CluePoints

Vertex – June 18th responses

July 2025

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M&A use case

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Use case M&A assets

- **Top 40 pharma – were** looking into assets for acquisition. Utilized the CluePoints platform to validate whether value was there within the studies they were buying into. Helped them make their final go-decisions.

- **Mid-Size Biotech -** Merger situation – DQA was able to detect fraud and merger was called off

- **Mid-sized Biotech** performed a Radar on their data (utilizing DQA) to help their sale go through on a lead. Led to **a Top 20 pharma** purchasing the whole company

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Data Volume – additional guidance

Risk-Based Quality Management (RBQM) and Data Quality Oversight

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Data volume guidelines for relative statistical results

Analysis Type	Dimension	Data Requirement #1	Data Requirement #2	Notes
DQA	Site	8 Sites	2 Patients/Site	When a site includes more than 20% of all data, statistical methods might lack statistical power to flag anomalies*
DQA	Patient	30 Patients		
DQA	Country	8 Countries	2 Patients/Country	When a country includes more than 20% of all data, statistical methods might lack statistical power to flag anomalies*

- The above rows can be treated as "OR" rather than "AND"
- This guideline is driven by simulations on fabricated data, see Trotta, L, *et al*. Detection of Atypical Data in Multicenter Clinical Trials Using Unsupervised Statistical Monitoring. *Clin Trials* 2019; 16(5): 512–22, DOI:10.1177/1740774519862564. We recommend sponsors to further discuss with CluePoints the best setup for those specific cases.

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Data volume guidelines for relative statistical results

Analysis Type	Dimension	Data Requirement #1	Data Requirement #2	Notes
KRI	Site	8 Sites	2 Patients/Site	1. Applies only to Relative Scores, Absolute KRIs are valid on any volume of data 2. When a site includes more than 20% of all data, statistical methods might lack statistical power to flag anomalies*
KRI	Patient	30 Patients		Applies only to Relative Scores, Absolute KRIs are valid on any volume of data
KRI	Country	8 Countries	2 Patients/Country	1. Applies only to Relative Scores, Absolute KRIs are valid on any volume of data 2. When a country includes more than 20% of all data, statistical methods might lack statistical power to flag anomalies*

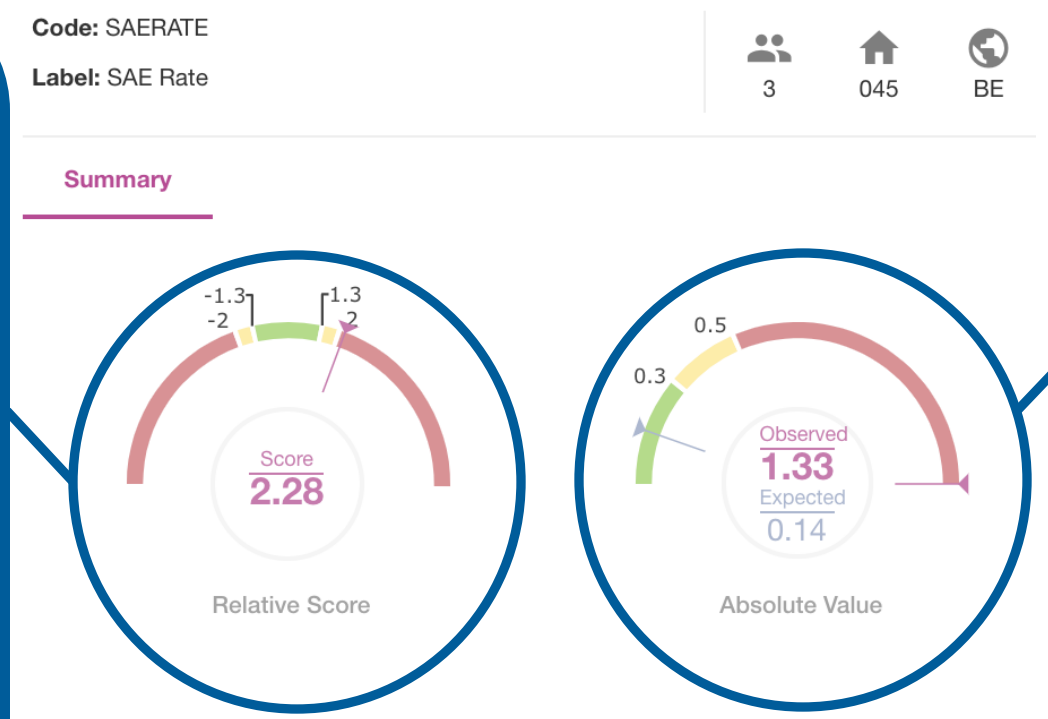
- This guideline is driven by simulations on fabricated data, see Trotta, L, *et al*. Detection of Atypical Data in Multicenter Clinical Trials Using Unsupervised Statistical Monitoring. *Clin Trials* 2019; 16(5): 512–22, DOI:10.1177/1740774519862564. We recommend sponsors to further discuss with CluePoints the best setup for those specific cases.

Relative Score and Absolute Value Explanation

The **Relative Score thresholds** define the risk based on how atypical the center observed value is compared to the study expected value for the selected KRI.

The higher the score (in absolute value), the more statistically atypical the center is.
A center can be at low risk, at medium risk, or at high risk.

A score of 1.3 represents a p-value of 0.05, a score of 2 represents a p-value of 0.01.



The **Absolute Value thresholds** are defined by the study team and are applied on the center observed value for the selected KRI.

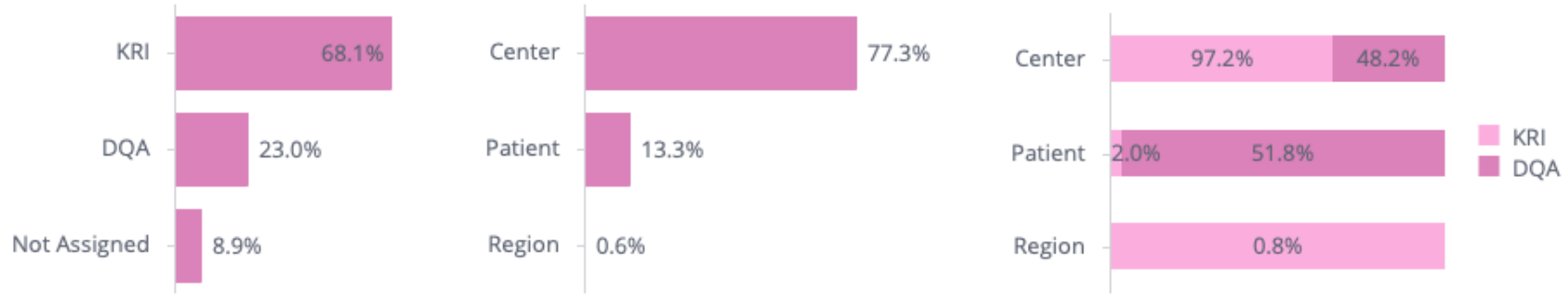
Note: Absolute thresholds can be defined by the study team if desired but are not mandatory.

Data volume guidelines for relative statistical results

Analysis Type	Notes
Duplicate Patient	Can be applied to any volume of data
Patient Profile	
RACT	
Beyond Clinical	
QTLs	

CluePoints Experience – Signals in Small Studies

- 15.7 signals per study in average (max ~55 signals in a study)
- 68.1% of the Signals are from a supervised, KRI approach
- 23.0% of the Signals were from an unsupervised, statistical detection approach
- 51.8% of unsupervised Signals were created by Patient-level analysis

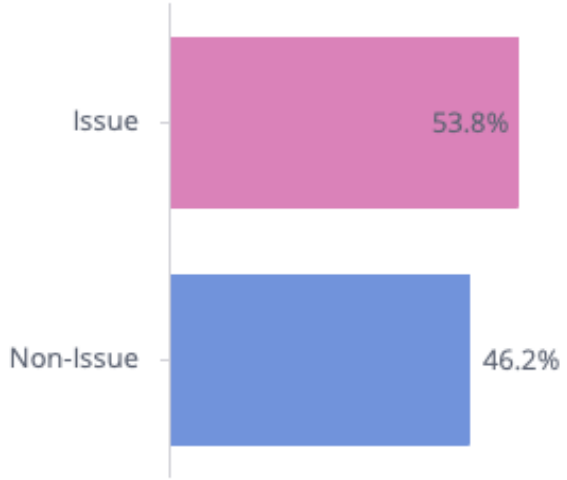


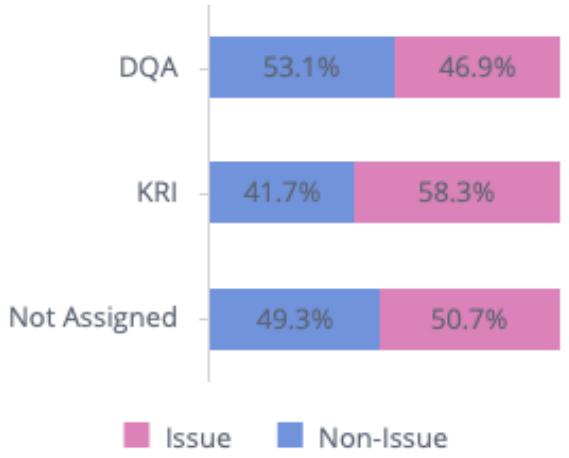
Very Similar results if we consider only <100 patients as small studies
Except the average number of signals per study that is growing (~54.9 signals per study)

CluePoints Experience – Issues flagged in Small Studies

Due to the low number of signals with user entry of Issue/Non-Issue for Small Studies defined as < 100 patients & < 8 centers (the feature is quite new in CMP),
The definition used for this analysis is < 100 patients only

- Signals considered as Issue by the user
  - 53.8% in total (total number of signal is around 5,609)
  - 46.9% of the DQA signals
  - 58.3% of the KRI signals



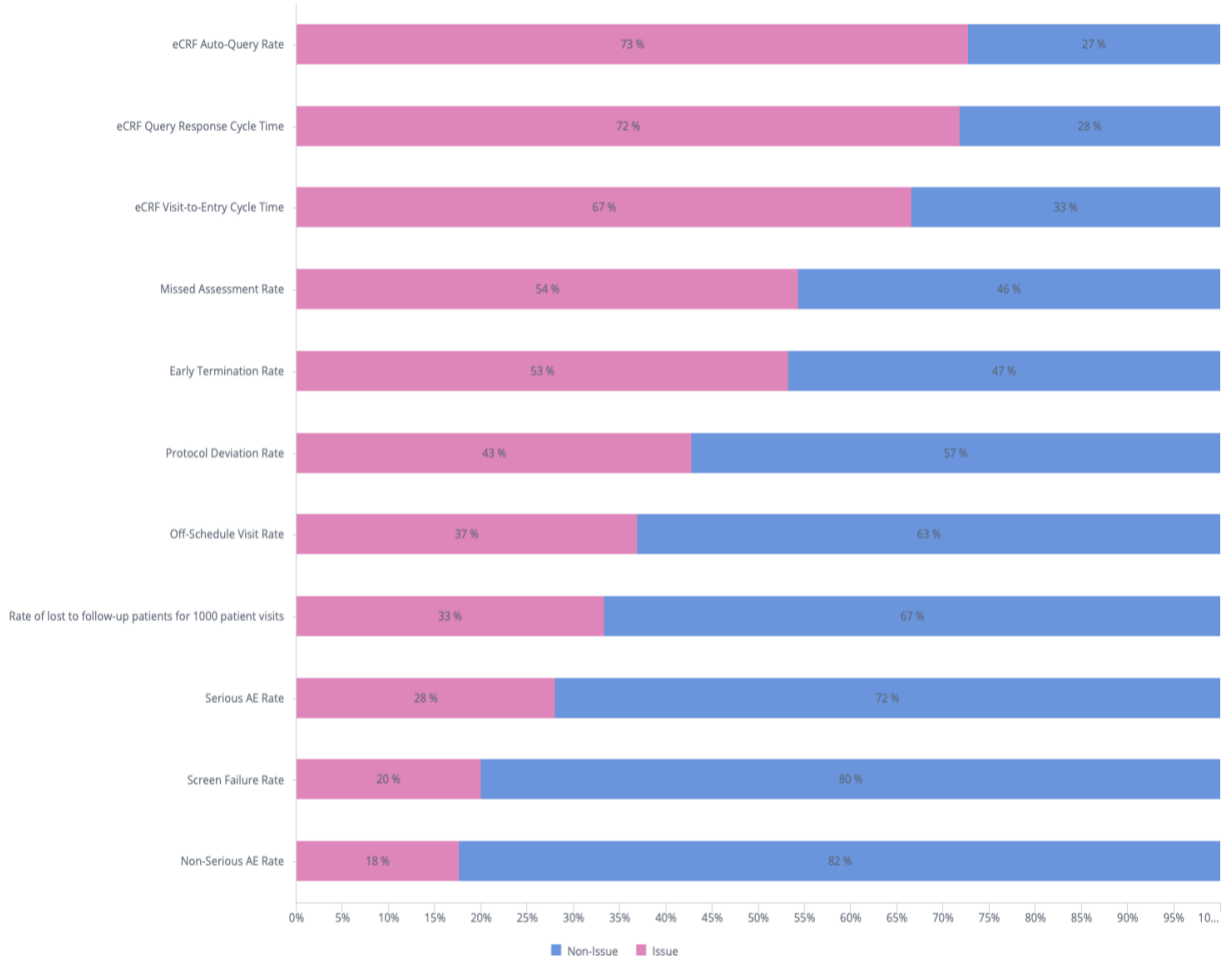


CluePoints Experience – KRIs in Small Studies (2/2)

Due to the low number of signals created on the selected KRIs for Small Studies defined as < 100 patients & < 8 centers,
The definition used for this analysis is < 100 patients only

- Among all signals created for the selected KRIs
  - 59.3% were predicted as issue
  - 40.7% were predicted as non-issue

- For 3 different KRIs, more than 65% of the signals were classified as issue
  - Auto-Query Rate (AQRATE)
  - Query Response Cycle Time (QUERCT)



CluePoints experience on small studies – KRIs

- The most frequently used KRIs in small studies correspond to CluePoints Standard KRIs

- Few others are frequently used as well
  - Rate of manual queries for the last 1000 datapoints per site (MQRATE)
  - Average time to resolve CTMS issues (SITEIAG)
  - Number of site issues reported in the issues and actions log per subject visit (STISSRT)
  - Number of subjects randomized per month (ENROLRT)
  - Proportion of patients who discontinued IMP (TDISRAT)

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CluePoints experience on small studies – Example of issues

- Entry delay (Site has been selected for audit due to entry delays)
- Data entry error
- Retraining needed (CRA discussed with SC regarding the eCRF guidelines and identified that the site lack with training in eCRF completion and timelines).
- Study equipment issue (eDIARY programming issue)
- Drug accountability (patient that did not return drugs)
- Non-compliance with protocol assessments

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Conclusion

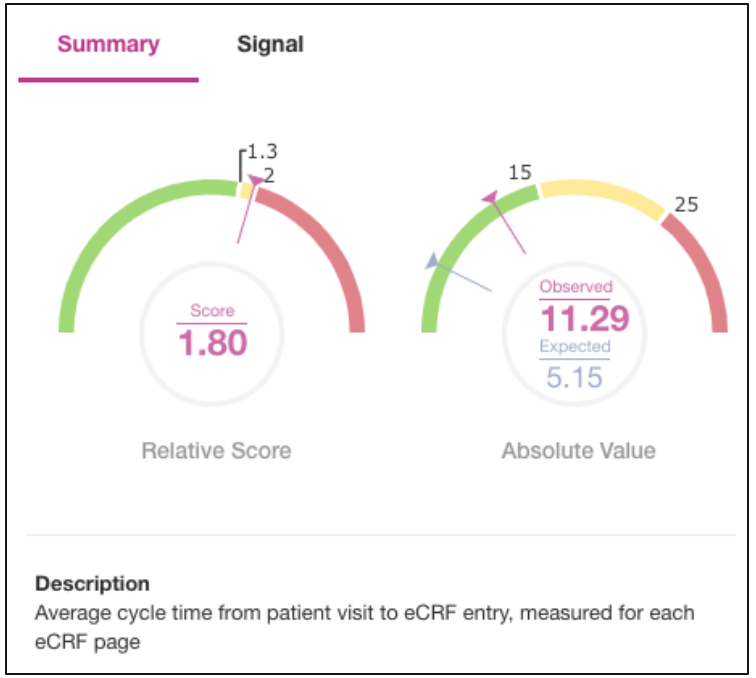
CluePoints has gained a fair experience in small studies

- DQA
  - 51.8% of the unsupervised signals are from the patient level analysis
  - 46.9% of the DQA signals are considered by the user as issue

- KRI
  - Most signals come from center level analysis (small proportions of Patient & Region signals)
  - Standard CluePoints KRIs are common in Small Studies
  - 59.3% of the KRI signals are considered by the user as issue
  - More than 65% of the signals created are predicted as issue for

Relative Key Risk Indicators - Guidelines

Experience suggests that with a limited number of KRIs (upto30),it is adequate to gauge statistical significance using unadjusted *P*-values; hence centers* are flagged if any KRI exceeds 1.3 (*P*-value less than 0.05).



* The same guidelines apply to country/region/patient

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References

- CluePoints guidelines from CluePoints Knowledge Base:
  - Using CluePoints on small studies:https://knowledge.cluepoints.com/hc/en-us/articles/360021017620-Using-CluePoints-on-Small-Studies
  - Setting expectations for pilot studies analysed by CluePoints using SMART: https://knowledge.cluepoints.com/hc/en-us/articles/360020464471-Setting-expectations-for-pilot-studies-analysed-by-CluePoints-using-SMART.

- Trotta, L, *et al*. Detection of Atypical Data in Multicenter Clinical Trials Using Unsupervised Statistical Monitoring. *Clin Trials* 2019; 16(5): 512–22, DOI:10.1177/1740774519862564.

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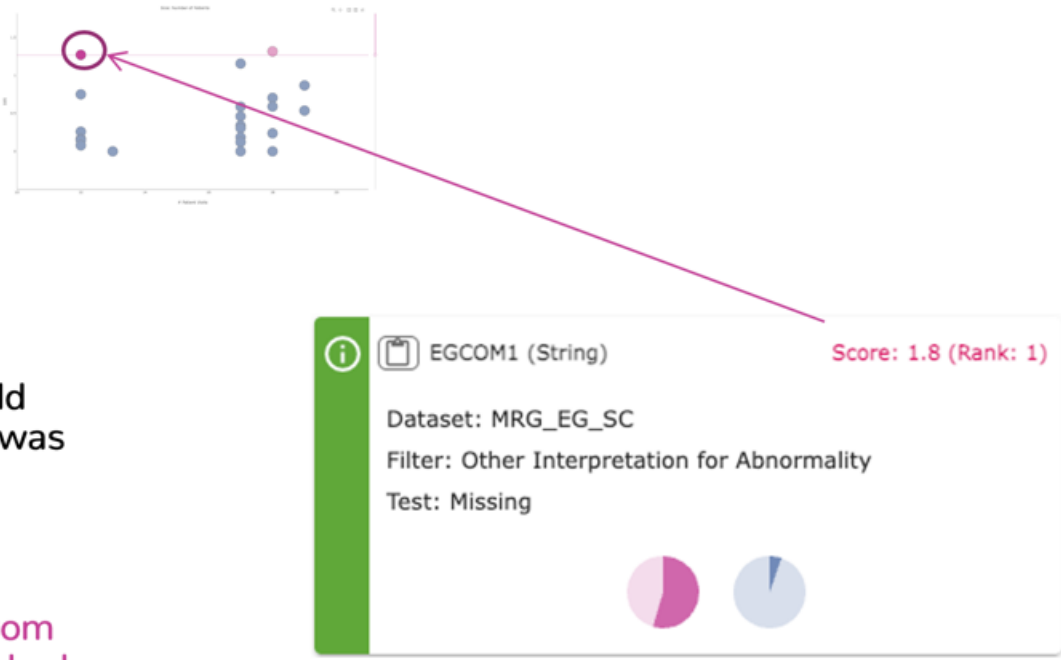
Case Study:

Patient Missing entries leading to discovery of systemically incorrect data entry by Study

Study Overview

Centers:	1	Therapeutic Area:	Neurology
Patients:	80+	Study Phase:	1



CluePoints Risk Detection

- Study with 24 randomized patients at the snapshot when DQA Analysis by patient flagged the issue.
- 1 Patient shown as outlier for **missing** data on the first field for abnormality description for ECG test results. The data was previously reviewed by CRA but no issue was was raised.

Root Cause Findings and Outcome

- For most patients, the field was being filled with details from non corresponding abnormalities. Most patients therefore had it incorrectly completed, and the outlier was the one correct.
- Data Entry was corrected and eCRF instructions were amended. The early detection also avoided that the data of newer screened patients have the same issue.

Ratio of incorrectly filled fields went from 60% to only 4.6% already on the following snapshot (2 months after).

Business Implications:

- Systemic issue for data entry found through positive outlier.
- Early discovery of the issue prevented propagation through trial
- Original Data corrected and preventive action for future put in place