



AR07 - Real-World Examples of eCOA Compliance and Audit Trail Review Using Advanced Statistical Methodology

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CluePoints



Quick Intro

- Nearly 20 years in the Clinical Research Space
- 15+ years at large CROs
- 10 years in RBQM Space, serving 20+ different sponsors across the industry in their RBQM efforts
- 10+ years in ClinOps (CRA, ClinOps Lead, Project Manager), with direct Data Management experience
- Former RBQM business system owner at large pharma company
- Key support on RBQM SaaS installations of 4 top-10 pharma companies
- Supported RBQM work at multiple mid- and small-pharma companies
- Worked in 3 different independent SaaS RBQM technologies as vendor, sponsor, and CRO
- VP of Customer Success at CluePoints

Today's Agenda

Background on Audit Trail

Established Methods of ATR

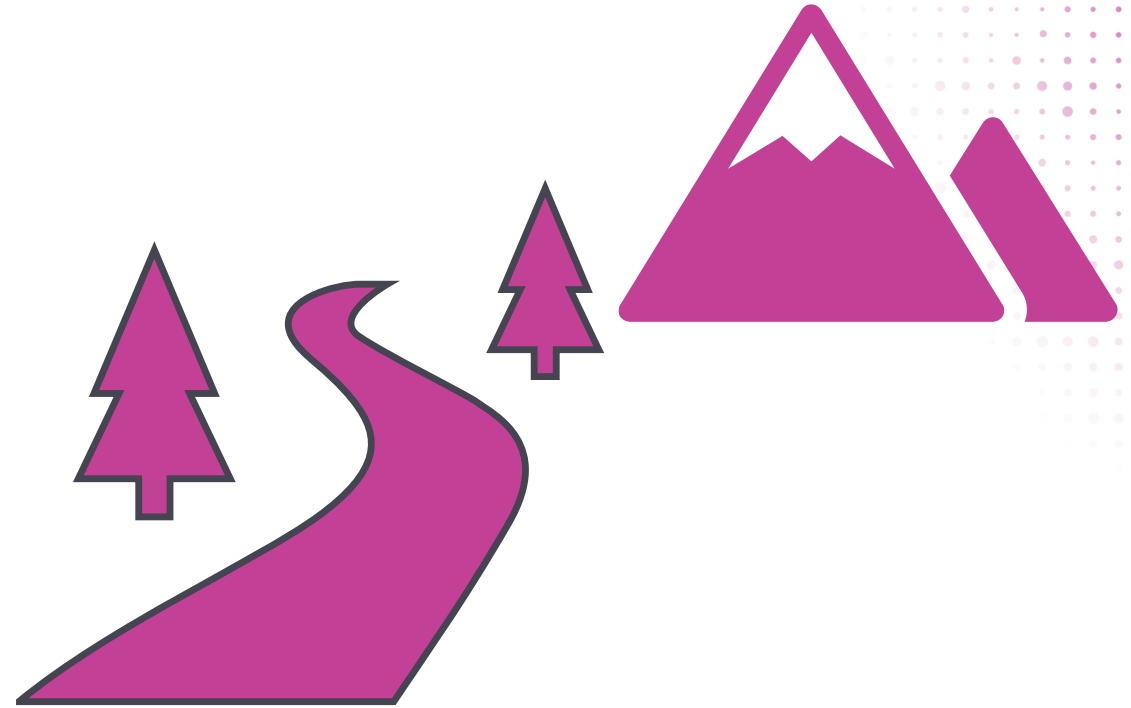
New Advances in Time-Based
Testing



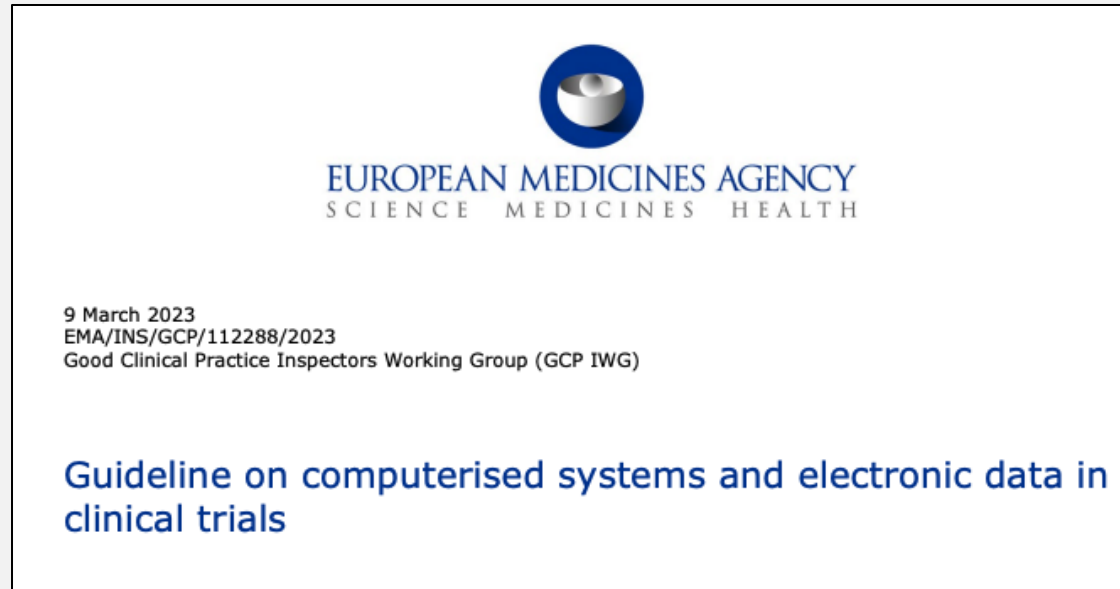
Part 1: Background on Audit Trail

Audit Trail Review - The What

- Audit Trail data sits within various eClinical Systems (ePRO, eCOA, etc.)
- Metadata could include or consist of the following:
 - Date/time of record creation
 - Login of end user Creating record
 - Role of person creating record
 - Data changes/modifications
- Should be human-readable within each system



Audit Trail Review – The Why



- “Procedures for **risk-based trial specific audit trail reviews** should be in place and performance of data review should be generally documented. Data review should focus on critical data. Data review should be proactive and ongoing review is expected unless justified. Manual review **as well as review by the use of technologies to facilitate the review of larger datasets** should be considered.”

Audit Trail Review – The Why

Means	2009–2012	2013–2016	2017–2020	Overall growth
Total Endpoints	16.6	17.2	21.1	27.1%
Total Eligibility Criteria	29.7	30.0	32.7	10.1%
Total Procedures Performed	159.7	186.9	267.1	67.3%
Percent of Total Non-Core Procedures	N/A	21.2%	24.7%	16.5%
Total Procedures per Patient Visit	11.3	12.4	13.8	22.1%
Total Countries	5.5	7.9	9.3	69.1%
Total Investigative Sites	43.6	58.3	58.0	33.0%

Increased Complexity of Trials

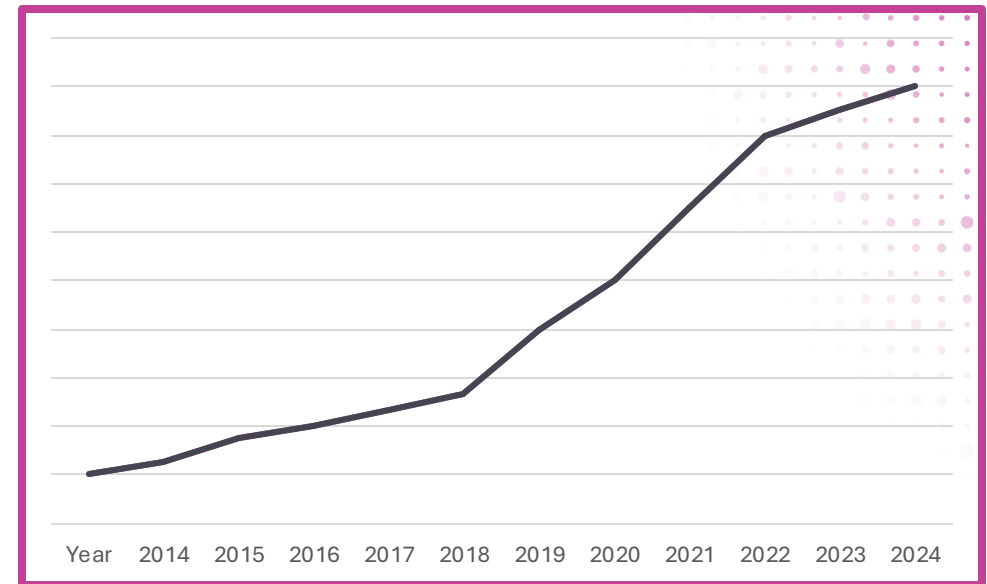
Additional Data Collected / Conduct Performed

More Data to Review and Conduct to Oversee

Rise In Digital Endpoints

- According to a 2021 Report by TCSDD, Phase III clinical trials generate an average of 3.6 million data points, **3x the amount of data collected by late-stage trials 10 years ago.**
- According to a 2024 Impact Report by the Tufts Center for the Study of Drug Development (TCSDD), **the use of digital endpoints has doubled every 3 years since 2014.**
- More than half of all digital endpoints are used to support secondary clinical trial outcomes. These endpoints are **very difficult to monitor and interrogate**

Use of Digital Endpoints 2014-Present





Part 2: Established ATR Methods

EDC Audit Trail Data

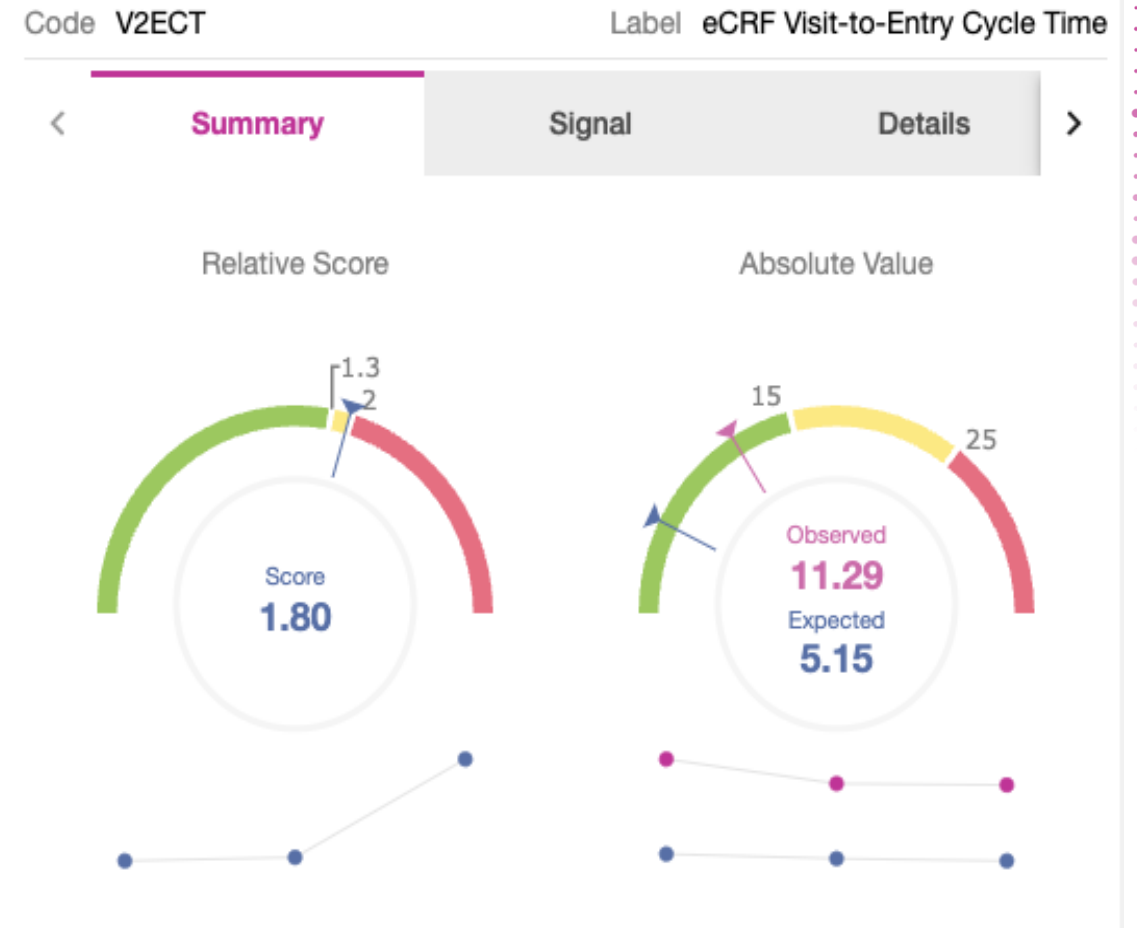
Audit Trail Risk Scenario: Long cycle time from patient visits until data entered into EDC

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.



Non-Query Data Changes

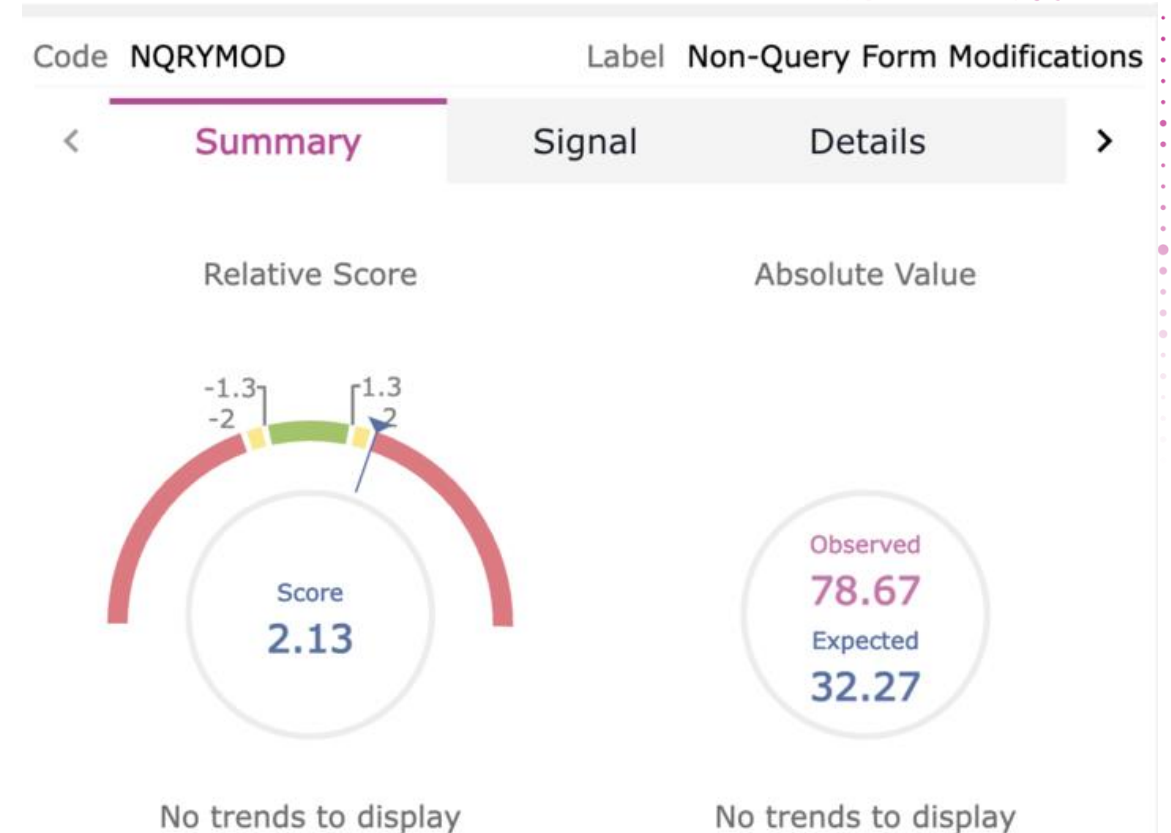
Audit Trail Risk Scenario: High levels of data changes

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.



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.

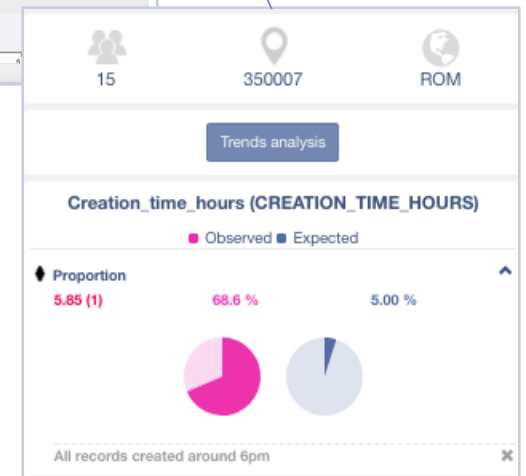
Root Cause Finding and Outcome

- 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





Part 3: New Advances in Time-Based Testing

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

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

Observed:

0.63

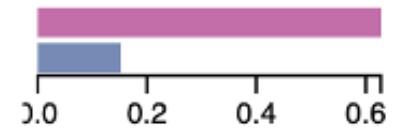
Average correlation between the timestamps of patients at this sites

Expected:

0.15

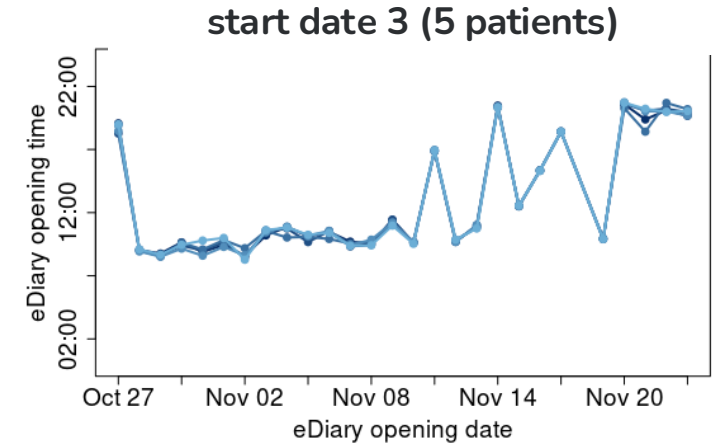
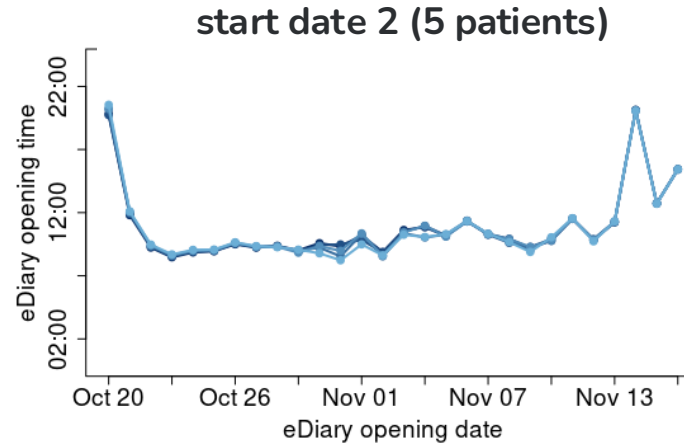
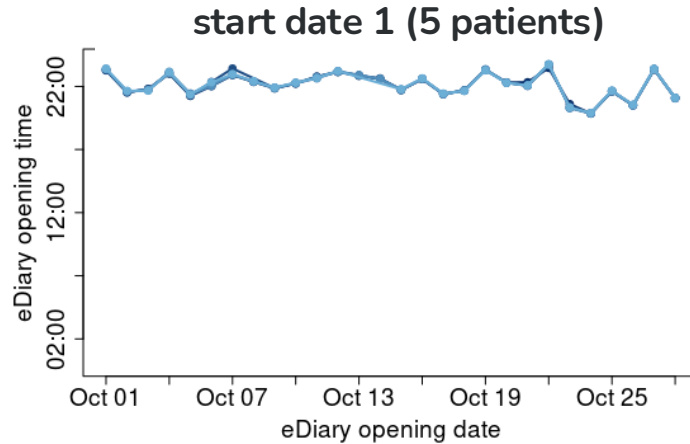
Study-wide average correlation between the timestamps of patients

4x

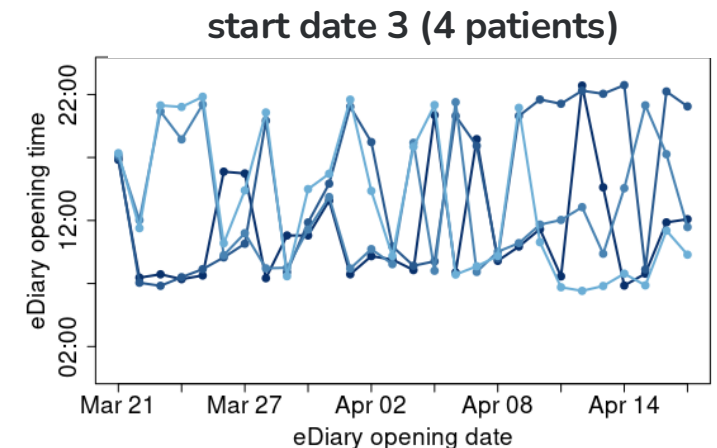
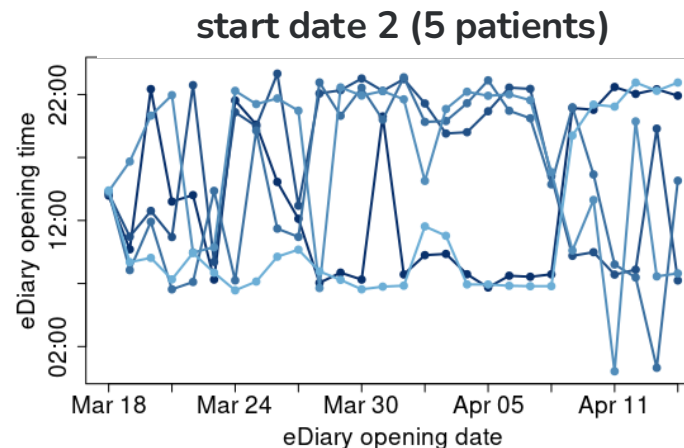
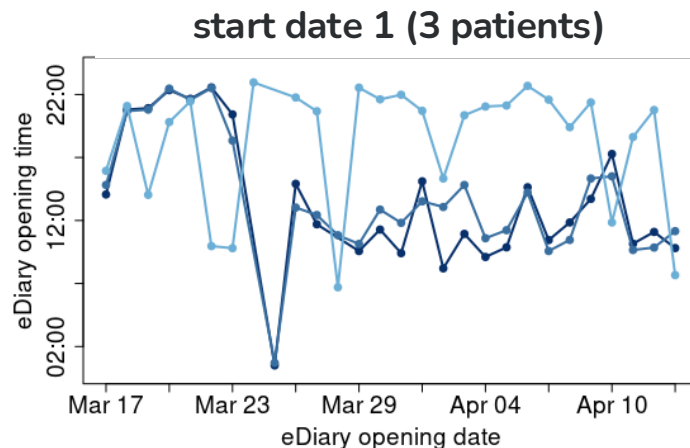


Patients at the site who started the study on the same date entered their daily eDiary around the same time each day

Atypical
Site



Typical
Site



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

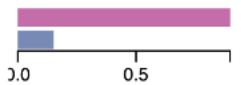
View groups ☒ View all

Observed:

0.9

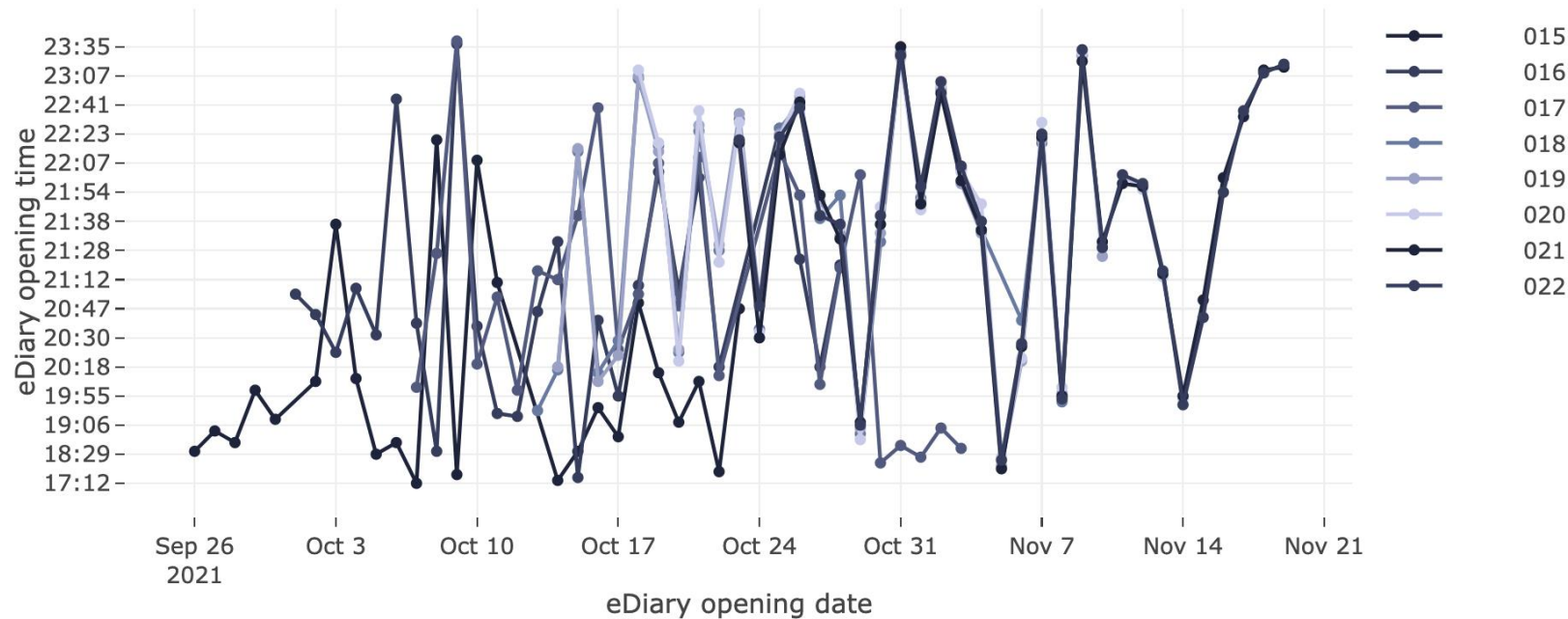
Expected:

0.15



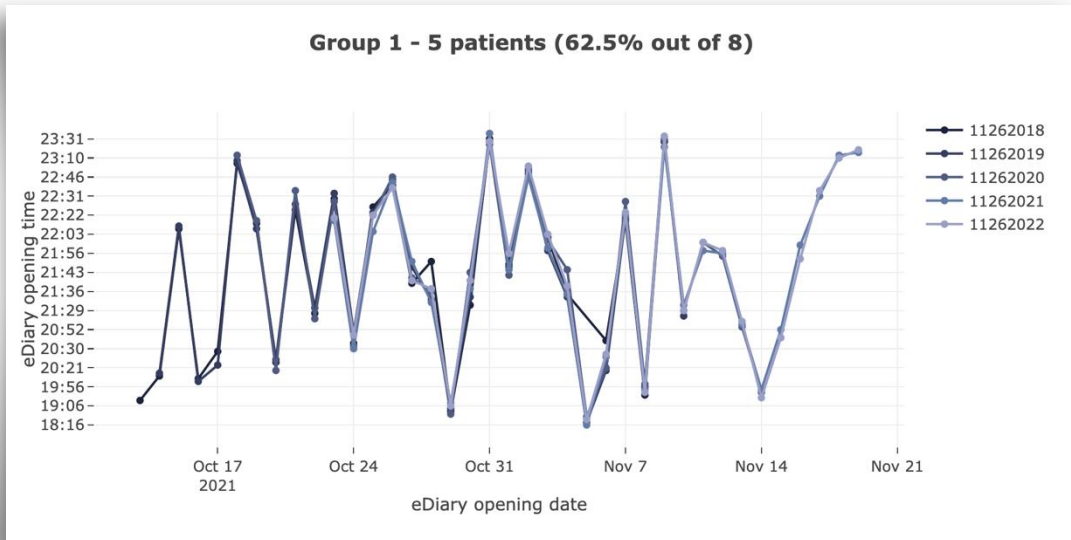
6x

All 8 patients

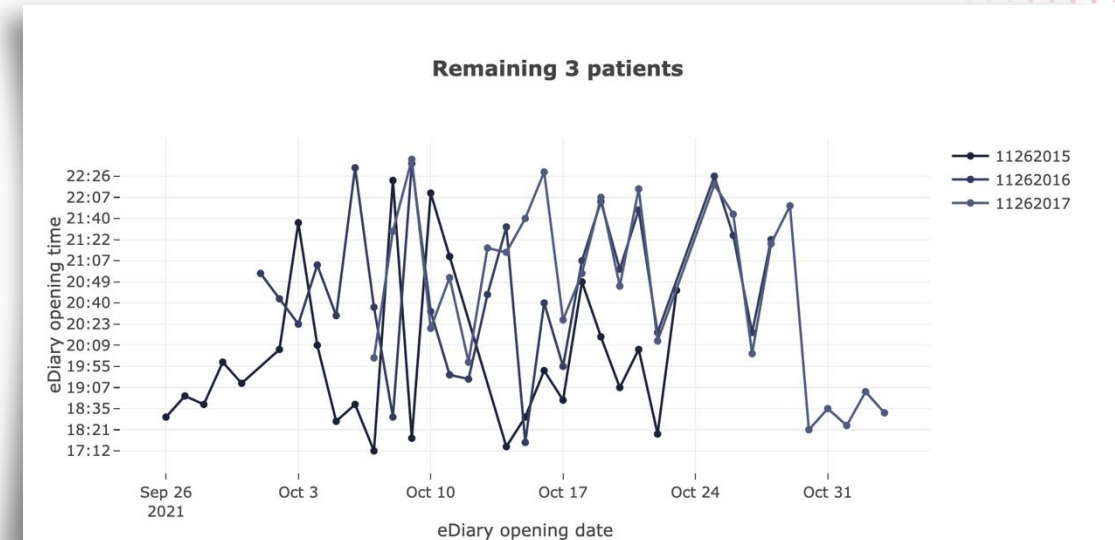


Analysis of Patient Sub-Groups – There is an Issue!

Sub-Group 1



Sub-Group 2





CluePoints Conclusion

As the complexity of
Clinical Trials
continues to rise, more
audit trail data is
produced

Audit Trail Review
activities can vary in
complexity, but provide
value in ensuring Data
Quality and adherence
to regulatory guidelines

Some Audit Trail
Review is better than
no Audit Trail Review,
but advanced Audit
Trail Review tools are
best at finding difficult-
to-detect issues

Data structure and
cross-functional buy-in
are required for
success



Thank you.

Questions?