RISK-BASED QUALITY MANAGEMENT IN RARE DISEASE TRIALS: AN OBSERVATIONAL PERSPECTIVE ON DATA INTEGRITY

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INTRODUCTION

Rare diseases affect over 300 million people globally (The Lancet Global Health, 2024). Low prevalence means small, dispersed cohorts, making recruitment slow and costly (Stoller, 2018). The natural history of many orphan conditions is poorly understood, complicating endpoint selection and study design (Liu et al., 2022b), and heterogeneity in small samples increases variability and underpowered analyses (Friede et al., 2018). Investigator inexperience with complex protocols further raises protocol deviations, screening failures, and data inconsistencies (PPD, 2016). Sponsors need targeted oversight to uphold data integrity and patient safety without overextending limited resources.

OBJECTIVES

To assess how risk-based quality management (RBQM) enhances data integrity and patient safety, facilitates oversight, ensures protocol adherence, supports anomaly detection, and meets regulatory requirements in rare-disease trials.

METHOD

A systematic literature review examined the effects of RBQM (and Risk-Based Monitoring). Though RBQM-specific studies in rare disease trials are limited, existing research and industry insights identify crucial data quality metrics for rare disease trials, e.g. protocol adherence, timely data entry, site performance, screening, and enrollment rates. Observations from an RBQM platform demonstrated the effect of monitoring and addressing these indicators proportionally using traceable Key Risk Indicators (KRIs).

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RESULTS

Rare disease trials are critical, as each patient can represent a large portion of evaluable data, making anomalies potentially trial-ending (Chen et al., 2024). Investigator inexperience and complex visit schedules drive high protocol deviations and screening failures. Data issues, such as delayed safety labs and inconsistent data entry, especially in multi-country trials, threaten patient safety and endpoint validity (Chen et al., 2024).

RBQM starts with prospective risk assessment to identify “critical-to-quality” elements, such as primary endpoints, safety assessments, informed consent, and key data captures. KRIs or Acceptable Ranges (ARs) are set to monitor risk events (ICH E6(R3), 2025; ICH E8(R1), 2021). Centralized Statistical Monitoring (CSM) further aggregates lab data, vital signs, query metrics, and site performance indicators. CSM models flag anomalies, and continuous KRI tracking triggers alerts when thresholds are breached, e.g. high deviation rates, data-entry lag, or screening failures. In rare disease trials, reliance on KRIs increases due to limited data points.

Empirical data shows substantial benefits in the application of RBQM. Andersen et al. (2023) reported a 50% reduction in primary efficacy endpoint errors under RBQM versus traditional monitoring. An industry survey found 83% of sites with KRI-triggered interventions improved data consistency versus 56% in conventional trials (De Viron et al., 2024). Stansbury et al. (2024) noted that though RBQM adoption has been slow, users achieve significant advantages while preserving safety and integrity. Sponsors can expect smoother regulatory inspections and clearer risk-management documentation under updated guidelines (ICH E6(R3), 2025).

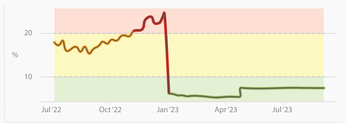

Figure 1: KRI indicating a **High % of Withdrawals** at a study level

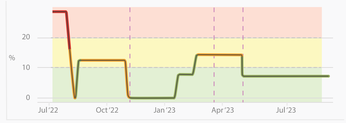

Figure 2: KRI indicating an **Under-recruitment** at a country level

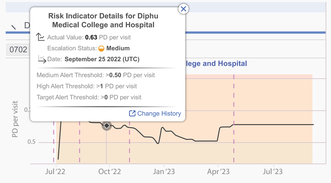

Figure 3: KRI indicating a **High Number of Protocol Deviations** at a site level

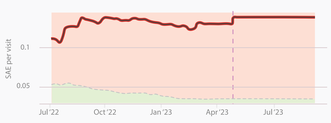

Figure 4: KRI indicating a **High Rate of Adverse Events** at a country level

CONCLUSIONS

RBQM offers a proactive, resource-efficient, and regulator-supported framework ensuring data integrity and patient safety in rare-disease trials. Focusing oversight on predefined critical risks and using centralized analytics for early detection minimizes issues such as protocol deviations, screening failures, withdrawals, underrecruitment, and safety events, while optimizing resources. In trials where each patient’s data is invaluable, RBQM offers a strategic advantage to accelerate therapy development for rare conditions.

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