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Work with me here...(or there or anywhere): Practical Cloud Collaboration with JMP Clinical for Clinical Trial Data Reviews

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ABSTRACT

JMP Clinical is a solution built on powerful analytics and data visualization of both SAS® and JMP® software. It provides a rich environment for generating clinical trials reviews driven by CDISC data standards (SDTM/ADaM) for safety analysis, fraud detection and data integrity/quality, operational monitoring and oversight, and data management. Configuration options to enable study and review sharing allow the solution to be a part of collaborative architecture for clinical trials data analysis and review. A scenario of such sharing using mapped network drives will be shown for generating clinical trial safety analysis reports including patient profiles and auto-generated patient narratives for medical monitor review.

With the increasing popularity and acceptance of cloud-based storage services, collaborating with colleagues, partners, regulatory agencies, and customers has never been easier. This presentation will also illustrate how, using Google Drive, JMP Clinical enables biometric teams to author and instantly share safety, efficacy, and operational reviews with monitors, medical writers, and sponsor executives. Furthermore, with automatic syncing capabilities, reviewer-generated status updates and comments are collected even while working offline. Once reconnected, reviewers receive notifications that alert them to the presence of new reviews or comments. This infrastructure supports a more flexible working environment, providing easy access of up-to-the-minute reports for personnel working in the field, even when access to the internet is tenuous. We demonstrate a simple example for the scenario of performing a clinical data science review and sharing medical anomalies with the appropriate medical staff.

INTRODUCTION

JMP Clinical is built on the premise that providing a user interface with dynamic graphical and tabular summaries directly linked to data dramatically increases efficiency in clinical trial safety and efficacy analysis. The solution, which leverages CDISC standards for the SDTM, ADaM, and SEND data models, provides role-based workflows and reviews for clinical data scientists, medical writers, data management, clinical operations, and biometrics teams. The system provides a variety of reports that analyze the special-purpose (DM, SV, SE, CO), events, interventions, and findings domains characterized by CDISC format to interrogate safety, efficacy, and data integrity signals. Reviews containing these analysis reports can be generated, saved and shared across biometric teams, medical monitors, and data managers. The software provides an architecture for adding studies and tracking ongoing snapshots of the study data; along with a notes infrastructure to add and view record/subject/site/country/analysis level review notes while performing data reviews. The software can be deployed on desktop applications and as a presentation server via Citrix XenAPP.

This paper address some of the critical aspects and challenges of collaborative clinical trial data review, including how you can leverage existing cloud-based storage services (Google Drive in this highlighting example) to create and deliver clinical reviews with JMP® Clinical software. Specifically, some of the challenges covered include the following:

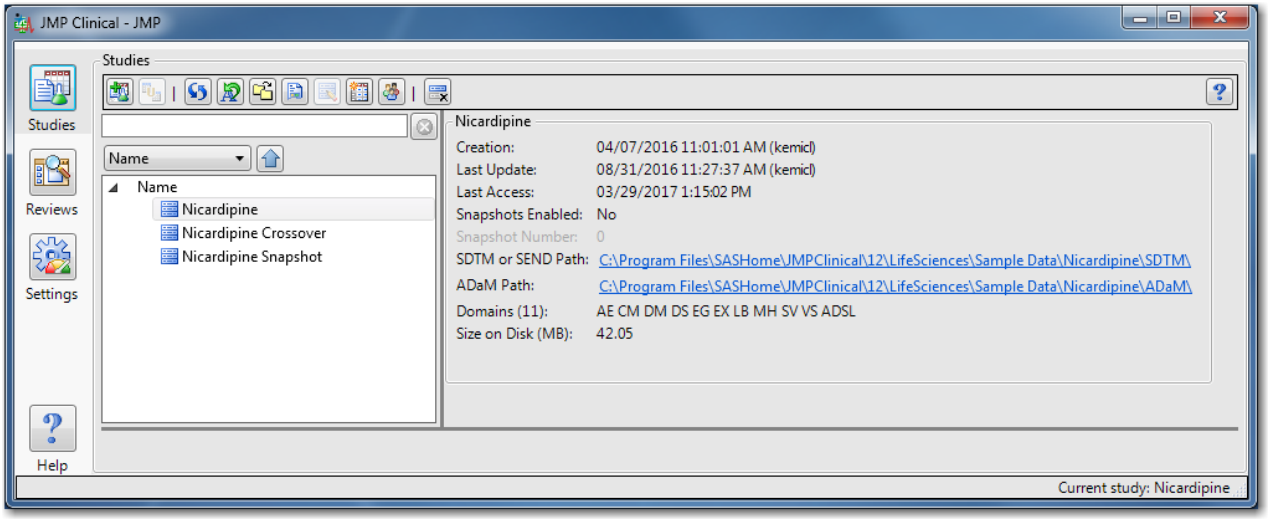
- The ability for data managers to add/manage/update clinical study data along with controlling/managing access for biometrics, monitors, reviewers.
- Allowing biostatisticians to create and easily share a collection of analysis reports with clinicians, medical monitors, and medical writers.
- Creating and sharing data review notes with collaborators on a clinical trial analysis team.
- Complexities of working in a shared “online” environment while also being able to work offline with

automatic synchronizing updates.

By reading this paper, you will learn how, with a few simple configuration settings, JMP Clinical enables you to author and instantly share safety, efficacy, and operational integrity reviews in a more flexible working environment

JMP CLINICAL STUDIES AND REVIEWS

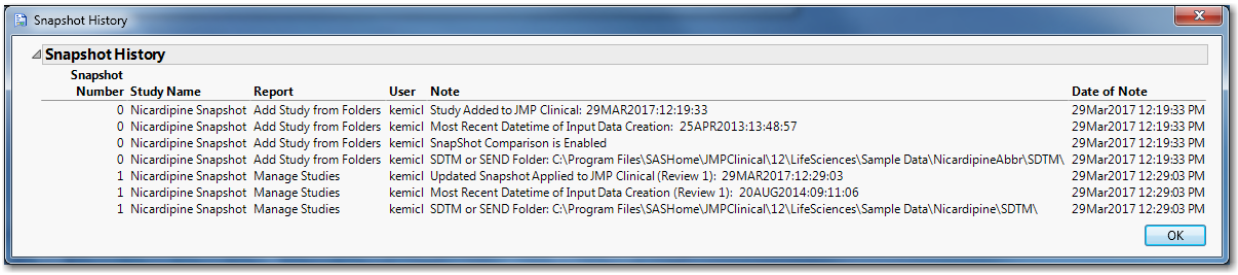
The screenshot shown in Display 1 highlights the study management options and tools in the JMP Clinical Main Starter Window. When a study is added to the system (by pointing to directories of SAS datasets formatted in the SDTM and/or ADaM standard), metadata is generated on the domains, including the variables each domain includes. A CDISC variable intelligence system evaluates which reports and the options available can be run for a given study. The data is then analyzed within the chosen clinical reports by dynamically generating and executing SAS® Macro programs. Reports are then displayed in a JMP Clinical review which can be saved and either manually or automatically shared.



Display 1. JMP Clinical Studies Main Window

MANAGING JMP CLINICAL STUDIES

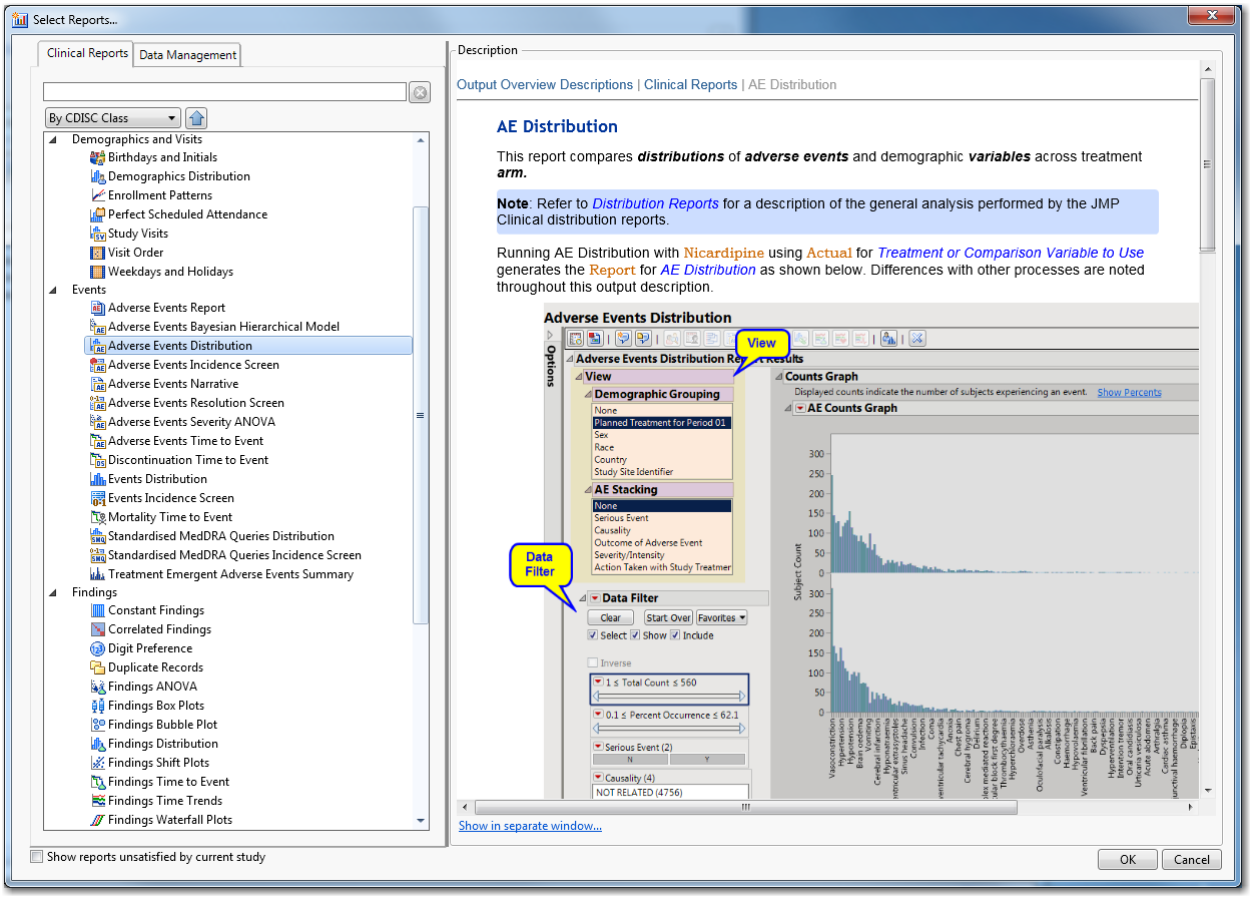
Several study management actions are available for data managers and users that have study management access. Studies can be updated with new snapshots and record level changes (based on key variables for each domain) are tracked for ongoing study data comparison. The screenshot in Display 2 shows an example snapshot history for an updated study. These subjects can be explored to create patient profiles, to view their review status distributions and to create reports on the study notes created by either the system or user(s).



Display 2. Snapshot History of a Study in the JMP Clinical System

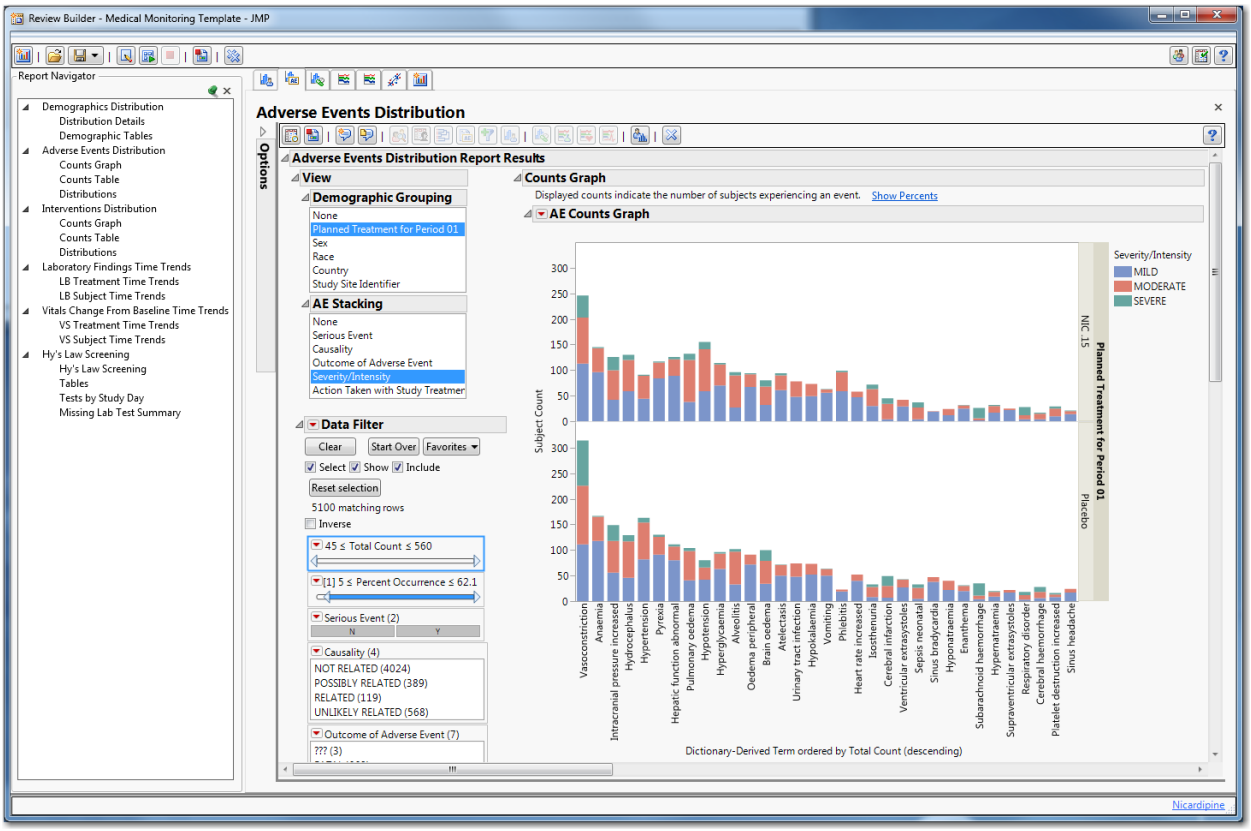
CREATING JMP CLINICAL REVIEWS

JMP Clinical supports various roles and access rights through system preferences configuration options (see JMP Clinical Configurations for further details). Study access for a given user honors directory and file path permissions for a study loaded into the system. The "Review Author" role assignment gives biostatisticians and medical reviews the capability to generate reports by selecting the particular analyses of interest. Display 3 shows the report selector tool and a sample of some of the reports available for creating a review.



Display 3. JMP Clinical Analysis Report Selection

The screenshot in Display 4 shows the results of a safety monitoring review generated by an example JMP Clinical Review template, which contains a collection of reports with specific options for understanding safety data signals coming from the demography, adverse event, concomitant medication, and findings (laboratory and vitals) domains.



Display 4. Building a JMP Clinical Review

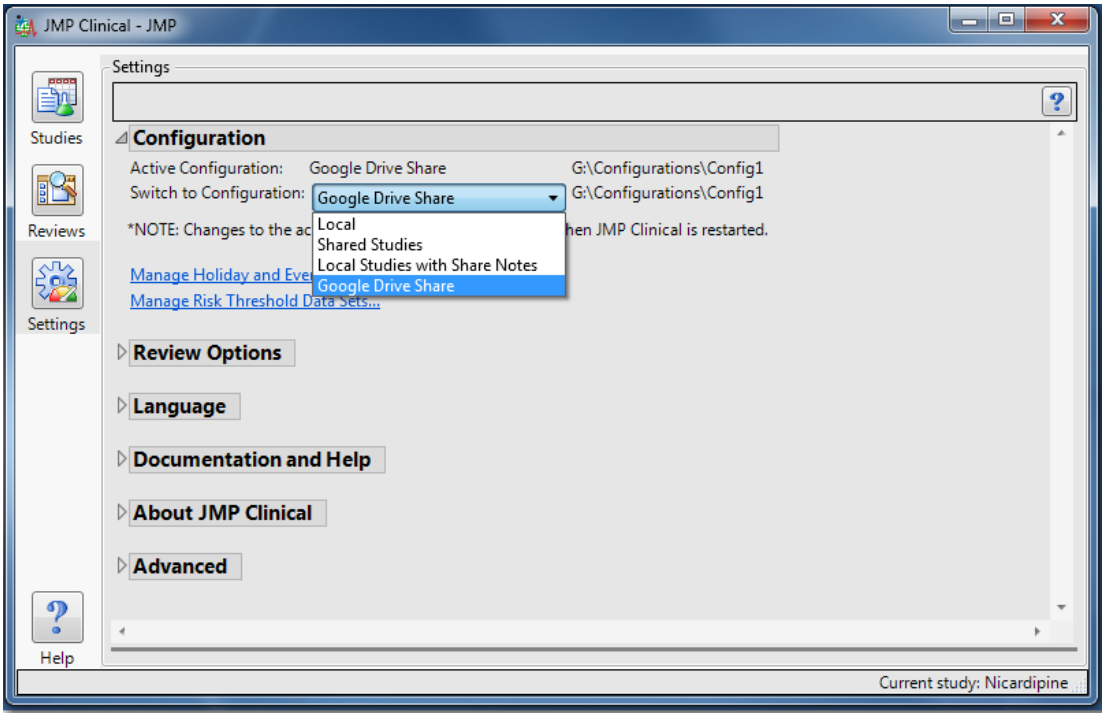
The Review Builder and subsequent Review Viewer tools offer in depth flexibility to understand and visualize data summaries, dynamically filter views based on patient cohorts and variable categories, perform further actions that drill down into related subject analyses, generate patient profiles and auto-generate adverse event narratives. From relevant reports in the review, study notes may be added or reviewed (aggregated across different users if applicable). If the review has been shared by a biometric team with a monitor that does not have study data access, actions requiring study data on the review are automatically removed to simplify your review tasks. Patient profiles generated during a review can also be embedded and saved into the review. When needed, you can generate a comprehensive static (PDF, word, PPT) report of the analyses in a given review that also tracks the date of creation, the study, review, any static and dynamic filters applied on the visual reports with the click of single button. The following role-based reviews are common use-cases of JMP Clinical:

- Clinical data integrity and operational site Risk-based Monitoring
- Medical monitoring and clinical data science for safety
- Patient profiles, tables, and event narratives for medical writing
- Data management of the ongoing collection of study data to identify stable and changing records
- Biometric analysis of safety and efficacy signals with Time-to-Event, Incidence, and ANOVA models

JMP CLINICAL CONFIGURATIONS

You can use the JMP Clinical system independently as described in the previous section; though the real gains in efficiency come from collaboration and quick communication. JMP Clinical supports multiple configurations to define distinct sets of directories where study metadata and report/review output can be stored. This is accomplished by setting up system file path preferences and settings preferences for a

given configuration. Simply put, a configuration is defined by a root directory (either a local or shared network path) to allow an organization to control and differentiate their collections of studies, reports, templates, notes, role assignments, etc. The following hyperlinked text describes setting up alternate JMP Clinical configurations. The screenshot shown in Display 5 depict the settings panel in the JMP Clinical Main Window. Here you can see the active configuration for the software and switch to alternate configurations. You can work completely locally or, using mapped network drives, share completely all studies, reviews, and notes; alternate configurations may support several variations of shared content in between.



Display 5. JMP Clinical Settings Window for Configuration

SHARED CONFIGURATIONS

There are several advantages to a shared study and reviews configuration, the foremost being that a data management team can uniformly add and control management/access of each study. System preferences annotate reviews built on outdated study data and limit shared study access from review actions if (for example) a new snapshot of the data has become available. Perhaps the main benefit is that you can partition the work responsibilities to appropriate parties, for example:

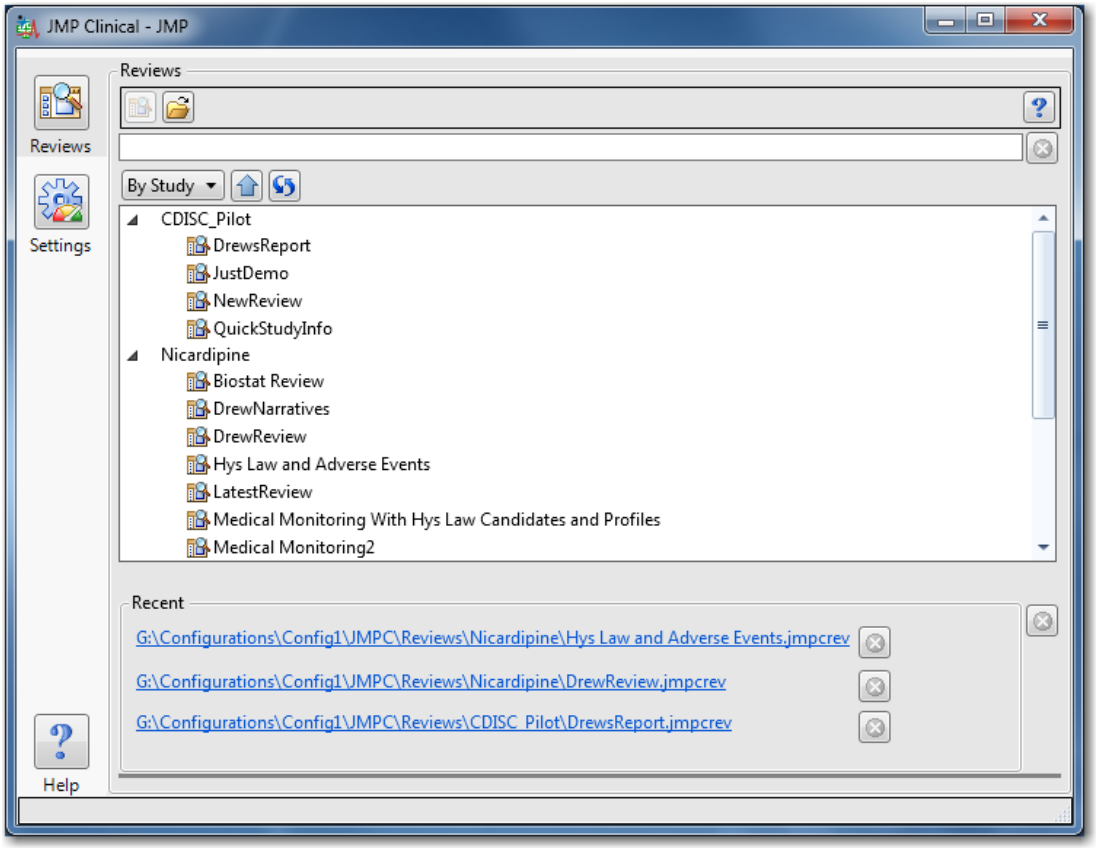
- Data managers will have sole control over study data management and updates.
- Biometrics teams can work as Review Authors to create analysis reviews to be shared with monitor teams. They can lock down access to what analyses are reviewed if necessary.
- Medical reviewers and monitors can work as Review Consumers to assess the medical signals found in the data summaries prepared for them.
- Centralized monitors can create data integrity reviews or RBM reports that can be shared with on-site staff for follow-up

Review Authors

Review authors can access (read-permission) JMP Clinical Studies created in the shared configuration to create and customize review templates and generate reviews for others to consume

Review Consumers

Review consumers may work in a much more limited environment than those that have rights to the Study Management and Review Author user roles. In fact, when a JMP Clinical user only has the Review Consumer role, they will be presented with a simplified interface that lists the reviews they can access from the shared configuration. Within the review, if the consumer still has file permissions to the study data, you can still perform report actions to create patient profiles and add/save notes to the system. Notes will be saved for each user and aggregated on request when viewing. The screenshot in Display 6 demonstrates the interface available to a Review Consumer.



Display 6. JMP Clinical Interface when in "Reviewer Only" Mode

JMP CLINICAL AND GOOGLE DRIVE

Now that you understand the system, it's time to realize the possibilities. Some level of knowledge of how cloud-based storage providers like Google Drive work is assumed and Google Drive in this paper is simply a highlighting example. Other cloud service providers such as Dropbox, Box, OneDrive, Amazon Drive, etc. could be employed in a similar manner.

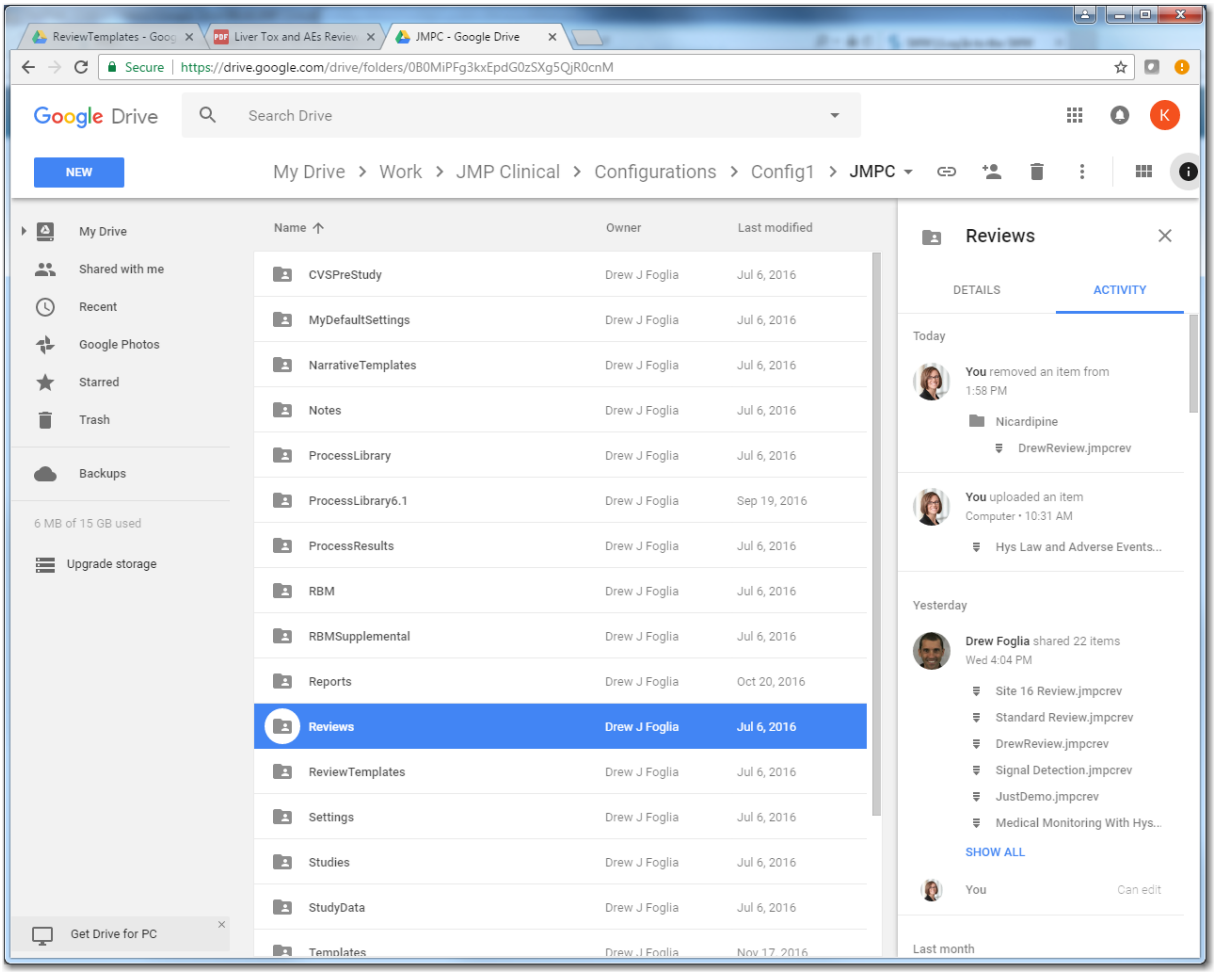
A JMP Clinical configuration, as described in the previous section, is defined solely by pointing to a UNC Path or mapped drive/directory that contains system and file path preferences files. When you install Google Drive on your desktop, you can create a mapped network drive that points to your Google Drive. This mapped drive (let's call it the G: drive) can now be used as the root directory for a JMP Clinical "Cloud" collaboration. JMP Clinical study metadata, review templates, reviews, notes, and static reports will automatically be written into Google Drive when connected to this configuration.

In support of shared configurations, study management operations, review output generation and notes-taking have been accordingly architected to avoid use-collisions through user-specified directories and

files (and corresponding aggregation when queried). Given that, the system can then utilize many of the built-in standard features of cloud-based technology, including managing file/folder activity, version management, and automatic synching and capabilities to work offline.

FILE AND FOLDER ACTIVITY

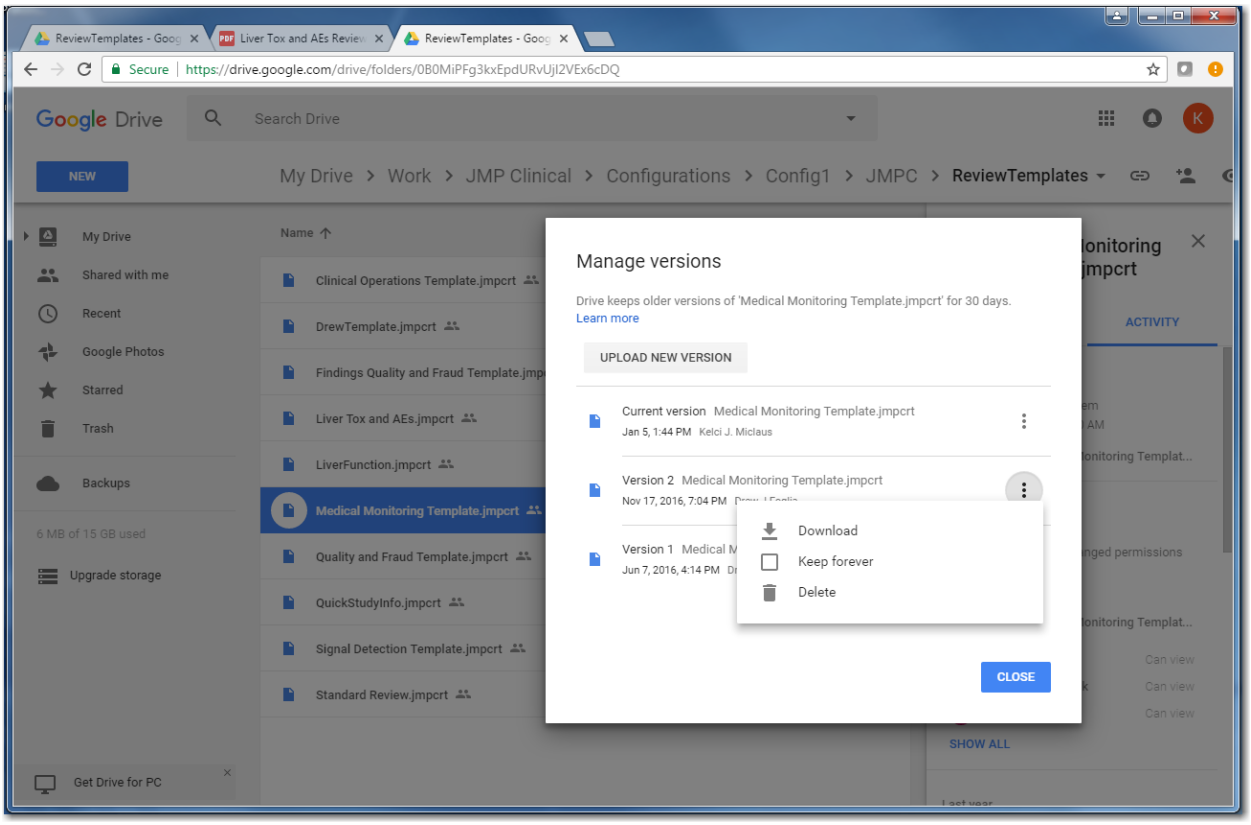
File management, permissions, updates, and activity of JMP Clinical operations while using a Google Drive configuration are automatically tracked by the cloud storage provider. The screenshot in Display 7 below shows the recent activity on the JMP Clinical Reviews folder below to allow the ability to track who has uploaded and modified reviews generated by JMP Clinical.



Display 7. File Activity for JMP Clinical on Google Drive

VERSION MANAGEMENT

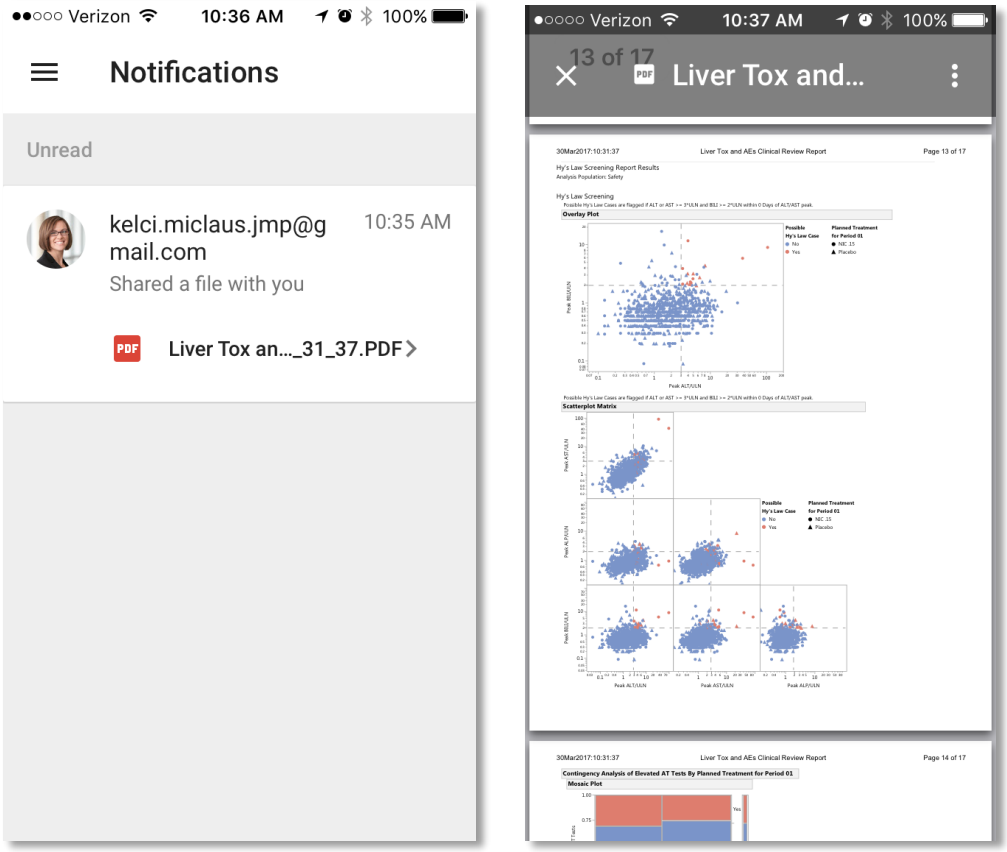
Along with activity, Google Drive also tracks versions of files shared on the drive. In the following screenshot in Display 8, we can manage the versions of ongoing Review Templates that are in use in JMP Clinical. You can download an older version and use JMP Clinical to build from that given version and save out a new current version and clean up older versions when necessary.



Display 8. Google Drive Version Management on a JMP Clinical Review Template

NOTIFICATIONS

A common request many companies have, is a way for notification or alerts for when a clinical data review is required or a review has been updated. When a JMP Clinical file in the cloud is uploaded and shared, email and phone alerts can quickly drive such action for a review. If you need to send a static review such as a pdf to someone on-site at a clinical trial or to someone without access to JMP Clinical, the JMP Clinical "Create Static Report" generates one-click PDF/Doc/PPTX files of a current JMP Clinical report analysis, review, or patient profile. Auto-generated Patient Narrative documents in RTF format can also be created by JMP Clinical and automatically uploaded to the cloud drive to share with medical writing teams. The screenshot in Display 9 shows a smartphone notification alert and access to a medical liver toxicity review within seconds of generating it with JMP Clinical with no further user-interaction required.



Display 9. Notification and Document Review on an IPhone

AUTOMATIC SYNCING AND WORKING OFFLINE

If you configure JMP Clinical to a mapped shared network drive, continued work on that configuration requires connectivity to the drive. By working with the Google Drive configuration, even when working offline, the drive stores continued work locally on the machine while offline and automatically syncs updated files when you can eventually reconnect. This allows continued work in areas where access to the internet is not guaranteed. Any notes, reviews, static reports, templates, etc. generated while working offline will become available for other users on the configuration when reconnected and those files get synchronized back to the cloud storage.

CLINICAL DATA SCIENCE REVIEW EXAMPLE

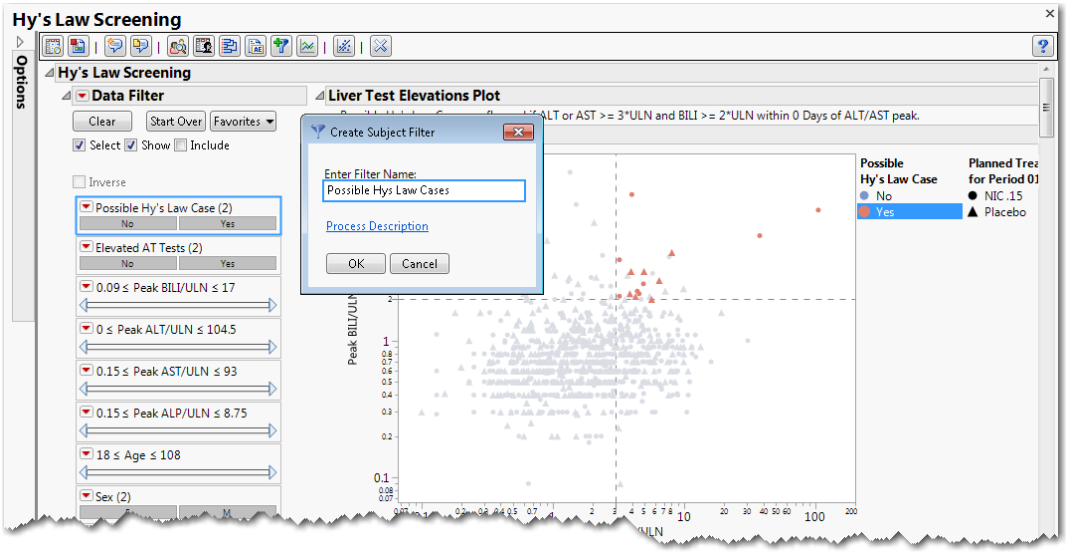
The following analysis review demonstrates the power and flexibility of using Google Drive as a configuration root directory of JMP Clinical.

We use an example clinical trial data in SDTM/ADaM format for evaluating the safety/efficacy of nicardipine hydrochloride for subarachnoid hemorrhage. The study was a two-week trial in 906 patients randomly assigned to intravenous nicardipine or placebo; 902 patients ultimately received treatment.

Liver toxicity is one of the most well-known safety pitfall of many clinical trials and one of the largest contributors to drug recalls. In this clinical data science review, I am performing summary analyses on laboratory (LB domain) measurements for liver-related tests (ALT, AST, BILI, ALP) specifically looking for

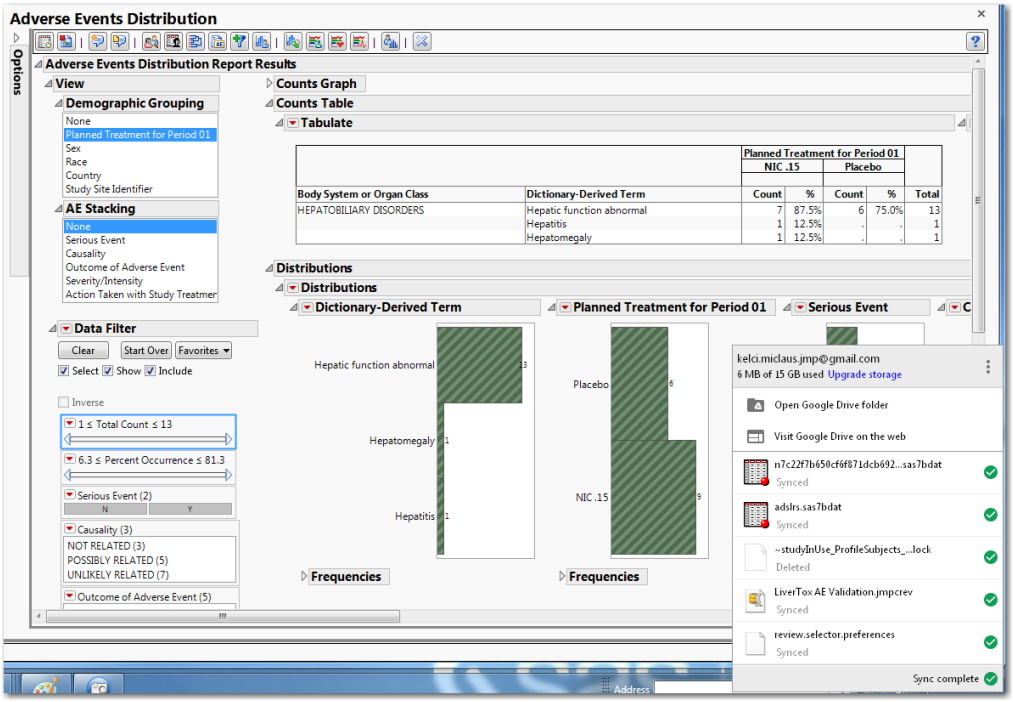
dangerous levels that may indicate liver toxicity based on the Hy's Law paradigm. I want to corroborate that any subjects that had dangerously elevated liver measurement records also had an appropriate hepatobiliary-type adverse event(s) recorded in the AE SDTM domain.

By running the Hy's Law Screening report in JMP Clinical, I can quickly select those subjects that meet criteria based on elevated liver laboratory measurements for potential toxicity and make a subject filter to be used in my next Adverse Event analysis summary.



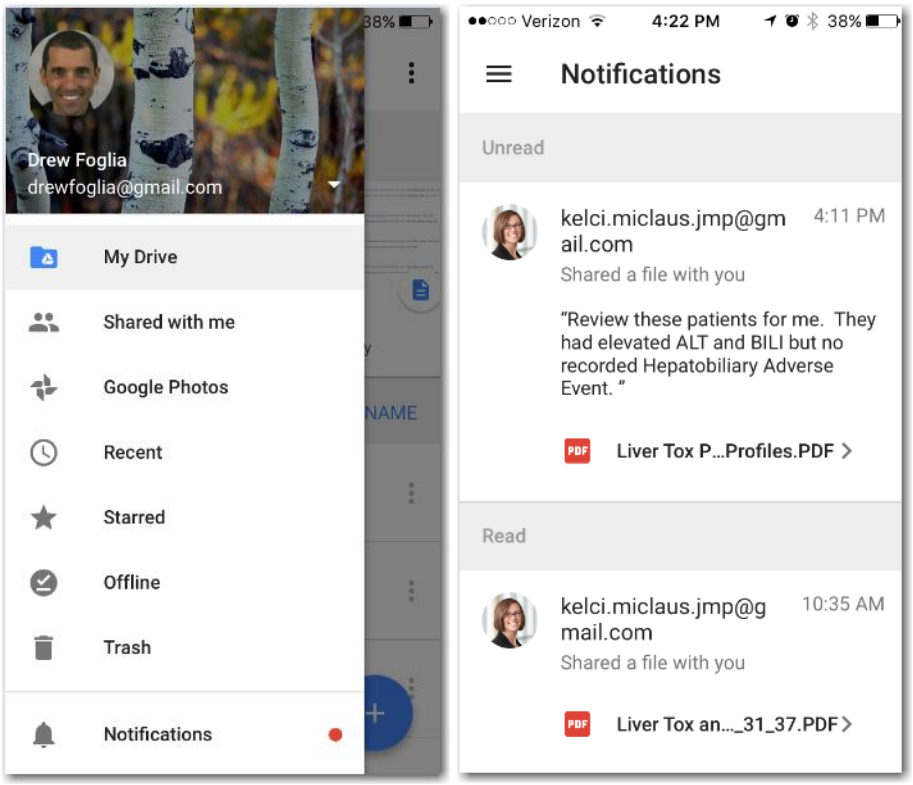
Display 10. Creating a Subject Filter during a Clinical Data Science Review

The next report in the review is an Adverse Event summary of hepatobiliary disorder system organ class codes using the subject filter created as shown in Display 10. Through looking at this report, I found 3 subjects who did not have the appropriate corresponding adverse event record accounting for liver issues during the trial. These three patients were profiled and their profiles were added to the clinical review, which was saved and synced to my Google Drive share as shown in Display 11.

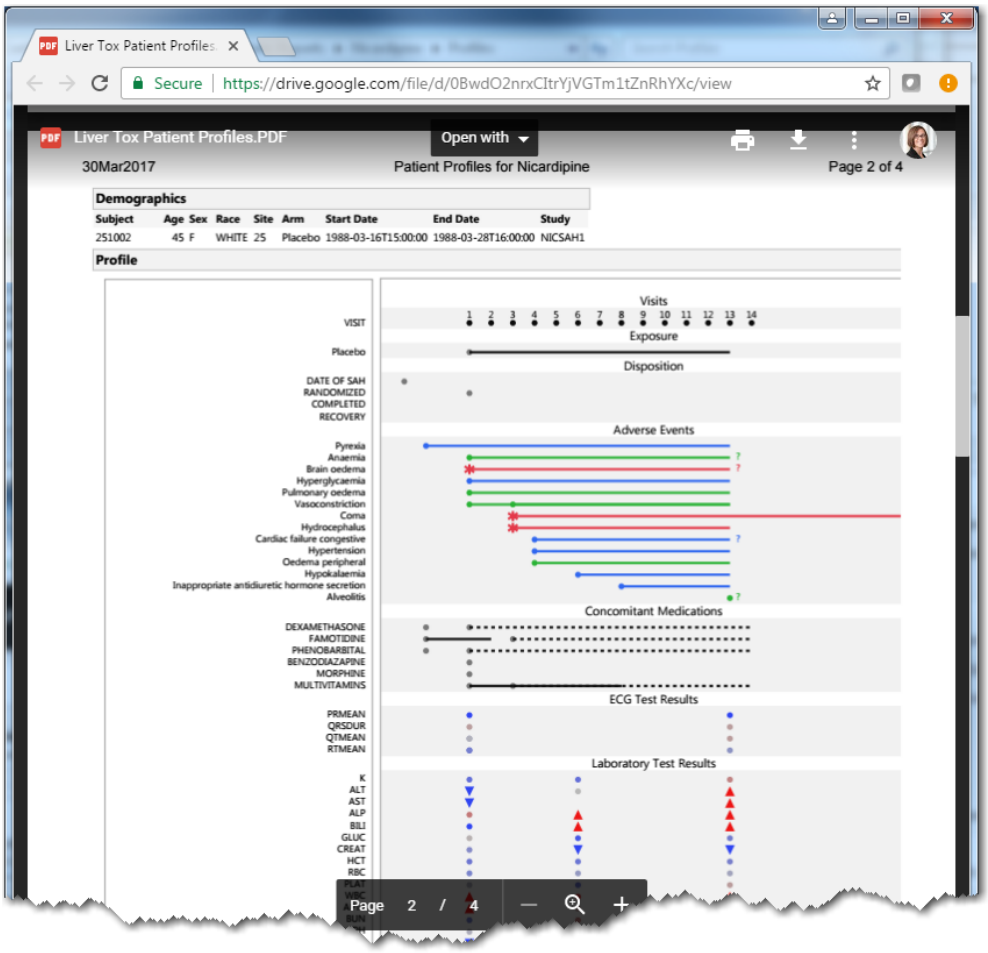


Display 11. Adverse Event Summary and Consequent Save/Sync of the JMP Clinical Review.

My medical reviewer (Drew) may not be on his laptop right now, so I generate and share with him a static report of the patient profiles so that he can immediately respond to the notifications that there are a few patients that need review. The screenshots of his phone notifications are shown in Display 12 and the following document of the profiles as shown in the browser is displayed in Display 13.

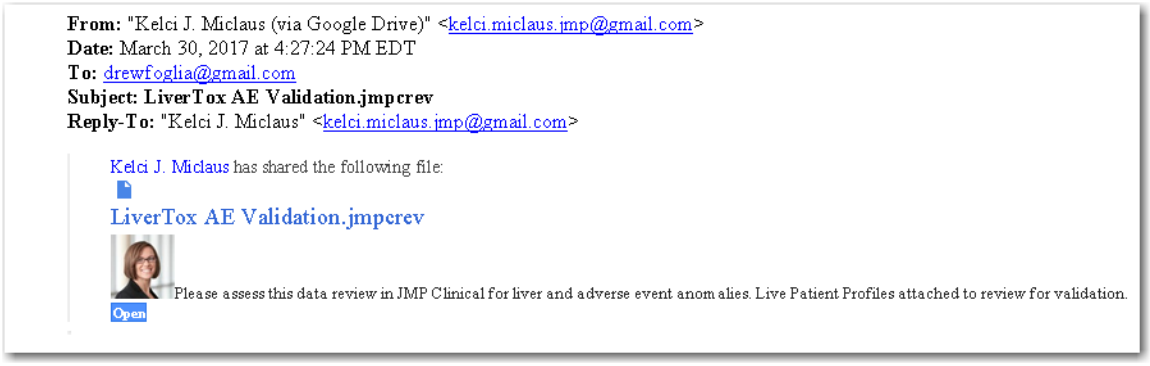


Display 12. Phone Notifications of Clinical Patient Profiles.



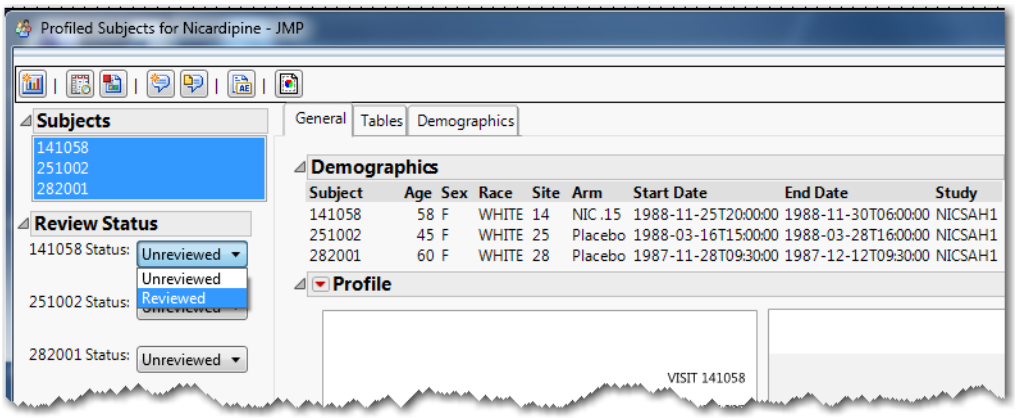
Display 13. Browser View of JMP Clinical Patient Profile Reports in Google Drive

When Drew is back at his desk, I need him to review the profiles live in JMP Clinical as well as the summary liver and adverse event reports I generated in my clinical data review. Display 14 shows the email notification for the JMP Clinical review that is available for him.



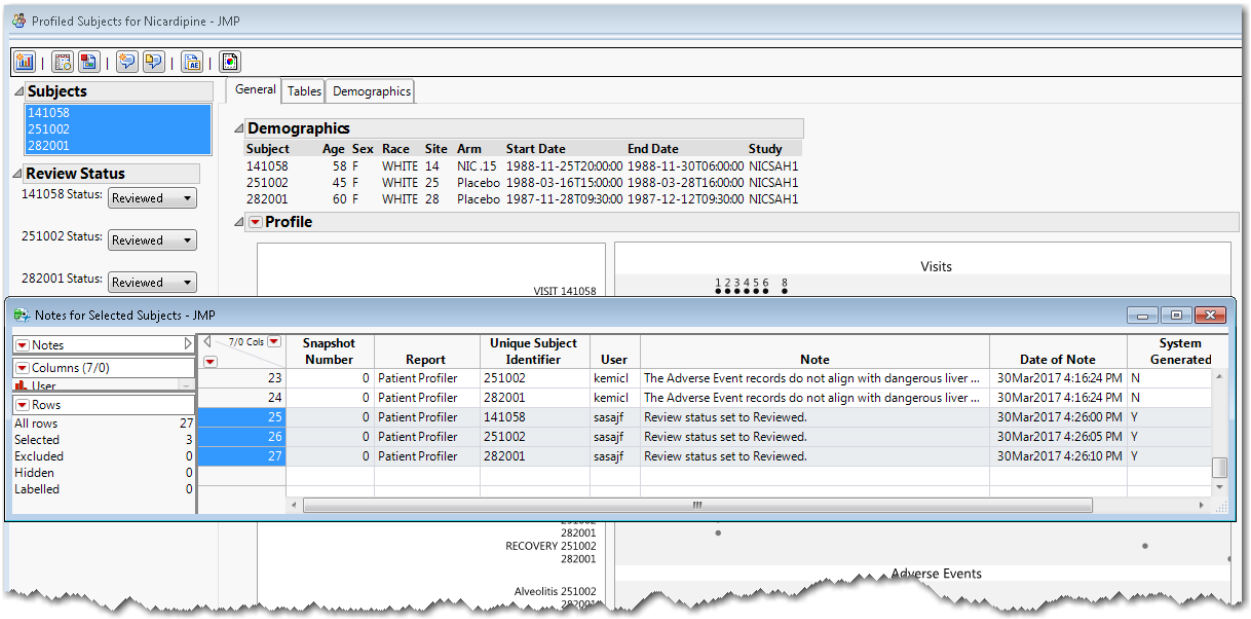
Display 14. Email notification of a Generated JMP Clinical Review.

Drew's job is to review the full patient data, corroborate as needed with others regarding why relevant adverse event records were not present and if everything looks right, set these patients' review status appropriately in the "live" JMP Clinical patient profile, his action is being shown in Display 15.



Display 15. Reviewer action to set the status of a Patient Profile Assessment

To finalize this clinical data science example, I review the latest review status (now set to Reviewed by Drew) on these profiles and can also access the study notes on the cloud to see when Drew reviewed these patients as shown in Display 16.



Display 16. Notes Regarding Review Status Accessed from Google Drive

CONCLUSION

JMP Clinical is a powerful application providing role-based reviews for those working with clinical trial data summaries. Leveraging the existing technologies of today's cloud-based storage providers, JMP Clinical enables organizations to collaborate more efficiently by sharing data, studies, reviews, and notes.

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

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