinical Research & Development

White Paper

Building Sustainable RBQM Frameworks: Challenges, Metrics, and Real-World Results

Introduction

Risk-based quality management (RBQM)—an approach to proactively manage risks in clinical trials to improve data integrity, patient safety, and resource utilization—is implemented in some 57% of clinical trials, according to a Tufts Center for the Study of Drug Development (CSDD) online survey.[1] Respondents to the 2024 survey represented pharmaceutical and biotechnology companies, as well as CROs, with 206 responses on 32 distinct RBQM methodologies. Levels of adoption were lower in companies that conducted fewer than 25 trials per year (48%) compared to those with more than 100 trials annually (63%). Barriers to adoption included lack of organizational knowledge, mixed perceptions of the value of RBQM, and inadequate change management skills.

Current Implementation of RBQM

RBQM implementation may have eight components, utilized in a fit-for-purpose manner: initial cross-functional risk assessment, ongoing cross-functional risk assessment, quality tolerance limits (QTLs), key risk indicators (KRIs), centralized monitoring, off-site/remote-site monitoring, reduced source data verification (SDV), and reduced source data review (SDR).[2] Appropriate involvement by other key functional groups such as medical and data management is also integral for operationalizing an effective RBQM approach. A survey by the Association of Clinical Research Organizations (ACRO) found that in 2024, 96% of clinical trials included at least one RBM or RBQM component.[3] Survey respondents represented seven CROs and 3,758 outsourced studies. This compares with 88% of 4,889 trials in 2021 having included at least one RBQM component, 77% in 2020, and 53% in 2019.[4] Increasing adoption of RBQM components is illustrated in *Figure 1*, with prevalence of these components shown in *Figure 2*.

The Evolution of RBQM

In its earlier stages, RBQM was often implemented as an add-on to existing clinical processes rather than as a holistic approach to monitoring. As RBQM has matured, more organizations have moved toward a fully integrated, cross-functional model that enables a constant feedback loop between clinical teams and other functional groups. In successful implementations, central monitoring findings are integrated directly into CRA activities, influencing decisions about monitoring scope, timing, and site management. Central monitoring insights may also inform data management, biostatistics, and medical monitoring activities. Despite this progress, adoption of this more mature RBQM model remains variable across the industry.

About RBQM

"Risk-based monitoring (RBM) and risk-based quality management (RBQM) offer a compelling approach to increase efficiency, speed, and quality in clinical trials by prioritizing and mitigating risks related to essential safety and efficacy data. Since 2013, the FDA and EMA have encouraged the use of RBM/RBQM, however adoption has been slow with limited understanding of the barriers to adoption."[5]

Figure 1: Increasing adoption of RBQM components in clinical trials[6]

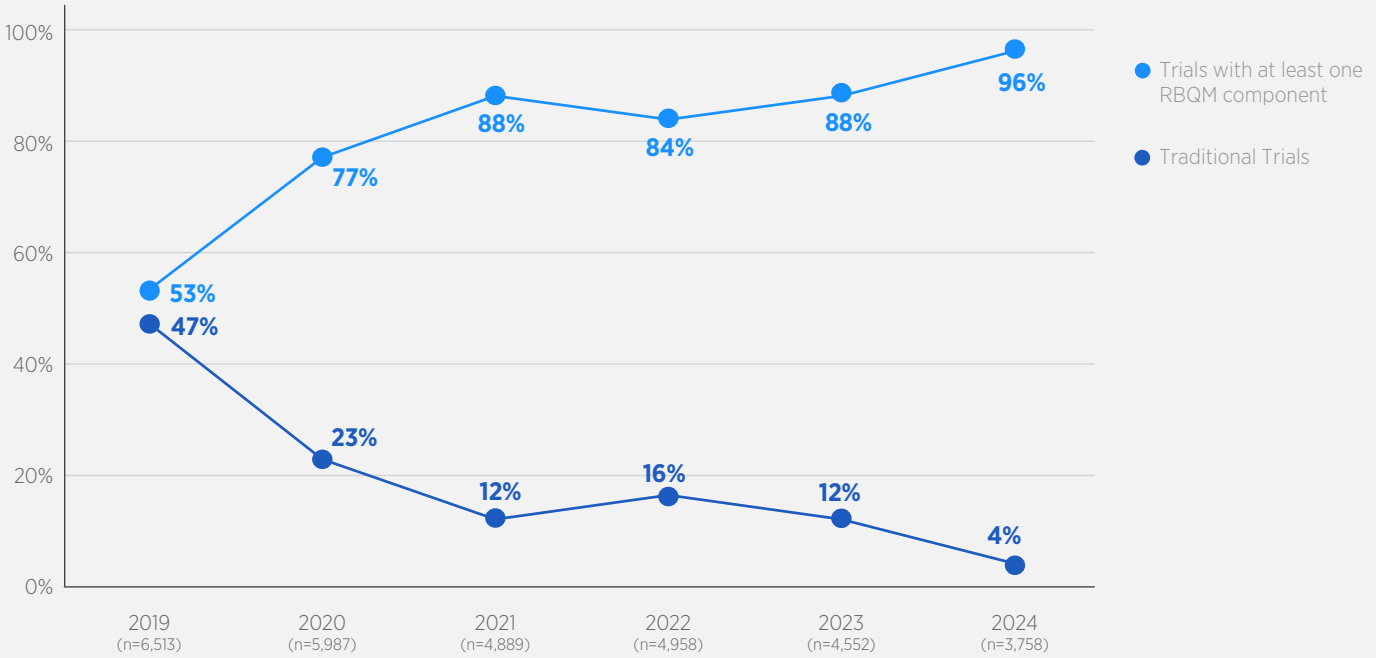
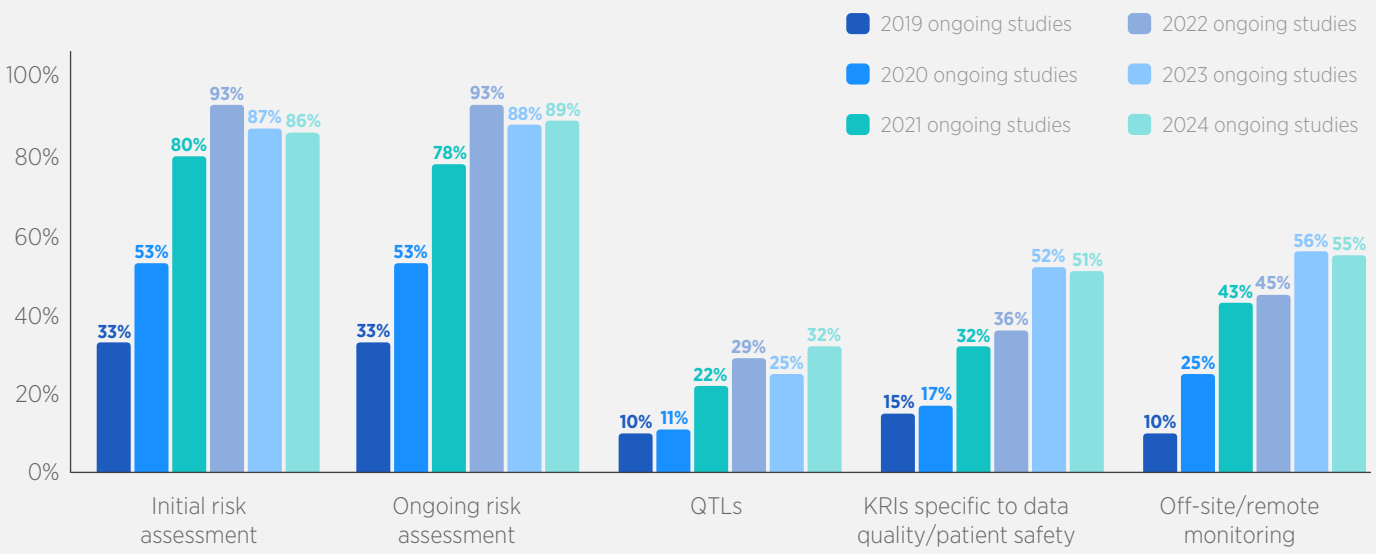


Figure 2: Prevalence of RBM and RBQM components in ongoing studies[7]



Elements of a Successful RBQM Strategy

Companies wishing to adopt RBQM should start with a risk assessment and progressively add components based on the organization's capabilities and functional tools. For example, organizations with minimal capabilities for data integration, perhaps limited to Clinical Trial Management System (CTMS) and Electronic Data Capture (EDC) data, may start by developing KRI dashboards to track operational metrics across sites. In contrast, organizations with more advanced data integration capabilities, incorporating sources such as EDC, Interactive Response Technology (IRT), labs, electronic patient reported outcomes (ePROs), and CTMS, can leverage these data to support more sophisticated study, site or patient-level visualizations and implement central monitoring approaches that augment or reduce the need for frequent onsite monitoring.

Once implemented, central monitoring can be applied at different levels depending on study needs, including study-level, site-level, or individual patient-level analyses. Patient-level central monitoring, in particular, enables earlier identification of potential protocol deviations and data quality issues, often before scheduled CRA site visits. This approach supports more targeted monitoring strategies and may reduce reliance on traditional 100% source data review (SDR)/source data verification (SDV), allowing for resources to be focused where risk is highest.

Combining central monitoring with a sampling of subject visits for SDR/SDV can reduce the time spent at the site by the CRA performing data review and allow CRAs more time to address improving critical processes, recruitment/retention, and evaluate regulatory compliance.

Integrated cross-functional processes are an essential foundation for RBQM strategies and should be flexible and configurable to the needs of each study. For example, if a study involves only four sites, a KRI dashboard may be unnecessary, since each site's performance can be viewed directly via monitoring visit reports. Similarly, for small clinical trials, there is

likely little need for study-level central monitoring. However, small studies can benefit from a patient-level approach, which can inform CRAs of where to focus their attention when on site. The need for various components of central monitoring should be re-assessed in a dynamic manner as each study evolves. For example, when moving into long-term follow-up, patient-level reviews can take place less frequently to reflect the level of patient activity.

The Value of Central Monitoring

RBQM offers many benefits, including the ability to identify issues more quickly than with traditional monitoring. The time to detect deviations can be reduced when a central monitor carries out patient-level reviews compared with when the CRA identifies these during scheduled monitoring visits. Central monitors can review data within 3–5 days of data being entered into the electronic source system such as EDC, ePRO, etc., while CRAs may wait as long as 6 weeks until an onsite visit is necessary.

In one Premier Research–managed study, an analysis compared time to protocol deviation (PD) detection by central monitors versus CRAs across both "important" and "non-important" PDs. The results showed that central monitors identified PDs 34% faster overall, with a 20% faster detection rate for important PDs and a 46% faster rate for non-important PDs. Similar results have been seen in reviewing data in other studies.

Further, RBQM enables cost efficiencies across two key areas of study delivery: monitoring and resourcing. By limiting reliance on 100% SDR and SDV, RBQM can reduce the frequency of onsite monitoring visits, thereby lowering costs associated with high-value resources and travel. RBQM also supports more efficient resourcing models by leveraging lower-cost central monitors, often deployed in global low-cost centers, to identify and document issues. This allows higher-cost CRAs to focus on working directly with sites to resolve findings and improve processes, while concentrating SDR/SDV efforts on critical areas such as eligibility, investigational product administration, and safety and efficacy endpoint collection.

The Evolving Role of Central Monitoring

Central monitoring was first introduced in very large studies, where it focused on aggregated analyses to identify trends and outliers across sites. Today, central monitoring supports more granular, patient-level reviews in smaller studies, and can be utilized as a key data quality surveillance tool, documenting protocol non-compliance, and intra-site variability in certain key assessments related to endpoints (like rater variability within a site, or one rater's inconsistency even with lack of variability). When an issue is detected in one patient or at one site that carries a great risk to patient safety or data integrity, central monitors can look for similar issues across all patients and all sites in an efficient and coordinated manner. In addition, central monitoring findings can be discussed at cross-functional meetings where data management, biostatistics, and medics can adapt their functional plans to better manage and mitigate the identified risks.

There is now enough evidence to support deploying central monitoring on every study regardless of size. This may be at the study-level, patient-level, or, for large and long-running studies, both study- and patient-levels. For studies that did not have central monitoring included at the start (perhaps because the capability didn't exist at the time), there is a growing trend to add this approach after the trial has been running for some time. In the following case study, central monitoring was added after the fact to determine what benefits might have been gained.

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A Case Study of Central Monitoring Assessment: Phase II Study in a Hematological Disease

A Phase II study did not originally include central monitoring; however, when concerns arose about inconsistent site performance in PK sample collection, the sponsor approached Premier to add central monitoring to the ongoing study. A study-level review was conducted using data that was integrated from various sources and displayed via visualizations for central monitoring review. As part of the central monitoring analysis, a retrospective review of various critical data domains was completed. Those included AEs/SAEs, ICF, labs, eligibility, protocol deviations, and IP compliance. One of the key areas of focus was PK collection/analysis, a primary endpoint of the study. Due to the complexity of PK collections, storage and shipment for various cohorts and protocol versions, as well as site staff and CRA turnover over the course of 4 years, this was the first area of analysis completed. The collection and tracking of this endpoint was further complicated by three EDC migrations, leading to varied and inconsistent interpretation of CRF completion guidelines by site staff. The review revealed a significant volume of certain missing PKs, isolated to particular sites—those with higher CRA and site staff turnover. Higher number of recorded PDs associated with PKs was the main risk signal that led to a more detailed review. In that case, both central monitoring and onsite monitoring activities identified issues with PKs, but having central monitoring sooner could have prevented some recurrent issues and reduced the volume of non-compliance.

Another trend identified through central monitoring was an expectedly higher incidence of adverse events among participants with more complex medical histories. To better understand this relationship, central monitors triangulated medical history, concomitant medication, and adverse event reporting rates to identify sites where the correlation between these domains showed a higher degree of variance than anticipated (e.g. some participants with a high number of medial conditions and concomitant medications had disproportionately low AE reporting compared to participants of similar complexity at other sites).

A review of critical data domains revealed a significant volume of certain missing PKs, isolated to particular sites—those with higher CRA and site staff turnover.

Sites with the greatest variance were then prioritized for granular, patient-level review, allowing central monitors to examine whether reported adverse events were consistent with participants' clinical profiles and treatment exposure. This deeper review identified additional adverse events that had not previously been captured in EDC.

In this case, the initial risk signal was driven by cross-domain rate analysis, which enabled detection of patterns not visible for CRAs since they review data one visit or one data point at a time. While onsite monitoring activities appropriately focus on individual patient records, the ability to evaluate trends across multiple data sources and across the entire study population allowed central monitoring to identify where focused follow-up would be most meaningful. Applying this type of analysis earlier in the study could have supported more timely data clarification and reduced the likelihood of recurrent under-reporting by allowing CRAs to target under-reporting sites for retraining.

Another central monitoring analysis looked at unexpected variation in protocol deviation rates related to investigational product dosing across sites. To better understand this pattern, central monitors reviewed dosing data, visit schedules, query activity, and protocol deviation records to identify sites where IP-related deviations appeared inconsistent with the complexity of dosing regimens and patient volume.

For example, several sites with similar enrollment and dosing requirements demonstrated markedly different patterns of documented IP deviations. In some cases, sites with a higher number of patients and patient visits recorded fewer deviations than sites with fewer patients, suggesting differences in documentation practices rather than true performance. Interestingly, one of the identified sites did not reveal any additional PDs despite being an outlier—likely indicating a better-performing site.

A targeted, patient-level review was then conducted to evaluate whether missed doses, dosing interruptions, and out-of-window administrations were captured in EDC. This analysis identified instances where dosing-related deviations had occurred but were not reflected in the protocol deviation log. Here, the initial signal emerged from a combined review of dosing data, query patterns, and protocol deviation records, which revealed trends that would not have been apparent when evaluating individual visits in isolation. Applying this type of cross-domain analysis earlier in the study could have enabled more timely clarification and helped minimize recurring issues related to IP.

Overall, the findings of the after-the-fact central monitoring analysis spanned eligibility, protocol deviations/important protocol deviations, AE and SAE reporting, and issues related to investigational product and endpoints. Most of these issues were confirmed as real, triggering several site audits. This case study presents a clear example of how shifting to a more modern and robust central monitoring approach can identify many issues proactively (and retroactively in this case) and improve overall data quality.

Premier recommendations for this clinical trial include:

- Continue prospective central monitoring reviews, with emphasis on known areas of risk.
- Conduct a full protocol deviation log reconciliation to ensure wording and classification are accurate.
- Perform additional onsite monitoring targeting the identified areas of risk and concern.
- Review eligibility form documentation in the trial master file (TMF) to ensure complete records are present.

Strengthening RBQM Approaches

Organizations often struggle with RBQM not because individual components are poorly designed, but because they are implemented without a cohesive, long-term strategy. A common pitfall is attempting to deploy multiple RBQM elements simultaneously without first defining how those components are intended to work together. In practice, this can lead to fragmented execution and limited operational impact.

An effective RBQM strategy typically begins at the enterprise level, with a clear vision for how risk will be assessed, monitored, and addressed across studies. From this foundation, individual components can be added incrementally and adapted modularly at the study level. Risk assessment is a critical first step, informing downstream decisions around patient-, site-, and study-level analyses, as well as the SDR/SDV sampling strategy. When these elements are designed to function cohesively, RBQM operates as an integrated system rather than a collection of disconnected activities.

In less mature implementations, RBQM components are often deployed in isolation. For example, organizations may adopt risk assessments or KRI dashboards while maintaining traditional monitoring approaches, such as 100% SDR and SDV, without clearly defining how insights from centralized analyses should influence CRA activities. This lack of integration is one of the most frequently observed weaknesses in RBQM programs and limits the ability to achieve desired outcomes such as improved efficiency, earlier issue detection, or cost savings.

Even when RBQM is not fully integrated at study start, opportunities remain to strengthen the approach during trial execution. Strategies can be refined as risks become more clear, additional data sources are incorporated, or operational challenges emerge. Adding or enhancing RBQM elements mid-study should be viewed as a maturation step rather than a corrective action.

A recurring challenge across organizations is insufficient documentation and follow-through of findings identified through central monitoring, particularly at the patient or study level. Without structured reporting and clear ownership, insights may not translate into action. Effective RBQM requires not only identifying risk signals, but also ensuring that findings are documented, communicated to the appropriate teams, and tracked to resolution.

In practice, structured site- and study-level reporting supports this integration by making central monitoring insights actionable. When findings are consistently documented and shared with clinical teams, they can directly inform CRA focus, site engagement, and corrective actions. This level of transparency and follow-through is essential for building confidence in RBQM and realizing its full value.

Conclusion

The Future: Need for Greater Adoption

The clinical trial sector should work to adopt centralized monitoring as part of RBQM to achieve more efficient and effective clinical trials. Centralized monitoring is still being underutilized despite the potential of increased patient safety oversight and improved data quality. Sponsors should consider the evidence that central monitoring is reliable and cost-effective, leaving CRAs with more time to work with sites on issue resolution and prevention. It is also critical to consider expanding central monitoring beyond EDC, which is just one of many ways that data is now collected. A continued focus on EDC places excessive burden on CRAs to find things in multiple source systems and identify discrepancies. If data from all sources are aggregated and displayed clearly, it becomes easier to identify and respond to discrepancies.

Experience suggests that overall risk assessment adoption is strong, but other risk-based components lag behind, meaning that companies may not be deriving the full benefits of performing the initial and ongoing risk assessment.[8] In an approach proposed by TransCelerate, a comprehensive risk-driven methodology can boost efficiency by altering the focus to central or off-site monitoring activities designed to identify potential issues sooner than a monitoring strategy that relies primarily on site monitoring visits.[9] This will hopefully advance the future obligation for the clinical trial industry to use centralized monitoring to produce more efficient and effective clinical trials, ensuring patient safety and data integrity.[10]

References

1. Dirks A, Florez M, Torche F, Young S, Slizgi B, Getz K. Comprehensive Assessment of Risk-Based Quality Management Adoption in Clinical Trials. *Ther Innov Regul Sci.* 2024 May;58(3):520-527. doi: 10.1007/s43441-024-00618-5. Epub 2024 Feb 16. Erratum in: *Ther Innov Regul Sci.* 2024 Sep;58(5):996. doi: 10.1007/s43441-024-00648-z. PMID: 38366107; PMCID: PMC11043178.

2. Stansbury N, Barnes B, Adams A, Berlien R, Branco D, Brown D, Butler P, Garson L, Jendrasek D, Manasco G, Ramirez N, Sanjuan N, Worman G, Adelfio A. Risk-Based Monitoring in Clinical Trials: Increased Adoption Throughout 2020. *Ther Innov Regul Sci.* 2022 May;56(3):415-422. doi: 10.1007/s43441-022-00387-z. Epub 2022 Mar 2. PMID: 35235192; PMCID: PMC8889871.

3. Association of Clinical Research Organizations (ACRO). *RBQM Landscape Summary Report.* June 2025. https://www.acrohealth.org/wp-content/uploads/2025/06/ACRO_2025-RBQM-Report_Final-062425.pdf

4. Adams A, Adelfio A, Barnes B. et al. Risk-Based Monitoring in Clinical Trials: 2021 Update. *Ther Innov Regul Sci.* 2023;57,529–537. doi: 10.1007/s43441-022-00496-9.

5. Dirks A, Florez M, Torche F, Young S, Slizgi B, Getz K. Comprehensive Assessment of Risk-Based Quality Management Adoption in Clinical Trials. *Ther Innov Regul Sci.* 2024 May;58(3):520-527. doi: 10.1007/s43441-024-00618-5. Epub 2024 Feb 16. Erratum in: *Ther Innov Regul Sci.* 2024 Sep;58(5):996. doi: 10.1007/s43441-024-00648-z. PMID: 38366107; PMCID: PMC11043178.

6. Association of Clinical Research Organizations (ACRO). *RBQM Landscape Summary Report.* June 2025. https://www.acrohealth.org/wp-content/uploads/2025/06/ACRO_2025-RBQM-Report_Final-062425.pdf

7. Association of Clinical Research Organizations (ACRO). *RBQM Landscape Summary Report.* June 2025. https://www.acrohealth.org/wp-content/uploads/2025/06/ACRO_2025-RBQM-Report_Final-062425.pdf

8. Stansbury N, Branco D, McDavid C, Stewart J, Surdam K, Olson N, Perry J, Liska J, Phillips L, Coogan A, Adelfio A, Garson L. Risk-Based Quality Management: A Case for Centralized Monitoring. *Ther Innov Regul Sci.* 2025 Mar;59(2):199-210. doi: 10.1007/s43441-024-00719-1. Epub 2024 Dec 11. PMID: 39663347; PMCID: PMC11880074.

9. TransCelerate BioPharma. *Position Paper: Risk-Based Monitoring Methodology.* May 2013. https://www.transceleratebiopharmainc.com/wp-content/uploads/2016/01/TransCelerate-RBM-Position-Paper-FINAL-30MAY2013.pdf

10. Stansbury N, Branco D, McDavid C, Stewart J, Surdam K, Olson N, Perry J, Liska J, Phillips L, Coogan A, Adelfio A, Garson L. Risk-Based Quality Management: A Case for Centralized Monitoring. *Ther Innov Regul Sci.* 2025 Mar;59(2):199-210. doi: 10.1007/s43441-024-00719-1. Epub 2024 Dec 11. PMID: 39663347; PMCID: PMC11880074.

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