Risk Based Data Quality Monitoring Utilizing Data Analytics and Recorded PANSS Interviews in Global Schizophrenia Trials

David G Daniel, MD¹ and Alan Kott, MD²
¹Bracket, McLean, VA and ²Bracket, Prague, CZ

BACKGROUND
- Outlier analysis of blinded data for aberrant rating patterns and patient selection anomalies can be paired with audio/video surveillance to cost effectively identify at-risk sites in global schizophrenia clinical trials.

METHODS
- Utilizing centralized, blinded data quality monitoring of 41,555 PANSS assessments in ten international schizophrenia clinical trials, norms were created for data patterns selected by sponsors as potentially at risk for measurement error or idiosyncratic patient selection. Based on these risk factors, a composite score or “dashboard” was created ranking each site based on quality measures. Sites of concern were subsequently subjected to more intensive, remote, centralized review of recorded patient interviews by external experts. The quality of recorded interviews and ratings was remotely assessed by independent reviewers for 2,943 PANSS assessments.

- In the illustrations of adaptive monitoring Sites 397 and 762 (site numbers fictionalized) were evaluated on four risk factors specified by the sponsor: 1) large between-visit PANSS changes; 2) erratic PANSS changes; or 3) 100% identical PANSS scores from visit to visit. If anomalies were determined by blinded data monitoring, additional scrutiny was employed by external review of recorded patient visits. Large between-visit changes were operationally defined as change >2 SD above the mean for that visit compared to other sites participating in the same protocol. Erratic between-visit changes were operationally defined as 2 consecutive visits with a large change as defined above and the changes had to be in opposite directions.

CONCLUSION
- Risk based outlier analysis of blinded data for aberrant rating patterns and patient selection anomalies can be paired with audio/video surveillance to cost effectively identify at risk sites in global schizophrenia clinical trials. Allowing sites to “opt out” of audio/video surveillance complicates interpretation of data anomalies. In addition, audio/visual surveillance has the potential to identify short point scoring irregularities that may not emerge in outlier analysis.

RESULTS
Summary of Results I:
- Based on independent review of audio and/or video recorded PANSS assessments, interview quality was rated as excellent, adequate with some deficiencies or inadequate in 75.44% (n=2221), 23.2% (n=683) and 1.36% (n=40) of visits, respectively.

Summary of Results II:
- Proper application of the PANSS instructions and anchor points was independently rated as excellent, adequate with some deficiencies, or inadequate in 75.98% (n=2236), 22.8% (n=671) and 1.22% (n=36) of visits, respectively.

Summary of Adaptive Monitoring Example I:
- The Site of Concern was an outlier on factors 1 and 2 (> 3 SD above the mean) but refused to allow interviews to be recorded for external review to allow independent assessment of measurement error. The site was not allowed to enroll additional patients.

Summary of Adaptive Monitoring Example II:
- The Site of Concern was not an outlier on large score or erratic score changes but more than 15% of visits were 100% identical. Recordings of patient interviews were scrutinized. The proportion of discordant PANSS ratings (>2 difference between site and independent rater) exceeded 60%.