

Creating Standard Analyses and Displays for Common Safety Assessments in Clinical Study Reports

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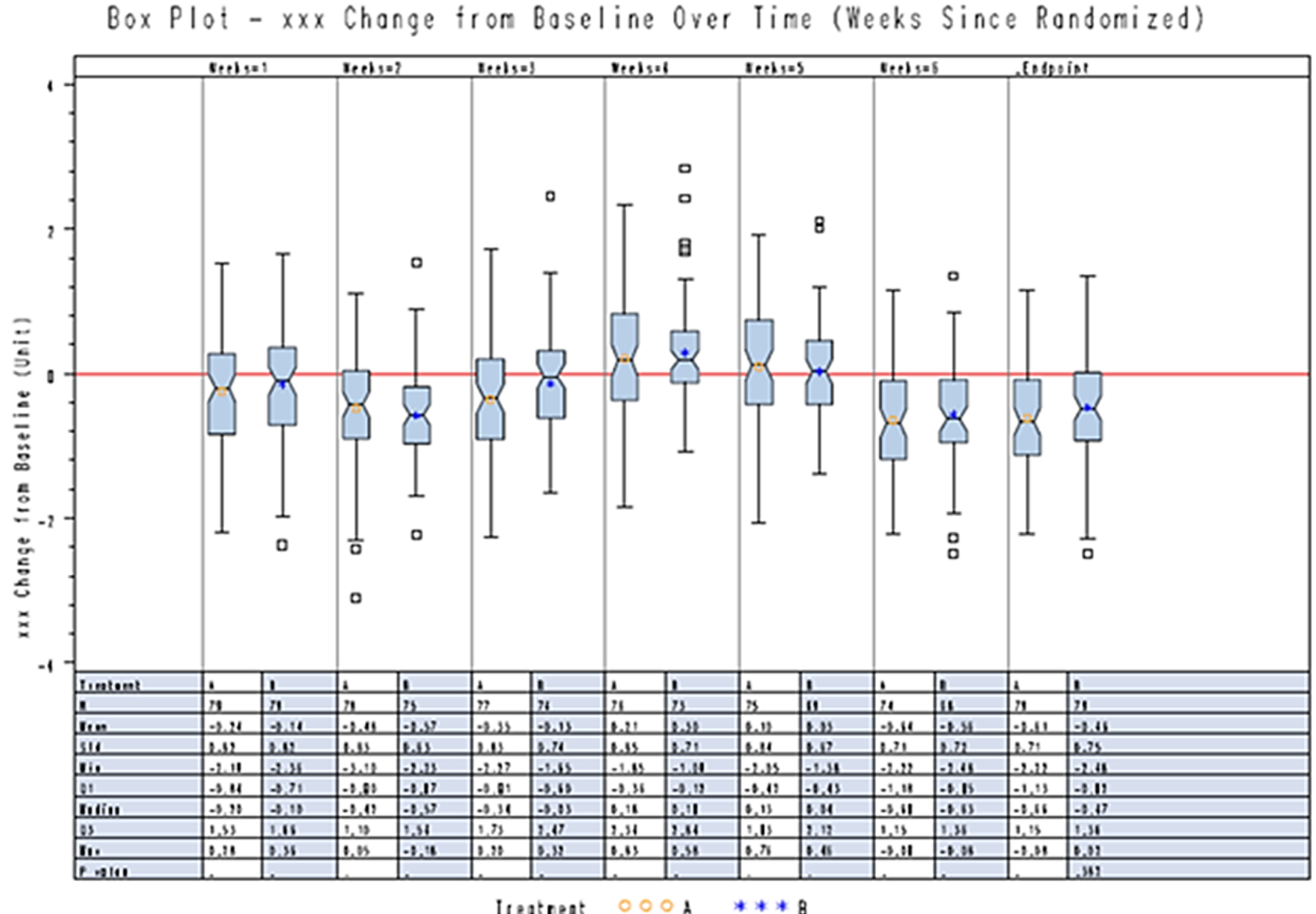
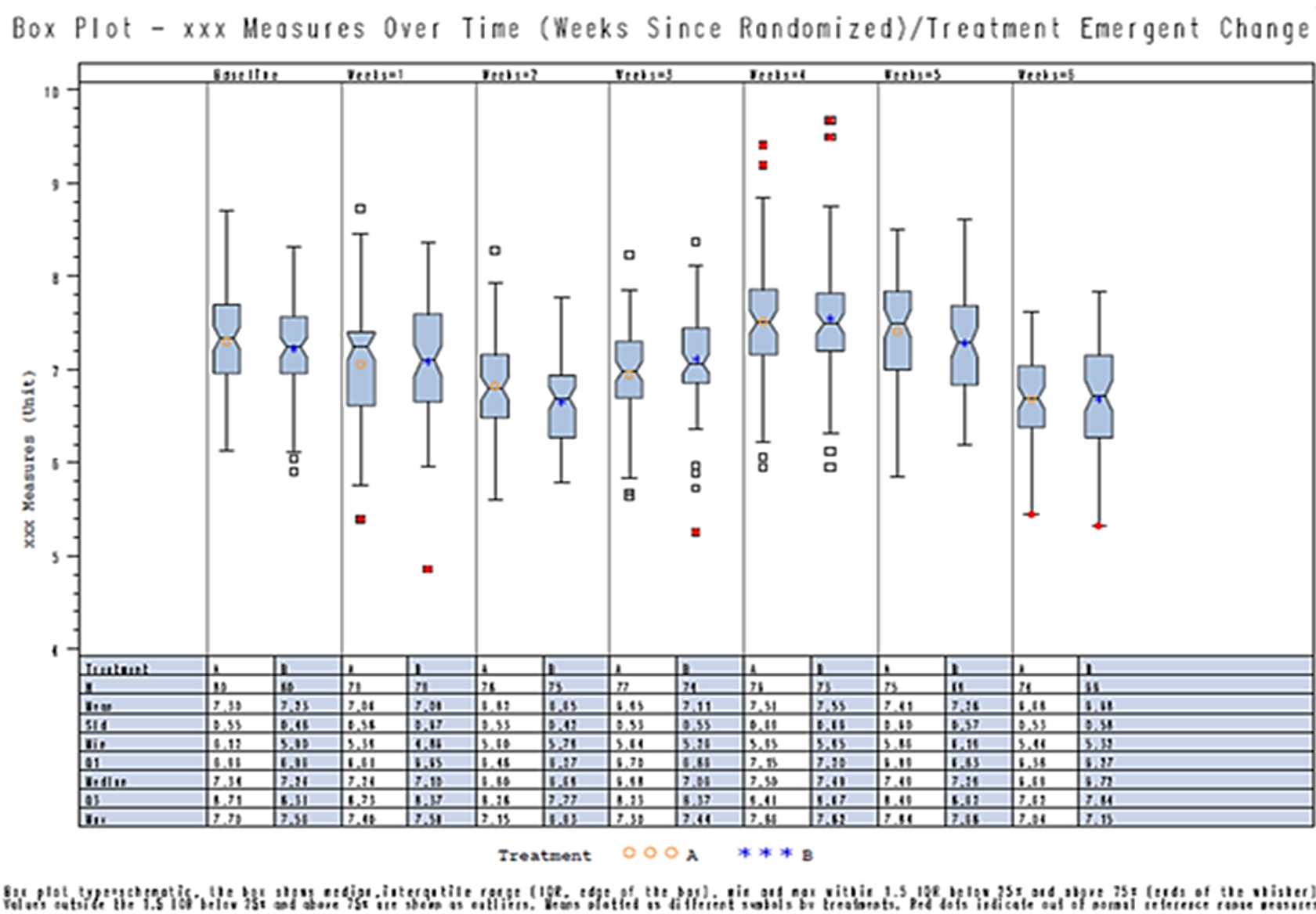
ABSTRACT

Industry standards have evolved over time for data collection (CDASH), observed data (SDTM), and analysis datasets (ADaM). Although substantial progress has been made, additional standardization can improve product development. Development of standard tables and figures with associated analyses will lead to improved product life-cycle evaluation by ensuring reviewers receive the desired analyses for the evaluation of patient safety. More importantly, having an organized process for shared learning of improved methodologies can lead to earlier safety signal detection and better characterization of the safety profile of our products. A cross-industry working group (the PhUSE Computational Science Symposium Development of Standard Scripts for Analysis and Reporting Working Group) is providing recommendations for analyses, tables, and figures for data that is common across therapeutic areas (laboratory measurements, vital signs, electrocardiograms, adverse events, demographics, medications, disposition, hepatotoxicity, pharmacokinetics). This poster will provide an update of this effort, and instructions for how to participate in the development and review process.

EXAMPLE DISPLAYS FROM THE WHITE PAPERS

Mean Changes–Boxplots

- Allows for visual inspection changes over time
- Can visually assess the potential impact of outliers on the central tendency summary statistic
 - Out of range values in red
- Easy to see treatment differences
- Summary table compliments box plot so numbers are available for textual summaries

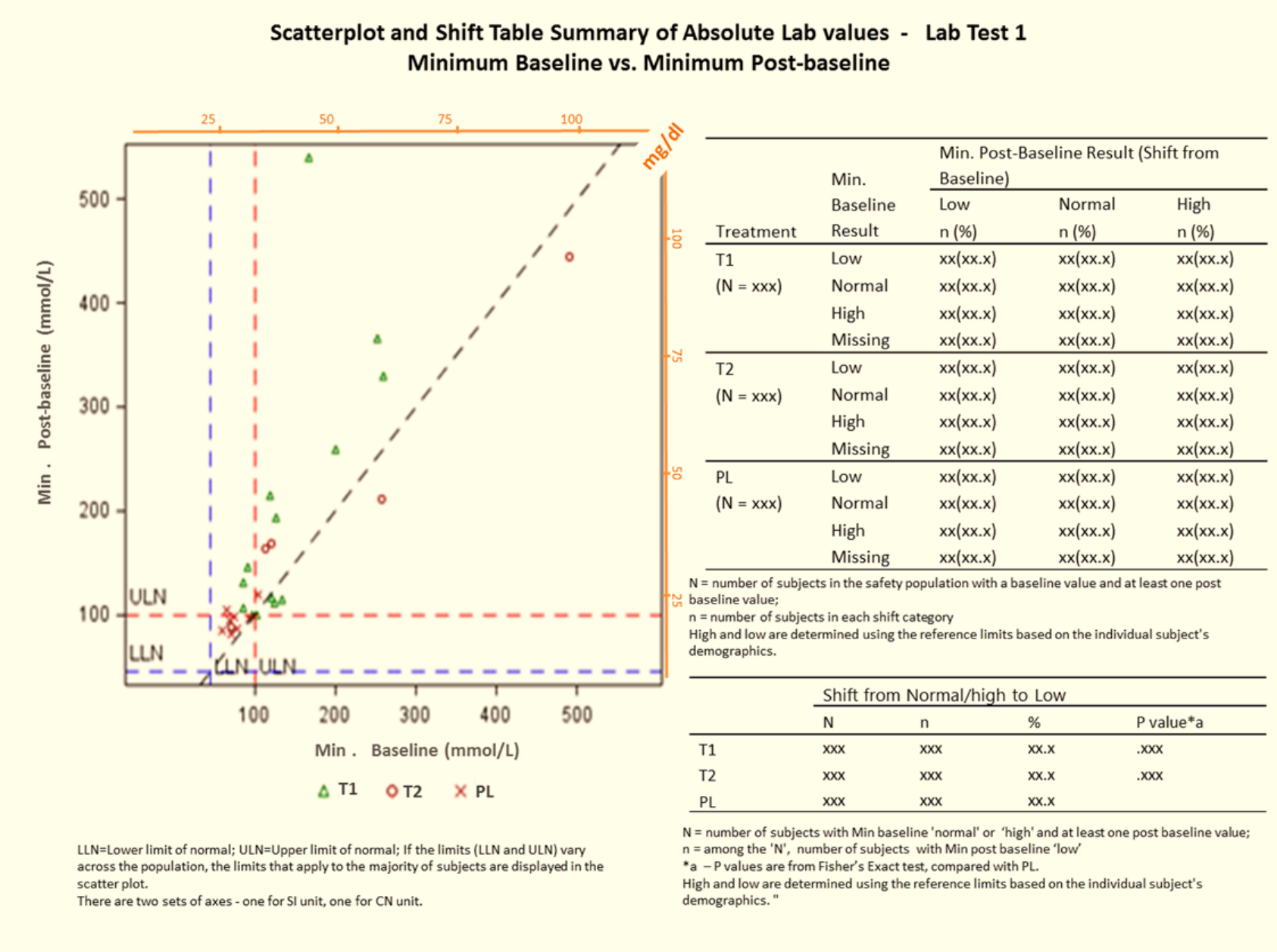
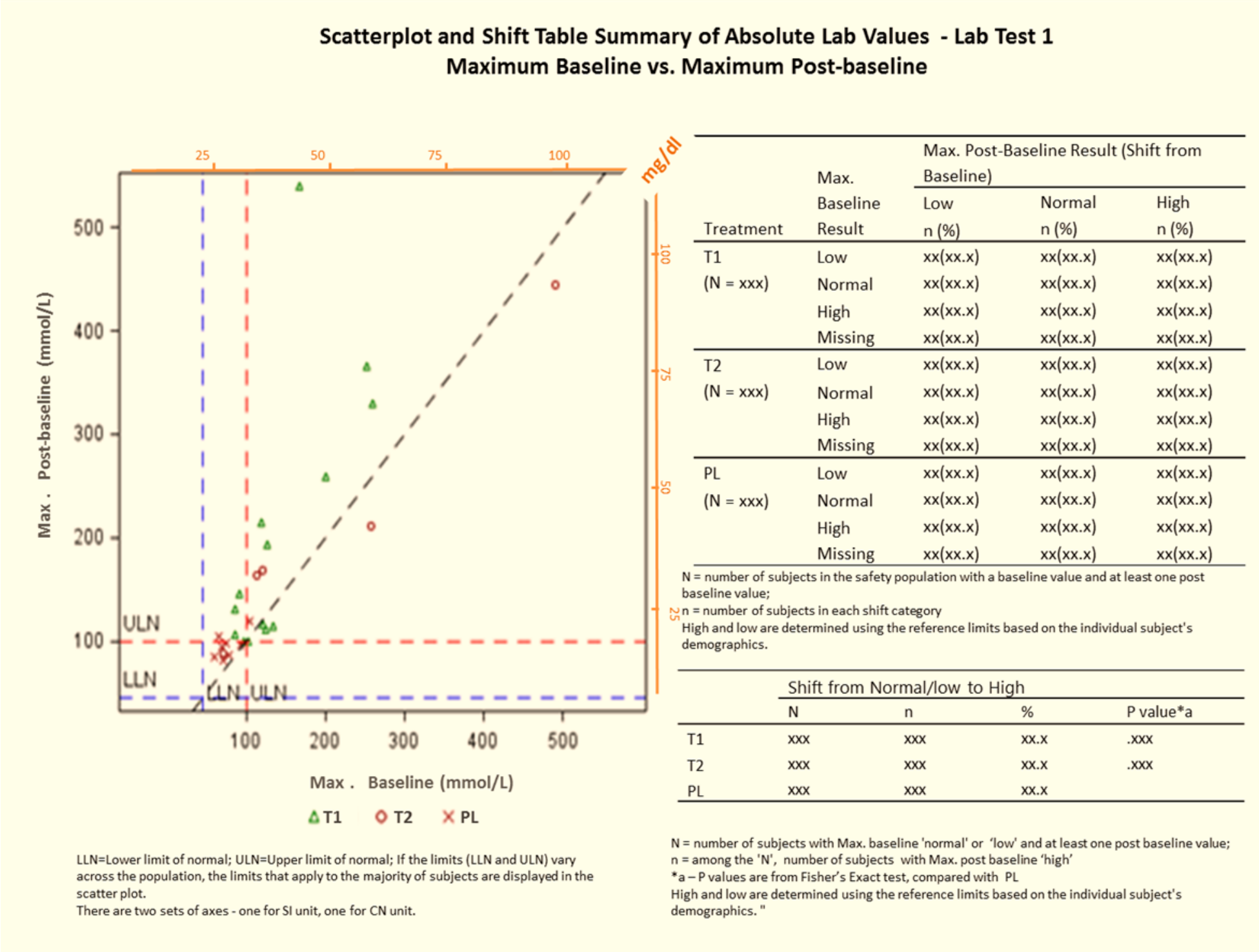
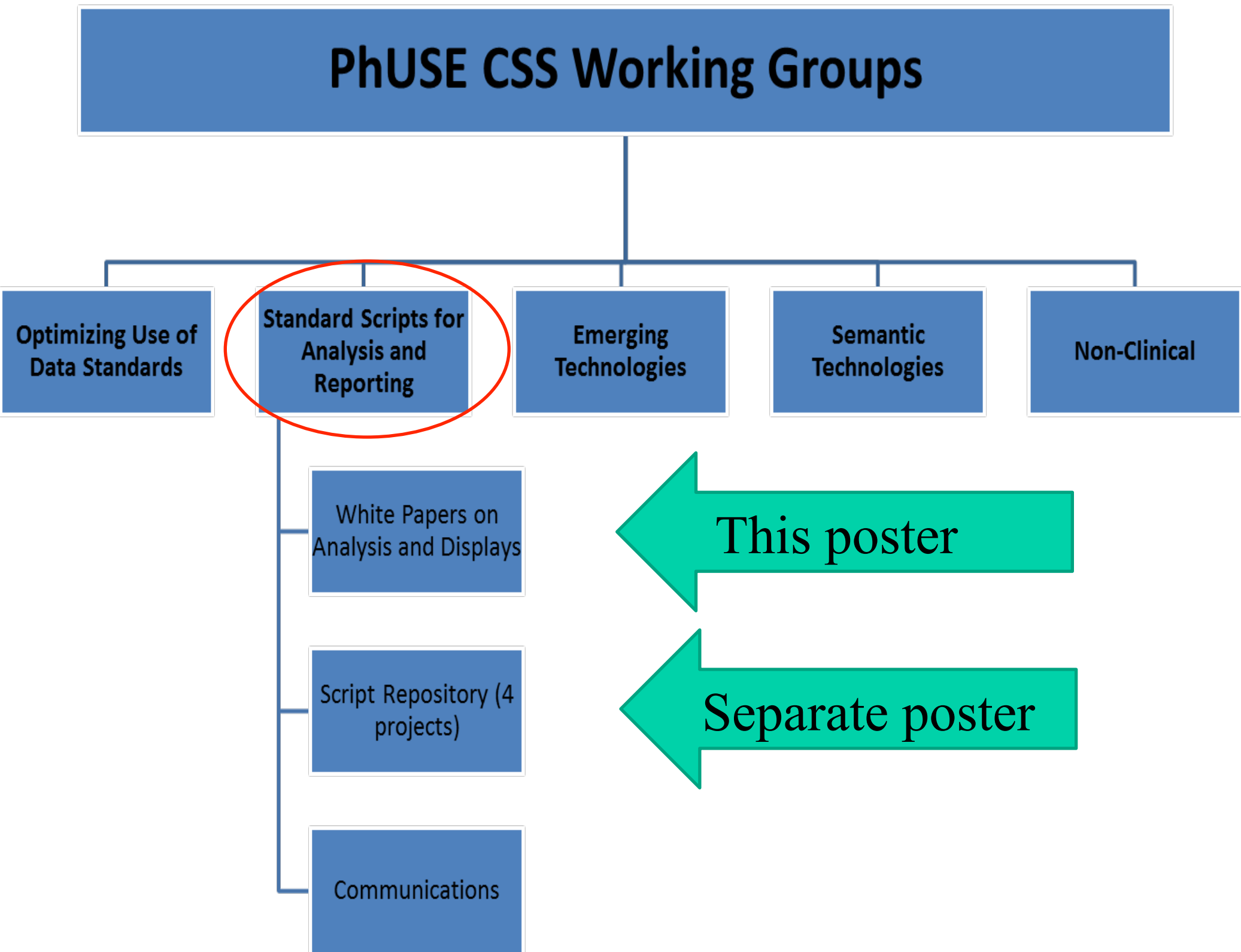


Outliers/Shifts

- Outliers/shifts analysis for numeric safety measures
 - Labs, ECGs, and Vital Signs
- Two pages per laboratory analyte
 - One for Max. baseline vs. Max. post-baseline
 - Another identical one for Min. baseline vs. Min. post-baseline
- Scatter plot
 - Shows patient-level information
 - Allows quick browsing through a large amount of information

- Shift table
 - Shows useful summary-level statistics
- Shift to high/low table
 - Shows concise summary-level statistics
 - Allows for easy assessment of treatment difference

THE BIG PICTURE – WHERE WE FIT IN

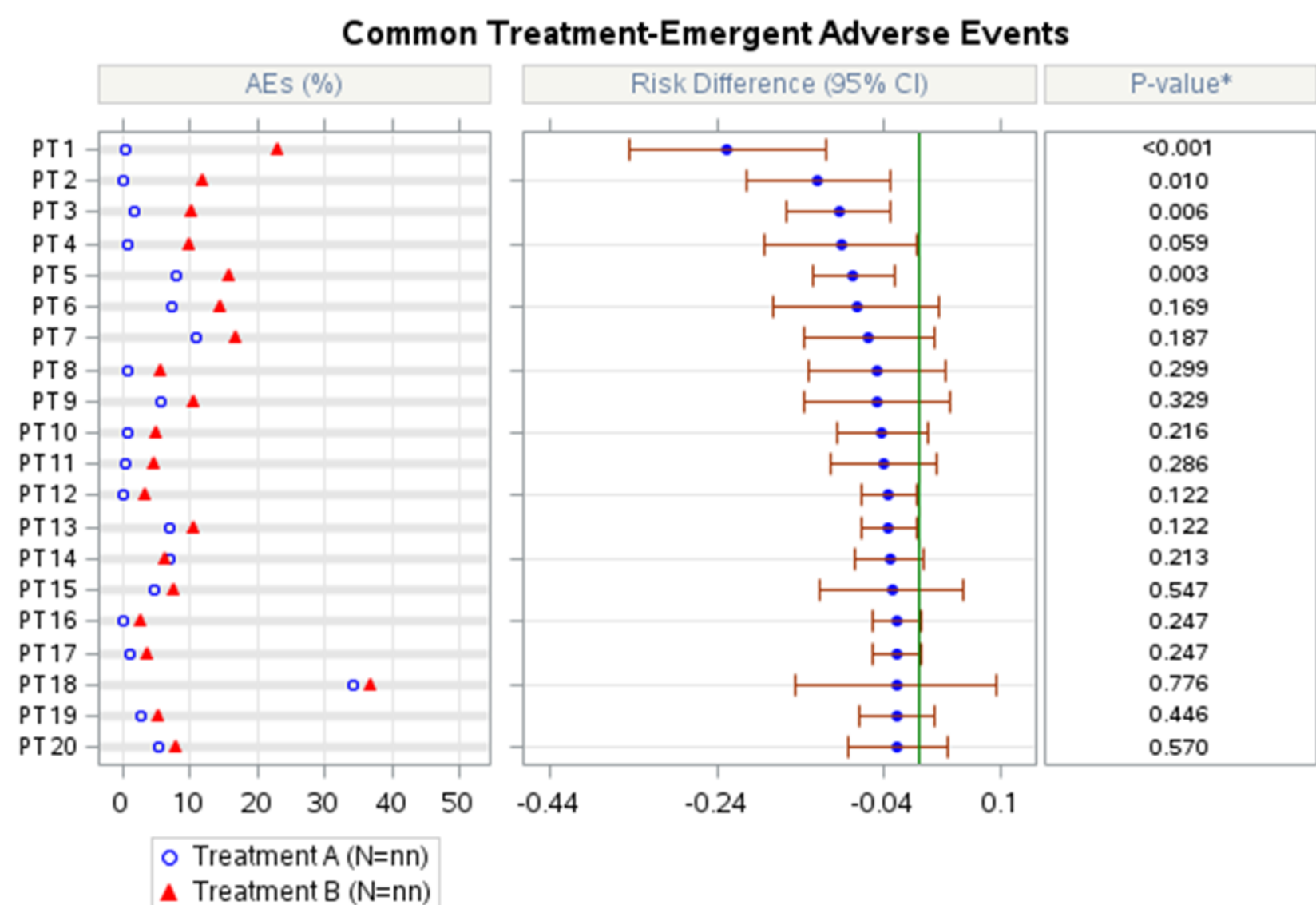


Adverse Events

- A single visual display that contains both percentages and risk differences

PhUSE WHITE PAPERS - STATUS

- Seven white papers at various stages
 - ECGs, Vitals, Labs – Central Tendency
 - Finalized October 2013
 - ECGs, Vitals, Labs – Outlier/Shifts
 - In progress
 - Adverse Events
 - In progress
 - Demographics, Disposition, Medications
 - In progress – Target Fall 2014
 - Hepatotoxicity
 - In progress
 - Pharmacokinetics
 - Finalized March 2014
 - QT Studies
 - In progress



Includes treatment-emergent adverse events of at least x% (before rounding) in Treatment X, sorted by risk difference
*P-value from Fisher's Exact Test

CONCLUSIONS

- Industry standards have evolved over time for data collection (CDASH), observed data (SDTM), and analysis datasets (ADaM).
- Development of standard tables and figures with associated analyses and code is the next step.
- Having an organized process for shared learning of improved methodologies can lead to earlier safety signal detection and better characterization of the safety profile of our products.
- We welcome new members! Contact information on www.phusewiki.org

Final White Papers: www.phuse.eu
Draft White Papers: www.phusewiki.org

Code to Create Tables, Figures, and Listings from the White Papers