

RBQM – The New Normal Vigilante for CROs with AI and ML

Presented by Vidya Muthukumar, Senior Data Strategist



Agenda

- ❖ **What is Risk-Based Quality Management?**
- ❖ **Why Risk-Based Quality Management?**
- ❖ **Current Trends in RBQM**
- ❖ **RBQM – New Normal with AI and ML**
- ❖ **Pros and Cons of RBQM**
- ❖ **Future of RBQM**
- ❖ **Questions**

What is Risk-Based Quality Management (RBQM)?

An improved monitoring model that optimizes clinical trial execution

Assessing & Mitigating Risk

The Risk-Based Quality Management (RBQM) model focuses on assessing and mitigating risks related to the protocol, and is in addition to the traditional risk assessment activities done on non RBQM studies

Focusing on Critical Data

In an RBQM model SDV is performed on only the most critical data elements of a study

Continuous Central Review

RBQM generally utilizes an element of centralized monitoring that uses a variety of processes, tools, and systems to continuously review overall study data to find potential issues where additional levels of monitoring may be needed

Monitoring Based on Risk

In an RBQM model, each site is monitored appropriately based on the amount of activity and overall performance of sites. On-site, remote and centralized monitoring can be employed based on the needs of each site

Industry Guidance for RBQM

Increased use of electronic systems and improvements in statistical monitoring present opportunities for evolved monitoring approaches



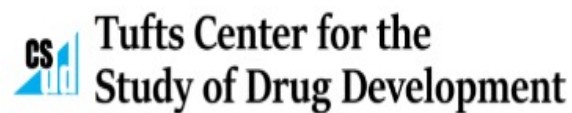
Support from Regulatory Agencies



“When good quality risk management and quality by design processes inform the development of RBM, effective implementation of RBM can maximize study quality by focusing monitoring activities on processes and procedures critical for the protection of trial participants and managing data integrity”



Large Data Aggregation



According to a 2018 Tufts Center for the Study of Drug Development report, the number of endpoints used in clinical trials rose 86% between 2001-2005 and 2011-2015. The number of sites increased 63% over the same time period. This increased complexity means more data to collect and learn from but also more patient burden.



Improved Quality and Safety



Effective RBQM implementation requires a strong collaboration between the sponsor and vendors that is based upon partnership alignment. No matter the size of the sponsor organization (e.g., large pharma, biotech), RBM and QbD principals should be rooted in a sound Quality Management System (QMS) framework to ensure human subject protection, product quality, clinical responsibility and reliability of trial results



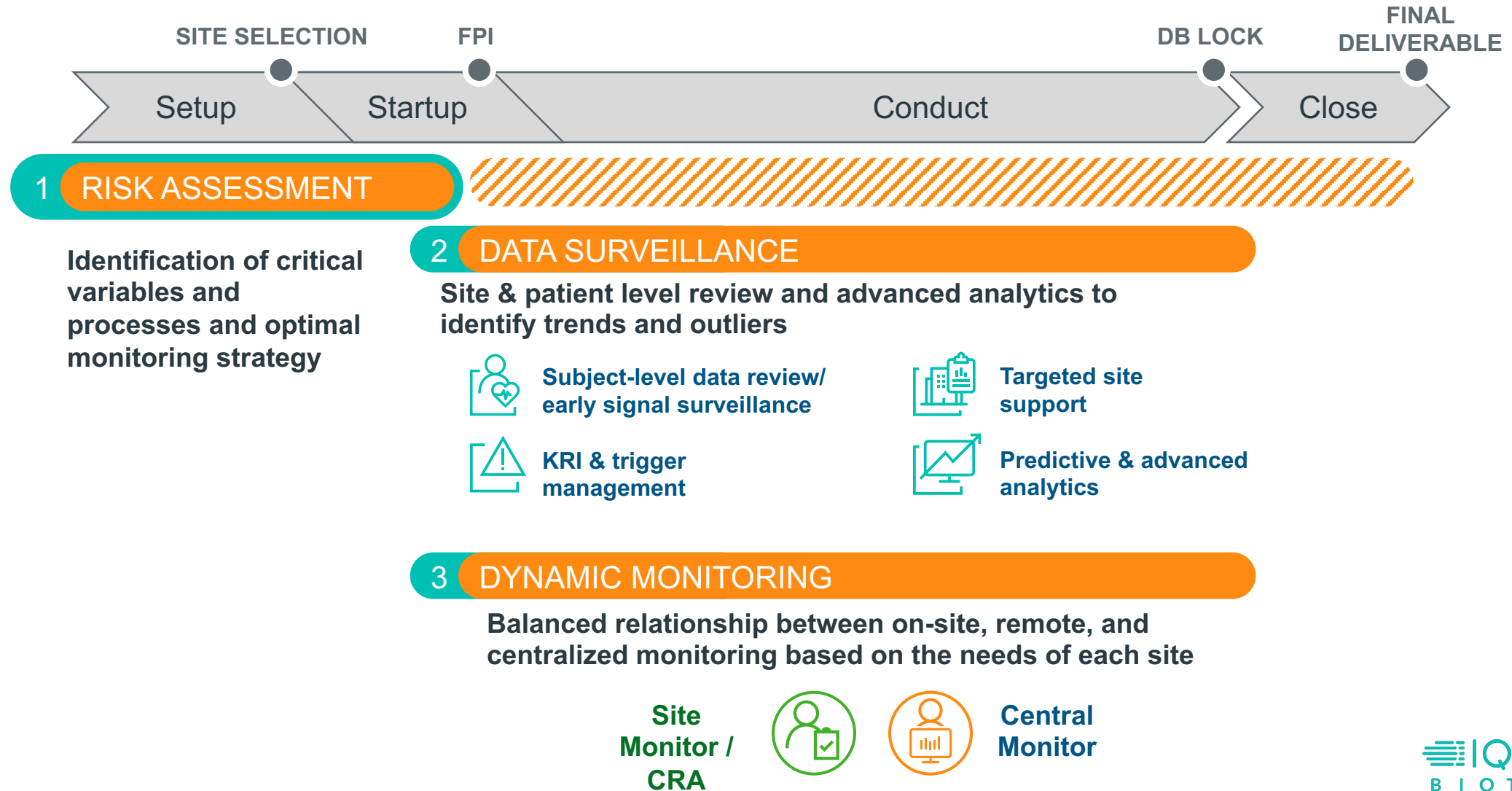
ICH-E6 R3* and ICH-E8 emphasis on risk strategy



- ICH E6 (R3) highlights technology being fit for purpose to enable the accurate reporting, interpretation, and verification of clinical-trial related information.

IQVIA's RBQM Approach

Identify & mitigate protocol risk, use the right monitoring approach, identify potential issues faster



Risk Assessment & Mitigation

Process and tool for conducting, documenting and mitigating risk



Outcome of Risk Assessment:

1. Risk assessment and mitigation plan (RAMP*)
2. Operational Risks: Key Risk Indicators identified
3. Scientific Risks: Critical / Key Data Variables documented
4. Monitoring strategy finalized

**Aligned to Transcelerate RACT (Risk Assessment and Categorization Tool)*

Critical Data /Processes (CD/P)

Primary and Secondary Endpoints

Essential Subject Safety

SAE recording and reporting

Informed Consent Process

Inclusion/ Exclusion Criteria (PE/SE)

Events leading to discontinuation of treatment

Variables related to dosing/ IP management

Other study-specific variables

Subject Sampling Strategy (SSS)

Subject Sampling Strategy for CRA to perform SDM during on-site MVs

Key Risk Indicators (KRI)

First Patient In (FPI)

Workload (SDV) Backlog

Missing Pages

Query Aging

Composite KRI

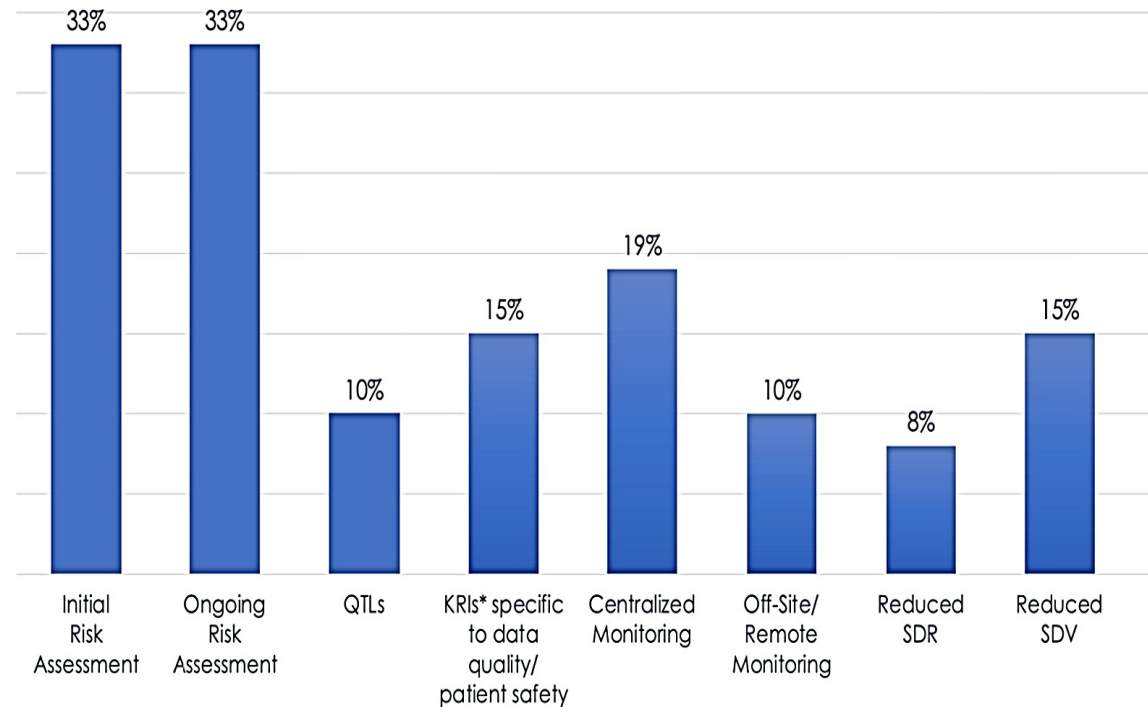
- Adverse Event Rate
- Serious Adverse Event Rate
- Query Rate
- Protocol Deviation Rate
- Overdue Action Items
- Screen Failure Rate

Individual KRIs - optional

- First Patient Screened
- Delay in FPS from SIV
- Subject discontinuation of IP

Current Trends in RBQM

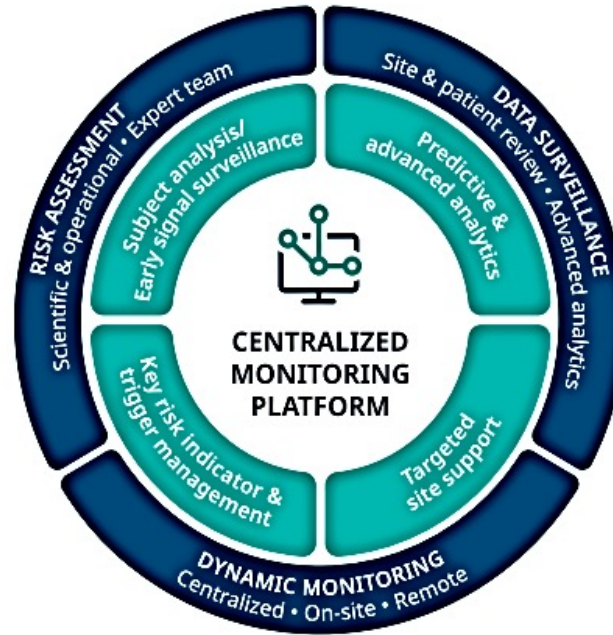
2019-20 Landscape of RBQM Components in Clinical Trials. Data represent the percentage of all 6,513 trials included in the survey, not just the subset of studies that have at least one RBQM component. *The KRI percentage does not include KRIs related to operations or performance*



Current Trends in RBQM

TECHNOLOGY AND DATA INTEGRATION

We collaborate with your IT team to integrate and validate your data, leveraging our unique centralized monitoring platform to speed operational readiness and effectiveness



CENTRALIZED MONITORING EXPERIENCE



Operational
since 2012

>600 Central
Monitoring staff



>17,000
sites
supported



>100,000
patients
monitored

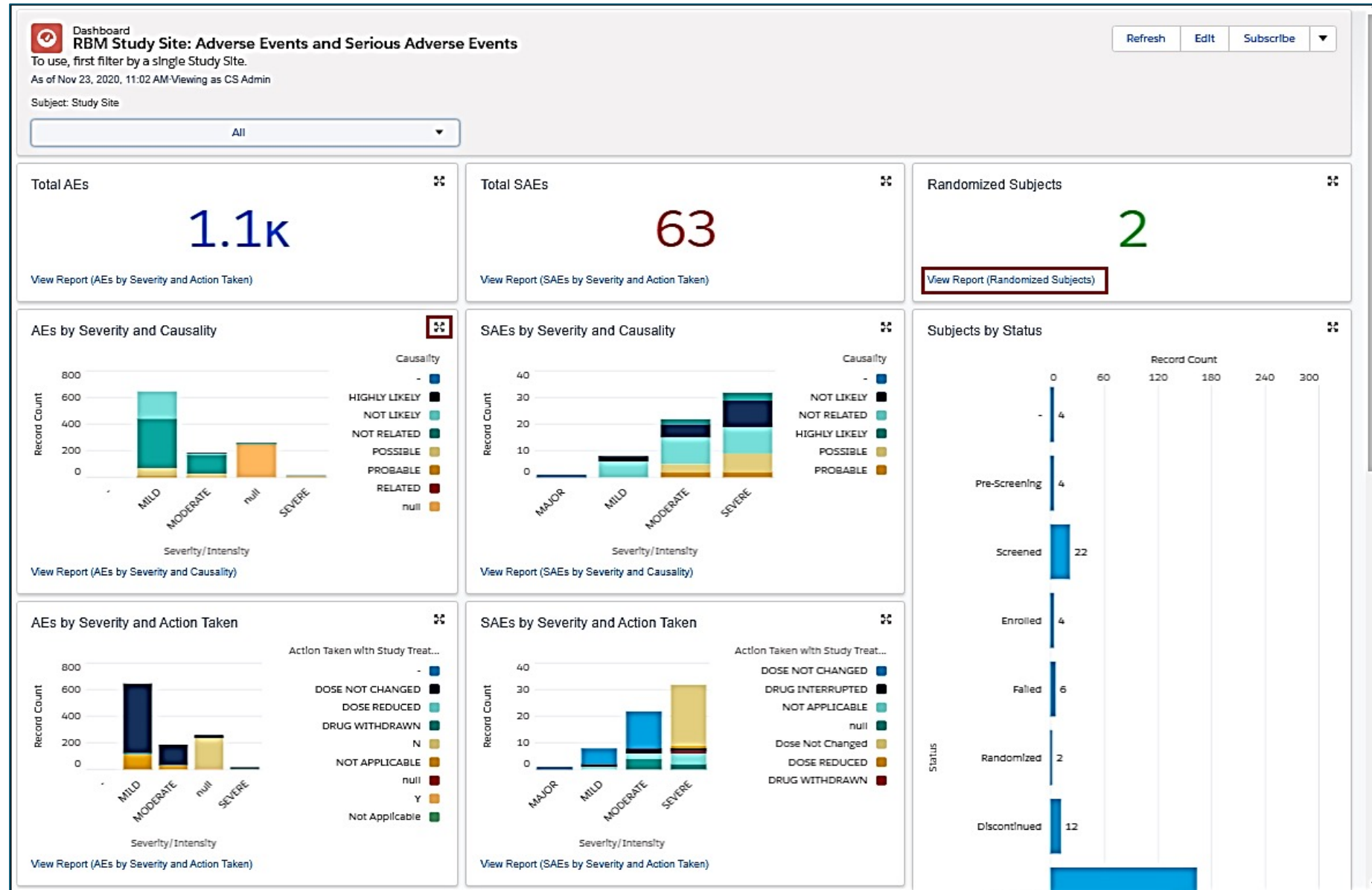


>70
sponsors

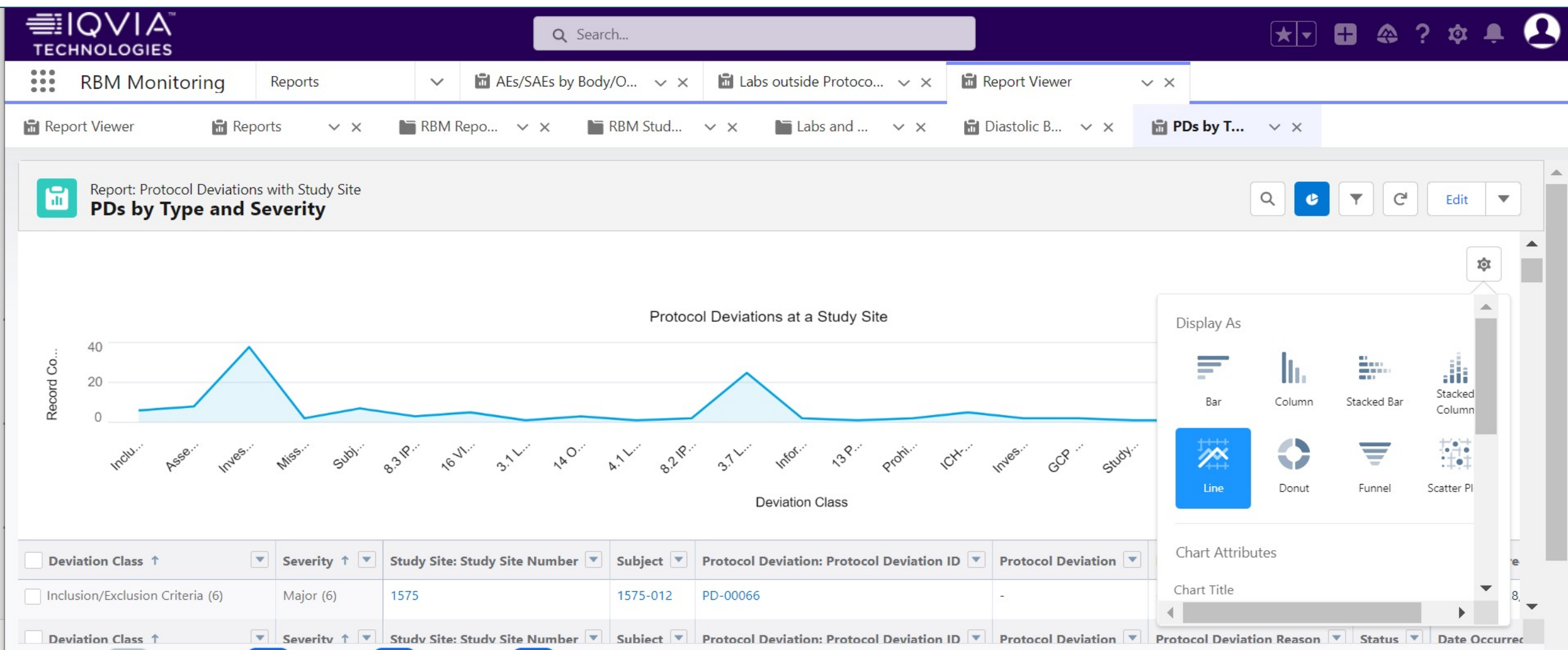
>170
studies



RBQM – New Normal with AI and ML



RBQM – New Normal with AI and ML



RBQM – New Normal with AI and ML

★
+
🏠
?
⚙️
🔔
👤

⋮ RBM Monitoring

Reports
▼

📊 Total Patients
▼
×

📊 Top AE/SAE...
▼
×

📊 Top AE/SAE...
▼
×

📊 Sites with H...
▼
×

📊 Site Subject...
▼
×

📊 Sample Rep...
▼
×

📊 Report Vie...
▼
×

📊 Report Viewer
📊 Reports
▼
×

📊 Site Subje...
▼
×

📊 Diastolic B...
▼
×

📊 Sites wit...
▼
×

📊

Report: Adverse Events with Subject
Sites with High AEs/SAEs

🔍
📄
⏏
🔄
Edit
▼

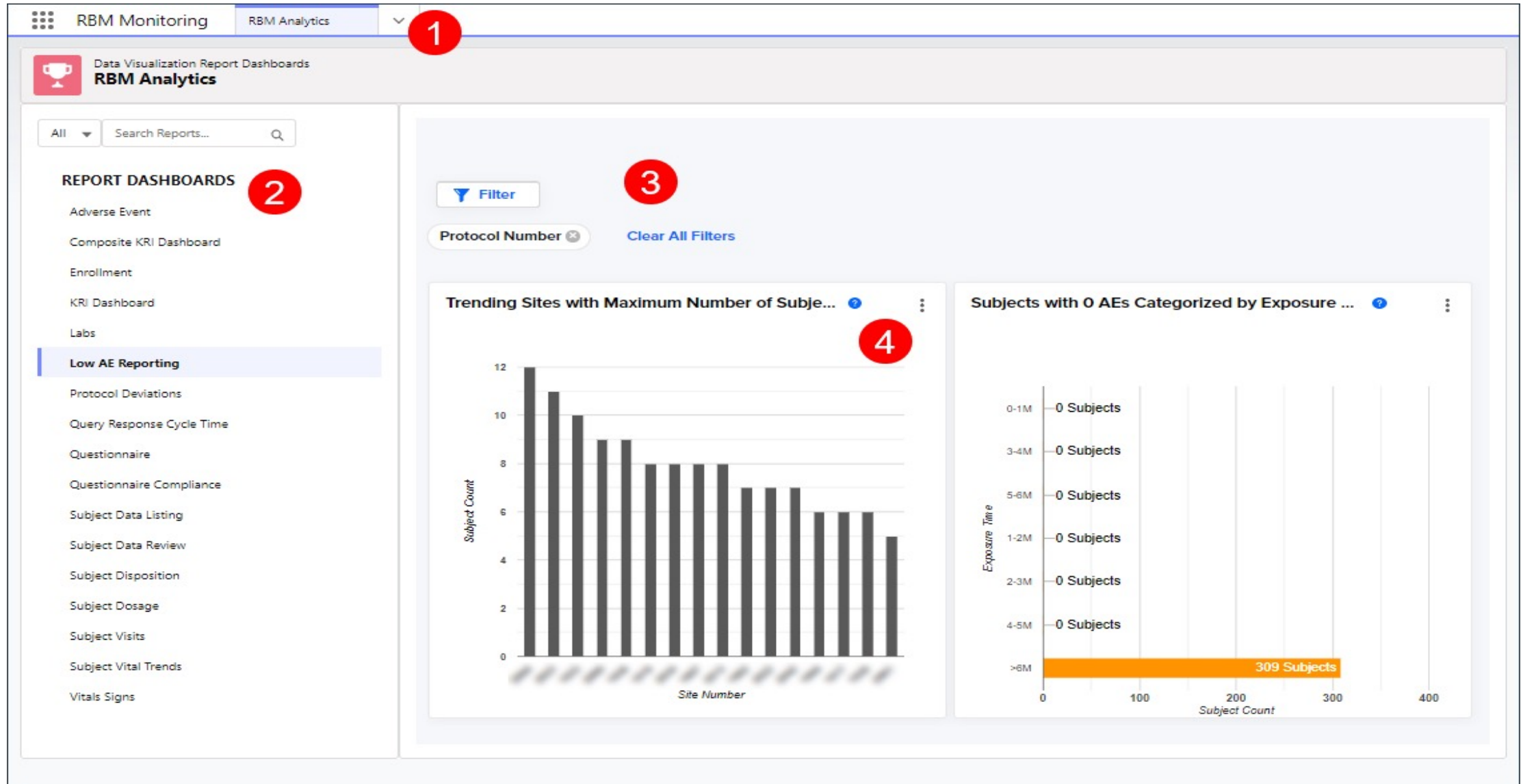
Subject Study Site

102

1575

☐ Subject: Study Site ↑ ▼	☐ Subject: Subject ID ▼	☐ Adverse Event: Adverse Event Name ↑ ▼	☐ Reported Term for the Adverse Event ▼	☐ Dictionary-Derived Term ▼	☐ Serious Event ▼	☐ Severity/Intensity ▼	☐ Start Date/Time of Adverse Event
☐ 102 (1)	102-011	7~2021-11-25T-:-:~+00:00~Headache, intermittent	Headache, intermittent	-	☐	-	2021-11-25T-:-:~+00:00
Subtotal		Unique: 1			0		
☐ 1575 (6)	1575-014	1~2021-10-07T00:00:00~FEELING SLEEPY	FEELING SLEEPY	-	☐	MILD	2021-10-07T00:00:00
	1575-014	2~2021-11-29T00:00:00~FEELING SLEEPY	FEELING SLEEPY	-	☐	MILD	2021-11-29T00:00:00

RBQM – New Normal with AI and ML



Pros and Cons In RBQM

Evolving Landscape and Accelerators

Innovations and challenges are requiring a new approach to clinical operations and monitoring



Increasing Costs

Increasing cost pressure paired with expanding development timelines

- Median R&D cost over last 10 years = **~\$1bn / product**
- Price and cost control regulations in US continue to gain traction



Expansion of AI & ML

Growing use of artificial intelligence and machine learning to streamline decisions and processes

- **77% of general consumers already interact with some form of AI technology**



Evolving Regulations

Variety of new initiatives put in place by the FDA to facilitate novel trial designs and rapid feedback.

- RBM, RWD use within trials, use of digital health tech, biomarkers, precision medicine approaches, etc.



RBM as the Standard



COVID-19 is driving increased adoption of RBM and remote monitoring approach

- RBM adoption increased as response to pandemic
- RBM accounted for higher study starts than non-RBM

Decentralized Trials & Digitization



Virtual and de-centralized trials, home nursing, and wearables all accelerated due to COVID-19

- **March 2020 telehealth visits surged 50%** amid the coronavirus pandemic

Broad Adoption of EMR & E-tech



Continued expansion of technology at site, including eSource, eConsent, eSIF, EMR and more

- **85.9% of office-based physicians using any EMR/EHR system**

Pros and Cons In RBQM

Category	Traditional	RBQM
Source Date Verification	100% SDV	Reduced SDV • Site monitor: focused on process review, source data review (SDR) / partial source data verification (SDV) • Central monitor: Data surveillance to assess and interact with site on follow-up actions
Data Surveillance	Limited to data management review	Extensive data surveillance provided by the centralized monitoring team • In a traditional model, data surveillance is limited to a cursory data management review that is focused on data consistency, and preset range limits • While data management is still done on RBQM studies, IQVIA RBQM has dedicated teams performing in depth data surveillance and data analysis that looks across data sets to spot trends that can indicate and predict issues in the study
Visits	At a predetermined frequency • Onsite monitoring visits • Site contacts	Data and risk-driven dynamic monitoring • On-site: visit is triggered by risk signals (i.e. issues / risks identified, accumulated data) or defined in the clinical operations plan (COP), generally less frequent than traditional model • Remote: focus on follow up on actions and assessment of protocol adherence
Additional Support	Not applicable	Site Monitor and Central monitor collaborate to work with the site CM: centralized monitoring of eCRF data and follow up with sites directly through email or via site monitor
Communication Level	Onsite monitoring visits and site contacts by the site monitor	Both the site monitor and central monitor are equipped with more information and able to have a more informed conversation on processes and trends identified in the study data

Pros and Cons In RBQM



12.5

**Days faster to
database lock**
vs. non-RBM studies

31%

Less SDV backlog
for RBM studies vs.
non-RBM studies

21%

**Reduction in patient
visit data entry lag**



Cost savings

Up to 25% cost savings when
compared to traditional monitoring



Improved patient safety

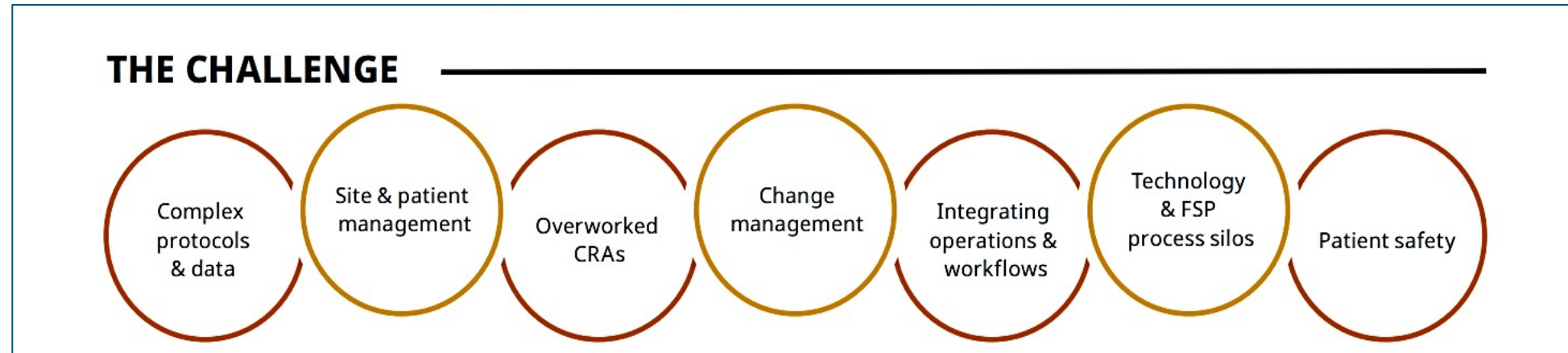
67% of queries resulted in data
base updates, with 74% of these
related to patient safety

References:

1) Branch, E. (2016, April 30). Ways to Lower Costs of Clinical Trials and How CROs Help. Retrieved January 21, 2019, from <https://www.americanpharmaceuticalreview.com/Featured-Articles/185929-Ways-to-Lower-Costs-of-Clinical-Trials-and-How-CROs-Help/>

Current Challenges In RBQM

Focus on change management and developing new workflows supported by integrating innovative technologies and multiple data sources



Future of RBQM

Next-Generation trials will rely on enhanced data assets to break down historical constraints and enable transformational study designs



Questions?