CluePoints

Turning artificial intelligence into human intelligence.

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

June 2025

VERTEX
THE SCIENCE of POSSIBILITY

Meet the CluePoints Team

Presenters…

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Our Session Aims Today…

- Validate our understanding of Vertex current Tech and Process, Gaps and Needs.
- Demonstrate the evolution of our RBQM solution to ensure compliance to ICH E6 (R3) guidelines and more efficient clinical trials
- Show our roadmap and future vision of CluePoints towards an integrated data review platform

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Today's Agenda

Time	Topic	Presenter
09:00 - 09:10	Introductions Understanding of Vertex goals	Jon Stone
09:10 - 09:30	CluePoints overall vision	Richard Young
09:30 - 10:30	ICH E6 R3 Impact on Global Compliance Impact on Data Reliability	Kristen Harnack
10:30 - 10:45	Break	
10:45 - 12:00	ICH E6 R3 Impacting Trial Efficiency Impacting Patient Experience	Kristen Harnack
12:00 - 13:00	Lunch	
13:00 - 15:00	CluePoints Roadmap/vision IQD, MSR, IMC	Richard Young
15:00-15:30	Wrap up/next steps	Jon Stone

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Medical and Safety Review

CluePoints' MSR Vision

Enable instream data review to accelerate time to DBL and ensure valuable medical and clinical scientists can spend more of their time reviewing data, ensuring patient safety and scientific integrity of the trial, and less time burdened with administrative tasks.

Improve the speed of the review process - track what has or has not been reviewed, quickly see new or amended data, and calculate the change.

Improve the speed and efficiency of the set-up process – libraries of visualisations that can be re-used.

Enable efficient communication between and within review teams through sharing and assignment.

Give medical reviews autonomy and freedom to configure their own dashboards and be able to quickly adapt to the evolving needs of the study.

Remove inefficiency in the process for raising queries by integrating with source EDC systems via API.

Audit trail of the review process to know who reviewed what and when.

Reduced duplication of queries between Medical/Safety and DM teams - see full history and current status of all queries related to a datapoint.

Facilitate the review process to enable reviewers to focus on what matters - combined supervised and unsupervised (stats & AI/ML) to detection of signals.

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Medical and Safety Review

Medical and Safety Review supports periodic review of study data using customizable dashboards to identify records of interest with outlying values, and track delta changes and communication workflow during frequent data refresh. This greatly improves the efficiency of the review process and enhances patient safety.

Challenge	How We Address
Infrequent data refresh and lack of identified changes in data	Ability to refresh the data at a predetermined frequency and identify delta changes between refreshes
Unable to easily identify what has changed (variable level) since last review.	Delta changes are highlighted at the variable level and the change of last review is calculated
Study preparation takes a lot of time to create specific visualizations	Library of standard visualizations and possibility to copy dashboards between studies
Swapping between systems to review data and raise queries.	Data can be reviewed and queried within CluePoints MSR tool, queries are raised to source via API
Requirement to have possibility to create dashboards for internal use of Medical & Safety reviewers	Possibility to create custom dashboards based on data available in the study
Long time to apply filters to identify most common outliers	Ability to define and save filters to quickly identify records of interest with outlying values

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MSR Demonstration

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Impact on Global Compliance

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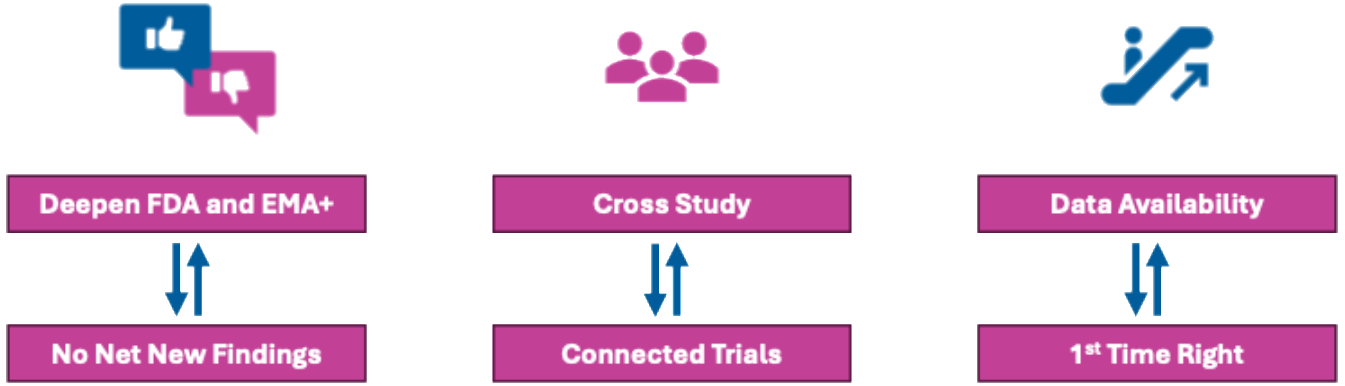
Impact on Global Compliance

Easier and faster regulatory approvals, consistent trial standards globally

Simple Statement of Intent

It is more than just automating science. It's really about amplifying human scientific creativity—unlocking insights and accelerating drug discovery and development.



Simple Example

Creating cross study learnings on the data point level and the behavioral level enable better execution. Exposing ALL data, enables faster decision making on all levels – true Agentic AI connectivity

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Renewed and Expanded Collaboration with FDA

FDA Extends CRADA with CluePoints to further explore a data-driven approach to quality oversight in clinical trials

2016 — 2019 — 2024

First CRADA with FDA Signed

New CRADA between FDA and CluePoints Signed as per below

01 **AI/ML**
Develop new AI/ML algorithms for improved anomaly detection.

02 **Audit Trail Review (ATR)**
Develop new tests to analyse date/time data for better oversight of data from (eCOA) and (ePRO) technologies.

03 **Updates to better support FDA processes**
Related to anomaly detection, review and follow-up, and site selection for inspection

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FDA Use of CP: Selection of Sites for Inspection

A Data Anomaly Detection Tool for Site Selection at FDA

Xiaofeng (Tina) Wang, Paul Schuette, Matilde Kam
Center for Drug Evaluation and Research, Office of Translational Sciences, Office of Biostatistics, Immediate Office

Background

- On-site inspections of clinical trial investigators are important to ensure the quality and integrity of the trial data and the reliability of the trial results submitted to the U.S. Food and Drug Administration.
- With the increasing size and complexity of the trials, statistical tools are needed to assist the site selection process and identify potentially problematic sites.

Methods

We describe our experience with a centralized statistical monitoring platform as part of a Cooperative Research and Development Agreement (CRADA) between CluePoints and the FDA.

Statistical Monitoring Applied to Research Trials (SMART):

- Applies battery of statistical tests to different types of variables in multiple domains

All Variables	Continuous Variables	Binary/Categorical Variables	Date Variables
Count Missing	Mean Between-Patient Variability Within-Patient Variability Global Outliers Sequence Outliers Identical Values Propagation Correlation	Proportion Transitions from Transitions to Initial Values	Saturday Sunday

- Compares subject/site level values for a variable to all sites in trial
- Computes a p-value corresponding to the site and the test

$$\mathbf{P} = \begin{array}{c} \\ \text{Site}_1 \\ \vdots \\ \text{Site}_i \\ \vdots \\ \text{Site}_m \end{array} \begin{array}{c} \begin{array}{cccc} \text{Test}_1 & \cdots & \text{Test}_j & \cdots \end{array} \\ \begin{pmatrix} p_{1,1} & \cdots & p_{1,j} & \cdots \\ \vdots & \cdots & \vdots & \cdots \\ p_{i,1} & \cdots & p_{i,j} & \cdots \\ \vdots & \cdots & \vdots & \cdots \\ p_{m,1} & \cdots & p_{m,j} & \cdots \end{pmatrix} \end{array} \begin{array}{c} \text{Test}_n \\ \begin{pmatrix} p_{1,n} \\ \vdots \\ p_{i,n} \\ \vdots \\ p_{m,n} \end{pmatrix} \end{array}$$

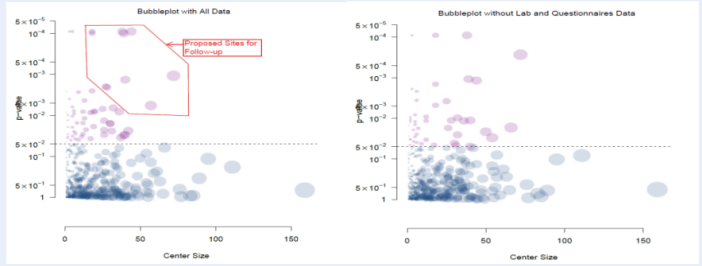
The data inconsistency score for Site_i is then computed as

$$S_i = \frac{\sum_{j=1}^{n} w_j \log(p_{i,j})}{\sum_{j=1}^{n} w_j}$$

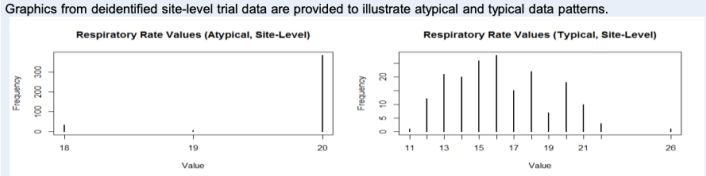
Results

An overall data inconsistency score is calculated from a high-dimensional p-value matrix to assess the inconsistency of the data between one site and the data from all sites. Sites are ranked by the data inconsistency score (-log(p), where p is an aggregated p-value). Operationally, only sites with highest ranks and larger sizes are recommended for inspections.

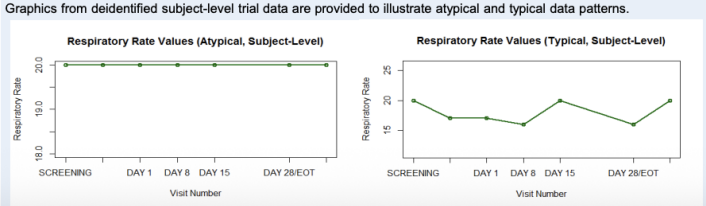
Results from one deidentified application are provided to demonstrate the data anomaly findings through the Statistical Monitoring Applied to Research Trials (SMART) analysis. Sensitivity analysis are performed after excluding laboratory data and questionnaires data.



Graphics from deidentified site-level trial data are provided to illustrate atypical and typical data patterns.



Graphics from deidentified subject-level trial data are provided to illustrate atypical and typical data patterns.



Results

Potential causes of data anomalies may include:

- Errors (technical problems, e.g. mis-calibrated thermometers)
- Sloppiness (incorrect report, e.g. under-reporting of AE)
- Tampering (fabricated, altered, or falsified data, e.g. modification of eligibility of criteria, or propagation of blood pressure)
- Sites that are atypical of the underlying population

Caveats and Limitations

- The software works best if there are at least 10 sites.
- Data preparation can be time consuming, but it is easier with SDTM data.
- If all the data are spurious, then an anomaly will not be detected. The software is designed to deal with problems primarily at the site level.
- The clinical significance of data anomalies may not be obvious.

Conclusions

- A data driven approach can be effective and efficient in selecting sites which exhibit data anomalies.
- Centralized Statistical Monitoring (CSM) can help ensure data quality and data integrity.
- CSM can provide insights to the statistical reviewers for conducting sensitivity analyses, subgroup analyses and site by treatment effect explorations.
- However, challenges exist with messy data and with the lack of conformance to SDTM data standards.

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Impact on Data Reliability

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Impact on Data Reliability

More accurate, real-time data and proactive issue resolution

Simple Statement of Intent

We can't compromise on scientific rigor while adopting AI. The two need to coexist. How do we unlock scientific potential ?

Consolidate, Automate

Intelligent Data Monitor

Next Best Action

Shift to Unsupervised

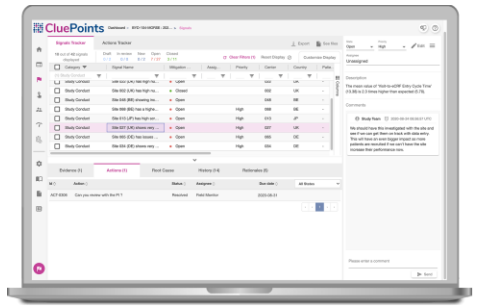
API First

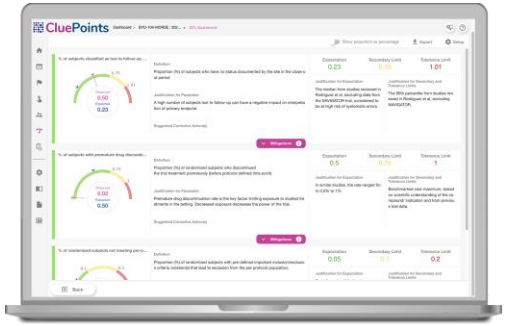
Agentic Robots

Simple Example

Autonomous Helpers: IMC has automated (99%) MedDRA coding, hits 96% on ACT codes in prototype. IQD has hit 100% sensitivity on first 20 studies at GSK

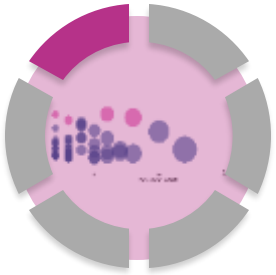
CluePoint's CMP is a *unique* modern integrated **Central Monitoring Platform** for signal identification & exploration



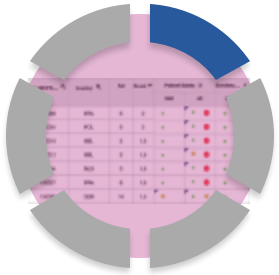


CENTRAL MONITORING PLATFORM

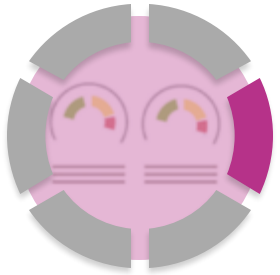
Risk Assessment Tool: Identify & Document Study Risk Factors



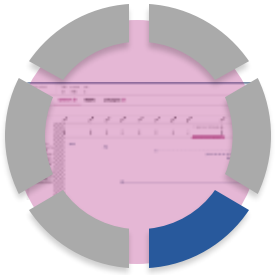
Data Quality Assessment: "DQA" Unsupervised Statistical Analysis to detect Unknown Risks



Key Risk Indicators: Monitor the Study Conduct using Operational and Clinical Data



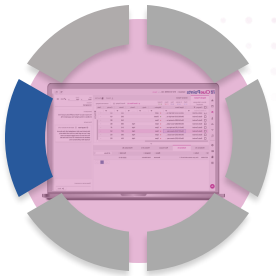
Quality Tolerance Limits: Monitor possible systemic issues



Patient Profiles: Visualize and Review Individual Patients

BEYOND Data Visualizations: Design and Explore Custom Dashboards

Duplicate Patients: Identify Duplicate Patients



Signal & Action Tracker & Risk Review Mgr.

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Value of a Combined Supervised & Unsupervised Approach: Greater Coverage of Issue Detection

SMART™ Engine

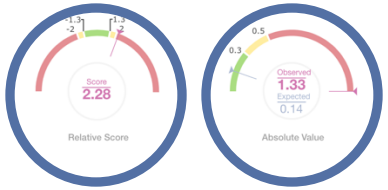
58% KRIs

42% DQA

- Protocol & GCP Compliance
- Study Equipment / Technology
- Data Cleaning / Data Entry

By Center

By Patient



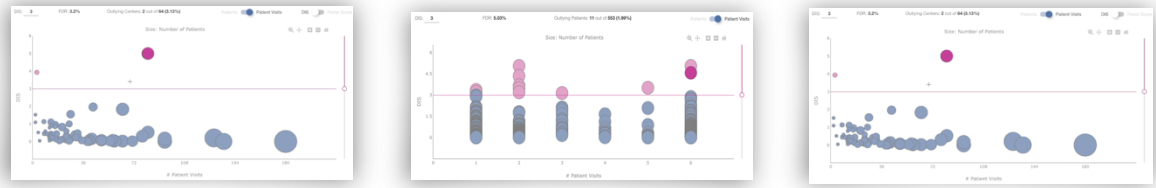
Absolute and Relative thresholds

The Score is computed by the SMART engine and reflects how atypical a center is compared to the other centers (observed vs. expected).

By Center

By Patient

By Region

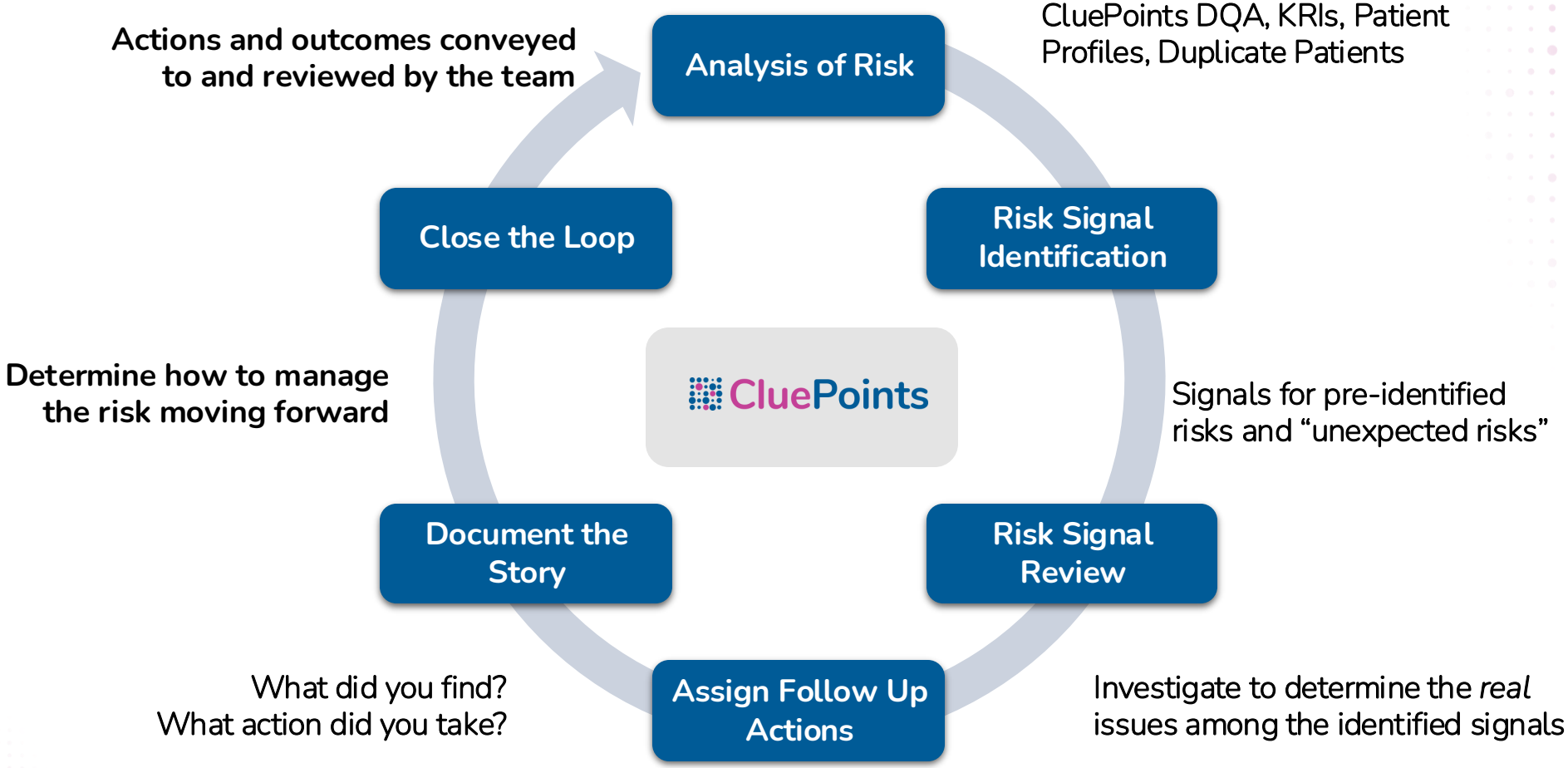


Unsupervised analysis of all clinical and key operational data

Detection of anomalies at site, patient and region level that remain undetected using traditional techniques.

Reference: S. Young, D. Beaudry, V. Pomerantseva, J. Rowe, The Eradication of False Signals in Monitoring, *Applied Clinical Trials-09-01,2022, Volume 31, Issue 9*

Demonstration Overview



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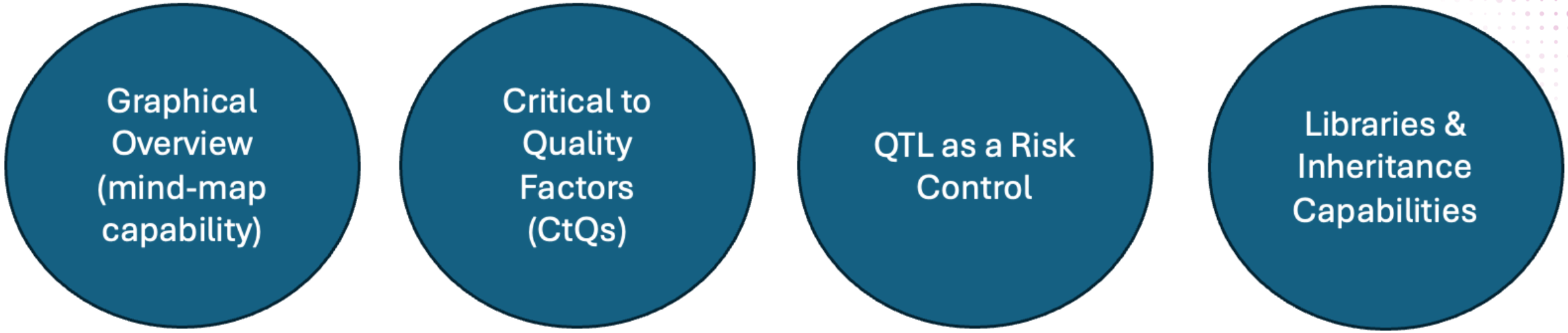
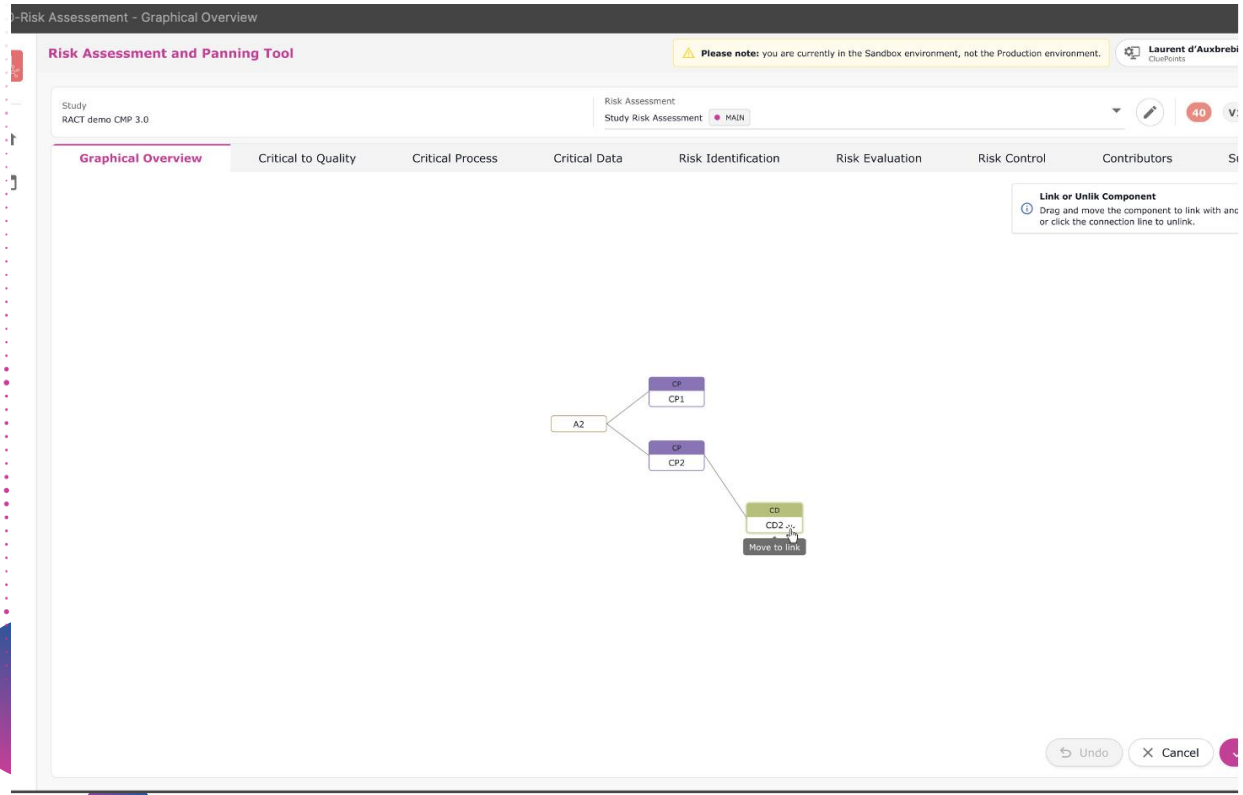
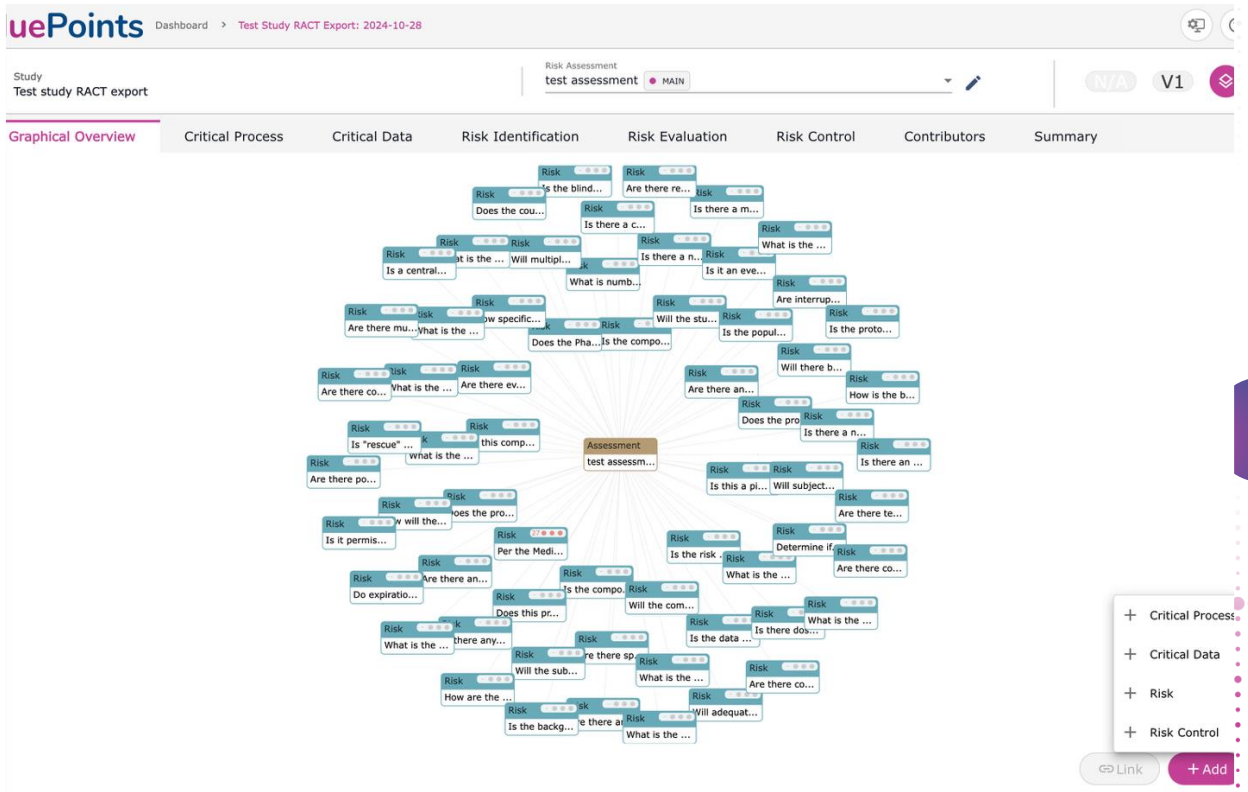
NextGen Risk Assessment



Graphical Overview (Mind Map)





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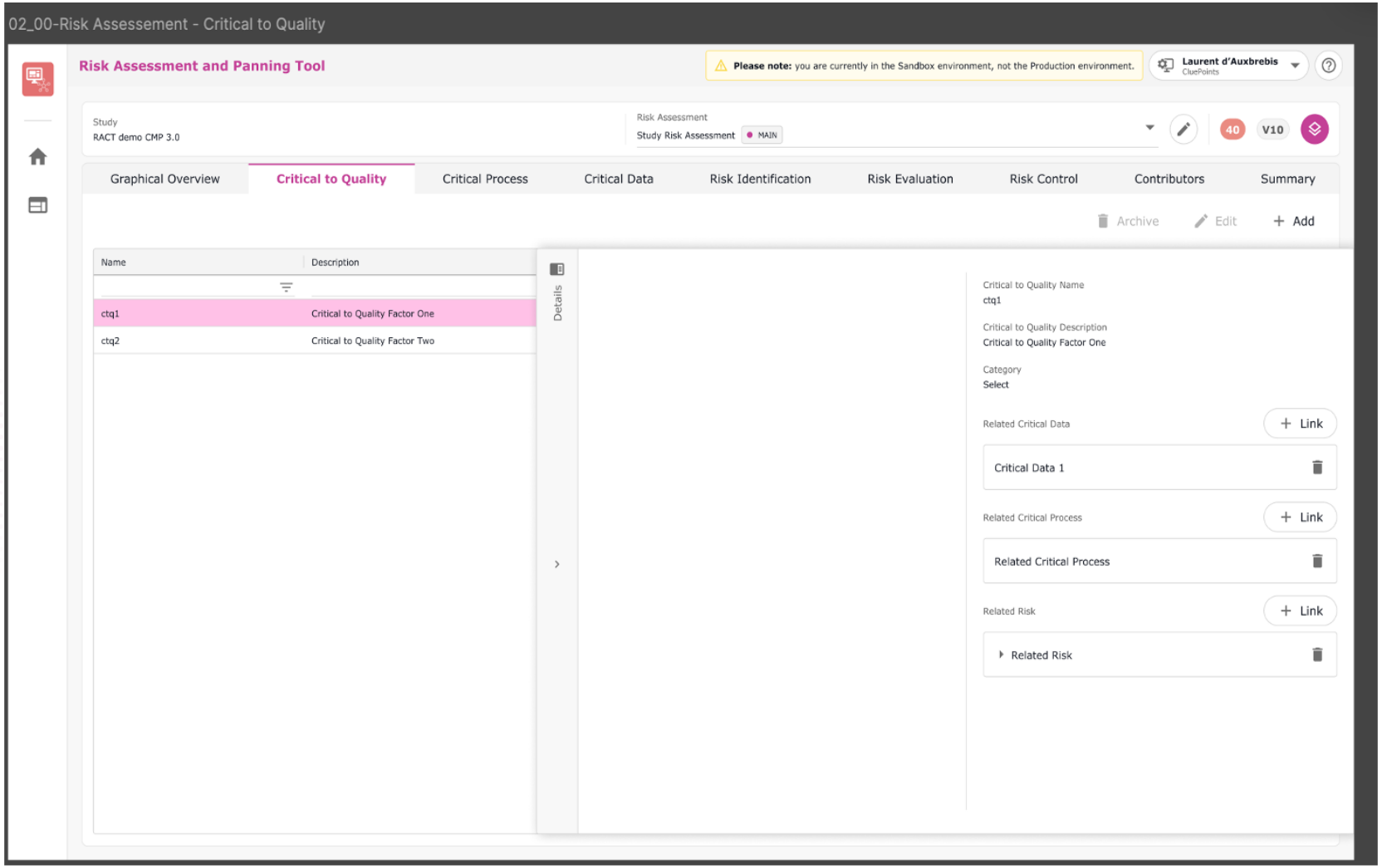
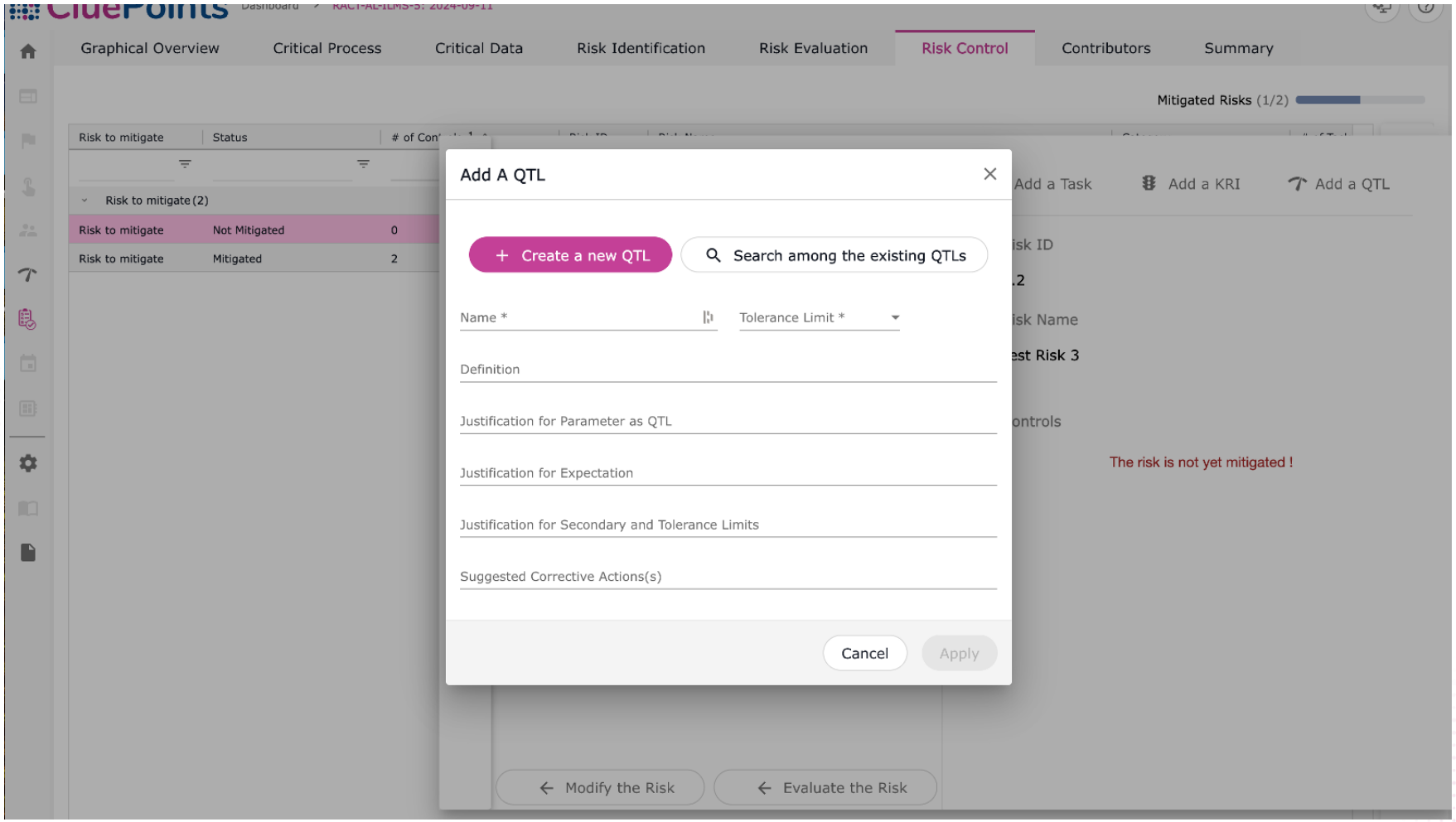
Critical to Quality Factors



QTL as Risk Control



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Small Studies

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Value from applying RBQM approach to early phase studies is distinct

Original Thinking

- Early phase (I or II) studies have fewer participants and sites.
- Assumed RBQM only highlights risks at site level; therefore, most effective in large scale studies with several sites.

Current Status

- 40% of all studies on CluePoints CMP solution are Phase I or II.
- 57% of all studies ACRO* looked at for using any component of RBQM were Phase I or II.

Reasons for Shift

- Regulatory guidance.
- Effectiveness of participant level risk indicators.
- Applying early phase lessons to Phase III planning and execution, including Quality by Design.

* Association of Clinical Research Organizations (ACRO) survey report

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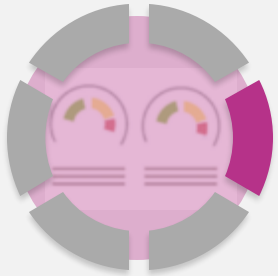
Core Platform Components – Any Study Size

RACT

Risk planning (critical process and data identification, risk identification, and risk mitigation planning) is an essential component of RBQM and applies to any and all clinical research including smaller studies

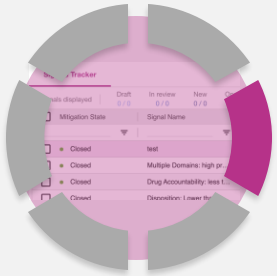
QTLs



Study-level monitoring should be considered for any/all clinical studies including those in early phase, per ICH E6 (R3).

Detection of study-level issues that may be impactful to overall study outcomes or patient safety

Issue Management



Integrated workflow to track and manage the follow-up and documentation of risks and queries identified within and/or outside of CluePoints.

Data Visualizations

Pre-configured and bespoke dashboards to enable exploration of the data exploration.

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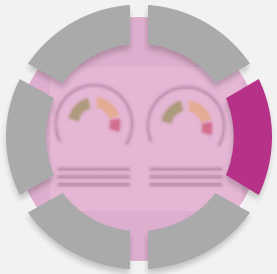
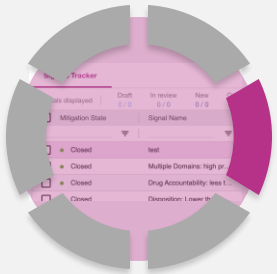
Analytics Based on Study Size

	KRIs	DQA	Patient Profiles
			
Site Level	Any number of standard and study-specific KRIs to detect specific risks of interest across centres & countries • Absolute Thresholds: Any Study Size • Relative Thresholds: (Min. 8-10 sites)	Unsupervised analysis of clinical and operational data (Min. 8-10 sites, 2 patients per site and 50 patients total)	Highly visual and configurable patient level reports
Patient Level	Patient-level KRIs can be used in conjunction with the Patient DQA to support effective medical and safety monitoring.	Patients assessed for atypical data patterns across all of their data and an overall DIS is computed for each patient.	Statistically unusual data patterns for each patient enables a prioritized risk review starting with the most atypical patients.
	(Min. 30 patients)		

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Early Phase & Small enrollment Study Adoption Evidence

Central Monitoring Use in Early-Phase and Small Enrollment Trials

December 11, 2024
By Steve Young
Sylviane de Viron

News *Article*

Applied Clinical Trials
Applied Clinical Trials-12-01-2024
Volume **33** Issue **12**

A review of industry methods and adoption trends in those trial segments.

Central monitoring is highly effective in detecting emerging quality issues in clinical trials, but debate continues over its use in early-phase and small enrollment studies due to typically lower data volumes and shorter study timelines. In this analysis, we summarized industry trends in early-phase and small trials using data from the CluePoints central monitoring platform. Out of the 1,062 studies using the platform, 140 were Phase I (13%), 378 were Phase II (36%), and across all phases we observed 175 trials with 100 or fewer enrolled patients (16%) and 65 more with 50 or fewer enrolled patients (6%).

Image Credit: © Murrstock - stock.adobe.com

Selection of 1,062 studies using CMP platform

- 140 Phase I (13%)
- 378 Phase II (36%)
- 175 trials with 100 or fewer enrolled patients (16%)
- 65 with 50 or fewer enrolled patients (6%).

Methods and Adoption: A Comparison

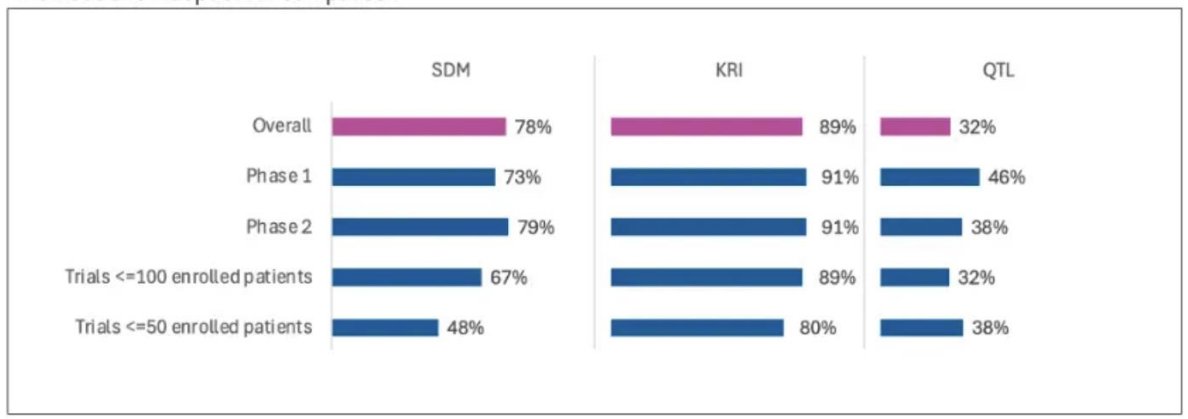

FIGURE 1. Adoption of SDM, KRI, and QTL tools across clinical trial phases and small studies.

SOURCE: CluePoints

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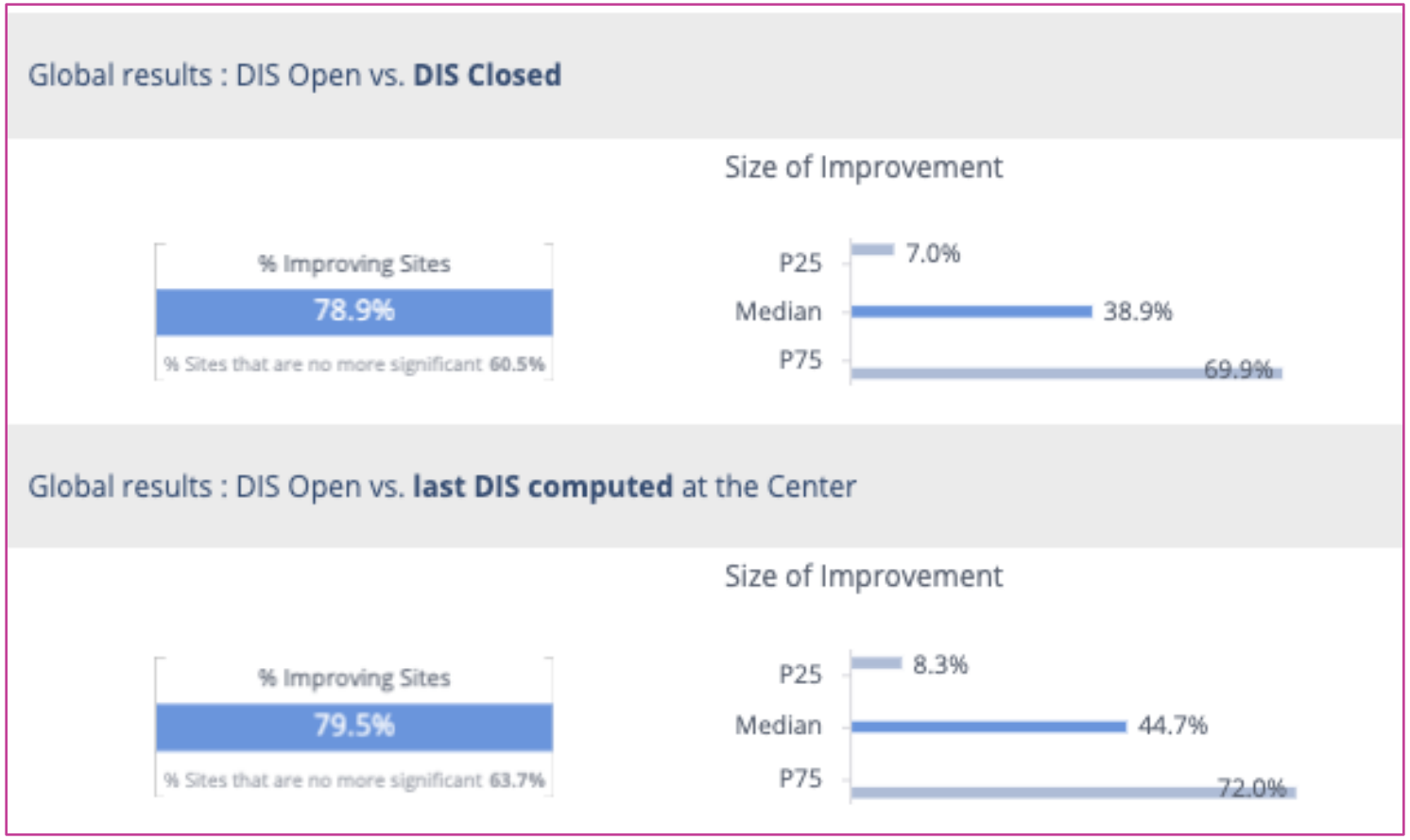
Quality is improving in 79% of the sites in early phases

125 completed early phase studies using CMP platform

- 590 atypical sites selected



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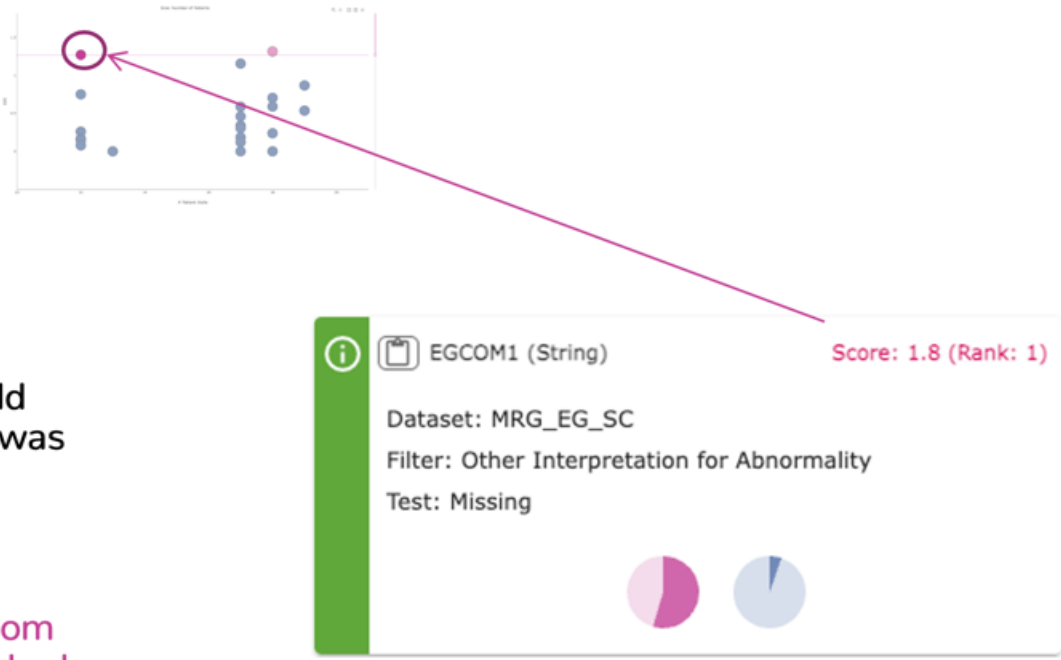
Case Study:

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

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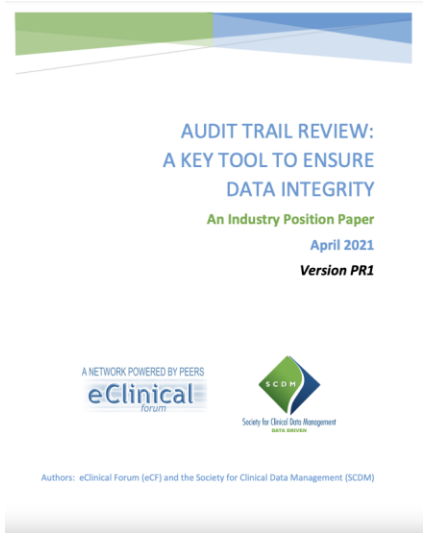
Audit Trail Review

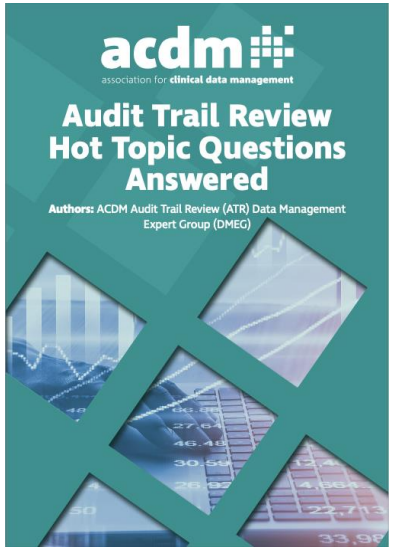
CluePoints: Partner in Key ATR Consortia

Co-Author on SCDM Position Paper

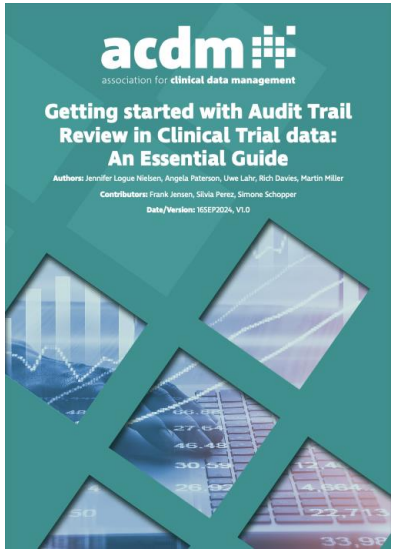


https://scdm.org/wp-content/uploads/2024/07/2021-eCF_SCDM-ATR-Industry-Position-Paper-Version-PR1-2.pdf

Member of ACDM ATR Data Management Expert Group (DMEG) and Co-Author on ACDM Guidance Papers



https://acdmglobal.org/wp-content/uploads/2024/05/ATR-Hot-Topic-Questions.pdf



https://acdmglobal.org/wp-content/uploads/formidable/47/Getting-started-with-Audit-Trail-Review-in-Clinical-Trial-data-An-Essential-Guide.pdf

Member of the eClinical Forum ATR Working Group

Contributing to the definition and prioritisation of ATR use cases and the scoping of analytical requirements for prioritised use cases

ATR Community of Interest Group

CluePoints user community formed to facilitate exchange of ideas and arrive at a group consensus around ATR best practice. Group's initial focus has been on capturing a comprehensive list of potential audit trail risks along with the corresponding potential root causes and potential systematic controls.

CluePoints

Increased Regulatory Focus

New regulatory guidance places a strong emphasis on the review of audit trails as a critical component of data and metadata management in clinical trials.


ICH harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

GOOD CLINICAL PRACTICE (GCP)

E6(R3)

Draft version

Endorsed on 19 May 2023

Currently under public consultation

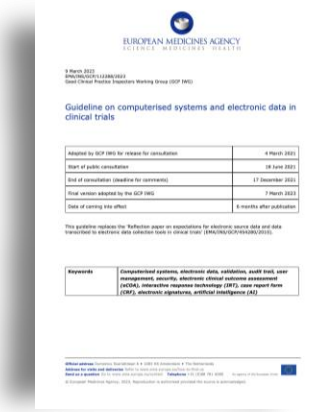
At Step 2 of the ICH Process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Assembly to the regulatory authorities of the ICH regions for internal and external consultation, according to national or regional procedures.

ICH E6 (R3)

- Ensuring that audit trails and logs are decipherable and **can facilitate analysis**;
- Encourage a "**risk-based evaluation**";
- Procedures for review .....should be in place ..... review should be a **planned activity**, and the extent and nature should be **adapted to the individual trial** and **adjusted based on experience during the trial**.

EMA Guideline on computerised systems and electronic data in clinical trials

- Sponsors should conduct **regular reviews of audit trails** to identify and investigate **suspicious activities** (unusual patterns or unauthorized access), **ensure data integrity** (not been tampered with or deleted), **detect and prevent data breaches**.
- Audit Trail Review should be **tailored to the specific risks and requirements of the trial**. It may include reviewing audit trails for specific data types, time periods, or user groups.
  - Methods of Audit Trail Review may include both manual review and use of **automated software tools**;
  - Encourage a **risk-based approach**, prioritizing the review of audit trails for **high-risk data or activities**.


EUROPEAN MEDICINES AGENCY

SCIENCE MEDICINES HEALTH

9 March 2022

EMA/769/GCP/112286/2022

Good Clinical Practice Inspectors Working Group (GCP IWG)

Guideline on computerised systems and electronic data in clinical trials

Adopted by GCP IWG for release for consultation	9 March 2021
Start of public consultation	18 June 2021
End of consultation (deadline for comments)	17 December 2021
Final version adopted by the GCP IWG	7 March 2023
Date of coming into effect	6 months after publication

This guideline replaces the 'Reflection paper on expectations for electronic source data and data transferred to electronic data collection tools in clinical trials' (EMA/INS/GCP/454280/2010).

Keywords	Computerised systems, electronic data, validation, audit trail, user management, security, electronic clinical outcome assessment (eCOA), interactive response technology (IRT), case report form (CRF), electronic signatures, artificial intelligence (AI)

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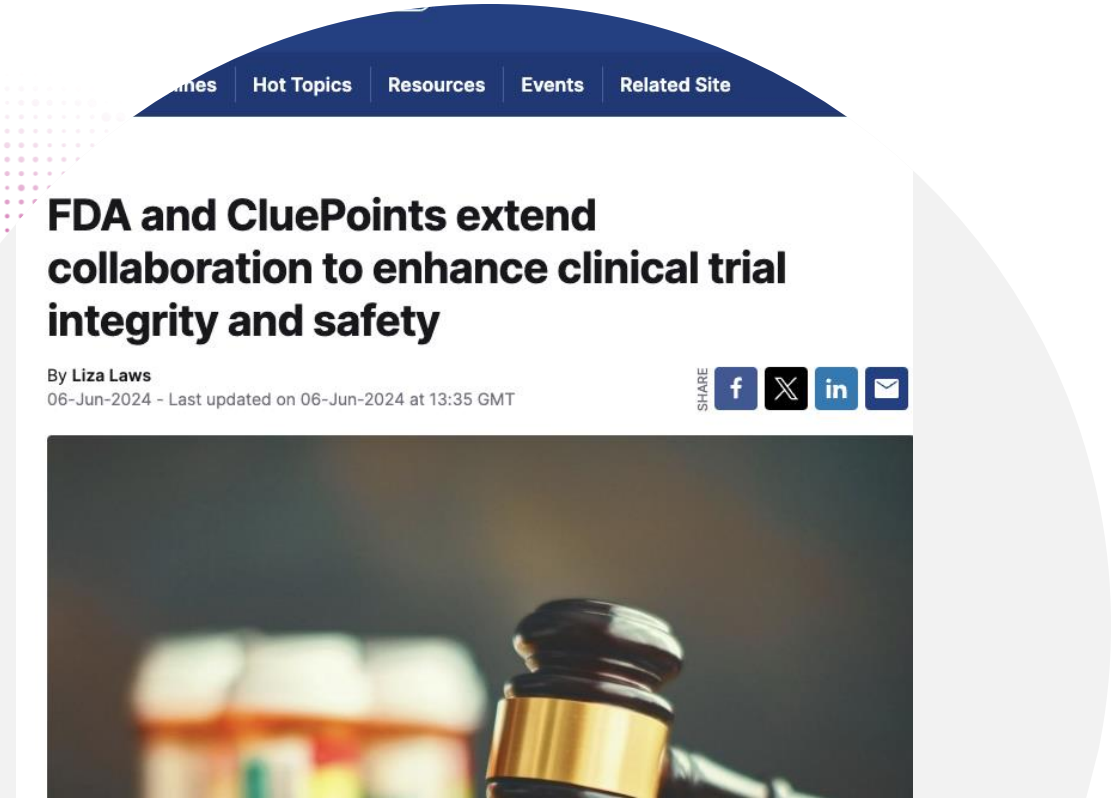
CluePoints

Renewed and Expanded Collaboration with FDA to include ATR



AI/ML

Develop new AI/ML algorithms for improved anomaly detection.

Audit Trail Review (ATR)

Develop new tests to analyse date/time data for better oversight of data from (eCOA) and (ePRO) technologies.

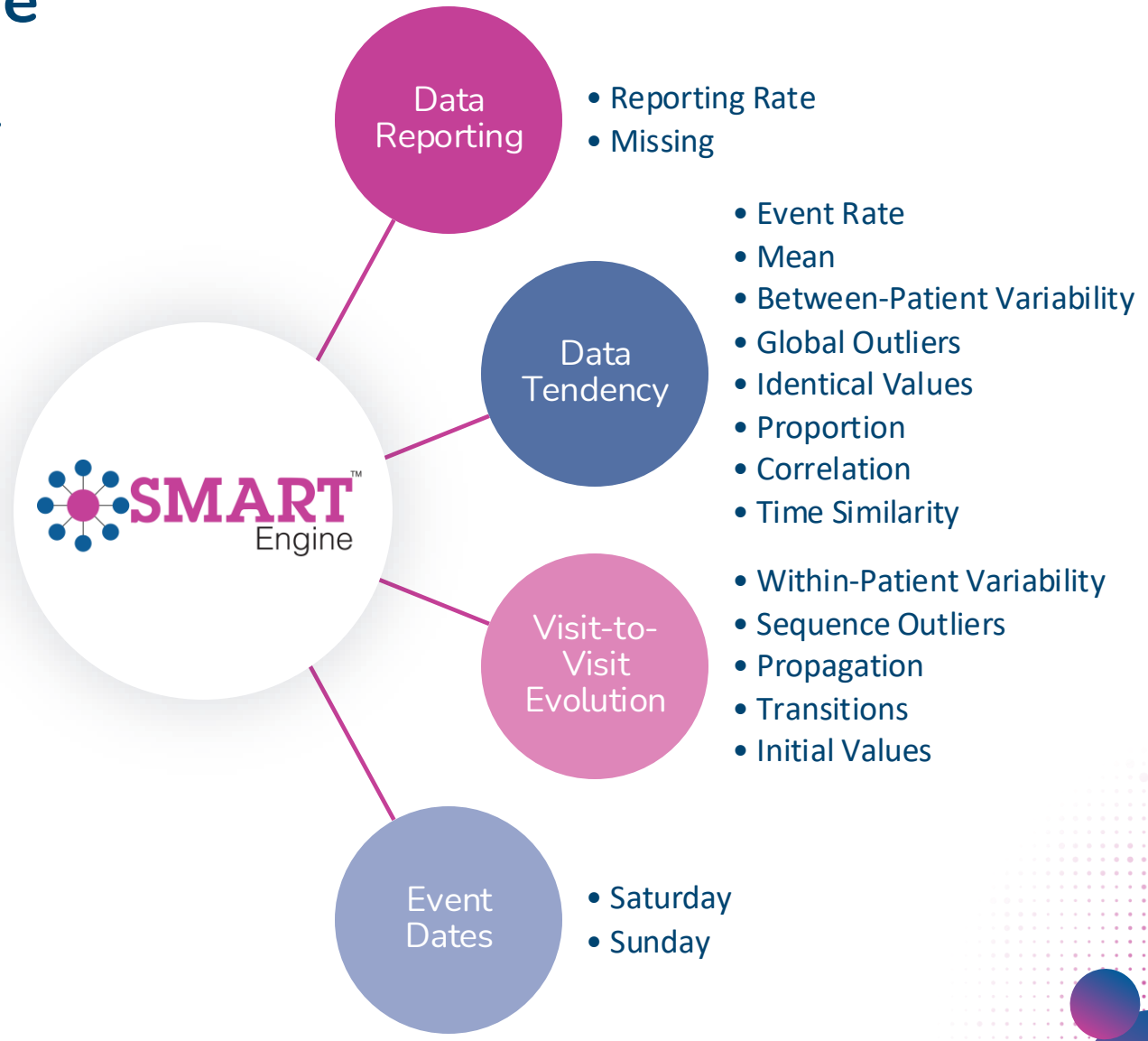
Updates to better support FDA processes

Related to anomaly detection, review and follow-up, and site selection for inspection

CluePoints

CluePoints SMART™ Engine

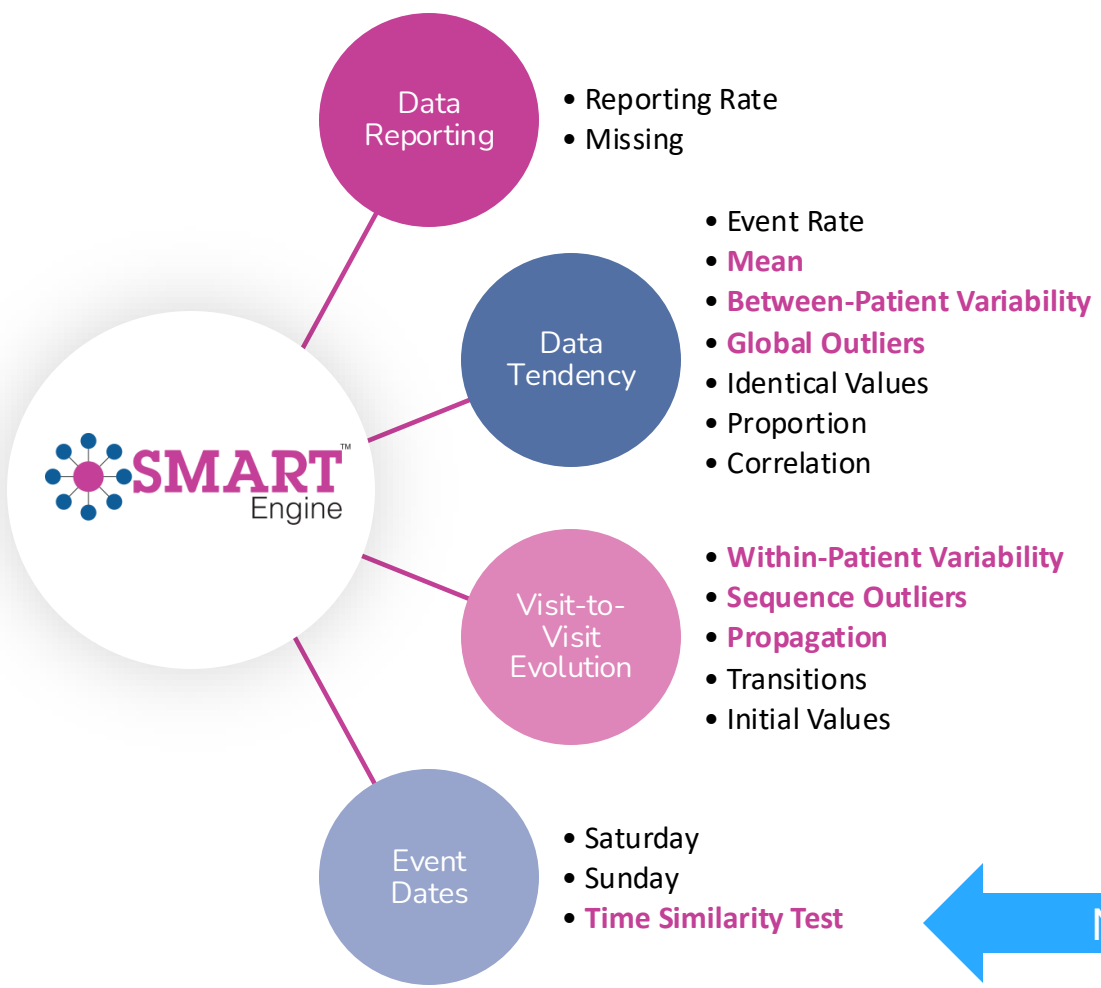
SMART™ compares the **data of each entity*** with the data of all entities in the study using the following **statistical tests:**



*Center, Patient or Country

CluePoints

Broadened Stats Engine to Enhance Audit Trail Review Capabilities and Enable the Testing of Data Collected at High Frequencies (e.g. daily ePRO data)



Event Based Tests (e.g. site visits)

Time Based Tests (e.g. frequent digital data)

6 current SMART tests expanded to support time-based tests of Audit Trail Data

NEW STATISTICAL TEST for time stamp data

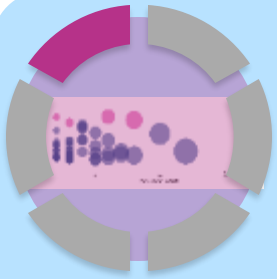
CluePoints

CluePoint's CMP enables and end-to-end ATR process from Risk Identification, Detection and Documentation.

CENTRAL MONITORING PLATFORM

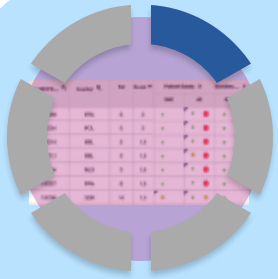
Risk Assessment Tool: Identify & Document Study Risk Factors

Identify Critical Audit Trail data, assess and evaluate risk and document Risk Control Strategy.



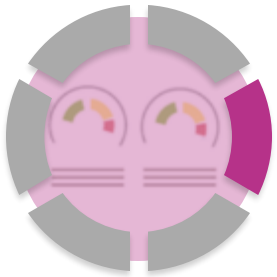
Data Quality Assessment: "DQA" Unsupervised Statistical Analysis to detect Unknown Risks

Review audit trail data with an unsupervised statistical approach to automate the review process.

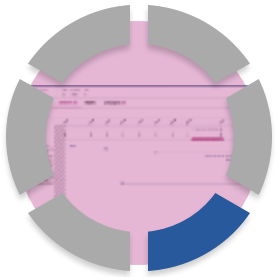


Key Risk Indicators: Monitor the Study Conduct using Operational and Clinical Data

Review audit trail data with a supervised statistical/threshold approach to detect expected risks.



Quality Tolerance Limits: Monitor possible systemic issues

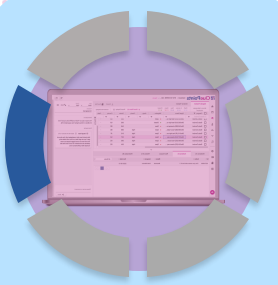


Patient Profiles: Visualize and Review Individual Patients

BEYOND Data Visualizations: Design and Explore Custom Dashboards

Enable a structured manual review of audit trail data.

Duplicate Patients: Identify Duplicate Patients



Signal & Action Tracker & Risk Review Mgr.

Document detected issues, root cause analysis, assign actions and document investigations and resolution.

CluePoints

Test Methods for ePRO / eCOA / wearables

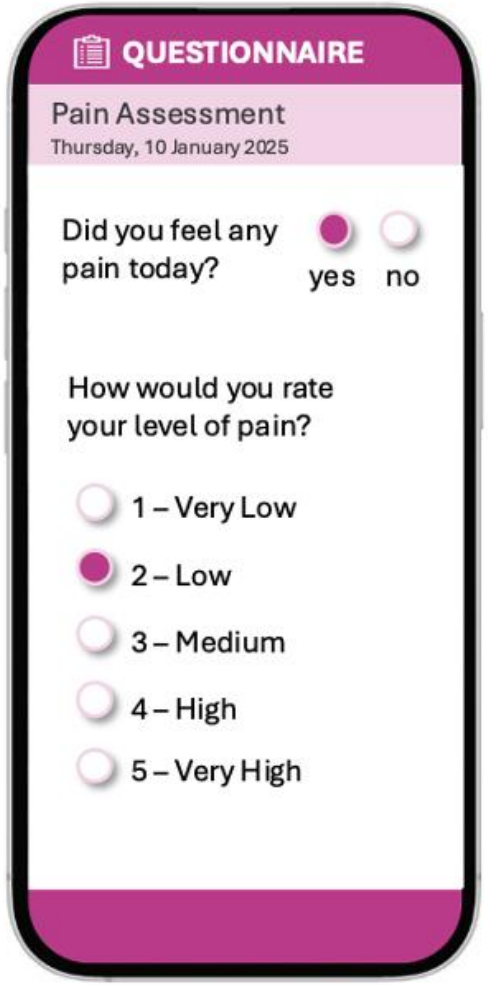
MONITORING OF TRIAL DATA

GLOBAL/SEQUENCE OUTLIERS
What are the measurements that are outlying

MEAN
What is the average score for an individual patient or group of patients

INTRA INTER-VARIABILITY
What is the variability in test scores for an individual patient or group of patients

MISSING
What are the data that are missing



GLOBAL/SEQUENCE OUTLIERS IN DURATION
What are the measurements that are outlying in their duration of assessment

MEAN/VARIABILITY IN DURATION
How long does it take to complete the assessment. What is the variability in the duration of the assessment.

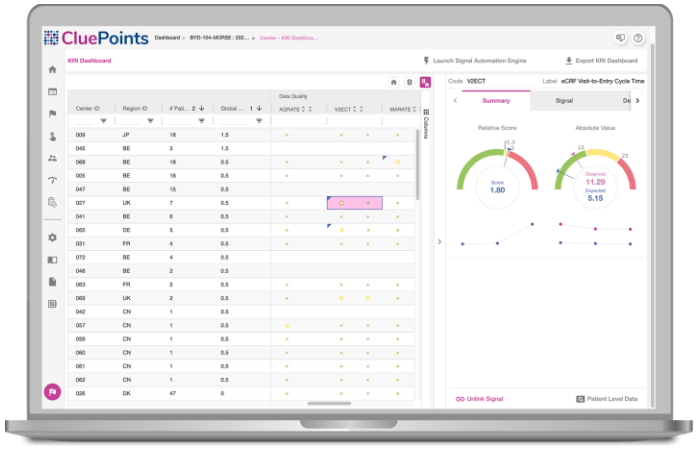
TIME SIMILARITY
Is there expected similarity in the time of the day of data entries

FREQUENCY OF UPDATES
What is the frequency of data updates

AUDIT TRAIL REVIEW

3 Modules Supporting Audit Trail Risk Detection & Visualisation

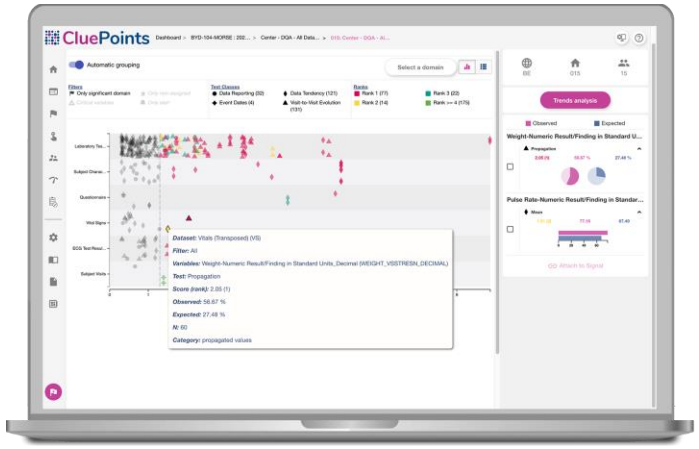
KRIs



Supervised review of *perceived risks*

E.g. EDC entry and query response

DQA



Unsupervised review of *unexpected risks*

E.g. issues with third party data

BEYOND

Summarise and explore audit trail data (and all other) data

CluePoints

Example KRI: EDC Audit Trail Data

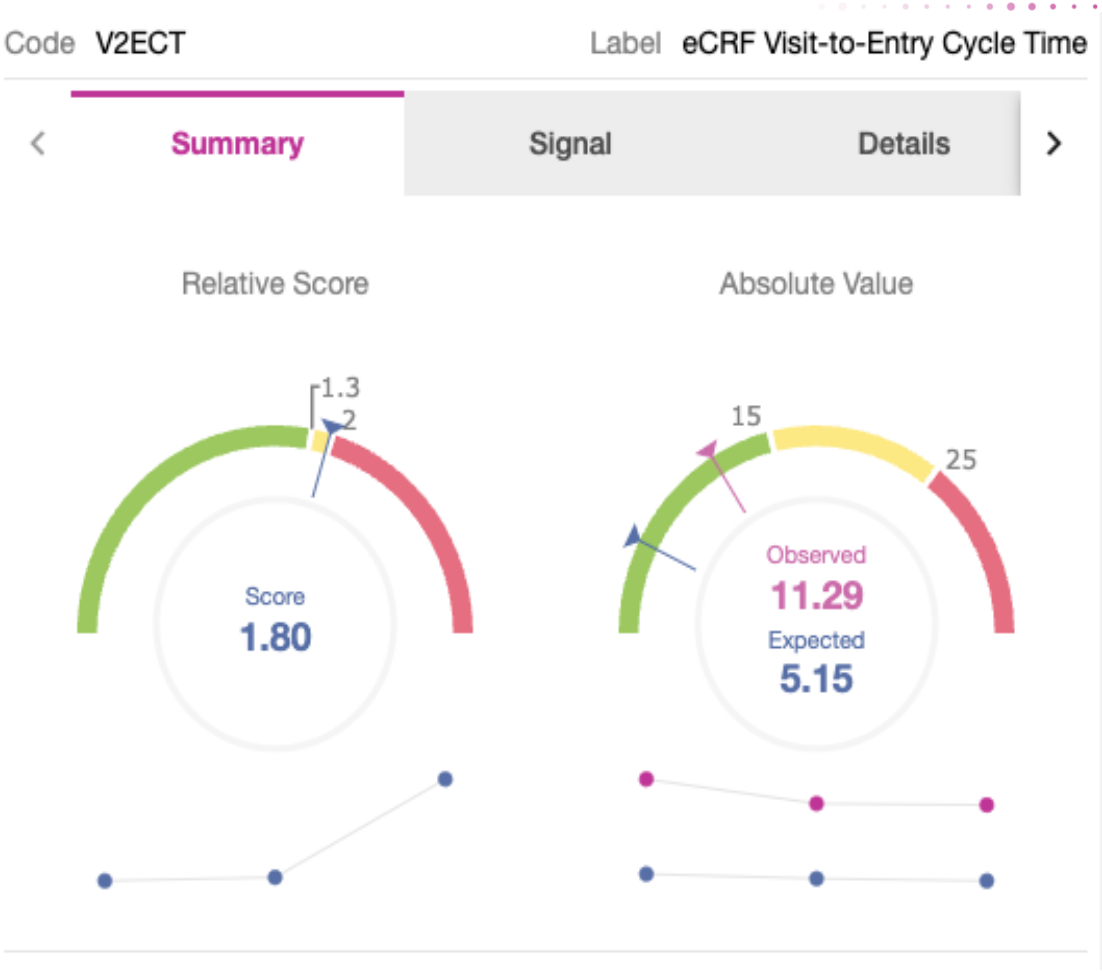
Audit Trail Risk Scenario: Long cycle time from patient visits until data entered into EDC

KRI: eCRF Visit-to-Entry Cycle Time (*V2ECT*)

Definition: Average cycle time from patient visit to eCRF entry

Rational For Use: Identify Sites that are highly delayed in entering patient visit data into the EDC system.

Possible Root Cause Issue(s): Site is too busy, under-staffed, inattentive, lack of understanding/sensitivity to importance of timely data entry.



CluePoints

Example KRI: EDC Audit Trail Data

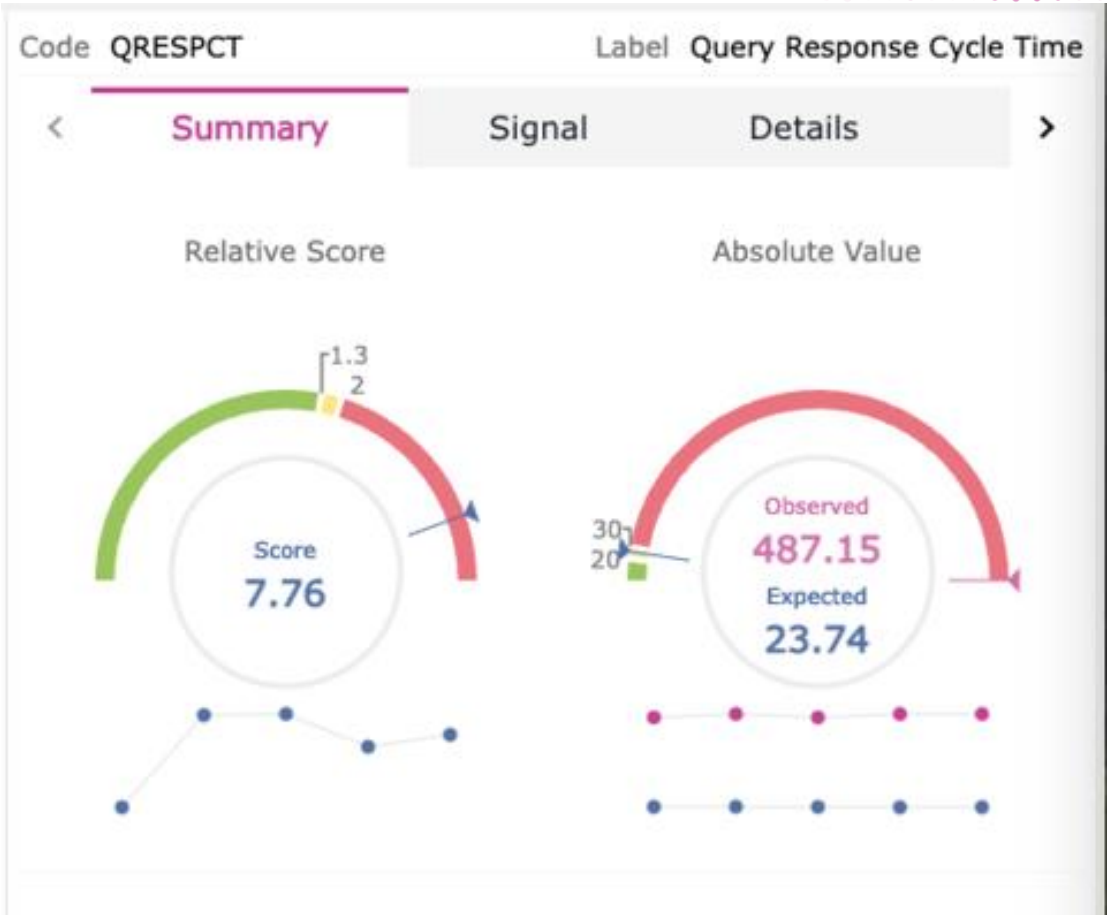
Audit Trail Risk Scenario: Long cycle time for sites to answer EDC queries

KRI: Query Response Cycle Time (*QRESPCT*)

Definition: Average cycle time from query generation to query response

Rational For Use: Identify sites that are slow in responding to manually generated (i.e., Data Mgt or Medical Monitor) queries.

Possible Root Cause Issue(s): Site is too busy, under-staffed, inattentive, lack of understanding/sensitivity to importance of timely query response.



CluePoints

Example KRI: Data Changes

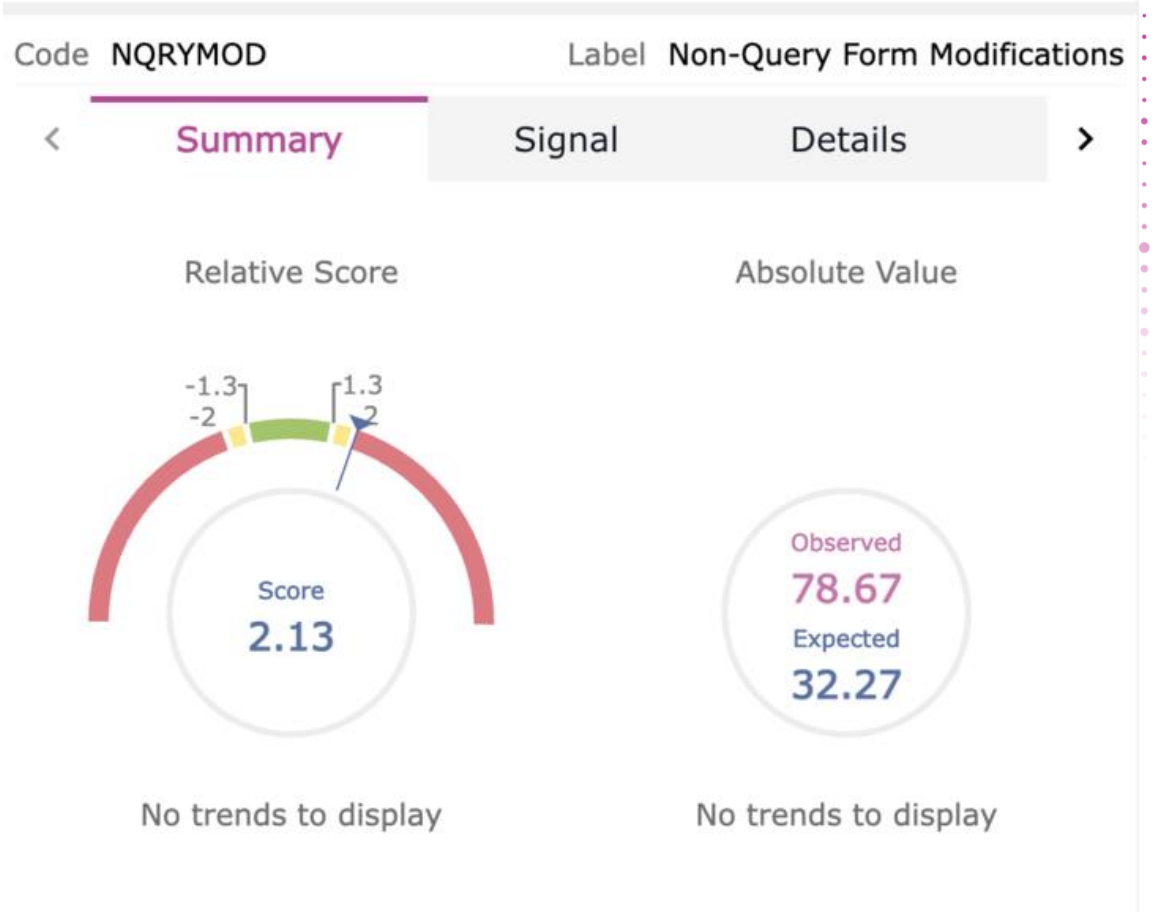
Audit Trail Risk Scenario: High levels of data changes

KRI: Frequency of data changes (in response or not in response to a query) e.g. *non-query form modifications*.

Definition: No. of data changes (in response or not in response to a query), total or over the past X days.

Rational For Use: Identify Countries, Sites or eCRF pages (critical / non-critical forms) that are changed more than expected.

Possible Root Cause Issue(s): Lack of understanding of protocol, EDC system, sloppiness in performing data entry, manipulation of data entry to make it fit.



CluePoints

Use case: identifying risks in ePRO audit trail data

Risk Scenario	Identify where there is an unusually close proximity in daily ePRO/eCOA entry times between patients at a site (compared to all other sites).
Potential Route Cause	• Site fabricating ePRO data • Site conducting group sessions with patients each day to guide their ePRO entries • Site erroneously directing patients to complete ePRO diaries/assessments at specific time
Risk Control	Time Similarity Test- between-patient time correlation
Definition	Measures how close in time patients at a site report their diary/ePRO data on the same date
Input Data	ePRO (or other device) audit trail data
Statistical Test	The average correlation between the timestamps of all pairs of patients at a site

ePRO Audit Trail Data – Analysis of ePRO Entry Times

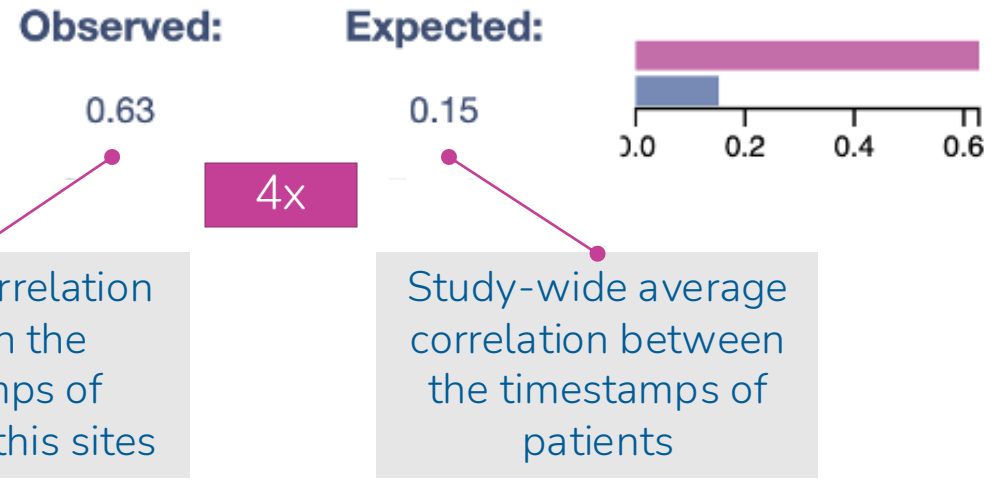
CP_CENTER	CP_PATIENT	DATETIME
1097		dd/mm/yyyy
1097	10971768	2021-10-01 23:16:14
1097	10971769	2021-10-01 23:18:32
1097	10971770	2021-10-01 23:20:14
1097	10971771	2021-10-01 23:22:42
1097	10971772	2021-10-01 23:24:38
1097	10971768	2021-10-02 21:30:59
1097	10971769	2021-10-02 21:32:54
1097	10971770	2021-10-02 21:34:39
1097	10971771	2021-10-02 21:36:39
1097	10971772	2021-10-02 21:38:37
1097	10971772	2021-10-03 21:40:00
1097	10971771	2021-10-03 21:41:55
1097	10971770	2021-10-03 21:43:49
1097	10971769	2021-10-03 21:45:25
1097	10971768	2021-10-03 21:48:16
1097	10971768	2021-10-04 23:00:47
1097	10971769	2021-10-04 23:02:31

Oct 1st

Oct 2nd

Oct 3rd

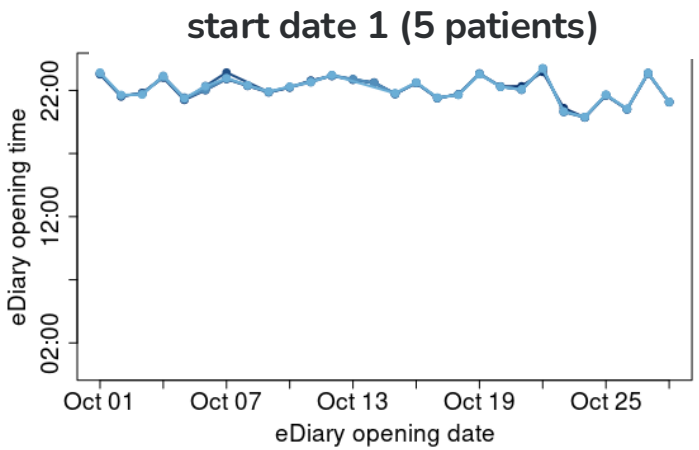
5 patients at the same site all entered their daily eDiary approximately 2 minutes apart every day during the study

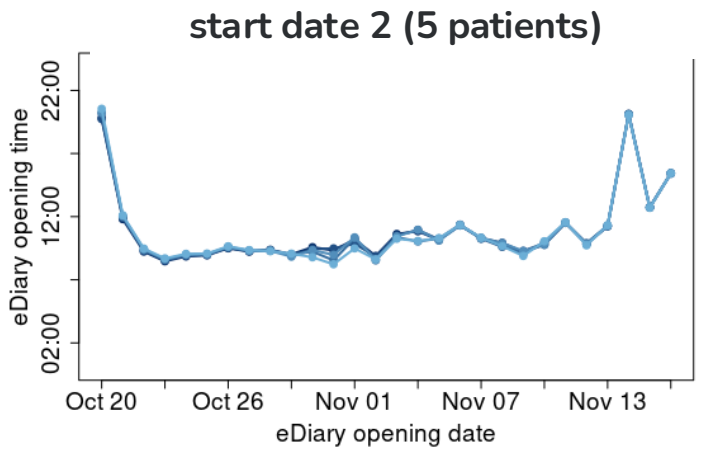


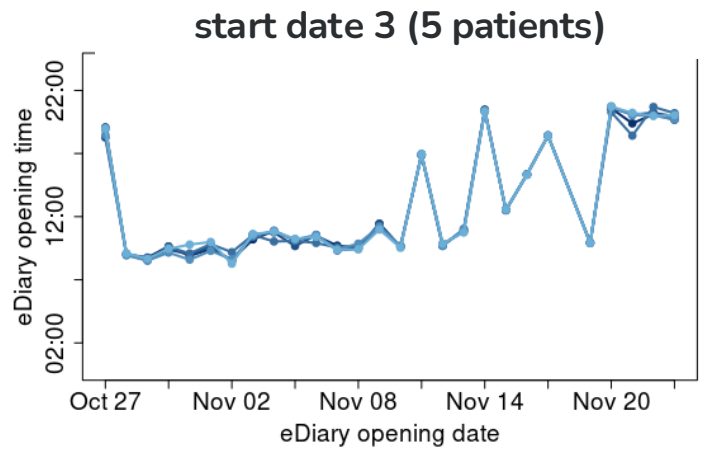
CluePoints

Patients at the site who started the study on the same date entered their daily eDiary around the same time each day

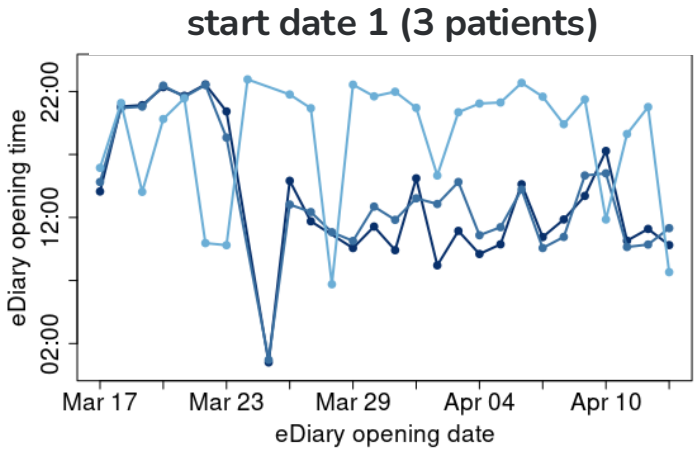
Atypical Site

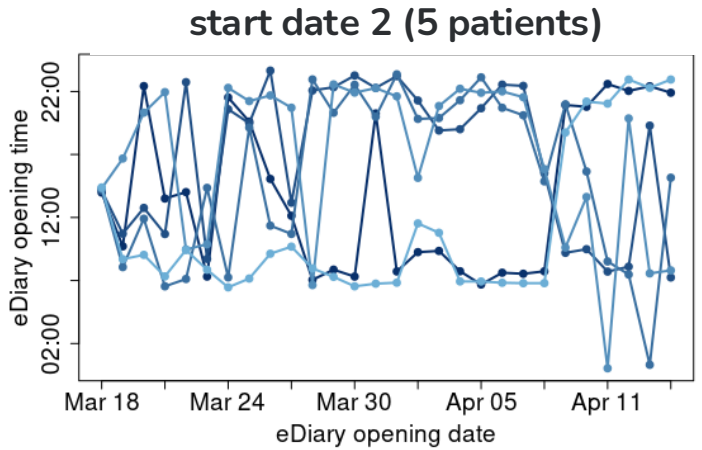


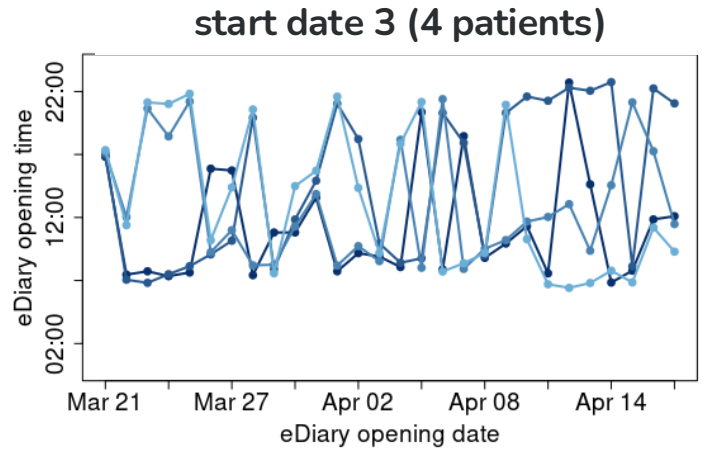




Typical Site

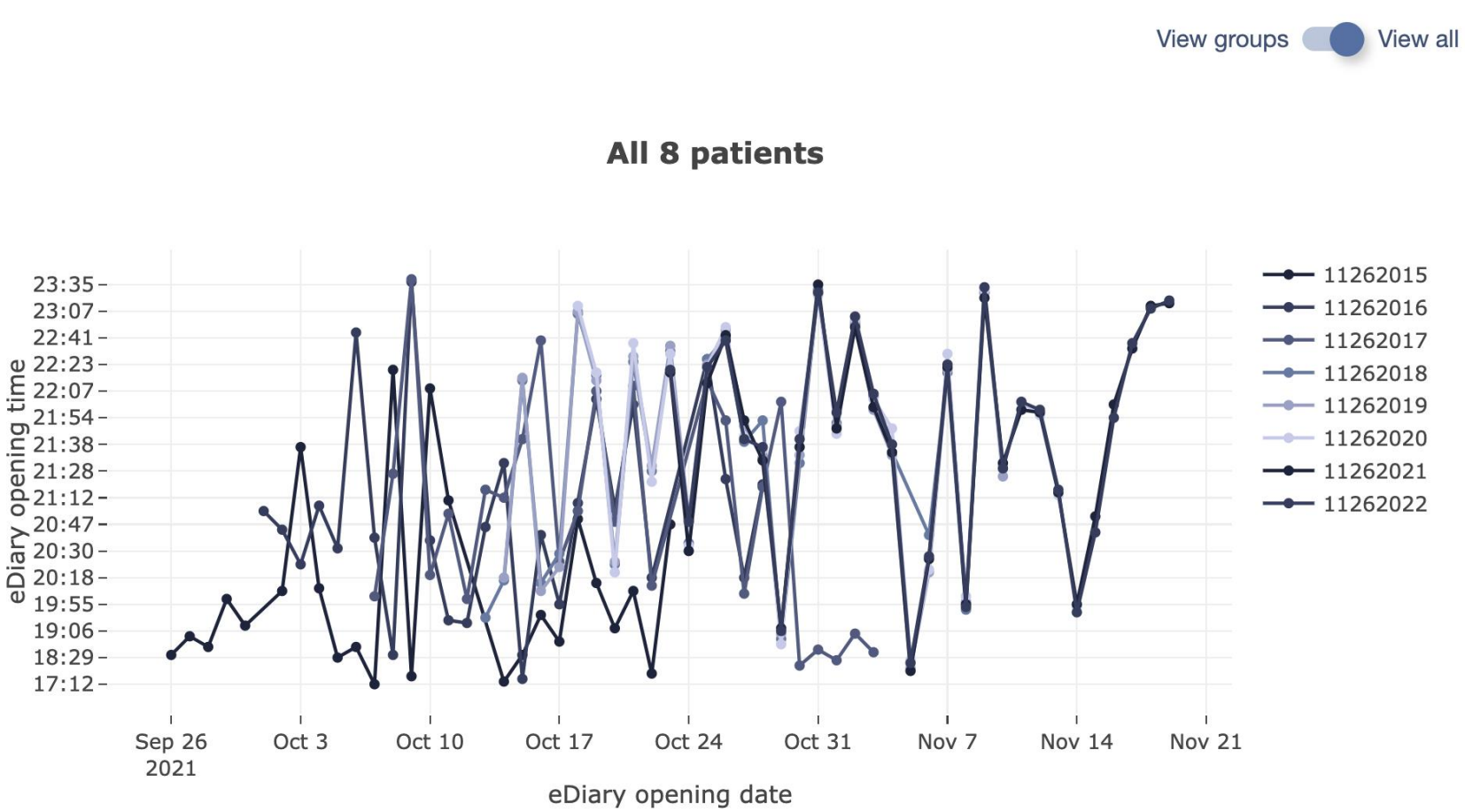


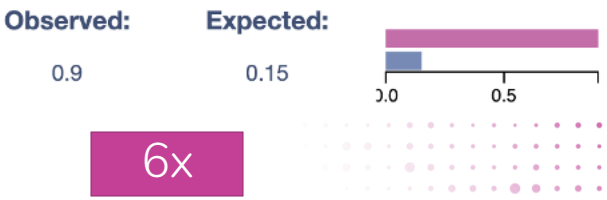




CluePoints

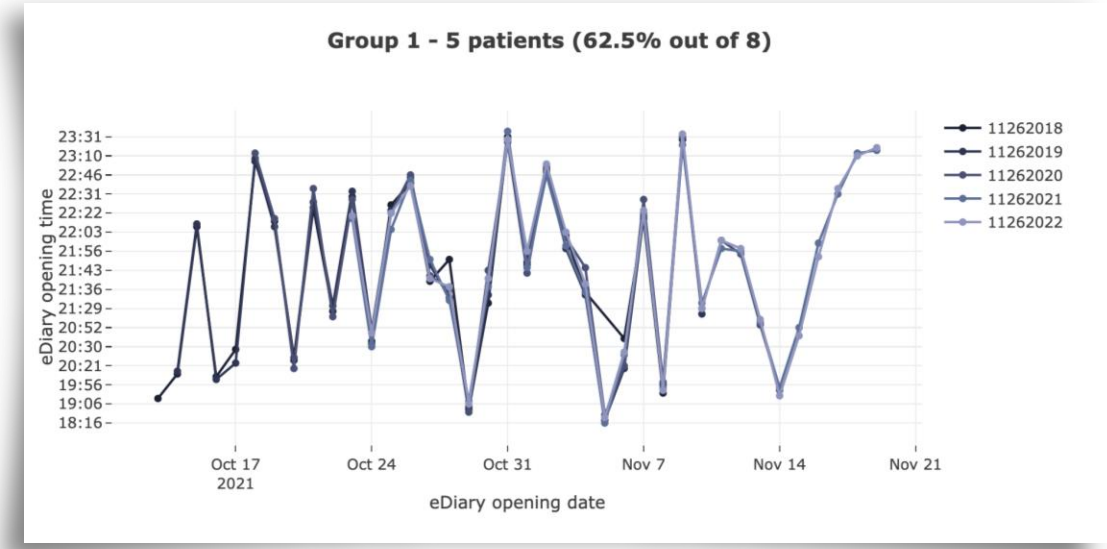
Analysis of All Patients at a Site – Is there an Issue?



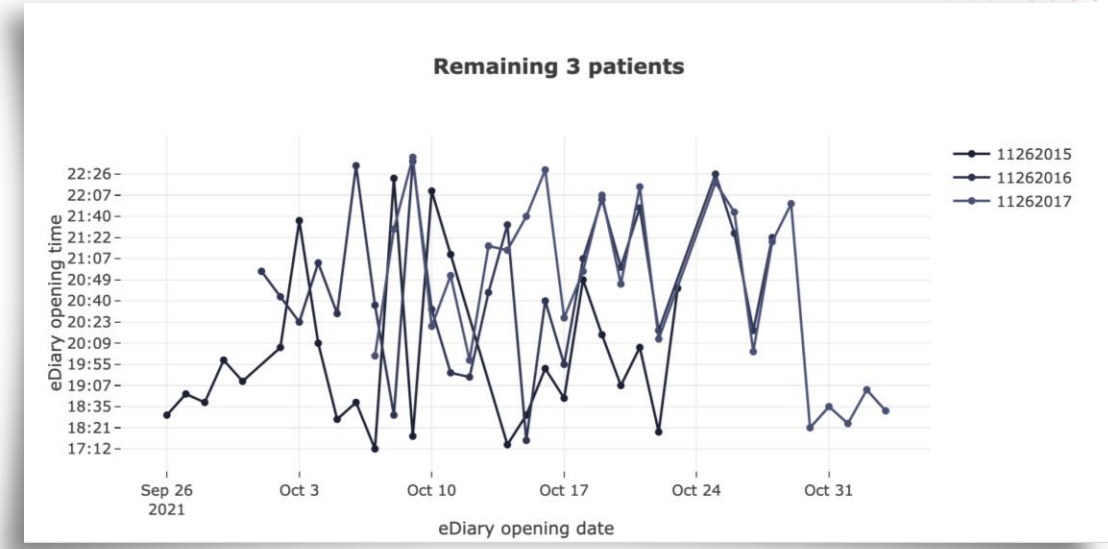


Analysis of Patient Sub-Groups – There is an Issue!

Sub-Group 1



Sub-Group 2

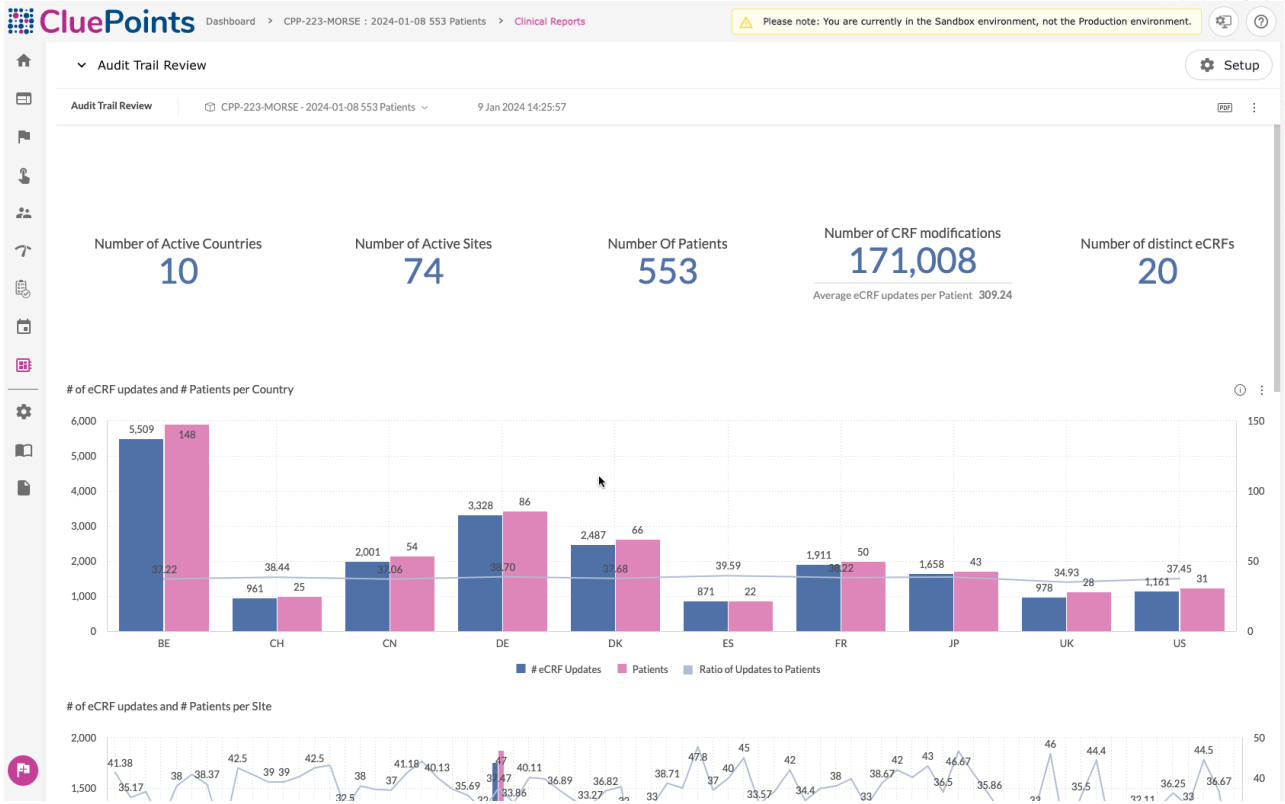


Visualise & Explore Audit Trail with BEYOND

Dashboards that surface audit trail data for exploration and review.

Summarised views by dimension of interest:

- Country
- Site
- Patient
- Form



Example – Looking at eCRF Updates across region, sites and eCRF Pages

Country

Site

eCRF Pages

CluePoints Use Case: Patient ePRO Diaries Falsified by Center

Study Overview

Centers:	50+	Therapeutic Area:	Chronic Disease
Patients:	500+	Study Phase:	3

CluePoints Risk Detection

- Center with 15 patients
- Nearly 70% of daily ePRO diary entries occurred in same hour of day (6 pm local time) across all patients.

Root Cause Finding and Outcome

- ePRO devices never distributed to patients. Daily diary entries "invented" by center staff, typically at close of business each day.
- Sponsor closed the center and removed all 15 patients from analyses.

Business Implications:

- Avoided potential skewing of study endpoint analyses
- Prevented potentially damaging regulatory inspection finding

CluePoints Use Case ID: 1505

CluePoints

CluePoints Use Case: eDiary programming error

Study Overview

Centers:	10+	Therapeutic Area:	Central Nervous System
Patients:	15+	Study Phase:	2

CluePoints Risk Detection

- In an eDiary dataset, one patient in the trial had only 'Clinician' as user role

  This was the only patient with such result, all other patients had Subject as user role

Root Cause Finding and Outcome

- Programming error discovered affecting eDiary proxy entries
- Updated programming and correction of all previously reported proxy entries.

DQA Results – Extreme Score

Business Implications

- Avoided mis-reporting of eDiary data

CluePoints

Impact on Trial Efficiency

CluePoints

Impact of Trial Efficiency

Reduced costs, fewer site visits, quicker decisions

Simple Statement of Intent

User-centered design is more than just the user interface in a browser or application. Embracing a data-product mindset is critical to establishing data as an asset

Control Tower	Control Room	API First
PTRS	Optimize Performance	Agentic Robots

Simple Example

AI solutions can't be delivered like traditional technology solutions, such as ERP systems. AI development cycles are much faster. What you build in the next three to six months might need to be retired in 18 months

CluePoints

SDR Sampling

Dynamic SDR Sampling

- Goal: To dynamically adjust the SDR sampling strategy for each site based on site risk.

  - Assess the site quality by assigning a global score to each site having at least one patient entered into EDC.
  - For each metric: a low, medium or high risk is assigned to each site in the CMP.
  - CMP derives automatically the site score based on the value assigned to each risk and the weight of each metric.

CluePoints

SDR Sampling: Why?

ICH E6 Compliance: enhances data quality and protocol and regulatory compliance.

Shift from 100% SDR to targeted SDR: dynamically adjust SDR based on site risk without compromising quality.

Reduces site monitoring costs: reduction in frequency of on-site visits or time on site, without compromising quality.

Focus monitoring efforts where they are needed most: smarter / risk based resource allocation: enables CRAs to focus on sites that need more support and on critical processes

CluePoints

SDR Sampling: Digitising The Process

Study Manager	Monitor	Study Manager	Central Monitor	Study Manager	Monitor	Study Manager
Define SDR Sampling Strategy Based on RACT Study Level RISK	Select Subjects for SDR and Perform SDR	Assess # of subjects randomized and initiate Site Quality Score	Perform Site Quality Assessment	Determine Site Specific SDR Sampling Strategy & Communicate	Select Subjects for SDR and Perform SDR	Initiate Repeat Site Quality Assessment

Site Initiation FPFV

8 – 12 weeks

SDR Sampling Strategy (e.g. data point, subject-level, visits-level) High Risk Medium Risk Low Risk	Based on RACT Study Risk Level	Determine if sufficient no. of randomised subjects to initiate Site Risk Score	Composite Score of KRIs Delta in Score (↑ ↓) is used to drive change in SDR sampling strategy	Determine change in SDR Sampling Strategy + communicate to Monitor	Based on Site Specific SDR Sampling Strategy

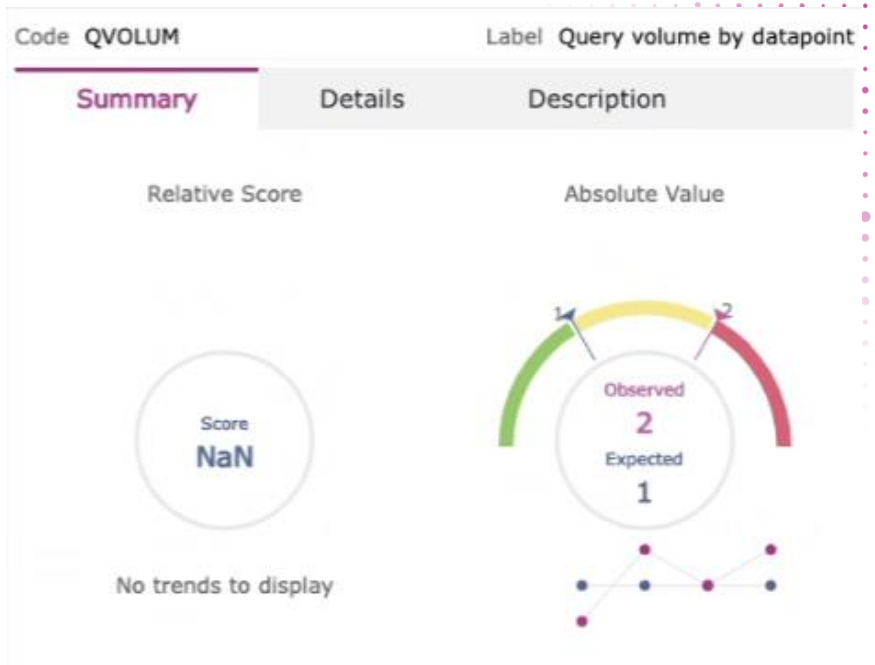
Example KRIs Determining SDR Sampling Strategy

Calculate Risk for Each KRI Metric

0 = low risk

1 = medium risk is identified

2 = high risk



* Incremental

Example KRI

Metric: Query volume

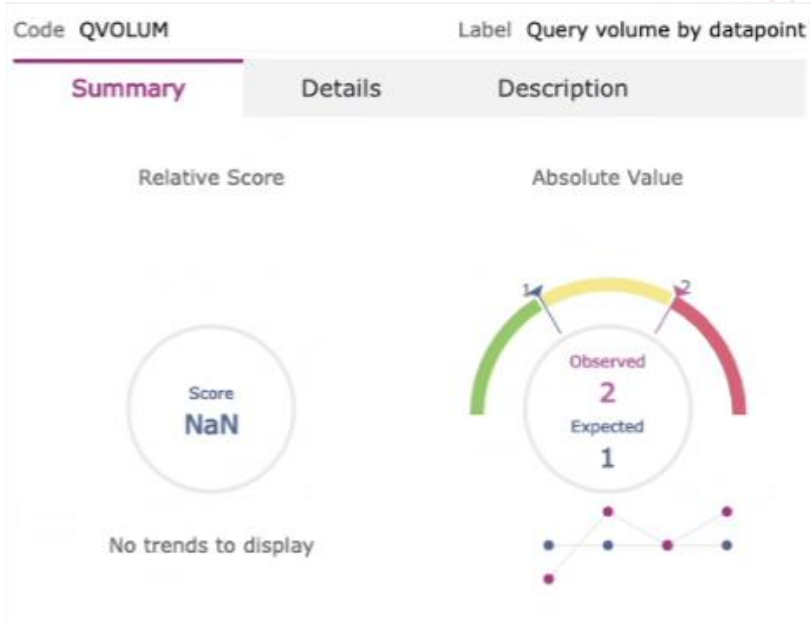
Definition: Rate of queries generated by datapoint for the site compared to the overall study data.

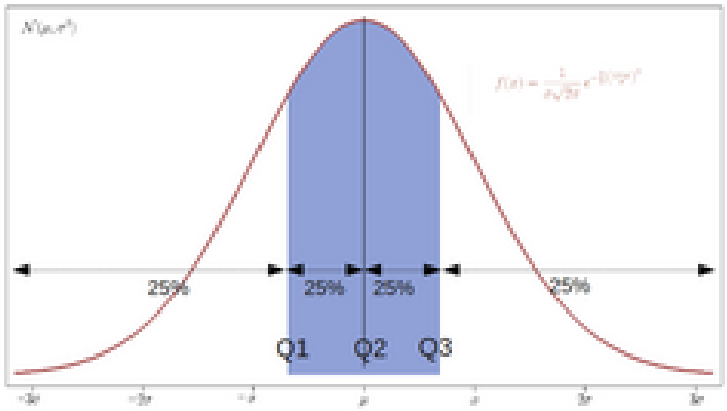
Risk Levels:

Risk Level	Thresholds	Risk Score
Low Risk	<= Q1 (0-25%)	0
Medium Risk	>Q1; <=Q3 (26-75%)	1
High Risk	>Q3 (>75%)	2

Notes:

- Keep only the datapoints (and corresponding queries) entered during the period of interest (the default period of interest is 6 months prior to the snapshot date).





CluePoints

Dynamic Data Driven Monitoring

CluePoints

Centralized Monitoring and Data Driven Site Monitoring are essential for RBQM

ICH E6 (R3)

3.11.4.1 Investigator Site Monitoring

appropriate). The frequency of monitoring activities should also be determined based on identified risks. Monitoring activities and their frequency should be modified as appropriate using knowledge gained.

(b) This monitoring activity may be performed on-site and/or remotely depending on the nature of the activity and its objectives.

3.11.4.2 Centralised Monitoring

(a) Centralised monitoring is an evaluation of accumulated data, performed in a timely manner, by the sponsor's qualified and trained persons (e.g., medical monitor, data scientist/data manager, biostatistician).

(b) Centralised monitoring processes provide additional monitoring capabilities that can complement and reduce the extent and/or frequency of site monitoring or be used on its own. Use of centralised data analytics can help identify systemic or site-specific issues, including protocol noncompliance and potentially unreliable data.

(c) Centralised monitoring may support the selection of sites and/or processes for targeted site monitoring.

SPOT

Suggest site visit schedule and type by workload and risk.

CMP

Identify systemic and site-specific issues from all data sources in timely manner.

Input signals to SPOT to modify site profile.

CTMS

1. Action from SPOT: Visit Schedule and Type.
2. Actions from CMP: Tasks to complete.

CluePoints

SPOT completes the cycle from analytics to actions…

Identifying Data Sources & What's Critical

Preparing & Processing Data

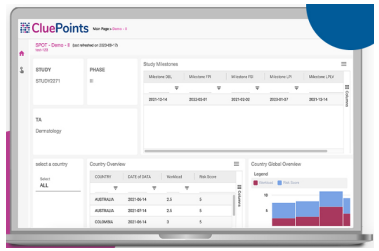
Identifying Data Anomalies

Documenting Root Cause Analysis *Centralised Monitoring Plan (%SDV/SDR)*

Visualize Site Risk & Monitoring Workload

Plan and Optimize Monitoring Strategy

Take Action



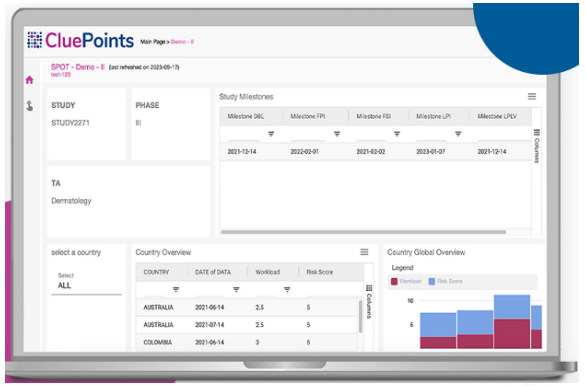
CluePoint's CMP

CluePoint's SPOT

CluePoints

What is SPOT?

- SPOT is an **entity profiling tool** that enables **data driven site monitoring capabilities** to improve the **planning, adaptation, execution** and **oversight** of MV activities.
- SPOT allows study teams to swiftly pinpoint anomalies and inefficiencies & translate ***site, country*** and ***regional level insights*** into actionable strategies.
- SPOT presents new data driven site monitoring approaches, offering a leap in addressing today's site-based monitoring challenges …



Efficient Monitoring Visit Planning

Rapid Site Performance Evaluation

Optimized Site Recruitment Strategies

Enable Targeted Source Data Verification & Review Strategies

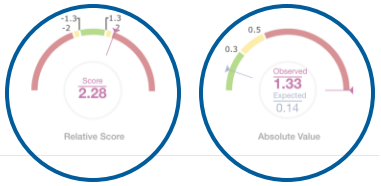
Enhanced CRA Performance Evaluation

CluePoints

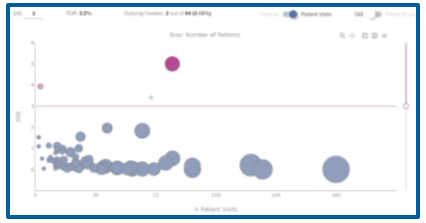
SPOT workflow

Input Data

KRIs



DQA



Clinical Data

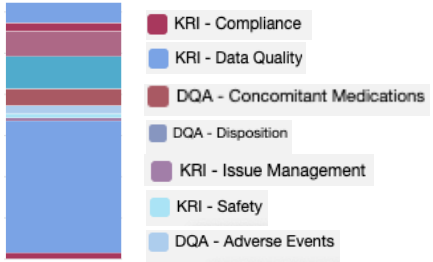
New & number of AE/SAEs,
Number of queries, …

Operation Data (CTMS)

MV Plan, Enrollment, Milestones, IMP, SDR & SDV
to be done, new ICF, …

Data Derivation

Site Level Risk Score Calculation



Workload estimation (backlog, new & predict)

Review Dashboards

Country level dashboard

Site level dashboard

Document & Take Action

Adjust Monitoring Activities

Reason & Rational

Plan/Modify MV Date

Create new MV
Update date of the MV

Modify MV Type

Change type (on site vs. remote),

Modify SDV Tier

Change SDV Tier

CTMS & EDC

CluePoints

90%+
Of all studies use CMP+SPOT

Proof Point #1

From FDA, Sponsors and CluePoints Together

30%+
reduction in number of monitoring visits

sanofi

90%+
reduction in number of database unlocks

Efficient Monitoring Visit Planning

Rapid Site Performance Evaluation

Optimized Site Recruitment Strategies

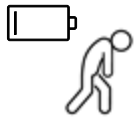
Enable Targeted Source Data Verification & Review Strategies

Enhanced CRA Performance Evaluation

CluePoints

Why SPOT

Improve MV Productivity	Reduce Travel and Expenses Costs	Support Achievement of Environmental Sustainability Goals
Reduce monitoring costs through data driven dynamic monitoring – focusing resources where they are needed most	Reduce travel costs through increased use of remote visits	Reduce carbon footprint and achieve a net-zero environmental impact
Ratio of on-site : off site MV Frequency: interval between MVs On-site days/Patient/Year		



Reduce CRA Burnout and Improve Employee Wellbeing	Improve MV Quality
Through more efficient workflows for CRA, reduce burnout, turnover and impact and on management Reduced unnecessary travel	Consistent approach to preparing and executing MV Align activities with each site's specific needs and risks - focus on what matters
Reduce CRA turnover over (past 12M)	Consistent approach to preparing for MV Align activities with each site's needs

CluePoints

Impact on Patient Experience

CluePoints

Impact on Participant Experience

Better recruitment, improved safety, and higher retention rates

Simple Statement of Intent

Data Democratization - the most striking impact is the ability to synthesize knowledge and generate hypotheses more efficiently.

Protocol Stress Test	Trial Execution	DMC / DSMB
⇅	⇅	⇅
Burden Assessment	Key Decision Automation	Trial Oversight

Simple Example

Adaptive Trials: protocol "benchmarking" for patient and site burden, leading to target setting for all down stream functions and an overall assessment of trial efficiency (and likely outcome ?)

CluePoints

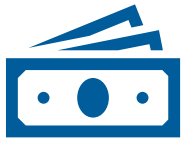
Patient Burden

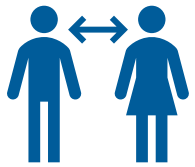
From Patient to……ESG ?

- Patient burden refers to the challenges and difficulties a patient faces in managing their participation is a trial;
- It encompasses not only the direct effects of symptoms and side effects but also the broader impact on daily life, relationships, and well-being.
- Compare expected / planned burden to actual


Physical Burden


Emotional Burden


Financial Burden


Social Burden


Treatment Burden


Trial Burden

CluePoints

Patient Compliance

Right Patient, Doing the Right Thing, at the Right Time

- Reduce errors: Ensuring the right treatment is given to the right patient at the right time minimizes the risk of medication errors, wrong-site procedures, and other harmful incidents.
- Improve efficiency: Standardized procedures and timely interventions reduce waste and improve the effectiveness of study/care delivery.
- Enhance patient satisfaction: When patients feel safe, heard, and that their care is personalized, they have a more positive experience.