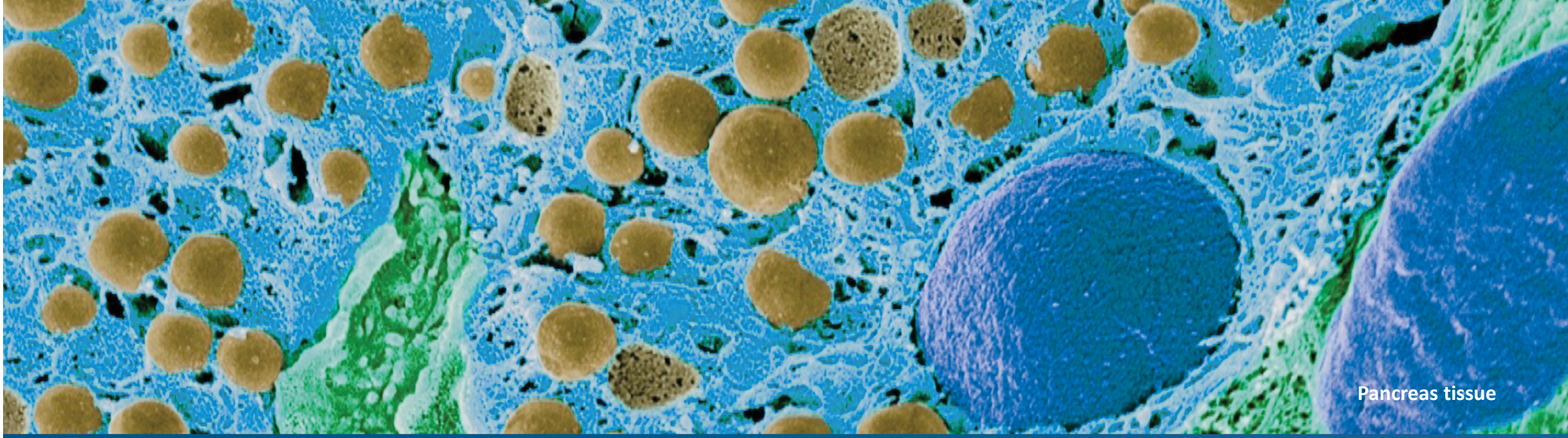

Data Visualization, Critical to Early Identification of Risk Signals

Agnes Verhoeven, Central Monitoring Manager

Marianne van de Ven, TA Lead Oncology

Risk Management & Central Monitoring

Janssen R&D| 01 November 2019

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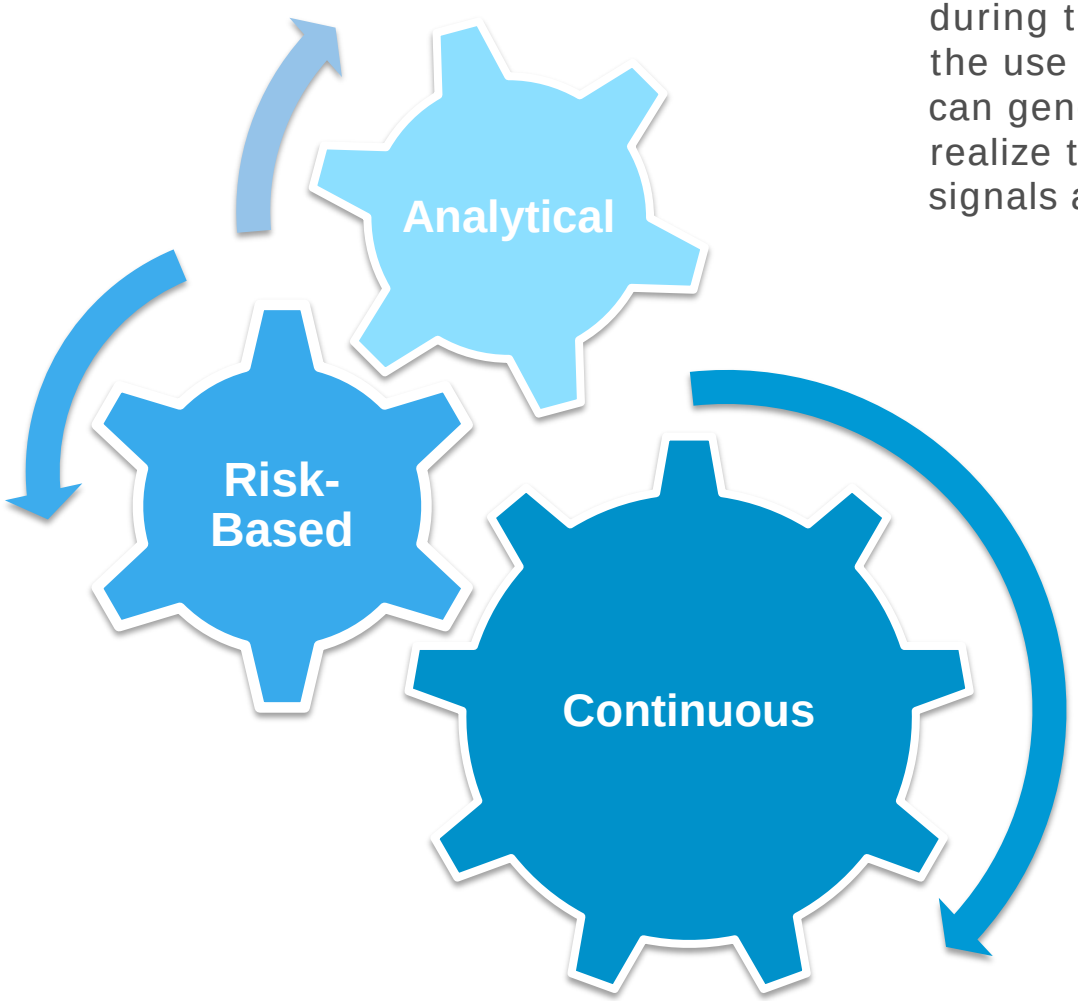
Central Monitoring at Janssen R&D

- Quality is the absence of errors that matter.
- Group formed in 2013 with 5 employees and has expanded to 50+ employees in 2019 across multiple Therapeutic Areas and Sectors.
- Our central monitoring capabilities have expanded and enhanced our ability to detect signals indicating potential risks, which can be recognized and actioned upon in a timely manner to drive data quality.

ARBM key concepts & principles

Risk-Based:

- A risk management plan that is **Targeted** to the data most critical to patient safety and data quality
- **Tailored** to meet the needs of the trial *and* the investigator site
- **Flexible** to be monitored according to the lifecycle of the trial and adjusted when needed



Analytical:
Quality-by-Design elements focused upon during trial setup, are then leveraged through the use of systems/tools (and the reports they can generate, allowing the organization to fully realize the power of analyzing data, to detect signals and trends that indicate a *potential* risk

Continuous Monitoring:
Pro-active and collaborative monitoring on a continuous basis by:

- **Site Managers** (via On-site and Off-site Monitoring Visits)
- **Central Team Members** such as Data Manager, Central Monitoring Manager, Study Physician

This Enables us to achieve the highest level of oversight through a mutual cost-beneficial approach for study teams

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Analytic Approaches to Support Risk-Based Monitoring

Standard Key Risk Indicators (KRIs)	Dashboard with *standard* operational and safety KRIs to indicate potential risks in countries/sites. Applicable across studies
Study-Specific Reports (SSRs)	Visualizations based on unique, *study-specific* Critical to Quality (CtQ) factors to identify potential risks in study/countries/sites
Central Statistical Surveillance (CSS)	Statistical analysis of entire trial data set to identify signs of intentional/unintentional noncompliance. Identifies sites that need further focused monitoring

Organizational Access to Data Visualizations

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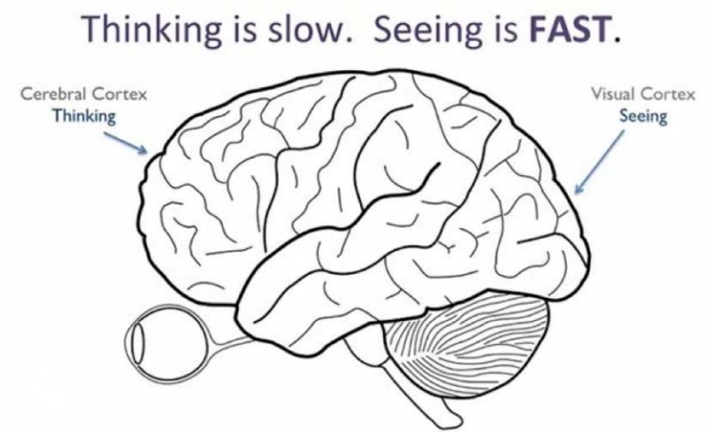
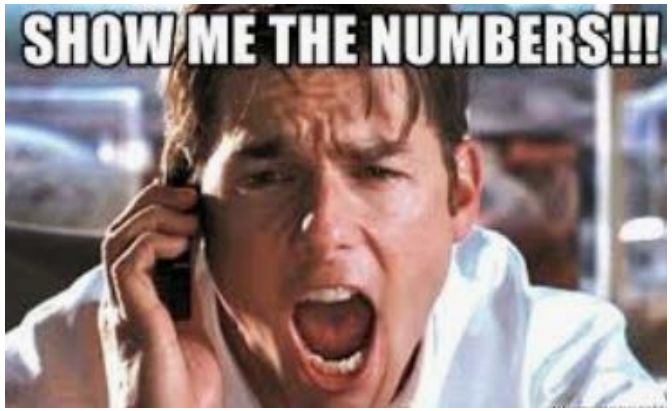
Note: Slide from Analytical Tools and Methods to Support Risk-Based Monitoring presentation, **Stephanie Clark** on behalf of Janssen at Duke Margolis Event, JUL 2019, Washington DC

Visualizations



According to research using brain imagery, visualization works because neurons in our brains, those electrically excitable cells that transmit information, interpret imagery as equivalent to a real-life action.



Data visualization can Identify areas that need attention or improvement.
Data visualizations make big and small data easier for the human brain to understand and visualization also makes it easier to detect patterns, trends and outliers in groups of data.

Centralized Monitoring

Key Risk Indicators

- KRI
- SSR
- CSS

Skin cells at 20x magnification

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Key Risk Indicators (KRIs) available for Standard Review

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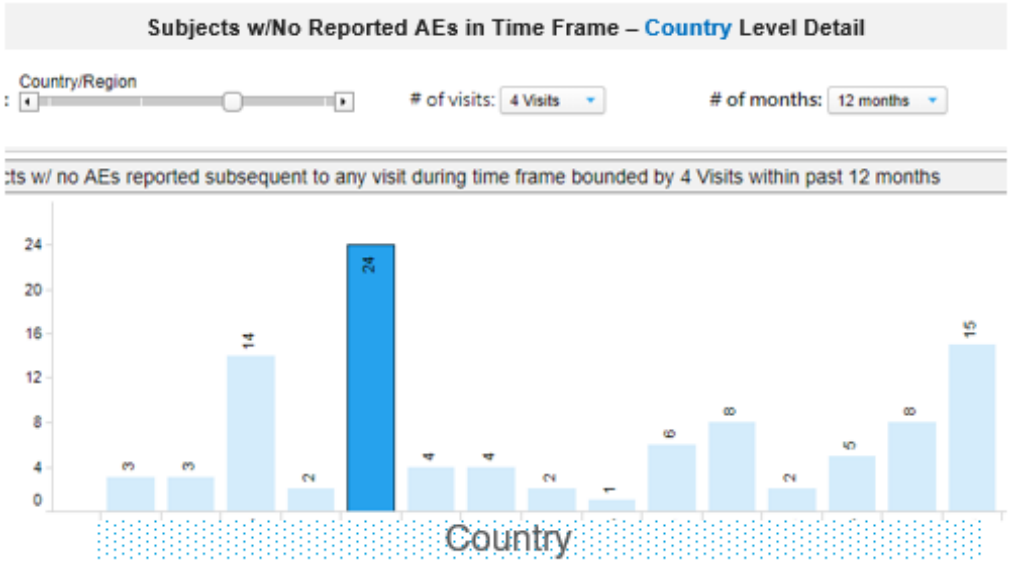
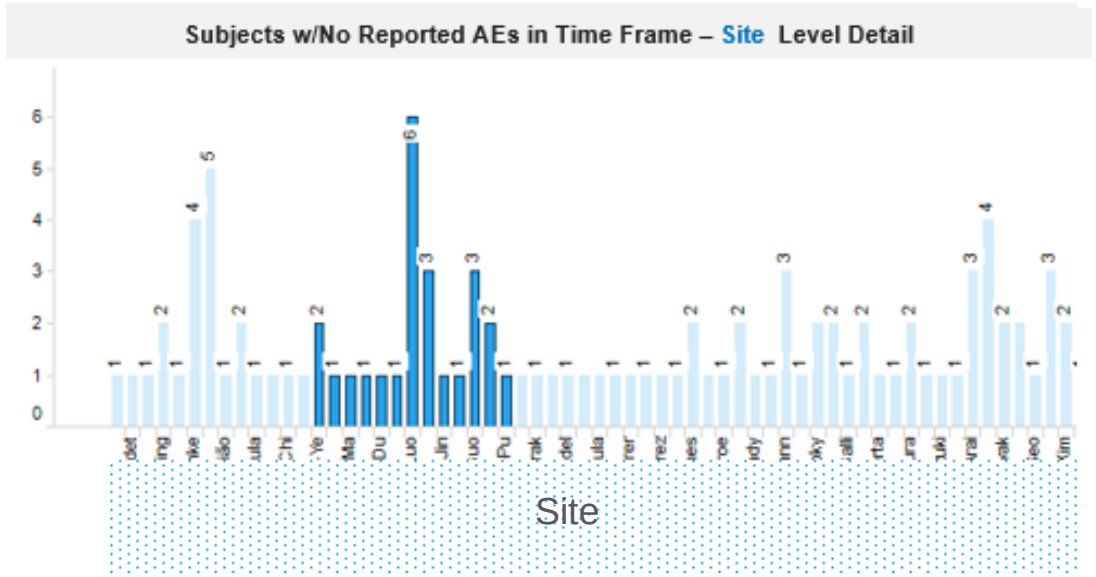
Standard Key Risk Indicator (KRI) – *example: No Reported AEs*





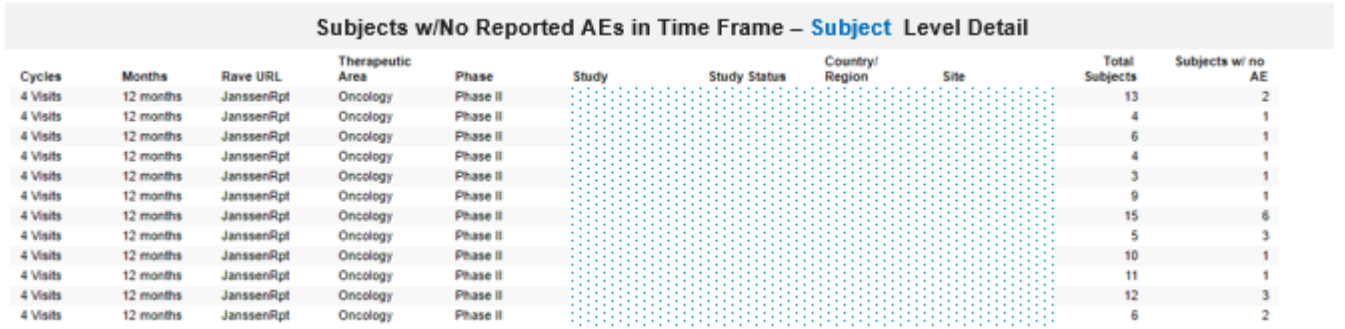
Related to subject safety

Dashboard created to identify and trend subject with no AEs or less AEs reported

ACTIONS:

- Raised signals in working group meeting
- Create a notification CRA to follow up with the site
- Appeared to be a data entry issue

DOCUMENTATION: fully documented in issue tracking system



Cycles	Months	Rave URL	Therapeutic Area	Phase	Study	Study Status	Country/ Region	Site	Total Subjects	Subjects w/ no AE
4 Visits	12 months	JanssenRpt	Oncology	Phase II					13	2
4 Visits	12 months	JanssenRpt	Oncology	Phase II					4	1
4 Visits	12 months	JanssenRpt	Oncology	Phase II					6	1
4 Visits	12 months	JanssenRpt	Oncology	Phase II					4	1
4 Visits	12 months	JanssenRpt	Oncology	Phase II					3	1
4 Visits	12 months	JanssenRpt	Oncology	Phase II					9	1
4 Visits	12 months	JanssenRpt	Oncology	Phase II					15	6
4 Visits	12 months	JanssenRpt	Oncology	Phase II					5	3
4 Visits	12 months	JanssenRpt	Oncology	Phase II					10	1
4 Visits	12 months	JanssenRpt	Oncology	Phase II					11	1
4 Visits	12 months	JanssenRpt	Oncology	Phase II					12	3
4 Visits	12 months	JanssenRpt	Oncology	Phase II					6	2

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Centralized Monitoring

Study Specific Reports

KRI

SSR

CSS

Skin cells at 20x magnification

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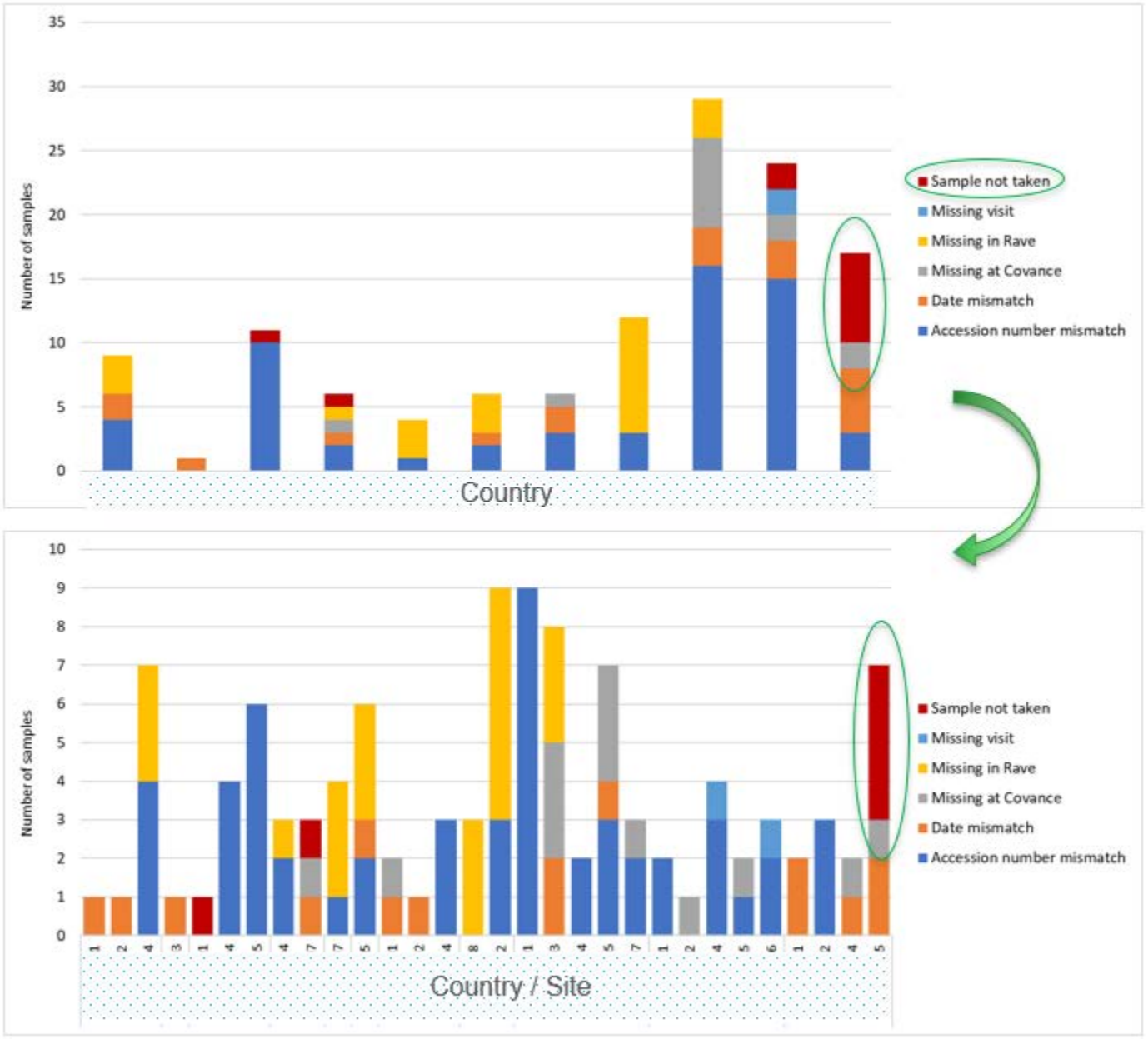
Study-Specific Reports (SSRs) – *example:* Biomarker Samples



Related to study endpoint

Report created to identify and trend samples not taken per protocol/not received at central vendor

Identified site where biomarker samples were not taken for two consecutive months

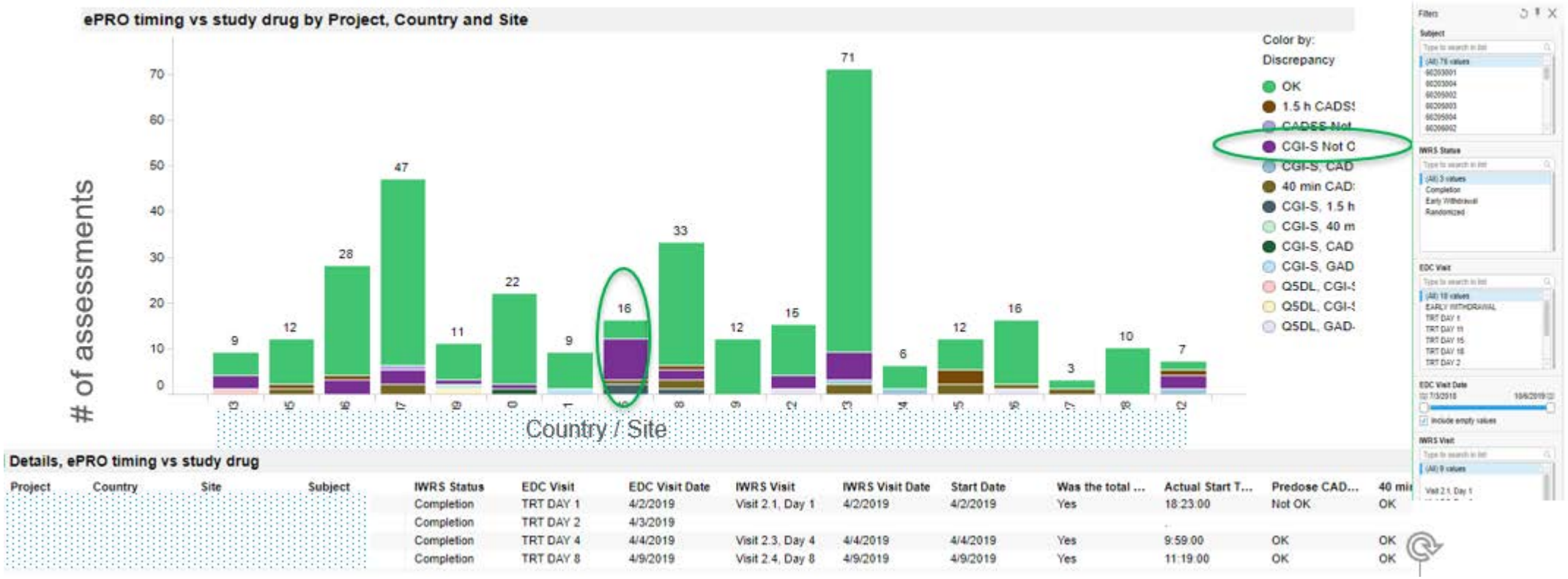
ACTIONS:

- Raised as a signal in working group meeting
- Site contacted and acknowledged confusion around protocol sampling process
- Site retrained, no recurrence

DOCUMENTATION: fully documented in issue tracking system

Example shown: Phase 3 Oncology study

Study-Specific Reports (SSRs) – *example:* ePRO on time



Related to efficacy

Report created to identify and trend sites who deviate from the ePRO timing schedule from the protocol.

Identified site where one particular assessment was not done according to the protocol schedule.

Immediately strikes the eye when data is converted to a visualization instead of a line listing

ACTIONS:

- The signal was discussed in the working group meeting
- Site was contacted and acknowledged the signal because the Sub-PI was asked to do an out-patient diagnosis at time of the study patients ePRO assessments
- This is a one time occurrence which was explained. It raised awareness by the site personnel and no recurrence occurred

DOCUMENTATION: fully documented in issue tracking system

Example shown: Phase 3 Neuroscience study

Centralized Monitoring

Central Statistical Surveillance

KRI

SSR

CSS

Skin cells at 20x magnification

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Central Statistical Surveillance (CSS)- basics

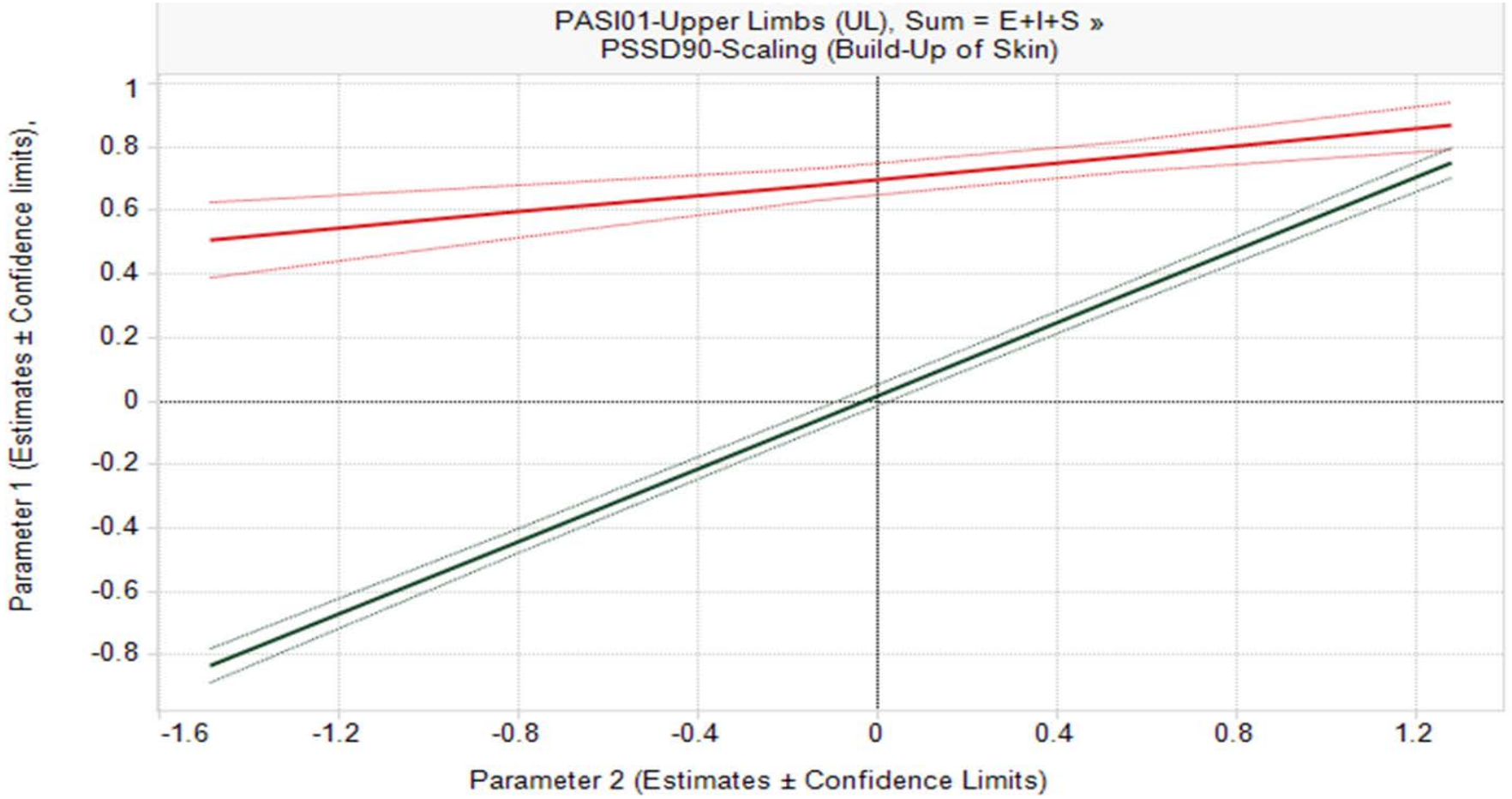
A combination of different statistical techniques to detect abnormal patterns in the data.

It uses the structured nature of clinical data

- Between clinical parameters: Different measures taken from the same subject at the same time should be related to each other (to varying degrees)
- Subject profiles over time: the same measurement from the same subject at different visits should be related
- Between subjects: the same measurement for different subjects should NOT be related

Example relationship between clinical parameters

Different relationship between questionnaire responses



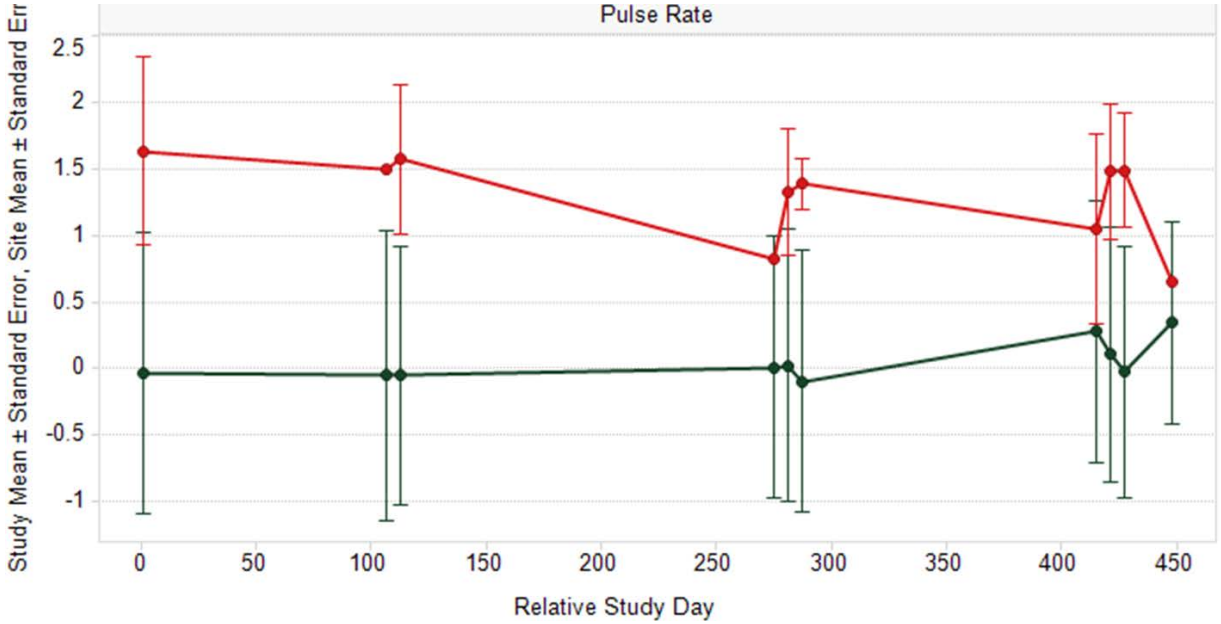
LEGEND:

- **RED LINE**: Site results
- **GREEN LINE**: Study results**

Study averages include all data with the exception of the site under review

Example site result changes over time

Pulse Rate test results are consistently higher than average



LEGEND:

- **RED LINE**: Site results
- **GREEN LINE**: Study results**

Study averages include all data with the exception of the site under review

Error bars represent the average difference between the test results at the respective study day

Parameter Averages v. Relative Study Day | Log-Normalized Values

ESCALATION

Central monitor determines which findings are true signals of potential risk and provides site by site summary to central study teams

Central monitor offers possible root causes and recommended follow-up actions:

- Review site level laboratory results to determine if there are any clinical issues
- Review source notes to ensure batching of subjects/samples is not done

Central study teams follow-up with local teams and/or vendors for further investigation or escalate compliance concerns to quality group

RESOLUTION

Depends on outcome of root cause analysis

Possible for-cause audits

DOCUMENTATION: fully documented in issue tracking system

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Centralized Monitoring

Conclusion & Summary

KRI

SSR

CSS

Skin cells at 20x magnification

Early identify risk signals in a clinical study is important and by using the visualization in the three-pronged approach to central monitoring, we are able to,

Identify,

- site/country risk signals early
- critical missing and discrepant data review and follow up
- protocol non-compliance

Quickly conduct root cause analysis and take timely and appropriate corrective and preventive actions

Be better prepared for database locks and inspections

More accurately forecast resource needs (targeted on-site monitoring)

Have clear insights to focus attention on errors that matter

Successfully implement a risk-based approach to monitoring with a robust central monitoring component

Visualization is an easy way to interpret the data for all roles and levels

Thank you

Agnes Verhoeven
averho10@its.jnj.com
Central Monitoring Manager

Marianne van de Ven
mvdven2@its.jnj.com
TA Lead Oncology

Questions?

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