

Next-Generation Risk-Based Monitoring: The Role of AI in Clinical Trial Oversight

Clinical trial monitoring has traditionally relied on routine on-site visits and exhaustive source data verification (SDV) to ensure patients' safety and data integrity. While effective at detecting individual errors, this approach is resource-intensive and often limited in its ability to identify systemic risk patterns across complex trials. In response, regulatory authorities advocated for more targeted, risk-proportionate oversight models. The European Medicines Agency's 'Reflection Paper on Risk-Based Quality Management in Clinical Trials' and the U.S. FDA's guidance on 'Oversight of Clinical Investigations – A Risk-Based Approach,' (2013) formally endorsed these strategies. Likewise, ICH E6(R2) and the evolving E6(R3) revisions emphasise systematic risk management throughout the trial lifecycle, integrating risk identification, assessment, control, communication and review.

To operationalise these principles, technology-enabled Risk-Based Monitoring (RBM) platforms emerged. However, early RBM tools were largely static, relying on predefined dashboards and rule-based triggers, which limited their ability to adapt to dynamic trial conditions. As clinical trials become increasingly complex with adaptive designs, decentralised data capture, wearable technologies and global operational networks, the limitations of rule-based RBM models have become evident.

Artificial Intelligence (AI), including machine learning and advanced analytics, represents a transformative evolution in monitoring. AI-augmented RBM shifts the focus from reactive detection of threshold breaches to predictive, adaptive and continuously learning risk management. By dynamically analysing large volumes of multi-source trial data, identifying subtle patterns, recalibrating risk models in real time and supporting multivariate pattern recognition, AI augments human expertise and enables proactive intervention. This evolution from manual, episodic SDV to technology-enabled RBM and now AI-augmented monitoring enhances trial efficiency, data integrity, patients' safety and regulatory compliance, marking a paradigm shift in how modern clinical trials are conducted.

Traditional Monitoring and 100% Source Data Verification

Historically, clinical trial monitoring relied heavily on frequent on-site visits by clinical research associates (CRAs) to ensure that study data were accurate, complete and verifiable. A cornerstone of this approach was 100% Source Data Verification (SDV), in which every data point recorded in the case report form (CRF) was systematically compared against the original source documents maintained at the investigative site. These source documents typically included medical records, laboratory results, imaging reports and other clinical notes documenting patient participation and study outcomes. The primary objective of this exhaustive verification process was to safeguard data

quality, ensure data integrity, warrant regulatory compliance and protect patients' safety throughout the trial.

While traditional monitoring with 100% SDV provided a high level of data confirmation, it was resource-intensive and operationally burdensome. Frequent site visits demanded substantial time and financial investment from sponsors and CROs, particularly in large, multicentre trials conducted across multiple regions. Moreover, this approach often emphasised transcription accuracy rather than proactive identification of systemic issues, such as protocol deviations, data trends, or emerging safety signals. As clinical trials became more complex, decentralised and global in scope, the limitations of this model became increasingly apparent, driving the adoption of more efficient and risk-proportionate monitoring strategies.

Key Limitations of Traditional Monitoring with 100% SDV:

- Delayed detection of quality issues and emerging safety signals.
- Limited ability to identify systemic risks or patterns across sites.
- High operational and financial burden.
- Significant workload for monitoring teams.

Emergence of Risk-Based Monitoring (Technology-Enabled RBM)

Risk-Based Monitoring (RBM) emerged as a modern approach designed to optimise monitoring efforts by prioritising activities that have the greatest impact on patients' safety and data quality. Regulatory authorities such as the US FDA and the EMEA encouraged the adoption of RBM frameworks, which were further supported by guidelines from the International Council for Harmonisation (ICH) through updates to Good Clinical Practice principles. RBM emphasises proactive risk assessment during trial planning, enabling sponsors and CROs to identify critical data points and processes that require focused oversight.

Under the RBM framework, monitoring activities combine centralised data review with targeted on-site visits based on predefined risk indicators. Techniques such as key risk indicators (KRIs), statistical data monitoring and centralised analytics allow sponsors and CROs to detect unusual patterns, protocol deviations, or site performance issues more efficiently. By shifting the focus from exhaustive verification to risk prioritisation, RBM enables more efficient allocation of monitoring resources while maintaining regulatory compliance and ensuring high standards of trial quality and patient safety.

However, there are some limitations of Technology-Based Risk-Based Monitoring (RBM) which include:

- **Dependence on Predefined Risk Indicators (KRIs):** RBM systems rely on predefined Key Risk Indicators and statistical thresholds



Figure: Evolution of Clinical Trial Monitoring

established during study planning, which may not capture all potential operational or clinical risks.

- **Limited Ability to Detect Complex Patterns:** Rule-based analytics may fail to identify subtle, multifactorial, or emerging patterns within large and heterogeneous clinical datasets.
- **Potential for Undetected Emerging Risks:** Because monitoring rules are predefined, novel or unexpected risks may remain unnoticed until they become significant.
- **Primarily Reactive Monitoring Approach and Limited Predictive Capability:** Many RBM systems identify issues only after deviations or anomalies occur rather than predicting them in advance. Traditional RBM tools lack the advanced predictive analytics needed to anticipate operational or safety risks early in the trial.

AI-Augmented Risk-Based Monitoring

Artificial intelligence (AI) introduces a new layer of analytical capability into RBM systems. AI algorithms can process vast amounts of clinical and operational data, identify subtle patterns and detect anomalies that may signal potential risks. Advances in AI and machine learning are now driving the next evolution of clinical trial monitoring. While traditional Risk-Based Monitoring (RBM) focuses on predefined risk indicators and centralised data review, AI-augmented RBM introduces advanced analytical capabilities that can process large and complex clinical datasets in real time. By applying machine learning algorithms to diverse data sources such as electronic data capture systems (EDC), randomisation tools, laboratory results, safety databases and operational metrics, AI systems can identify patterns, correlations and anomalies that may not be easily detected through conventional monitoring methods.

One of the key advantages of AI-augmented monitoring is its ability to enable predictive risk detection rather than relying solely on retrospective analysis. Machine learning models can analyse historical trial data, site performance metrics and patient-level information to predict potential issues such as enrolment delays, protocol deviations, or data inconsistencies. These predictive insights allow sponsors and clinical operations teams to intervene earlier, reducing the likelihood of significant operational or quality issues as the trial progresses.

AI-enabled monitoring platforms can also significantly enhance centralised monitoring capabilities. By continuously analysing

incoming trial data, AI systems can dynamically generate risk scores for investigative sites, patient cohorts, or specific study parameters. These dynamic risk assessments help prioritise monitoring activities and guide targeted site visits, enabling clinical research associates and clinical project managers to focus their efforts on high-risk areas that require closer oversight. As a result, monitoring resources can be deployed more efficiently while maintaining high standards of data quality and participant safety.

Importantly, AI-augmented RBM does not replace human expertise but rather enhances the decision-making capabilities of clinical trial management team. Clinical Research Associates (CRAs), medical monitors, data reviewers and clinical project managers remain essential for interpreting AI-generated insights and making informed clinical and operational decisions. By combining advanced analytics with expert clinical judgment, AI-augmented monitoring represents a powerful approach for improving trial quality, operational efficiency and proactive risk management in modern clinical research.

AI-augmented RBM leverages machine learning, natural language processing, and advanced analytics to enhance risk detection and prediction. These core capabilities include:

Predictive Risk Modeling: Traditional Risk-Based Monitoring (RBM) platforms primarily rely on predefined thresholds and rule-based triggers. For example, a site may be flagged when serious adverse event numbers exceed a specified threshold value or patient enrolment numbers are lower than the expected number or protocol deviations surpass established limits. While these approaches help identify safety or operational or data quality issues, they typically detect problems only after deviation patterns have already occurred, making traditional RBM largely reactive. In contrast, AI-enabled RBM leverages historical and real-time trial data to identify patterns that may signal emerging risks. Machine learning models can detect early indicators of operational risks such as patient recruitment rate, CRF completion rate or data integrity issues, data inconsistencies, protocol deviations, or delays in safety reporting before they exceed predefined thresholds. By shifting from retrospective signal detection to predictive risk intelligence, AI enables earlier intervention and more proactive trial monitoring and oversight. This capability is particularly valuable in fast-enrolling Phase II and Phase III trials, where delayed detection of issues can quickly propagate across multiple investigative sites.

Multivariate Risk Pattern Detection: Traditional technology-based RBM systems typically evaluate risk indicators independently,





such as adverse event frequency, query rate, or protocol deviations, using predefined thresholds. In contrast, AI-enabled monitoring systems apply multivariate analytics to examine multiple variables simultaneously, enabling the identification of complex relationships and hidden correlations within clinical trial data. For example, patterns such as rapid patient enrolment combined with a number of protocol deviations or consistent laboratory values with unusually low variability across multiple patients, or high screen-failure rates coupled with aggressive enrolment rates may indicate potential site-level risks that rule-based systems could overlook. This multidimensional analysis enhances the sensitivity and precision of centralised monitoring, allowing earlier and more reliable identification of emerging operational or data quality issues.

Dynamic and Adaptive Risk Modeling: Traditional Risk-Based Monitoring tools typically rely on static risk models established during study initiation, where key risk indicators (KRIs) and thresholds are defined and remain largely unchanged throughout the trial. In contrast, AI-enabled monitoring systems support dynamic and adaptive risk modeling by continuously analysing evolving clinical trial data. As site performance, enrolment trends, CRF completion rate, query rate, and protocol compliance patterns change over time, the system can recalibrate risk signals and adjust monitoring priorities accordingly. This adaptive approach allows monitoring strategies to better reflect real-world trial dynamics rather than relying solely on assumptions made during protocol planning.

Scalability and Integration of Multi-Source Trial Data: AI-enabled RBM platforms are designed to process large volumes of clinical trial data from multiple sources in real time. These systems can integrate data from electronic data capture (EDC), ePRO/eCOA platforms, wearable devices, imaging systems, laboratory data and remote monitoring technologies. By automatically harmonising and analysing these diverse data streams, AI systems can manage high-velocity datasets without requiring proportional increases in manual review. This scalability makes AI-based monitoring particularly well-suited for complex and data-intensive clinical trials involving a large patient pool.

Ongoing Centralised Monitoring Instead of Periodic Review: Traditional centralised monitoring is often conducted through periodic reviews, such as weekly, bi-weekly or monthly evaluations supported by static dashboards. In contrast, AI-enabled RBM enables continuous centralised monitoring by automatically analysing new data as it becomes available in the eClinical systems. Risk scores can be updated in real time, allowing emerging anomalies to be detected earlier and appropriate alerts to be generated. This shift from periodic review to continuous monitoring and oversight improves responsiveness and reduces the time between the emergence of risks and corrective action.

Higher Cost Efficiency and Resource Optimisation: Monitoring remains one of the major cost drivers in clinical trials. While traditional Risk-Based Monitoring (RBM) has reduced the frequency of on-site visits compared with legacy monitoring models, substantial manual effort is still required for centralised data review and signal interpretation. AI-enabled monitoring can automate routine analytical tasks such as anomaly detection, trend analysis and risk scoring, thereby reducing the burden on monitoring teams. This allows resources to be focused on high-risk sites or critical data elements rather than being uniformly distributed across all sites. As a result, monitoring efforts can be more efficiently targeted, potentially lowering overall study costs while maintaining or enhancing trial quality.

Improved Objectivity and Consistency in Monitoring: AI-enabled RBM helps reduce variability by applying standardised analytical models and algorithms across studies. Risk signals and scores are generated using consistent, data-driven methods, providing a more objective basis for monitoring decisions while still allowing for human oversight. This standardised approach can improve consistency in monitoring practices and strengthen the transparency and defensibility of oversight during audits and regulatory inspections.

Challenges and Limitations of AI-Augmented Risk-Based Monitoring

Despite its significant potential, the implementation of AI-Augmented

Risk-Based Monitoring (RBM) presents several practical and operational challenges. One of the primary challenges is data harmonisation and integration. AI systems must aggregate and analyse data from multiple clinical trial systems, including electronic data capture (EDC), randomisation tool (RTSM), safety databases, laboratory information systems and clinical trial management platforms etc. These systems often use different data formats, standards and data structures, which can complicate integration and require extensive data normalisation. Variability in data quality, incomplete datasets and delayed data entry can further affect the reliability and performance of AI-driven analytical models.

Another key consideration is algorithm transparency and regulatory acceptance. Many machine learning models operate as complex analytical systems, making it difficult to clearly explain how specific predictions or risk scores are generated. Regulatory authorities may require a high degree of transparency, validation and documentation to ensure that automated decision-support tools do not compromise patient safety, data integrity, or regulatory compliance. In addition, organisations may encounter technical and operational challenges when integrating AI solutions with existing legacy clinical systems that were not originally designed to support advanced analytics or continuous data processing.

Operational adoption also represents an important challenge. Successful implementation of AI-augmented RBM requires organisational readiness, including appropriate infrastructure, skilled personnel and changes in monitoring workflows. Study teams must be trained to interpret AI-generated signals and incorporate them into risk management processes without over-reliance on automated outputs. To address these challenges, sponsors and contract research organisations (CROs) should establish strong governance frameworks that include transparent algorithm validation, robust data quality management, and clearly defined human oversight. Phased implementation strategies like starting with pilot programmes and gradually expanding AI capabilities, can further facilitate the responsible and effective integration of AI technologies into clinical trial monitoring.

Conclusion

AI-augmented Risk-Based Monitoring (RBM) represents a transformative shift in clinical trial monitoring and oversight, moving beyond reactive, threshold-based approaches to predictive, adaptive and continuously learning systems. Traditional RBM relies on static risk models, periodic data review, and manual interpretation of predefined indicators, which can limit responsiveness and sensitivity to emerging risks. In contrast, AI-augmented RBM leverages historical and real-time trial data to detect subtle patterns, generate dynamic risk scores and continuously recalibrate monitoring priorities. Features such as multivariate pattern recognition, automated anomaly detection and predictive modeling enable continuous, data-driven oversight that is more precise, scalable and aligned with the operational realities of complex, modern clinical trials.

Importantly, AI does not replace clinical judgment; rather, it augments human expertise by automating routine monitoring tasks and providing actionable insights, allowing study teams to focus on high-value decision-making and strategic oversight. When implemented with robust governance, transparent algorithm validation and phased operational integration, AI-augmented RBM can enhance patients' safety, ensure data quality, maintain data integrity, optimise resource allocation and improve regulatory inspection readiness. By combining predictive intelligence with adaptive monitoring, AI-Augmented RBM empowers sponsors and CROs to transition from reactive problem-solving to proactive risk

management, setting a new standard for efficient, high-quality and future-ready clinical trial monitoring.

REFERENCES

1. U.S. Food and Drug Administration. Guidance for Industry: Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring, 2013.
2. European Medicines Agency - Reflection paper on risk based quality management in clinical trials, 2013
3. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. ICH E6(R2) and E6(R3) Good Clinical Practice Guidelines.
4. Hurley C, et al. Risk-based monitoring tools for clinical trials: A systematic review. *Contemporary Clinical Trials*, 2016.
5. Agrafiotis DK, et al. Risk-based monitoring of clinical trials: An integrative approach. *Clinical Therapeutics*, 2018.
6. Adams A, et al. Risk-Based Monitoring in Clinical Trials: 2021 Update. *Therapeutic Innovation & Regulatory Science*, 2023.
7. Vyas, N.R. Future of risk-based monitoring in clinical trials. *International Journal of Clinical Trials*, 2020.
8. VKB Parasaram. Real-Time Clinical Trial Monitoring with AI-Powered Analytics. *Journal of Advances in Pharmaceutical Sciences*, 2025
9. David B. Olawade et al. Artificial intelligence in clinical trials: A comprehensive review of opportunities, challenges, and future directions. *International Journal of Medical Informatics*, 2026
10. Rahul Aggarwal et al. The potential of artificial intelligence in clinical trials. *European Journal of Clinical Investigation*, 2026;
11. FDA Guidance: Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products Guidance for Industry and Other Interested Parties, January 2025
12. Ashok Ghone, The Book "Risk-Based Approach To Clinical Trial Management" Published in October 2018
13. RK Ravindran et al. Evaluating the Effectiveness of Risk-Based Monitoring and Artificial Intelligence-Driven Strategies in Clinical Trial Management: A Data-Driven Analysis. *International Journal of Advanced Engineering Research and Science (IJAEERS)*, 2026
14. Benbow JH et al. Harnessing Artificial Intelligence to Transform Clinical Trials and Cancer Care: Opportunities and Challenges. *The Cancer Journal*, 2025
15. Vishakha Verma et al. Clinical Trial Monitoring: An Overview of Risk-based Approach. *Journal of Young Pharmacists*, 2023

Ashok Ghone



Ashok Ghone, PhD, MBA, is the CEO and Founder of MedInventas, bringing nearly 25 years of experience across the pharmaceutical, medical device, and CRO industries. He brings deep expertise in global clinical research, spanning clinical operations, project management, trial execution and process innovation. Ashok has successfully led cross-functional teams across local, regional and global studies in both early- and late-phase development, as well as in multiple therapeutic areas. A recognised thought leader in clinical operations excellence, he has played a pivotal role in designing and implementing frameworks for risk-based and centralised monitoring, operational process optimisation and clinical team enablement through the use of data intelligence. At MedInventas, Ashok offers domain expertise and strategic direction for developing AI-powered eClinical systems designed to transform clinical operations, trial management, and medical writing. His vision focuses on empowering life sciences organisations and CROs with intelligent, adaptive and compliant AI ecosystems that improve quality oversight, accelerate study delivery and enhance decision-making.

Email: ashok.ghone@medinventas.com