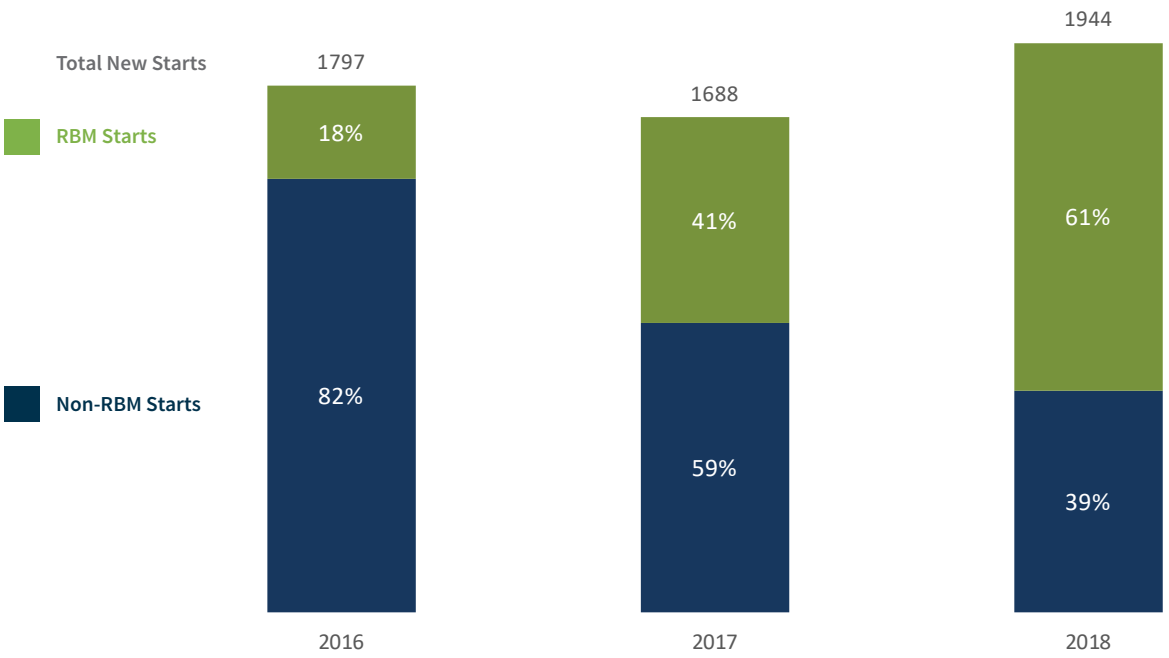
THE RISK-BASED MONITORING LANDSCAPE IN 2019

In 2019, the Association of Clinical Research Organizations (ACRO) surveyed its members on Risk-Based Monitoring (RBM) processes and implementation.

RBM-ENABLED NEW TRIAL STARTS ARE GROWING AS A PROPORTION OF TOTAL STARTS



In 2016, new trial starts using RBM technology comprised 18% of all starts. That proportion has risen to 61% as of 2018.

Definition of RBM in Survey: "Risk-Based Monitoring: An adaptive approach to clinical trial monitoring that directs monitoring focus and activities to the evolving areas of greatest need which have the most potential to impact subject safety and data quality."
Source: TransCelerate BioPharma Inc. (2017). Section 5 The Next Frontier of RBM - Glossary: Key Terms Defined
https://www.transceleratebiopharmainc.com/rbminteractiveguide/the-next-frontier-of-rbm/glossary-key-terms-defined/

CROs ARE INVESTING IN AN RBM-ENABLED FUTURE

Over the last 3-5 years, **ALL ACRO member companies** have made significant investments to advance RBM:

- **Workforce** - Reshaping and adding more positions to support the growth of RBM. Members have developed diverse, cross-functional training programs to support new technologies and processes.
- **Technology** - Building in-house software infrastructure and solutions and partnering with technology vendors to enhance RBM offerings. New generations of RBM offerings have built on years of experience.
- **Processes** - New and updated methods to support and improve RBM across clinical research.

ALL ACRO member companies routinely recommend RBM in their contract bids.

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RBM IMPLEMENTATION

***Examples* of RBM trial evaluation metrics reported by ACRO survey respondents**

QUALITY IN RBM TRIALS

- Enhanced ability to identify and manage patient eligibility issues, unreported adverse events and protocol deviations, helping to monitor safety risks
- Central data reviews enabled early detection of quality issues, allowing sites to identify data issues and make early corrections
- 16% reduction in critical and major findings in site audits
- 17% better detection of significant deviations
- 4x lower error rate in critical data in a head-to-head comparison of RBM to traditional 100% SDV approach
- 45% reduction in the number of missing pages in RBM trials versus traditional trials

EFFICIENCY AND SPEED IN RBM TRIALS

- 10-day reduction in data management cycle time for a large sponsor implementing a new RBM technology
- A smaller biotech has seen database locks go from 30-60 days from Last Patient Visit (LPV) to about 5 days
- 40% faster database lock timeline compared to non-RBM trials
- 20% reduction in SDV, resulting in more than $1M savings for a mid-sized sponsor in the first year
- 3-15% savings over traditional monitoring, depending upon the level of SDR/SDV included
- 21% reduction in subject visit data entry lag

CHALLENGES

Despite the increasing use of RBM, ACRO member companies report challenges that limit wider adoption

PERCEPTION MANAGEMENT

When sponsors request 100% SDV, it is often due to their comfort level with traditional oversight methods and the perception that 100% SDV is the only way to ensure data quality, and thus a "lower risk" market application.

Emerging biopharmaceutical companies with limited portfolios tend to be the most reluctant, choosing what they see as a "safer" strategy of "checking" every data point.

Sponsors perceive audit and inspection findings at research sites, with findings for non-critical discrepancies, as further support for 100% SDV.

Sponsors may also request RBM initially, but then identify additional data points as critical, resulting in little reduction in SDV.

EXPECTATION MANAGEMENT

Non-directive guidance creates varied performance expectations regarding RBM implementation (eg. reduced SDV/SDR) by sponsors, CROs and research sites.

Varied interpretations of ICH E6 (R2) requirements relating to RBM and quality tolerance limits (QTL), creates variability in inspection findings.

Variability in inspection findings creates variability in stakeholder incentives – positive and negative – to implement RBM.

RBM implementation requires consistent and ongoing investment in change management by all parties, including regulators, sponsors, CROs and investigative sites.

ACRO and CRO Forum Members

Bioclinica, Covance, ERT, ICON, IQVIA, Medidata, Oracle, PAREXEL, PPD, PRA Health Sciences, Premier Research, Syneos Health, Veeva

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