



JMP Clinical lets data monitors explore incoming blinded data, identifying clinically impossible outliers in real time. Medical and statistical reviewers can investigate study data on an ad hoc basis or after clinical databases are locked.

A hallmark of JMP Clinical is its fluidity of movement between results for the entire trial and for specific subjects. Choose individual subjects from any graph and JMP Clinical can generate a patient profile from CDISC data, the globally recognized standard for clinical analysis and reporting. The customizable view lets you examine analysis results for one outlier or by groups according to race, sex or other characteristics. Just summarize, select, zoom in and drill down on specific details – adverse events, medical history, vital signs, and now physician comments and substance use – to display any combination of safety domains.

JMP Clinical uses CDISC data, the FDA's preferred format for clinical analysis and reporting. It organizes the review process, working behind the scenes to automate the analytics and reporting, allowing you more time to interpret and understand the results.

The software now supports 12 core CDISC domains for safety and efficacy review: demographics, adverse events, medical histories, disposition, exposure, concomitant medications, lab results, electrocardiograms, vital signs, physician comments, substance use and subject visits. With simple configuration, JMP Clinical can analyze results from any CDISC Findings domains as well.

As one of the first tools that inherently understand ADaM data, JMP Clinical is a great option for clinicians and biostatisticians migrating into the modern review environment. Its optional 64-bit

platform brings even more power to the analysis of vast data sets.

JMP Clinical is also a valuable tool for reporting during the submission process. It formulates adaptable patient narratives that medical writers can finesse and include in the Clinical Study Report (CSR) for NDA submission, cutting down on this time-consuming step, which is required for FDA approval.

You can also rely on JMP Clinical to:

- Explore data visually and interactively, replacing static tables and listings.
- Examine relationships between events, findings and interventions using dashboard visualizations of distributions and incidence screen analyses by demographic interactions.
- Select specific time windows for almost any analysis.
- Share reports easily, streamlining communications between internal reviewers, and then between sponsor organizations and regulatory agencies.
- Fit advanced statistical models, including those with time windows (Figure 1).
- Compare results across testing sites or countries with mapping capabilities (Figure 2).

The Clinical Starter menu (Figure 3) helps you load CDISC studies and follow FDA reporting guidelines in logical sequence. A customizable, menu-driven desktop system lets you see and explore safety and efficacy data from every angle, and then easily share findings with others. You also can use dialogs to manipulate data on the fly and streamline interactions between collaborating groups.

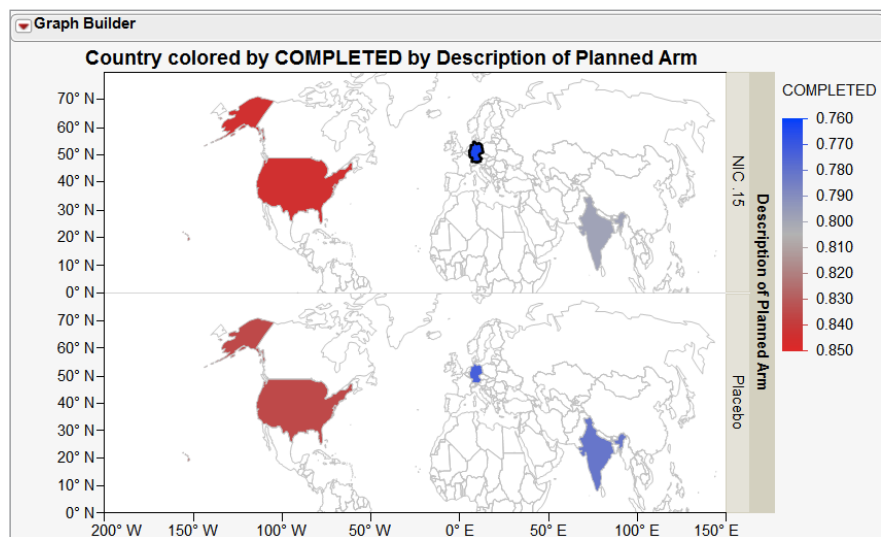


Figure 2. The mapping feature in Graph Builder lets you choose any variable for geographic display.

“JMP Clinical doesn’t replace the statistician or the SAS programs. Rather, it “bridges the clinical-statistical divide.”

Mark Williams, Vice President and CIO, Applied Clinical Intelligence

## Interventions

The Exposure Summary process identifies differences in dose and duration of exposure across treatment groups, providing context for all downstream analyses (Figure 4). JMP Clinical includes options to choose the number of dosing groups and the duration of the time window.

Incidence screens of concomitant medications and substance use allow clinicians to identify drug-drug interactions.

## Events

Following FDA Reviewer Guidance principles and ICHE3 guidelines, JMP Clinical enables analysis of event rates and estimation of risk over time, while helping you rapidly explore events, such as medical history, disposition and adverse events, as well as possible differences in subgroups. You can easily select these subgroups with Distribution dashboards that summarize by age, sex, race, treatment group and site.

Incidence screens, the principal safety analyses for adverse event identification, perform a Cochran-Mantel-Haenszel test, yielding volcano plots of multiplicity-adjusted p-values by risk difference, relative risk or odds-ratio (Figure 5). The bubble size indicates the total incidence of an event that occurs for both treatments combined. For an alternative view, create a relative risk plot from the same report (Figure 6). Select adverse events (bubbles) of interest to determine the frequency of co-occurrence in the study population using a Venn Diagram (Figure 7).

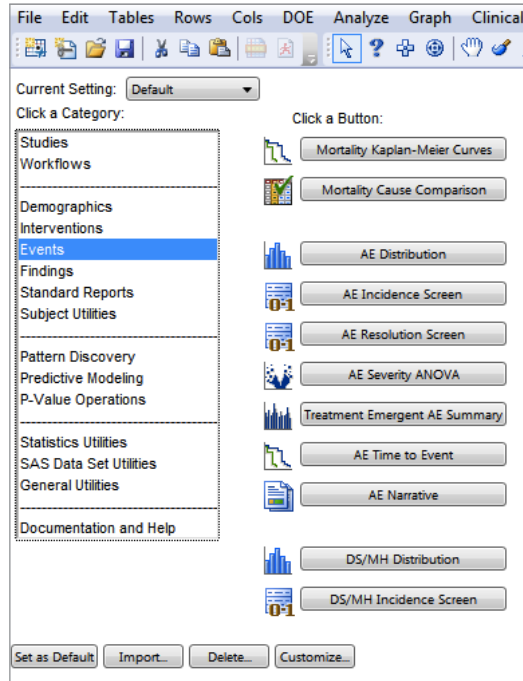


Figure 3. A simplified Starter menu helps users easily choose specific reports and analyses for dynamic visual exploration.

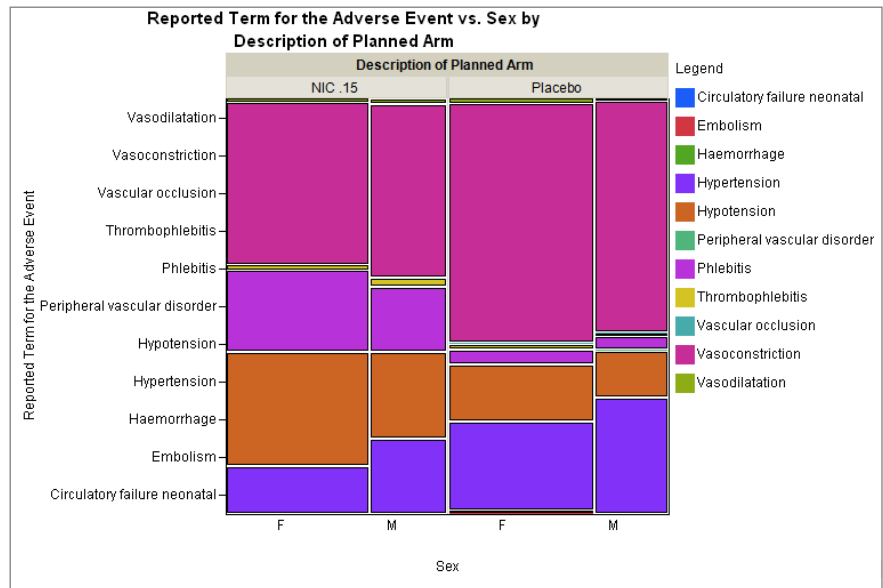


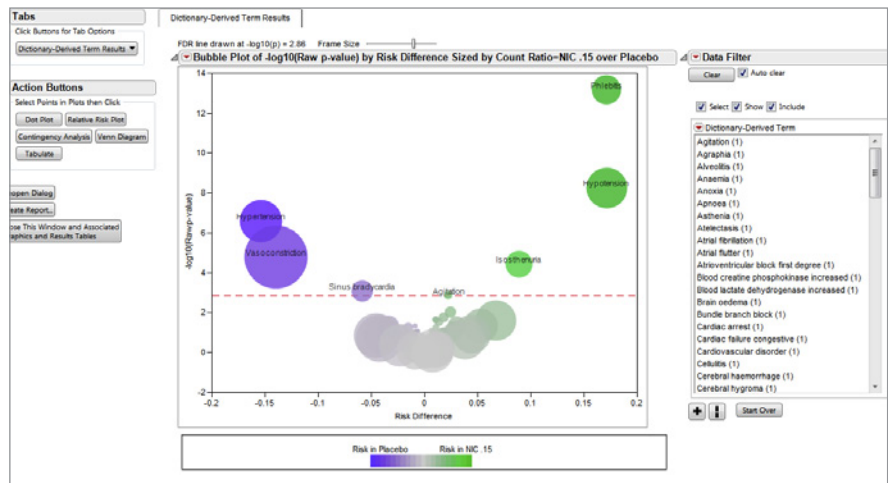
Figure 4. Use Graph Builder’s Mosaic Plot to compare adverse events, here from the vascular body system, by sex across treatment groups.

JMP Clinical utilizes multiple testing methods, such as Holm, Hochberg, Bonferroni or the double false discovery, mitigating the risk of over-reporting adverse events. The MedDRA hierarchy allows examination of verbatim terms, preferred terms, higher level terms, higher level group terms, as well as Standard MedDRA Queries, to help you discern adverse event patterns across treatment groups. The software also lets you compare the incidence of any of these term levels across the duration of the trial (Figure 1). For a more in-depth discussion of these features, please see “A Primer on JMP Clinical Incidence Screens.”<sup>1</sup>

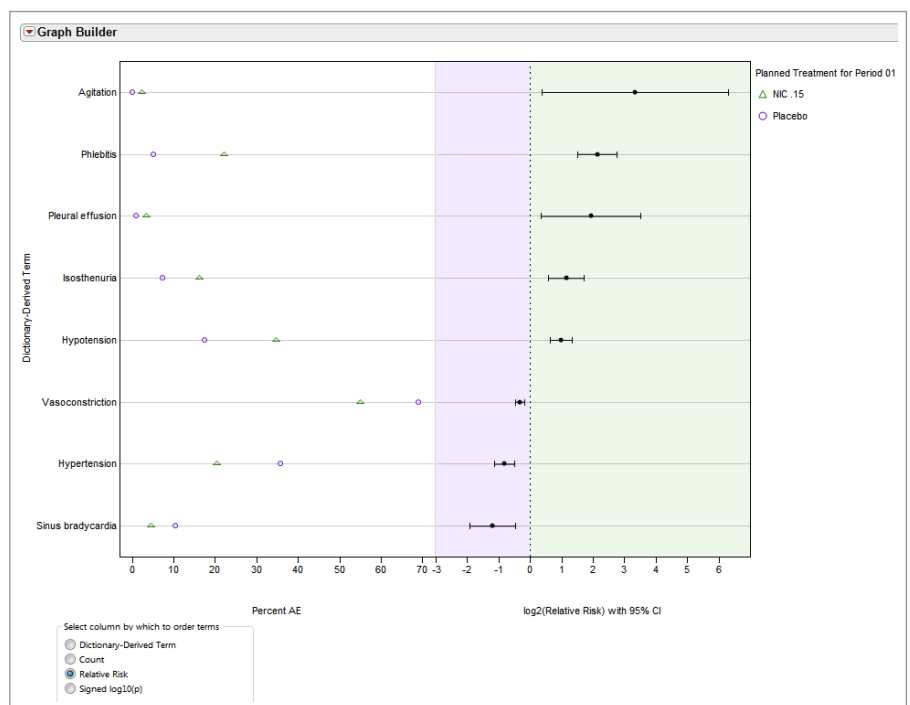
With JMP Clinical, you can determine the onset of an adverse event and its outcomes with time-to-event analyses and resolution screening, respectively. JMP Clinical facilitates time windowing in most analyses, and the AE Resolution Screen lets you monitor adverse event outcomes during a specified time window. The Severity ANOVA uses an average ranked severity, or toxicity grade score, as the dependent variable in the analysis of variance, helping clinicians to confirm whether severity differences are of concern in the safety population.

## Findings

Determining treatment compliance and establishing baseline values for lab measurements is important for all clinical reviewers. Often these data provide the means to determine both efficacy and safety evaluations. JMP Clinical equips medical reviewers with analyses for both measures of central tendency and outlier



**Figure 5. A volcano plot reveals significant adverse events across treatment groups. Focus on the upper left and right corners of the graph to identify the significant adverse events. From this dashboard display, select an Action Button and drill down for details.**



**Figure 6. From the volcano plot, drill down to a relative risk plot to sort easily by count, relative risk, significance or dictionary-derived terms.**

<sup>1</sup> Zink, R. (2011) A Primer on JMP® Clinical Incidence Screens. [jmp.com/incidencescreens](http://jmp.com/incidencescreens)

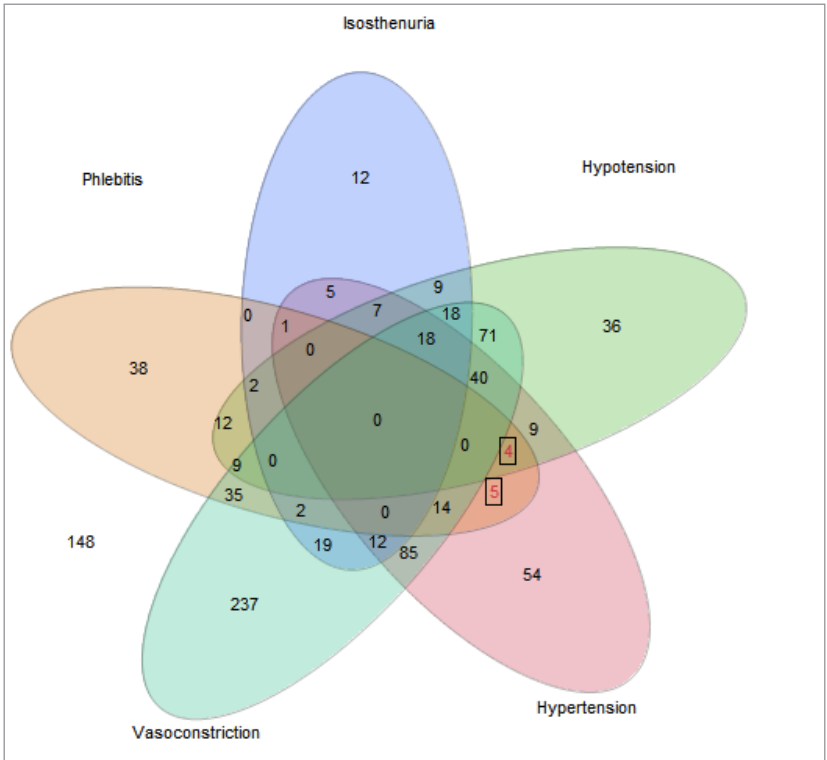


Figure 7. From the volcano plot, a Venn diagram helps identify co-occurring adverse events for subjects in the study. Then select subjects for clustering or profiling.

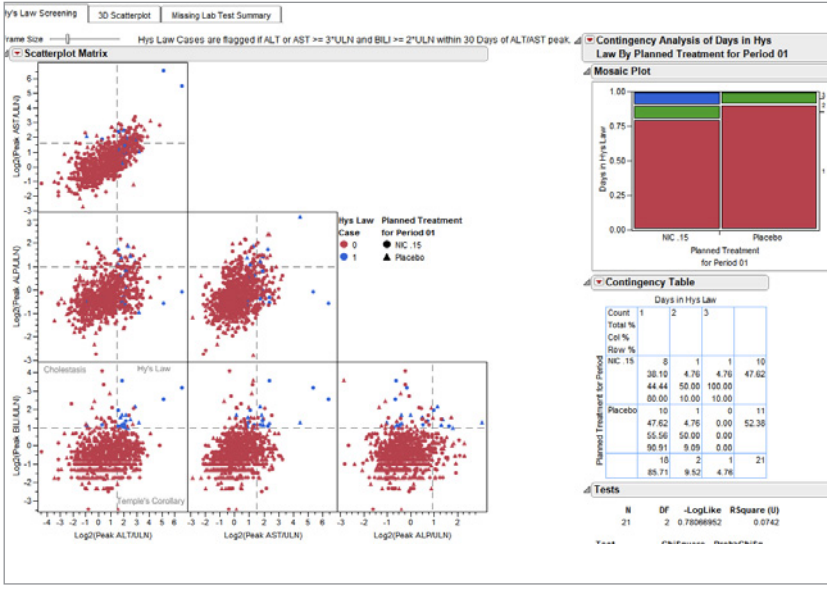


Figure 8. The industry-standard Hy's Law display in JMP Clinical is interactive for selection of subjects. A dashboard containing a scatterplot matrix of transaminases and bilirubin; mosaic plot of days until bilirubin elevation and missing lab tests report tab.

detection so that they can quickly identify potentially harmful symptoms that develop during the clinical trial.

Nearly all of the visualizations recommended in the FDA Reviewer Guidance are available in JMP Clinical without any programming. Distribution displays, box plots, shift plots, time trends, scatterplots and bubble plots can all be leveraged to explore any Findings domain of interest. Interactive bubble plots show the rate of change for multiple lab tests, measuring trends over time across treatment groups or other categories. Baseline ANOVA analysis measures the change from baseline on the trial via box plots or shift plots, a prescribed analysis from the guidance documents. A scatterplot in the form of a volcano plot displays a summary view of significantly different lab tests.

The Findings time-to-event process permits you to use value cutoffs to arbitrarily define an event from any Findings domain before performing an analysis. For example, one might define a hypertension event as systolic blood pressure greater than 140 mm Hg and diastolic blood pressure greater than 90 mm Hg. This helps a reviewer double-check the frequency and count of previously defined events.

JMP Clinical evaluates liver toxicity, a primary safety focus of clinical trials, by identifying subjects who meet the Hy's Law criteria described in the Drug Induced Liver Injury Guidance document set by the FDA. This hepatotoxicity analysis assesses transaminase measurements (ALT or AST) above 3\*ULN with total bilirubin above 2\*ULN within a specified number of days after transaminase

“It was clear early on that JMP Clinical will help us achieve a quicker turnaround in the drug approval process. I believe JMP has hit a home run with this tool.”

Steve Wong, Senior Director Statistical Programming, Biometrics Department, Gilead Sciences Inc.

elevation. An industry-standard scatterplot matrix displays Hy’s Law along with a mosaic plot to confirm the number of days subjects experienced elevated liver test measurements (Figure 8). Finally, a tabular report in the dashboard display shows the number of subjects who missed the laboratory tests necessary for Hy’s Law determination.

### Subject review and reporting

Automated patient profiles and patient narratives reduce the time and complexity of creating output for review and submission to the FDA. Along with subject clustering and subject filters, these features enable medical officers to quickly generate hypotheses about particular groups or subgroups within the study population.

JMP Clinical lets you instantly generate patient profiles for an individual (Figure 9) or group of subjects (Figure 10), simply by selecting subjects from a Hy’s Law graph, box plots or shift plots, to name a few. Reviewers and medical writers can also record and save unstructured text about any subject or group, noting, among other things, cases of death, serious adverse events and reasons for discontinuation. Patient profiles are customizable, displaying data from any combination of the core safety domains. Once the reports are tailored, they can be printed in PDF or RTF, making for straightforward communication of findings among review groups.

JMP Clinical can also compose a configurable patient narrative for each subject who experienced a serious adverse event during the clinical trial. Reviewers and medical writers enjoy the speed of this programmed process, using the write-ups as a starting point for the final patient narratives compiled in the Clinical Study Report (CSR) required by the FDA.

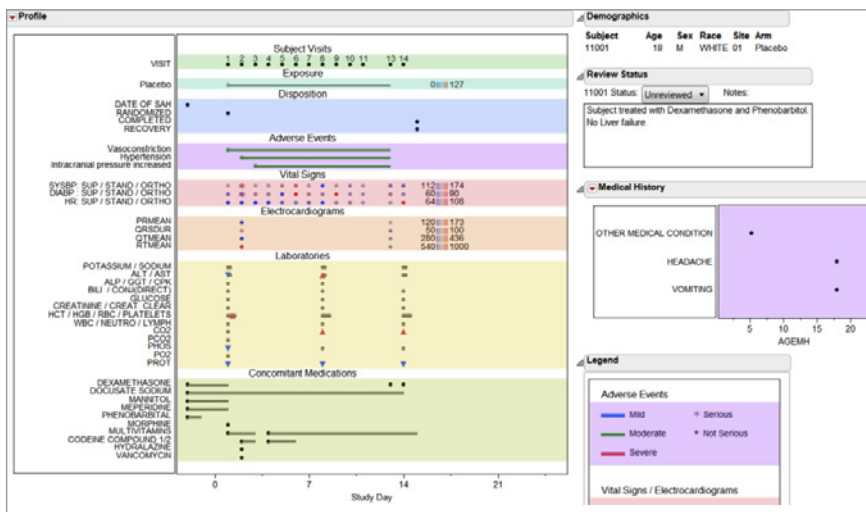


Figure 9. A patient profile dashboard allowing configuration of clinical information, notes for reviewers and printing to PDF documents.

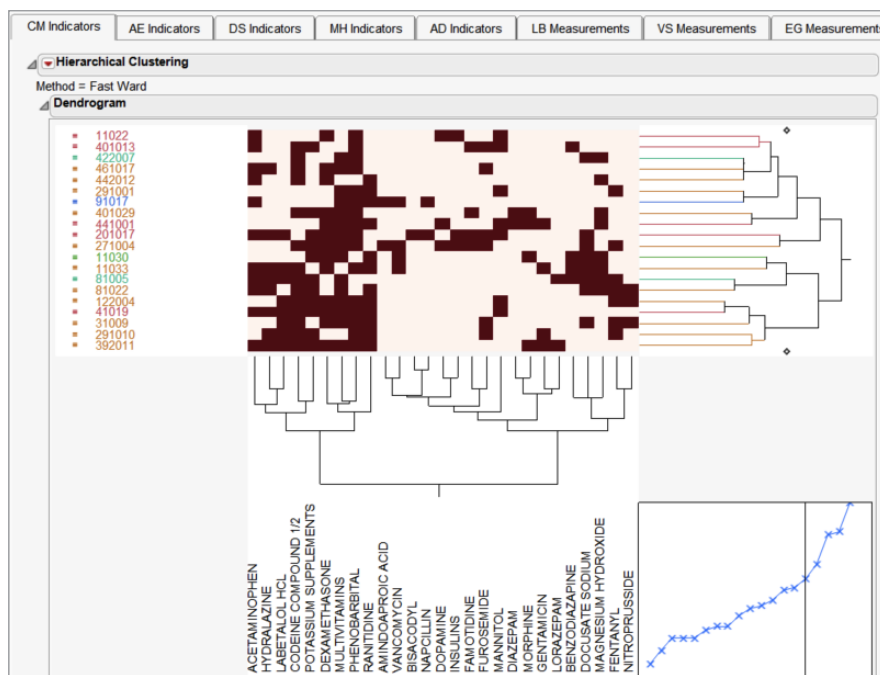


Figure 10. A Hierarchical Cluster report with two-way clustering identifies relationships between individual subjects and the events, findings and interventions included in the safety analyses for the study.

## JMP® Clinical Features

Linking dynamic JMP® visualizations with robust SAS® Analytics, JMP Clinical provides a Starter Menu that allows users rapid and focused point-and-click access to a variety of analytical processes for:

### Studies

- Add a **Study** that contains CDISC-formatted SDTM and/or ADaM data from SAS data sets or transport files.
- Create ADSL data sets and other types of ADaM data on the fly by collecting relevant slices of SDTM data.
- Rename a study or its associated folders, or delete parts or all of it with **Manage Study**.
- **Check Required Variables** in SDTM and ADaM folders for all variables required in JMP Clinical analytical processes to produce a table of results indicating missing variables and affected processes.

### Workflows

- Use **Basic Safety Workflow** to perform a complete set of standard safety data analyses with only a few mouse clicks.
- Create custom workflows with **Workflow Builder**.
- Employ **Journal Builder** to create a journal file containing results of user-specified processes.

### Demographics

- Compare **Distribution** of demographic variables across treatment arms via a oneway ANOVA or contingency analysis.

### Interventions

- Generate an **Exposure Summary** of drug exposure duration for subjects across entire study or specified time window.
- Compare **Distribution** of concomitant medications and substance use variables across treatment arms.
- Use **Incidence Screen** to perform an incidence analysis of concomitant medications or substance use between two or more treatment groups to produce a volcano plot of relative risk, risk difference or odds ratio.

### Events

- Create **Kaplan-Meier Survival Curves** and associated statistics, grouped by treatment arm.
- Compare cause-of-death frequencies between treatment arms via a contingency analysis with **Mortality Cause Comparison**.
- View **Distribution** of adverse events, subject disposition or medical history across treatment arms.
- With **AE Incidence Screen** perform an incidence analysis of all adverse events or Standard MedDRA Query terms across two or more treatment groups to produce a volcano plot of relative risk, risk difference or odds ratio. Optionally perform the incidence screen using the Double FDR methodology of Mehrotra and Adewale (2011)

to discover true signals by incorporating a grouping variable, such as body system, into the analysis.

- Analyze incidence of adverse event resolution across treatment arms using **AE Resolution Screen**.
- Perform **AE Severity ANOVA** to explore severity for each distinct adverse event that differs between time periods and/or treatment groups.
- Create tabular and graphical overviews of **Treatment Emergent Adverse Events** for the safety population by treatment arm.
- Determine time to first occurrence of an adverse event using **AE Time to Event** to perform log-rank and Wilcoxon tests between treatment groups.
- Generate **AE narratives** for clinical study reports on all AEs or SAEs with option to capture all adverse events within specified time frame surrounding AE start date.
- Use **DS/MH Incidence Screen** to perform an incidence analysis of disposition or medical history across two or more treatment groups to produce a volcano plot of relative risk.

### Findings

- Compare **Distribution** of laboratory, vital signs and ECG findings across treatment arms.
- With **Baseline ANOVA** efficiently screen all findings measurements that differ across treatment groups over the entire study or for a defined time window.
- Display **Shift Plots** to compare test measurements for a specified findings domain at baseline versus on-therapy values and performs a matched pairs analysis.
- Display **Box Plots** by treatment group representing the change from baseline in measurements for each test for specified findings domain across various specified time windows or points in the study.
- Visualize **Time Trends** for findings measurements for each subject across the timeline of the study.
- Track a pair of findings measurements over time with an animated **Bubble Plot** and select subjects of interest to display their time profiles.
- Define events using one or more findings tests to be analyzed in a **Time to Event** analysis.

### Hy's Law Screening

- Visualize peak values over the duration of a study for lab measurements pertaining to Hy's Law for detecting potential liver toxicity for all subjects across treatment arms.
- Calculate number of days subject experiences elevated liver test measurements to identify individual Hy's Law cases.
- Perform contingency analysis to compare the incidence and frequency of potential liver toxicity across treatment arms which may be used to evaluate the possibility of drug-induced liver injury (DILI).
- Tabulate number of subjects with missing lab tests.

## JMP® Clinical Features, cont.

### Standard Reports

- Generate a Study Visit Attendance Report, various Standard Safety Reports and a report of study Comments in RTF and PDF formats.

### Profile Subjects

- Examine patient profiles from any CDISC domain.
- Drill down to view demographics, disposition, safety, findings, medical history and comments for any subject.
- Profile multiple subjects simultaneously, side by side.
- Create customized patient profile templates.
- Create a PDF report and AE narrative from drill-down views.

### Other Subject Utilities

- **Cluster Subjects** to search for hidden patterns in interventions, events and findings within or across domains.
- Create interactive **Venn Diagrams** with up to five variables.
- Tailor data views using complex queries with **Data Filter**.
- **Apply Subject Filter** to any analytical process.
- **Review Status Distribution** of the subjects in a study.
- **Create Cross Domain Data** suitable for clustering, pattern discovery and predictive modeling.

### Pattern Discovery & Predictive Modeling

- Perform interactive partial correlation analysis on clusters of events to adjust for potential confounding.
- Employ dimension-reduction techniques such as principal components and multidimensional scaling to highlight major structural trends in your data.
- Compare results across nine different major predictive modeling methods, with numerous options and tuning capabilities.
- Customize predictor filtering during model construction.
- Perform predictive modeling for survival analysis.
- Assess the impact of sample size using a Learning Curve analysis.
- Sophisticated cross-validation with adjustable hold-out and iteration options to enable comparison of relative performance across multiple models.
- Learning Curve analysis assessing the impact of sample size.



SAS Institute Inc. World Headquarters +1 919 677 8000

To contact your local JMP office, please visit: [www.jmp.com](http://www.jmp.com)

SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc. in the USA and other countries. ® indicates USA registration. Other brand and product names are trademarks of their respective companies.  
Copyright © 2010, SAS Institute Inc. All rights reserved. 104419\_S73280.0811