Visual Analytics in Risk-Based Monitoring (RBM) of Clinical Trials
Visual Analytics tool developed specifically for reviewing clinical data

- Intuitive user interface to perform safety and efficacy review through clinically relevant reports and data visualizations
- Understands ‘patient’, ‘baseline’, ‘endpoint’, etc.
- Integrated with all industry standard clinical data sources
- Dynamic multi-study pooling
- Built-in ‘patient identification/drill down’
- Patient review tracking (with critical data review)
- Many clinical data specific graphics, tabulations, profiles, risk assessments, etc. including defining critical data
JReview

Integrated with industry standard clinical data sources – UI consistent

- **Data Management Systems:**
  - Oracle Clinical, Oracle Clintrial
- **EDC Systems:**
  - Medidata Rave, Oracle Inform (reporting database), DataLabs
- **Drug Safety Systems:**
  - Oracle ARGUS, ARISg, Oracle AERS
- **Data Warehouse Environments:**
  - Oracle LSH (JReview built-in LSH ‘connector’)
  - Oracle CDC
  - Entimo EntimICE
  - eClinical Solutions eGreX
  - SAS Drug Development
  - FDA – JANUS/CTR (new environment)
- **SAS environments – ‘pure SAS environment’**
- **Custom configured customer database environments.**
- **CTMS data via dblink, etc.**
Facilitating Modernization of the Regulatory Review Process

Source: Liliam Rosario, Ph.D., Director, Office of Computational Science, PhUSE CSS 2014
JumpStart the Regulatory Review: Applying the Right Tools at the Right Time to the Right Audience
JReview Standard Analysis – Hy’s Law Plot

Source: Lilliam Rosario, Ph.D., Director, Office of Computational Science, PhUSE CSS 2014
JumpStart the Regulatory Review: Applying the Right Tools at the Right Time to the Right Audience
Members of TransCelerate have identified clinical study execution as the initiative’s initial area of focus. Five projects have been selected by the group for funding and development, including: development of a shared user interface for investigator site portals, mutual recognition of study site qualification and training, development of risk-based site monitoring approach and standards, development of clinical data standards, and establishment of a comparator drug supply model.
Risk Based Monitoring (RBM)

◆ Traditional monitoring
  ● 100% Source Data Verification
  ● Error detection not in real time but at time of visit
  ● Monitoring visits scheduled based on data volume or periodically
  ● Reactive
  ● Random and highly error-prone
  ● Extensive resource utilization and cost

◆ Risk Based Monitoring
  ● Centralized (data-driven) monitoring
  ● Real-time error detection and continuous monitoring
  ● Monitoring visits triggered by risk indicator thresholds
  ● Proactive
  ● QbD built-in via intelligent data tools and processes
  ● Cost savings via targeted onsite monitoring
Risk Based Monitoring (RBM)

Monitoring Recommendations (FDA/EMA)
◆ Conduct a risk assessment to identify and evaluate risks to critical study data and processes
◆ Design a monitoring plan tailored to address important and likely risks identified during risk assessment

Risk Metrics
◆ Site Performance Metrics:
  ● Enrolment and randomization rates, screen fail rate/reason, dropout rate/reason, protocol violations, milestones, documentation/audit, monitoring visit attributes, ...

◆ Site Quality Metrics:
  ● Over/underreporting of lab measurements, AE rates, CTC grades, ...

◆ Site Data Metrics:
  ● eCRF entry, query rates against eCRFs, source data verification of eCRFs, missing pages, lag between visit and CRF data, lag between queries and responses

➢ Site Scores: Combining metrics for rapid (adaptive) assessment
Out of the box Analytics support for Risk Based Monitoring

◆ Centralized monitoring teams can define key risk categories and indicators from all clinical & operational source data available, set thresholds, and specify suggested actions

◆ The JReview RBM Data Browser allows for the design of aggregated risk-based monitoring reports which can be scheduled in regular intervals to push monitoring activity plans out to site monitors/CRAs

◆ Periodic ‘risk factor’ batch execution

◆ The newly developed native iPad app provides easy access to key RBM metrics and recommended actions for CRAs and monitors in the field

◆ Visualization of risk evolution by site/country/region based on multiple risk indicators & -categories
RBM Risk Indicator Definition

Key Risk Indicators, thresholds, & suggested actions
Definition within JReview with test run ⇒ scheduled periodic execution
RBM Data Browser

Risk Indicator Result Visualization by site, country, or region - subset by attributes - interactively sort any columns for site ranking
Site Distribution Over Time

Site Distribution (Box Whiskers) over time – for selected site & RBM rule results table
RBM Treemap

Site – Risk Indicator weight visualization – Tree Map visualization
RBM Statistics enabled via R/SAS Programs or Import SQLs

- In addition, R- and SAS programs may be executed from within JReview after definition and registration in the JReview STAT Program Registration Browser
- STAT programs and program groups can be executed from the Object Explorer like any other JReview objects
- Alternatively, RBM-related statistical models may be embedded in import SQLs for processing upon data import

Example: Listing of the exposure-adjusted adverse event rate per study site, taking into account the total treatment duration (AEs per patient year)
Statistics enabled via R & SAS programs

Source: http://gersonides.com/minmaxscatbox
JReview RBM iPad App

New native iPad app provides easy access to key RBM metrics and recommended actions for CRAs and monitors in the field.
ICS thoughts on Risk Indicators

How we do it:
- JReview ‘template’ for custom definition of risk indicators - providing ultimate flexibility in risk indicator definition
- ‘Standard library’ based on CDISC
- Flexibility of range definitions for ‘thresholds’ – 5 levels indicator results

Different types of Risk Indicator characteristics
- Indicators based on absolute values, ranges, etc. - regardless of % of population they catch (counts, %, etc.)
- Dynamic indicators, ‘rolling average’ – outliers from group – Z scores
- Risk indicator weighting factors
- Risk categories – not lumping into a single risk score – but by categories
- Risk Categories, Project, Study, Region, Site ‘drill down’ capabilities -> to site level (& patient ID)

Then what ... - when a risk indicator fires -> taking action, recording action, etc.

Review over time to determine effects of actions

Open interface accessing the information available on risk indicator
Thank You!

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