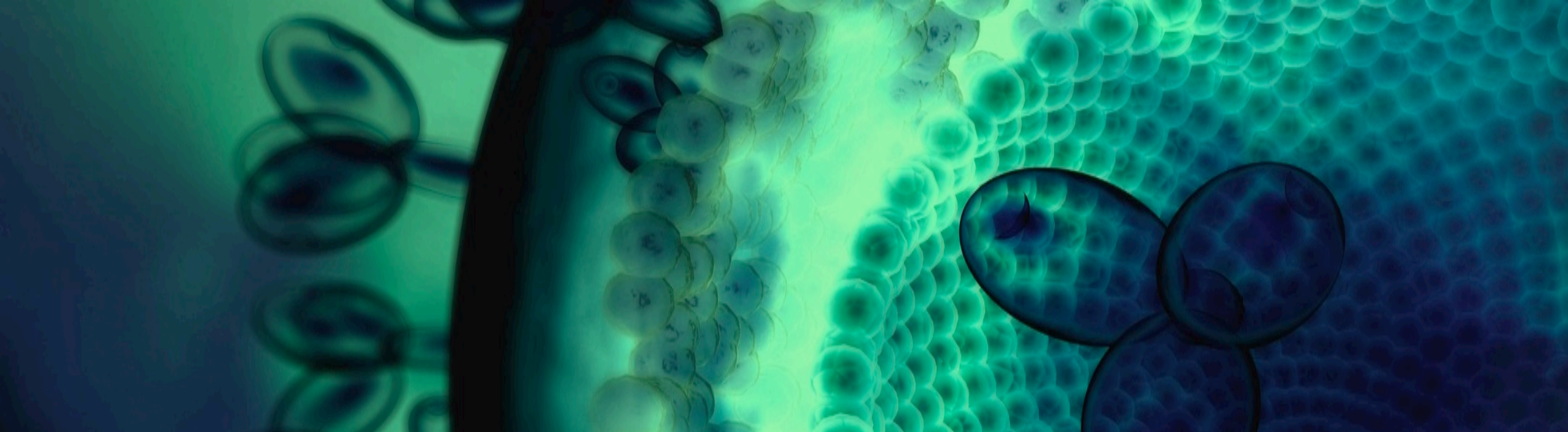




Practical Implementation of Central Statistical Surveillance in Clinical Trials

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Pictured above: The structure of HIV.

Disclaimer

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Agenda

- Introduction and Background
- Methods/Requirements
 - Staff Training
 - Process
 - Communication of Observations
- Conclusions

Introduction and Background

PAST:

- How do we best ensure that our clinical data is of the highest quality while ensuring patient safety and maximizing efficiencies?
 - Traditional Monitoring
 - Heavy resource burden
 - Potential for high cost
 - Lacks a targeted/risk-based approach



Introduction and Background

Present:

- How do we evolve our methods of clinical trial management to improve efficiency and effectiveness?

We evolve and improve our oversight mechanisms

– Risk Based Monitoring 1.0

- Risk based Approach
- Standard Critical to quality factors
- Tailor to Study Needs



Introduction and Background

Future:

- How to we leverage new technologies to improve our current processes?

By implementing new, innovative oversight mechanisms.

- Risk Based Monitoring 2.0

- Adds Central Statistical Surveillance

- Statistical Tool to identify potential data errors, trends, outliers, etc.
 - Allows for detection of issues that are undetected or difficult to detect by other methods
 - Unintentional errors (i.e. poor data entry, equipment malfunction, mis-interpretation of protocol)
 - Intentional errors (i.e. fabricated or falsified data)

Methods: Successful Implementation of CSS

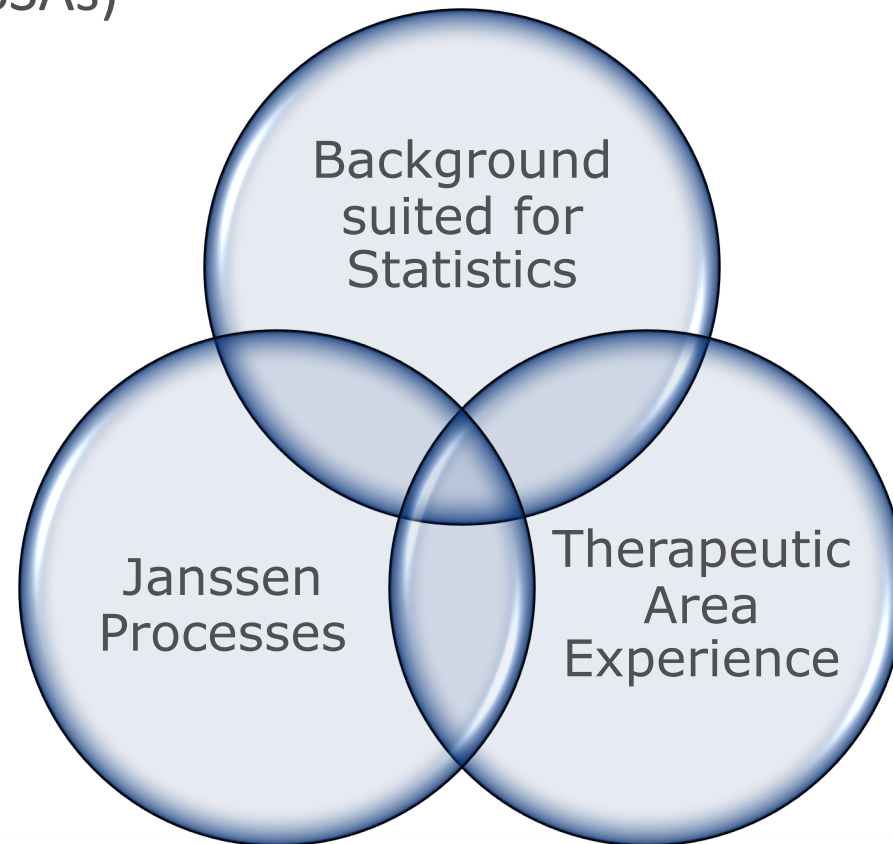
As processes evolve it is key to ensure a sound implementation road-map

- Pilots
- Scalable
- Robust Training
- Strong Process
- Proper Documentation

Methods: Staff Training

Selecting CSSAs

Identify Central Monitoring Managers (CMMs) to be trained as Central Statistical Surveillance Analysts (CSSAs)



Methods: Staff Training

Training Execution

- Intensive, 3-day training session included:
 - Statistics behind the Model
 - How outputs are converted into an interactive dashboard
 - How to interpret the dashboard
 - How to Translate the observations noted in the dashboard from statistical terms to easily actionable clinical terms
 - Didactic and hand-on exercises

Methods: Staff Training

Piloting

- CSSAs were TA aligned
- One trial assigned
- One-on-one sessions with Subject matter Expert
- Group sessions/discussions

Methods: A Detailed Process

- Must be clear, repeatable, scalable
- Leveraged the strong RBM infrastructure in place within Janssen
- No need for updates to/creation of new SOPs

Methods: A Detailed Process

CSS Analysis added to
RBM pan (requirements &
frequency defined)



Methods: A Detailed Process

CSS Analysis added to
RBM pan (requirements &
frequency defined)



CSSA completes
analysis & prepares
results



Methods: A Detailed Process

CSS Analysis added to
RBM pan (requirements &
frequency defined)

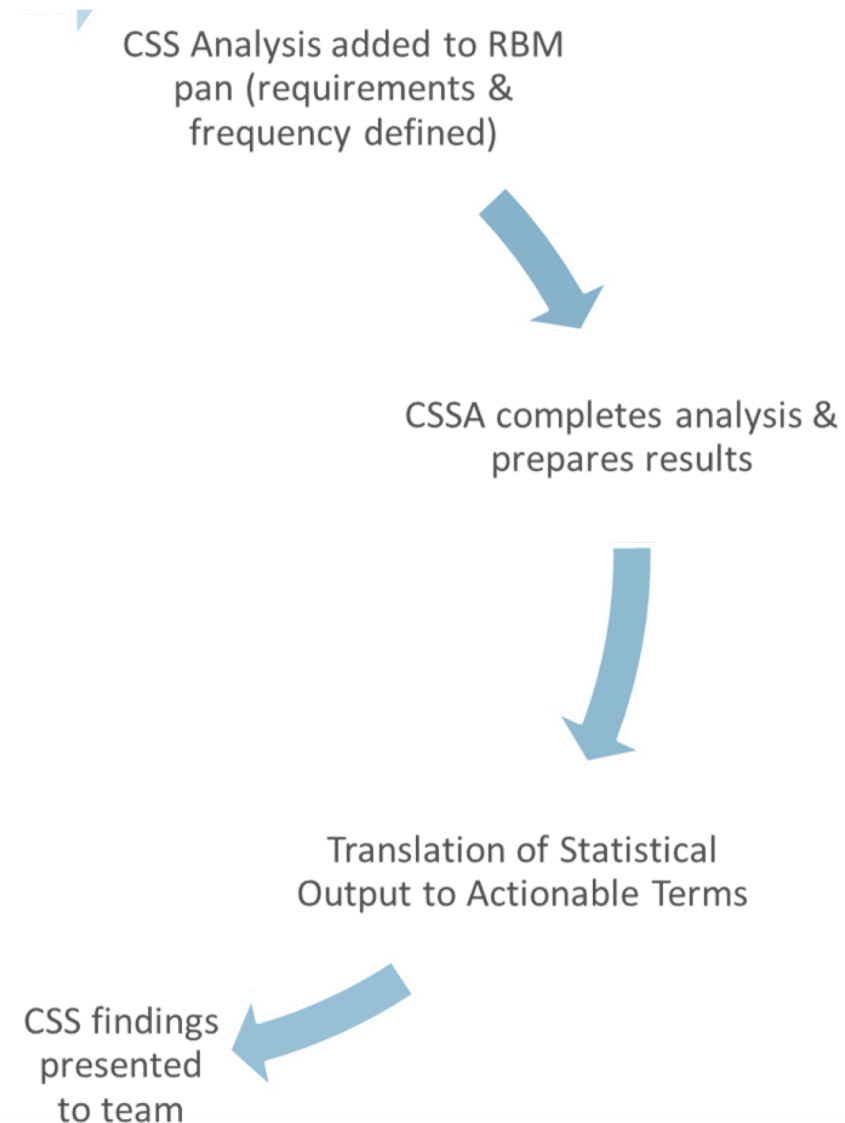


CSSA completes
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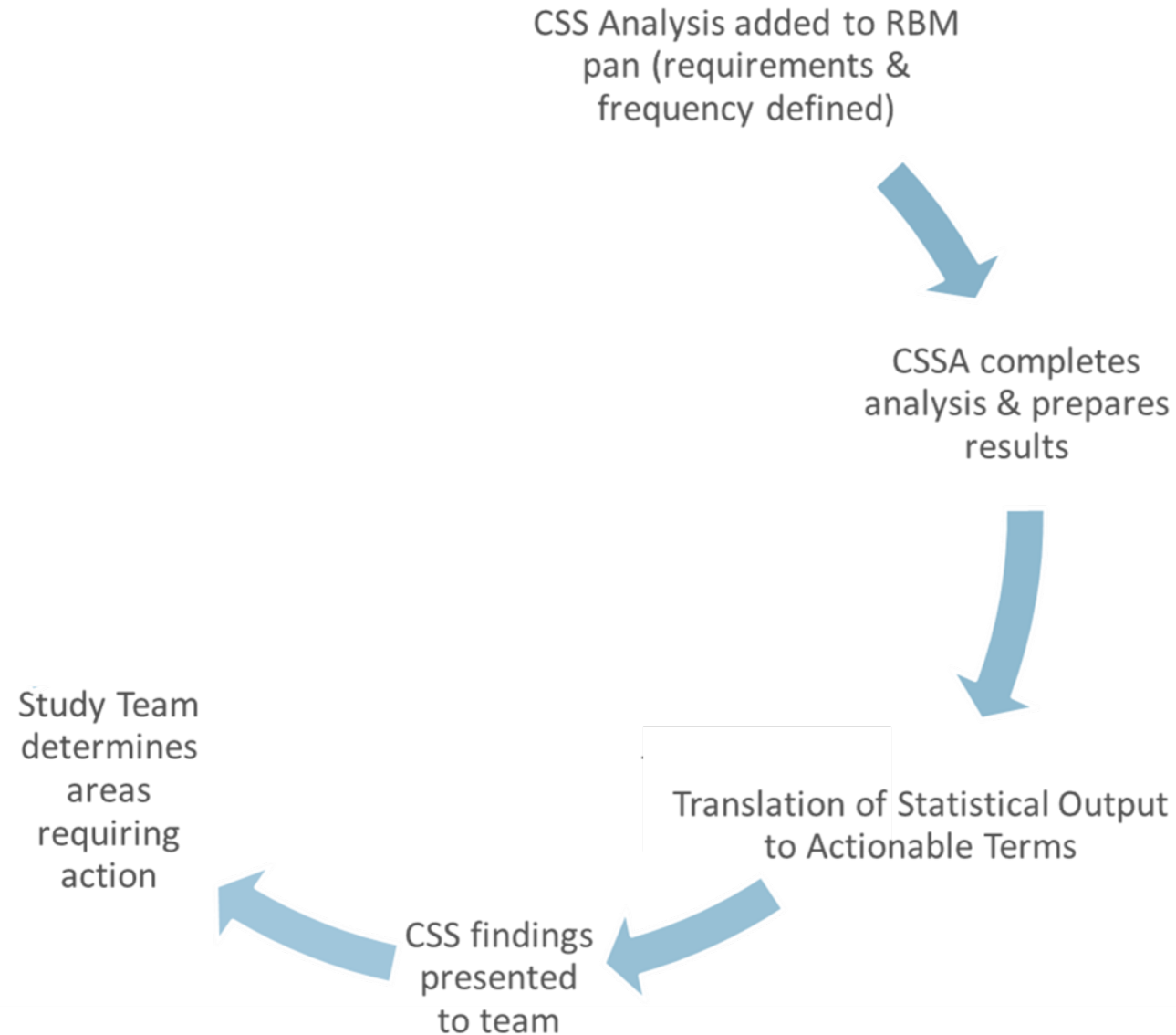


Translation of
Statistical Output to
Actionable Terms

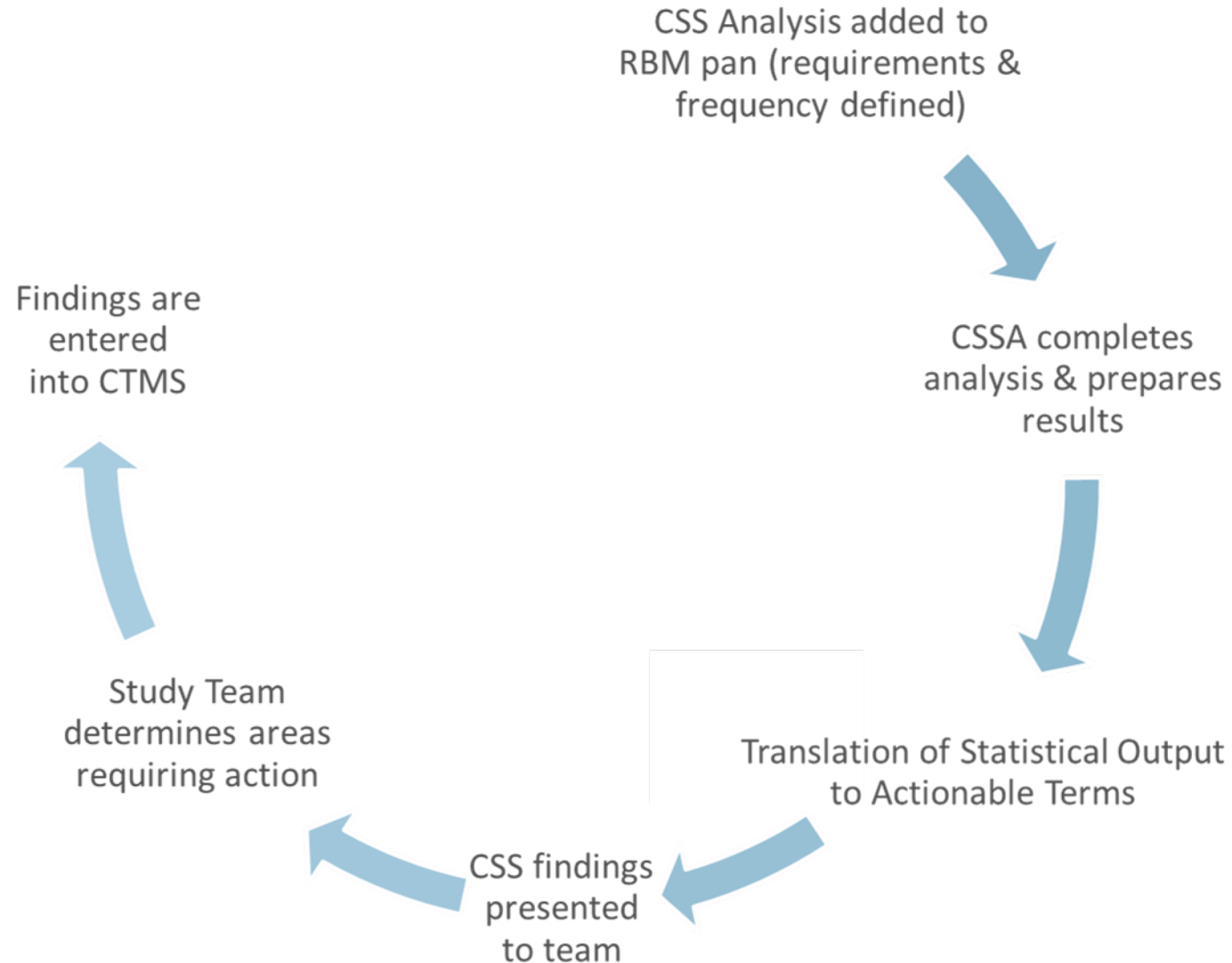
Methods: A Detailed Process



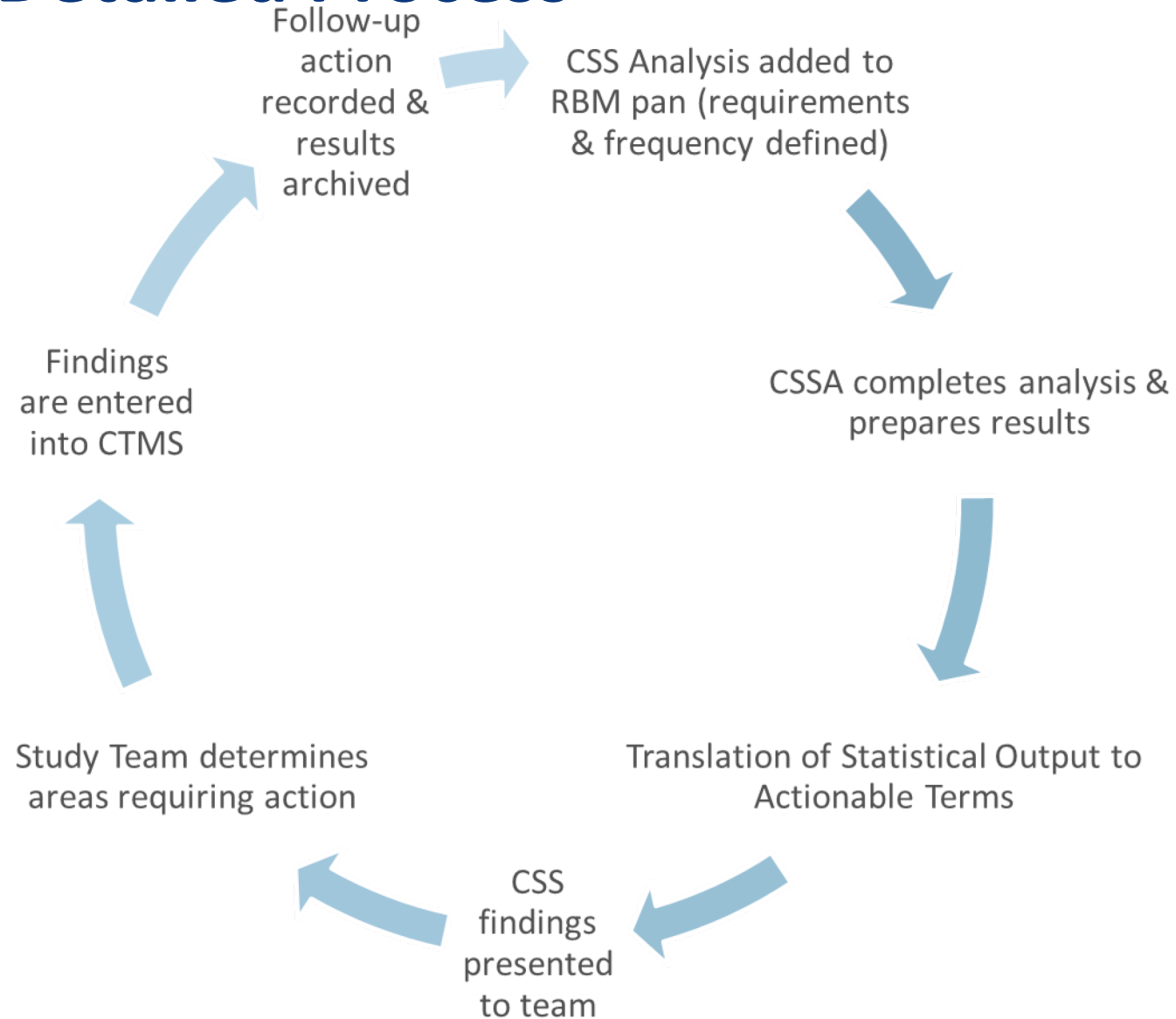
Methods: A Detailed Process



Methods: A Detailed Process

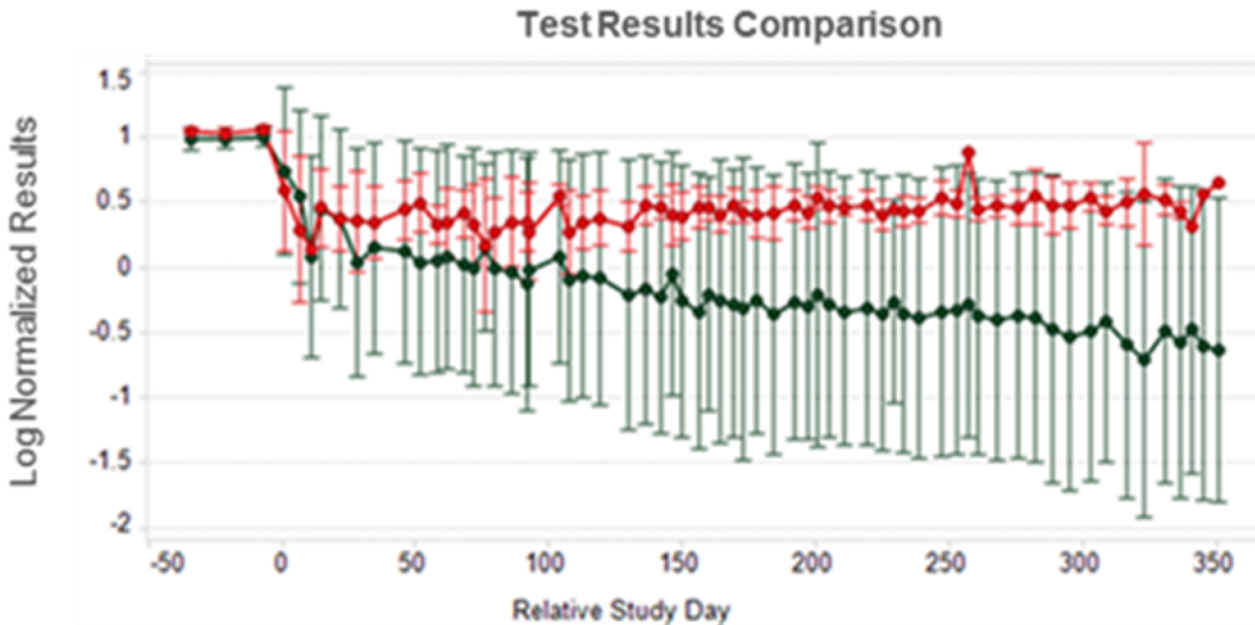


Methods: A Detailed Process



Methods: Communication of Observations

Translation of statistical outputs to actionable terms for clinical operations staff



LEGEND:

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

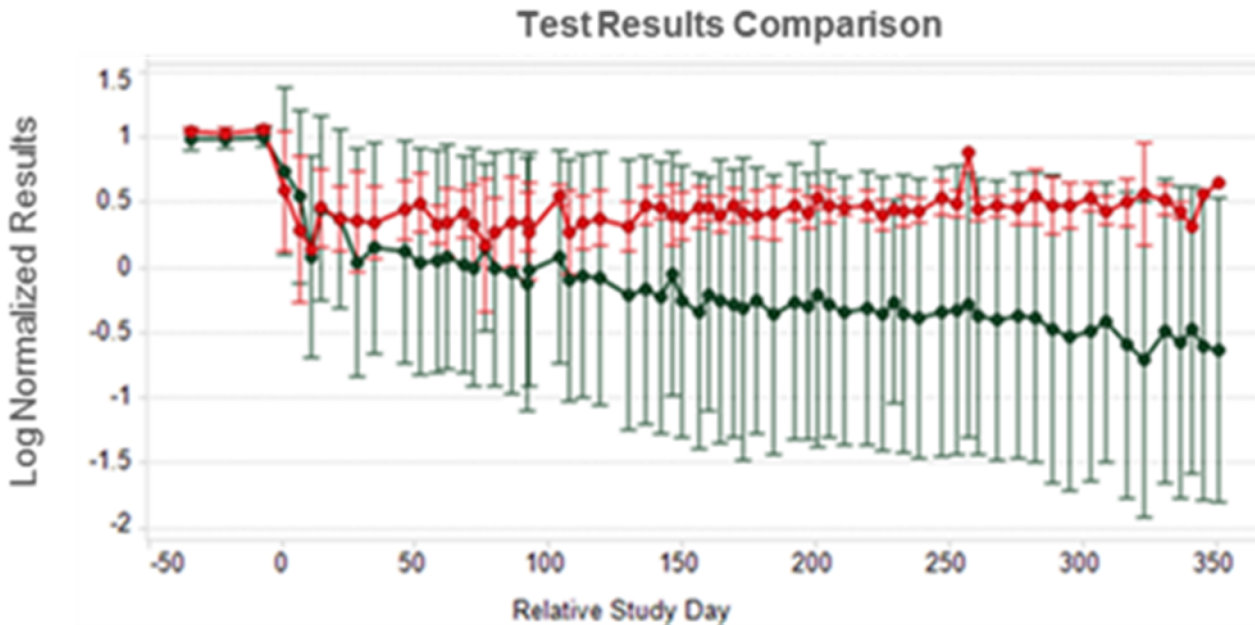
Error bars depict the standard error at each study timepoint

Statistical Terms:

- There is statistically significant evidence that, at the site, test result variance is very low. Specifically observed:
 - Low between subject variance
 - Low within subject variance

Methods: Communication of Observations

Translation of statistical outputs to actionable terms for clinical operations staff



LEGEND:

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

Error bars depict the standard error at each study timepoint

Actionable Terms:

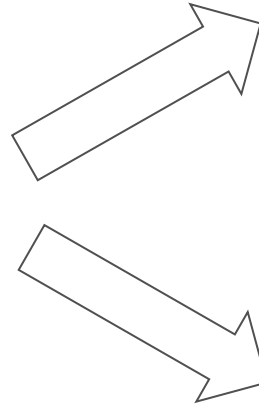
- Subject test results at the site are more similar than expected
 - Test results among subjects at study visits are closer together in value
 - The test result profile changes less over time

Methods: Communication of Observations

Providing action recommendation & potential root causes

Actionable Terms:

- Subject test results at the site are more similar than expected
 - Test results among subjects at study visits are closer together in value
 - The test result profile changes less over time



Follow-up Actions Terms:

- Medical review of subject test results
- Review of site procedures for test administration

Potential Root Causes

- Demographic similarities among subjects
- Scale not administered as intended

Conclusions

- When rolling out a novel technology to a large organization consider the following:
 - Robust training
 - Creation of support infrastructure for new staff
 - Minimize process disruption
 - Standard Documentation
 - Clear and effective communication pathways
- This process will allow CSS to grow within Janssen, further enhancing clinical trial oversight and operational efficiency

Thank You

Giordano Lo Regio

Dolly Ugi

Amy Loescher

Kris Lauwers

Stefan Van Yper

5-Nov-2018

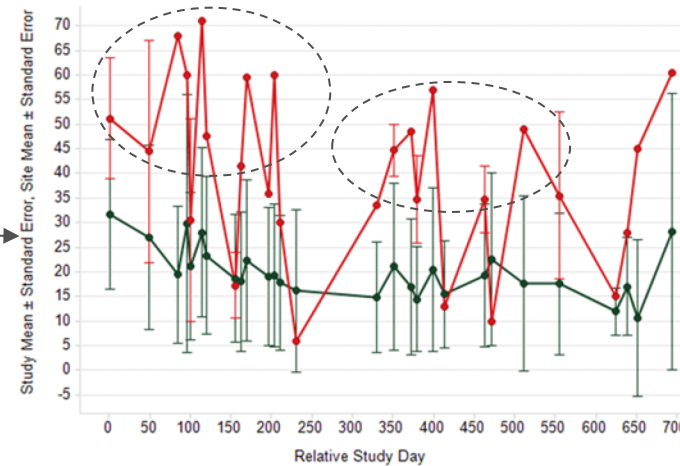
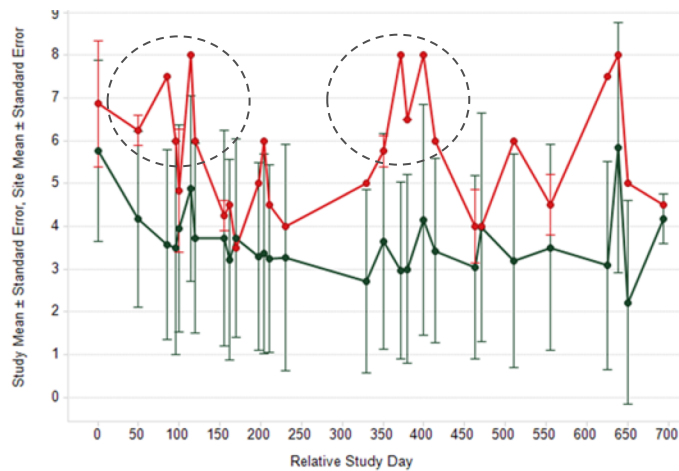
References

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2. Central Statistical Surveillance in Clinical Trials. Kris Lauwers, Stefan Van Yper, Giordano Lo Regio.
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• 5-Nov-2018

Back-up Slides

Case Study



LEGEND:

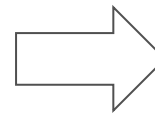
- **GREEN LINE:** Study results**
- **RED LINE:** Site results

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

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

Statistical Terms:

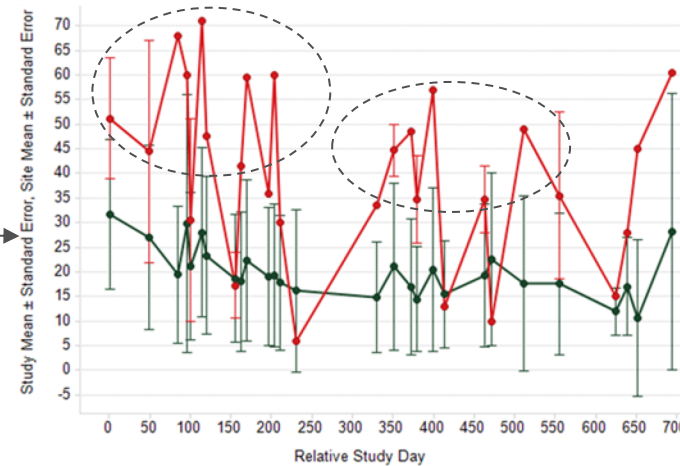
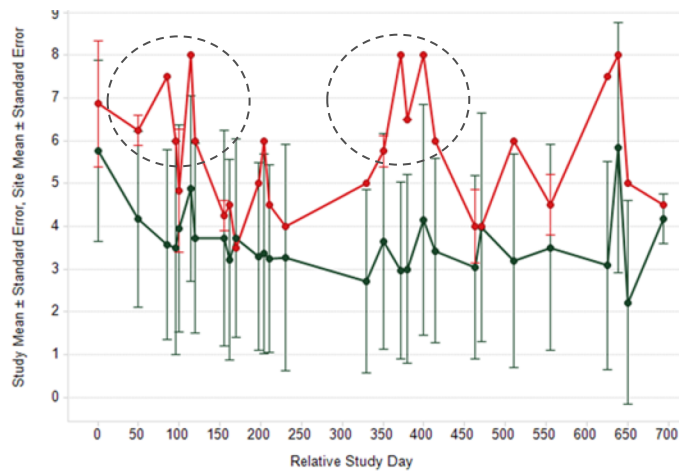
- There is statistically confirmed that:
 - questionnaire results at the site are larger in magnitude
 - there are study days where the variance is minute or 0.



Actionable Terms:

- Subject test results are greater in value than expected
- Subject test results, at some visits, are closer together in value

Case Study



LEGEND:

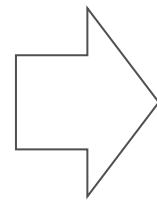
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Study averages include all data with the exception of the site under review

Follow-up Actions:

- Medical review of subject test results (study physician)
- On-site review of site process for test and administration and calculation



Follow-up Results:

- On-site review of source notes found that the site staff was calculating components of the assessment prior to entry in EDC. Since all calculations were programed to occur in EDC.
 - All site staff re-trained regarding procedures for collecting the data per protocol and EDC Completion Guidelines.