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Simplify the safety and effectiveness research of drug development process

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ABSTRACT

The evaluation of drug safety and efficacy is a very important step in the process of new drug development. Through safety assessment, drug safety issues can be identified and resolved early, ensuring the safety of patients. Through effectiveness evaluation, the therapeutic effect and safety of drugs can be evaluated, and the therapeutic effect and quality can be improved. During the evaluation process, it is common to encounter issues such as slow/inefficient review based on static tables, summarized numbers, and lists, and inability to establish dynamic connections between charts and subject files, which greatly affects the efficiency and accuracy of the evaluation.

This article will introduce how an interactive statistical discovery tool called JMP Clinical can achieve efficient safety and effectiveness assessments, helping pharmaceutical companies to deeply explore and analyze clinical data, discover the patterns and correlations behind the data, and provide strong support for drug research and development and decision-making. With the help of visual output mode, interactive tables and graphics are used to accelerate the discovery and disclosure of trends and outliers that are easily hidden by spreadsheets.

The specific content will include based on standard CDISC format clinical data, how JMP Clinical can automatically generate over 60 clinically relevant analysis output reports with one click, including but not limited to electronic medical records, centralized electronic data review, adverse event description reports, RECIST standard visualization charts, exposure/adverse event summary reports, standardized MedDRA queries, trend analysis of various indicators, etc. This article will also cover how to quickly create interactive clinical data visualization reports based on non-standard EDC and manual source data through JMP Clinical, including the frequency of adverse events in different treatment groups, visit counts, trend of changes in laboratory test results and follow-up time, as well as the visualization of the distribution of subjects of different ages in different research centers including laboratory abnormal results and SAE. Finally, this article will introduce how to generate a comprehensive visual dashboard through simple merging to conduct a comprehensive safety analysis of laboratory test results, adverse events, and subject demographic characteristics, to explore and understand the safety of drugs for different patient groups.

INTRODUCTION

As a clinical data review tool used by the FDA, JMP Clinical software can greatly simplify data discovery, analysis, and reporting in clinical trials, and improve the efficiency and accuracy of safety and efficacy data research in drug development. Customized workflows, templates, and reporting tools based on user roles allow medical personnel, clinical data scientists, medical editors, clinical operations personnel, data administrators, and biostatisticians to easily view and explore trends and outliers and exchange their findings with each other.

APPLYING THE JMP CLINCIAL MODULE TO PROCESS SDTM AND ADAM DATASETS BASED ON STANDARD CDISC FORMAT CLINICAL DATA

- Clinical data scientists and medical monitors can assess safety and effectiveness issues with just a click on a button and can also delve into customized patient profiles and patient narratives by creating interactive reports on adverse events, concomitant medications, tumor response analysis, and laboratory measurement analysis.

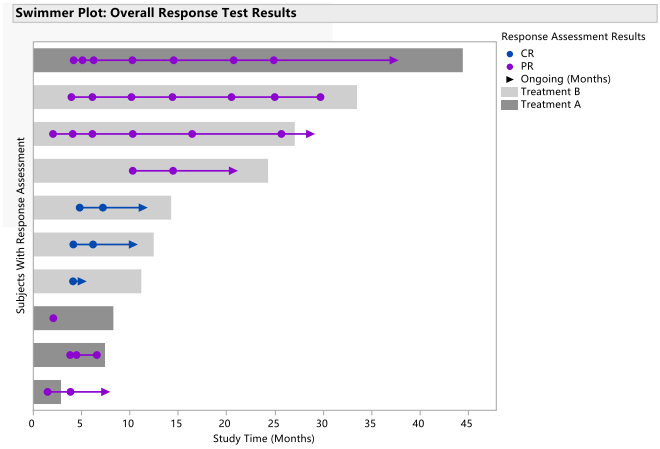


Figure 1. Swimming plot

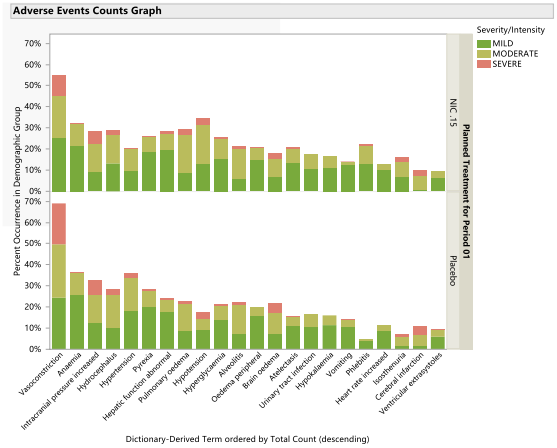


Figure 2. Percentage plot of adverse events in different treatment groups

- Medical researchers only need to select the subjects, and JMP Clinical will immediately generate patient profiles for a single subject or a group of subjects in a visual and intuitive manner.

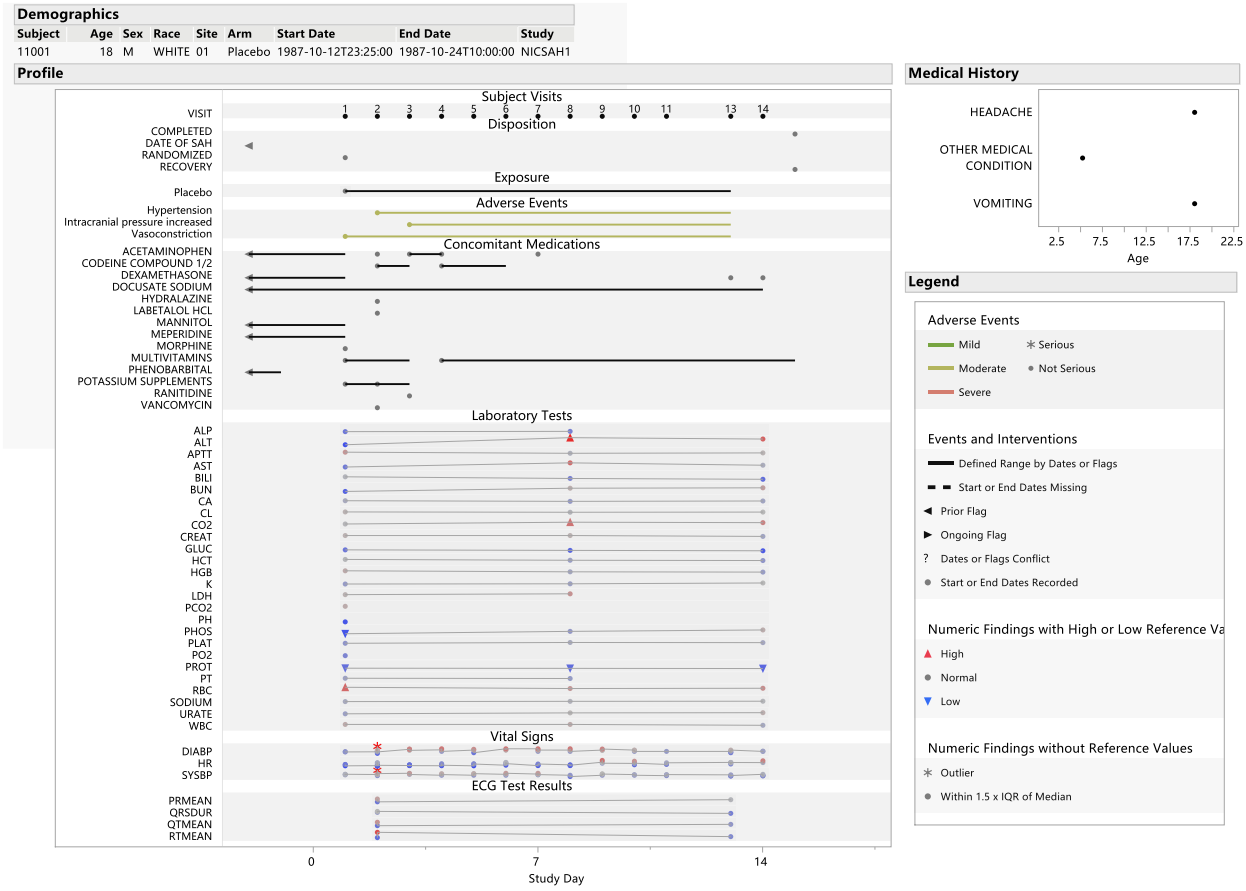


Figure 3. Patient Profile

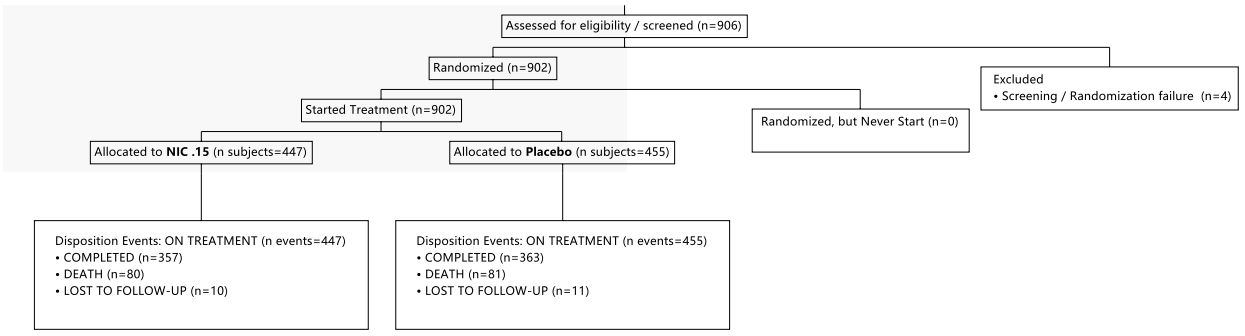


Figure 4. Study Flow Diagram

- The automatically generated exposure summary report can help clinical researchers identify differences in dose and duration of exposure between treatment groups, providing background reference for all subsequent analyses. It can also screen for the occurrence of concomitant medication and substance use, help identify drug interactions, and analyze the distribution of risks, event occurrence rates, and estimate changes over time.
- Through adverse event time analysis and resolution screening, you can confirm the occurrence and results of adverse events. JMP Clinical supports standardized MedDRA queries to help researchers

identify adverse event patterns across different treatment groups.

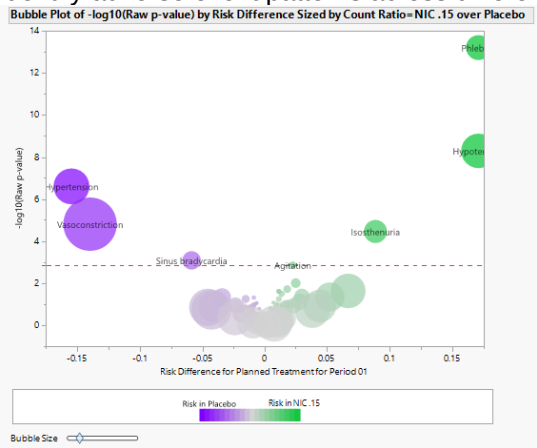


Figure 5. Adverse Events Incidence Screen

- By using FDA prescribed guidelines and industry standard visualization methods, and utilizing JMP Clinical's quantitative indicators of concentration trends, outlier detection, and trends over time, medical researchers can quickly identify potential harmful symptoms, including hepatotoxicity, that may occur in clinical trials.

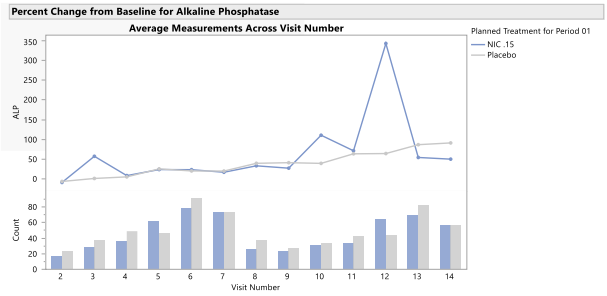


Figure 6. Findings measurements Time Trends

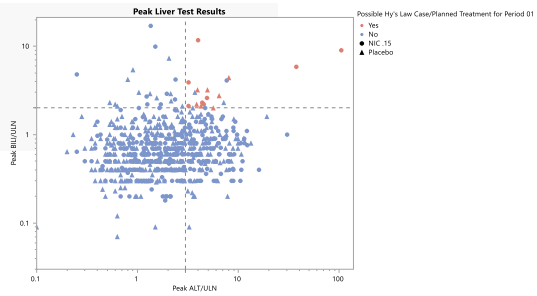


Figure 7. Hy's Law Screening

- Adverse event narratives are usually time-consuming and labor-intensive. With JMP Clinical, medical editors can automatically generate patient profiles and patient narratives, reducing the time required to create output results and reducing operational complexity.

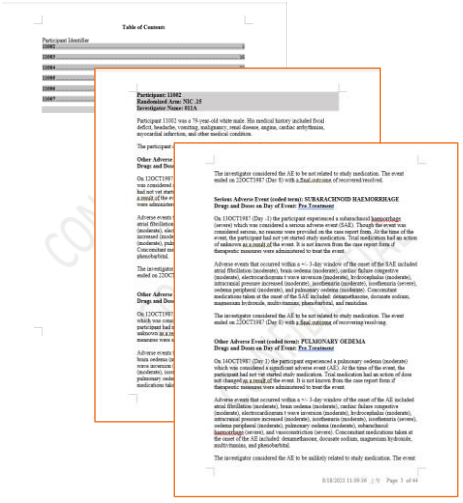


Figure 8. Adverse Events Report

- JMP Clinical can help clinical researchers reduce data quality risks that may hinder regulatory agency submissions or drug approval, by identifying data anomalies at the supplier, investigator, clinical trial center, and national level, and identifying factors that lead to safety or data quality damage. With the risk indicators recommended by TransCelebrate BioPharma, the test center level can present an overview of risk levels marked by color, making it easy to identify any test centers that require timely attention.

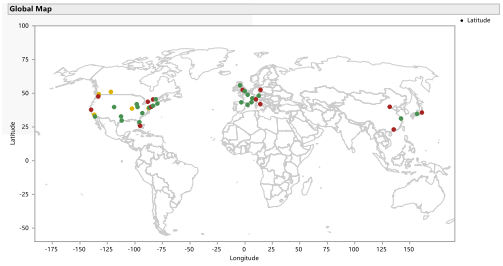


Figure 9. RBM Site-Level Maps

	Study Site Identifier	Country	City	State or Province	Monitor	Site Category	Vendor	Overall Risk Indicator	Overall Risk Indicator ...	Overall Risk Indicator ...	Overall Risk Indicator Safety
1	01	USA	New York	NY	Monitor G	Veteran	Vendor A	0.719	0.056	0.607	0.940
2	02	USA	Orlando	FL	Monitor F	Experienced	Vendor A	0.748	0.448	0.218	1.081
3	03	USA	Indianapolis	IN	Monitor E	Experienced	Vendor A	0.228	0.497	0.000	0.275
4	04	FRA	Paris	Ile-de-France	Monitor I	Experienced	Vendor C	0.721	0.027	0.000	1.255
5	05	ITA	Milano	Lombardia	Monitor H	Novice	Vendor C	1.820	3.660	2.120	1.210
6	06	USA	Philadelphia	PA	Monitor G	Experienced	Vendor A	1.457	1.289	0.000	2.227
7	07	CHN	Guangzhou	Guangdong Sheng	Monitor K	Experienced	Vendor B	0.949	1.107	0.000	1.383
8	08	GBR	Birmingham	Birmingham	Monitor J	Novice	Vendor C	0.991	1.052	0.000	1.472
9	09	CAN	Montreal	Quebec	Monitor A	Veteran	Vendor A	0.851	0.629	0.356	1.153
10	10	USA	Baltimore	MD	Monitor G	Experienced	Vendor A	0.635	0.432	0.000	1.003
11	12	DEU	Berlin	Berlin	Monitor H	Experienced	Vendor C	0.886	1.346	0.008	1.210
12	14	CAN	Toronto	Ontario	Monitor A	Veteran	Vendor A	1.028	0.850	1.368	0.902
13	16	USA	Seattle	WA	Monitor B	Experienced	Vendor A	0.769	1.282	0.669	0.691
14	17	USA	Los Angeles	CA	Monitor C	Experienced	Vendor A	0.715	0.327	0.000	1.169
15	18	JPN	Osaka	Osaka	Monitor L	Novice	Vendor B	0.466	1.155	0.109	0.472
16	19	CAN	Ottawa	Ontario	Monitor A	Experienced	Vendor A	0.661	0.682	1.178	0.398
17	20	FRA	Marseille	Provence-Alpes-...	Monitor I	Veteran	Vendor C	0.429	0.382	0.027	0.641
18	21	ESP	Barcelona	Cataluna	Monitor I	Experienced	Vendor C	0.274	0.169	0.000	0.437
19	22	CAN	Calgary	Alberta	Monitor B	Experienced	Vendor A	0.929	0.058	0.067	1.571
20	23	USA	Chicago	IL	Monitor E	Veteran	Vendor A	0.415	0.095	0.225	0.580

Figure 10. RBM Report Results Description

- Biostatisticians can use unique Bayesian hierarchical models to identify rare but potentially high-risk adverse events in clinical trials.
- The software can also help data management researchers visually monitor the status of all data and quickly discover new, modified, deleted, or duplicate data. This can accelerate database locking and ensure that subsequent analysis is always based on valid data. Even if you are not a statistician or programmer, you can detect fraudulent data or other data quality issues, and easily identify intentional or unintentional errors in individual subjects or clinical center related data by aggregating clinical trial data.

APPLY JMP MODULE TO PROCESS NON-STANDARD EDC AND MANUALLY SOURCE CLINICAL DATA

The diversity of manually sourced clinical data in EDC hinders the possibility of the Clinical module generating clinical related reports with one click. However, with the help of the JMP module, the visualization of non-standard clinical data can be easily achieved through simple mouse click and drag, without the need for any coding throughout the entire process.

Common application scenarios and screenshots of some demonstrations:

1. Quickly achieve data aggregation and generation of derived indicator columns:
    - Summarize the frequency and number of adverse event
    - Summarize the changes in the number of adverse events under different CTCAE levels, or calculate the changes in adverse event levels with dose during the DOT climbing process
    - Quickly identify records of laboratory results exceeding the standard by deriving indicator columns
2. Diverse visual statistical graphics:
    - The frequency of adverse events containing adverse event level information in different treatment groups
    - Trend of changes in visit counts and laboratory test results over time
    - The distribution of subjects at different research centers and ages, and the information of subjects with laboratory indicators above the limit and serious adverse reactions should be displayed in the graph
    - Spider chart, swimming pool chart, waterfall chart, and survival curve closely related to tumor efficacy
3. Generate customized listings according to requirements:
    - Review the checklist for the relationship between laboratory indicators and AE for each subject
    - Based on custom logical rules, merge a Listing checklist containing multi-dimensional clinical data from multiple sources such as DM, DS, SV, and CM
4. Generate comprehensive reports:
    - Linkage display of multiple clinical data tables and derived graphics, including demographic information, adverse event information, and laboratory indicator information
    - View electronic medical records of each subject's visit time, adverse events, and changes in laboratory indicators for a small amount of clinical data
    - Customized PM query table containing multi-dimensional information

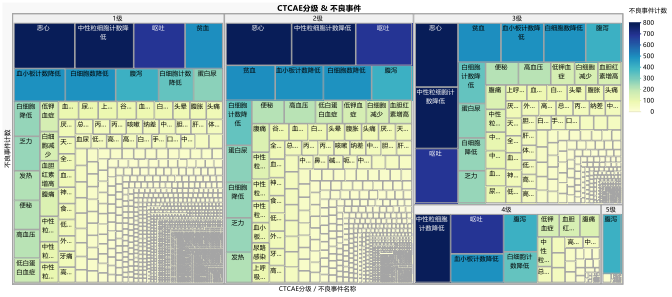


Figure 11. Tree plot of CTCAE Graded Adverse

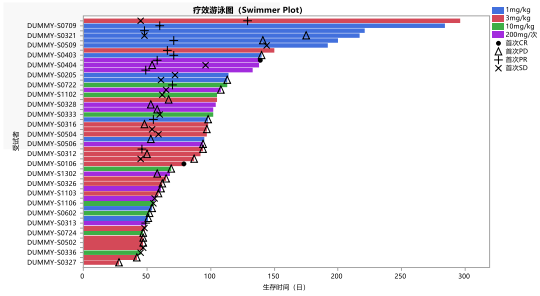
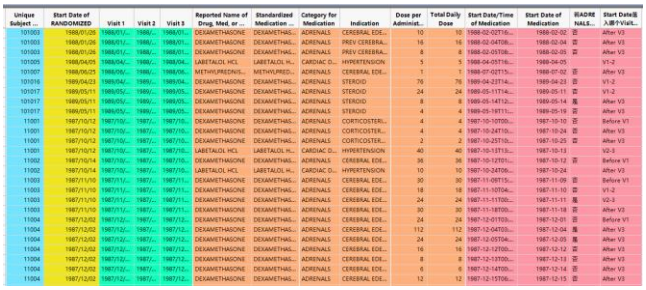


Figure 12. Swimming plot based on non-standard data



Unique Subject ...	Start Date of RANDOMIZED	Visit 1	Visit 2	Visit 3	Reported Name of Drug, Med, or ...	Standardized Medication ...	Category for Medication	Indication	Dose per Administ...	Total Daily Dose	Start Date/Time of Medication	Start Date of Medication	是ADRE NAILE...	Start Date是入排予Visit...
101003	1988/01/26	1988/01/...	1988/...	1988/01...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CEREBRAL EDE...	10	10	1988-02-02T16:...	1988-02-02	否	After V3
101003	1988/01/26	1988/01/...	1988/...	1988/01...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	PREV CEREBRA...	16	16	1988-02-04T08:...	1988-02-04	否	After V3
101003	1988/01/26	1988/01/...	1988/...	1988/01...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	PREV CEREBRA...	8	8	1988-02-05T08:...	1988-02-05	否	After V3
101005	1988/04/05	1988/04/...	1988/...	1988/04...	LABETALOL HCL	LABETALOL H...	CARDIAC D...	HYPERTENSION	5	5	1988-04-05T16:...	1988-04-05		V1-2
101007	1988/06/25	1988/06/...	1988/...	1988/06...	METHYLPREDNIS...	METHYLPRED...	ADRENALS	CEREBRAL EDE...	1	1	1988-07-02T15:...	1988-07-02	否	After V3
101016	1989/04/23	1989/04/...	1989/...	1989/04...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	STEROID	76	76	1989-04-23T14:...	1989-04-23	否	V1-2
101017	1989/05/11	1989/05/...	1989/...	1989/05...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	STEROID	24	24	1989-05-11T14:...	1989-05-11	否	V1-2
101017	1989/05/11	1989/05/...	1989/...	1989/05...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	STEROID	8	8	1989-05-14T12:...	1989-05-14	是	After V3
101017	1989/05/11	1989/05/...	1989/...	1989/05...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	STEROID	4	4	1989-05-15T11:...	1989-05-15	否	After V3
11001	1987/10/12	1987/10/...	1987/...	1987/10...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CORTICOSTER...	4	4	1987-10-10T09:...	1987-10-10	否	Before V1
11001	1987/10/12	1987/10/...	1987/...	1987/10...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CORTICOSTER...	4	4	1987-10-24T10:...	1987-10-24	否	After V3
11001	1987/10/12	1987/10/...	1987/...	1987/10...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CORTICOSTER...	2	2	1987-10-25T10:...	1987-10-25	否	After V3
11001	1987/10/12	1987/10/...	1987/...	1987/10...	LABETALOL HCL	LABETALOL H...	CARDIAC D...	HYPERTENSION	40	40	1987-10-13T13:...	1987-10-13		V2-3
11002	1987/10/14	1987/10/...	1987/...	1987/10...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CEREBRAL EDE...	36	36	1987-10-12T01:...	1987-10-12	否	Before V1
11002	1987/10/14	1987/10/...	1987/...	1987/10...	LABETALOL HCL	LABETALOL H...	CARDIAC D...	HYPERTENSION	10	10	1987-10-24T06:...	1987-10-24		After V3
11003	1987/11/10	1987/11/...	1987/...	1987/11...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CEREBRAL EDE...	30	30	1987-11-09T15:...	1987-11-09	否	Before V1
11003	1987/11/10	1987/11/...	1987/...	1987/11...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CEREBRAL EDE...	18	18	1987-11-10T04:...	1987-11-10	否	V1-2
11003	1987/11/10	1987/11/...	1987/...	1987/11...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CEREBRAL EDE...	24	24	1987-11-11T00:...	1987-11-11	是	V2-3
11003	1987/11/10	1987/11/...	1987/...	1987/11...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CEREBRAL EDE...	30	30	1987-11-18T00:...	1987-11-18	否	After V3
11004	1987/12/02	1987/12/...	1987/...	1987/12...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CEREBRAL EDE...	24	24	1987-12-01T03:...	1987-12-01	否	Before V1
11004	1987/12/02	1987/12/...	1987/...	1987/12...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CEREBRAL EDE...	112	112	1987-12-04T03:...	1987-12-04	是	After V3
11004	1987/12/02	1987/12/...	1987/...	1987/12...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CEREBRAL EDE...	24	24	1987-12-05T04:...	1987-12-05	是	After V3
11004	1987/12/02	1987/12/...	1987/...	1987/12...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CEREBRAL EDE...	16	16	1987-12-12T00:...	1987-12-12	否	After V3
11004	1987/12/02	1987/12/...	1987/...	1987/12...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CEREBRAL EDE...	8	8	1987-12-13T00:...	1987-12-13	否	After V3
11004	1987/12/02	1987/12/...	1987/...	1987/12...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CEREBRAL EDE...	6	6	1987-12-14T00:...	1987-12-14	否	After V3
11004	1987/12/02	1987/12/...	1987/...	1987/12...	DEXAMETHASONE	DEXAMETHAS...	ADRENALS	CEREBRAL EDE...	12	12	1987-12-15T06:...	1987-12-15	否	After V3

Figure 13. Based on custom logical rules, merge the Listing checklist of multi-dimensional clinical data sources

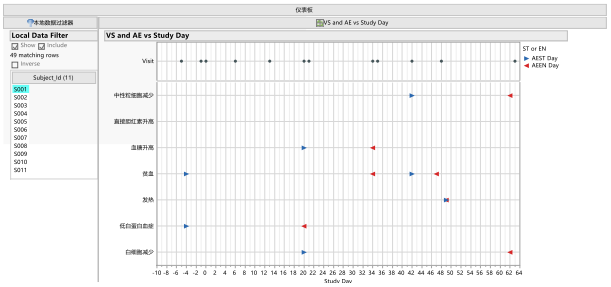


Figure 14. A simple patient profile generated based on non-standard data, mainly reflecting the relationship between visit time and occurrence of adverse events。

A simple example will be used to demonstrate the mutual invocation of clinical data information tables containing DM, AE, and LB, achieving the generation and merging display of specified graphics, as shown in the following figure.

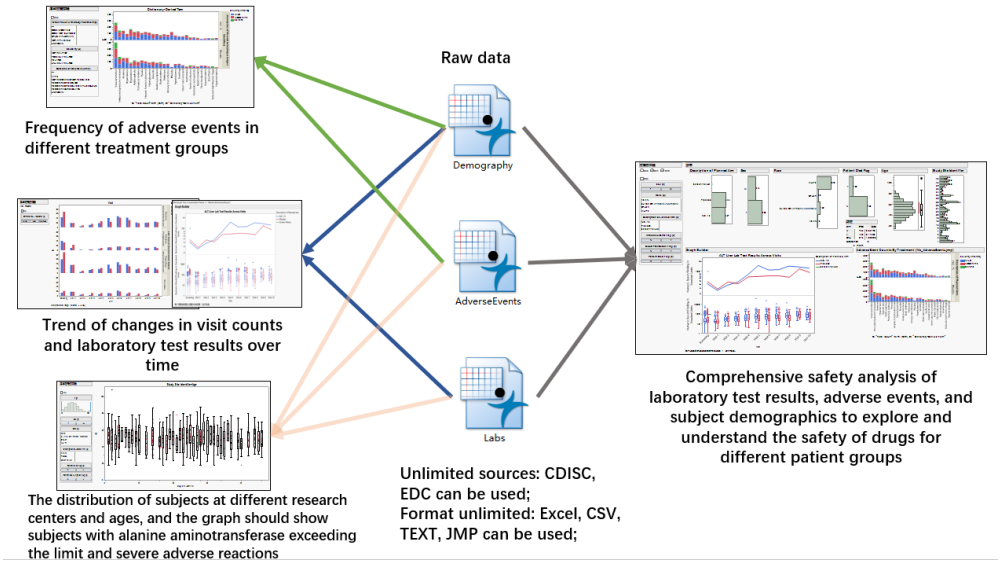


Figure 15. Demonstration Case Implementation Diagram

To achieve the above process, some functions of JMP need to be utilized, including:

- Cross referencing of table data, with options for direct and virtual connections
- Generate a custom graphics generator for the graphics platform
- Implement dashboard function for merging and interactive viewing of multiple graphics

The first step is to establish a virtual connection and achieve mutual referencing of information from different data tables. By clicking on the "Unique Subject Identifier" column in the data table DM as the Link ID, and clicking on the "Unique Subject Identifier" column in the data table AE and LB as the Link reference, you can view the information of the data table DM in the data table AE and LB.

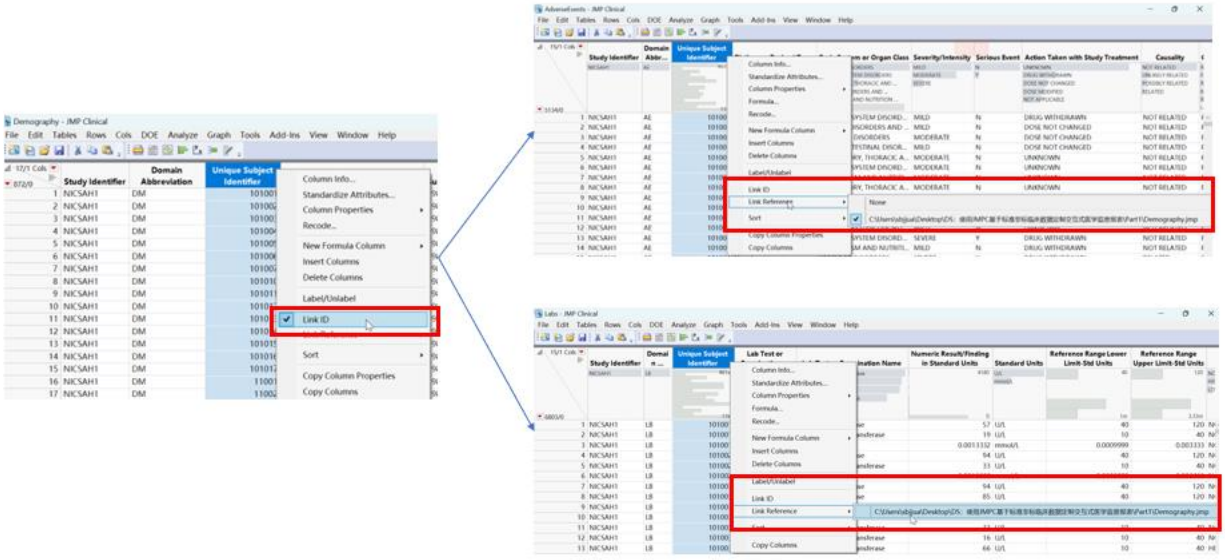


Figure 16. Demonstration of virtual connection implementation

Step 2: By utilizing the graph generator function and using simple drag and drop operations, it is possible to quickly draw a bar chart of the frequency of adverse events occurring in different treatment groups, as well as a trend chart of visit counts, laboratory test results, and follow-up time in different treatment groups.

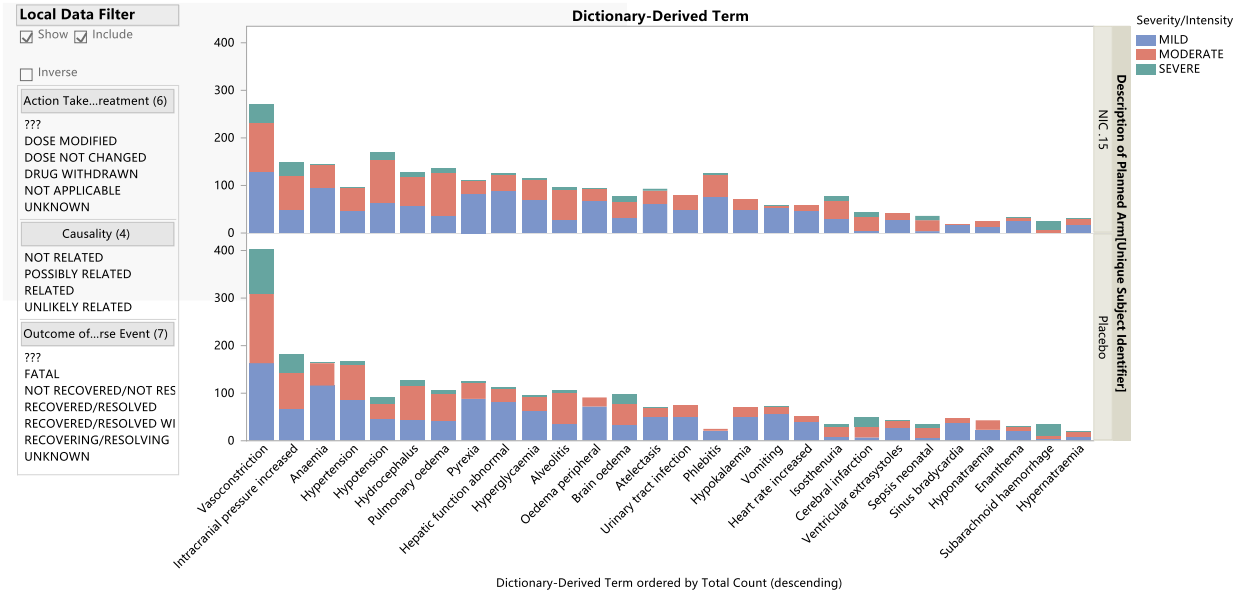


Figure 17. The frequency of adverse events in different treatment groups based on the level of adverse event

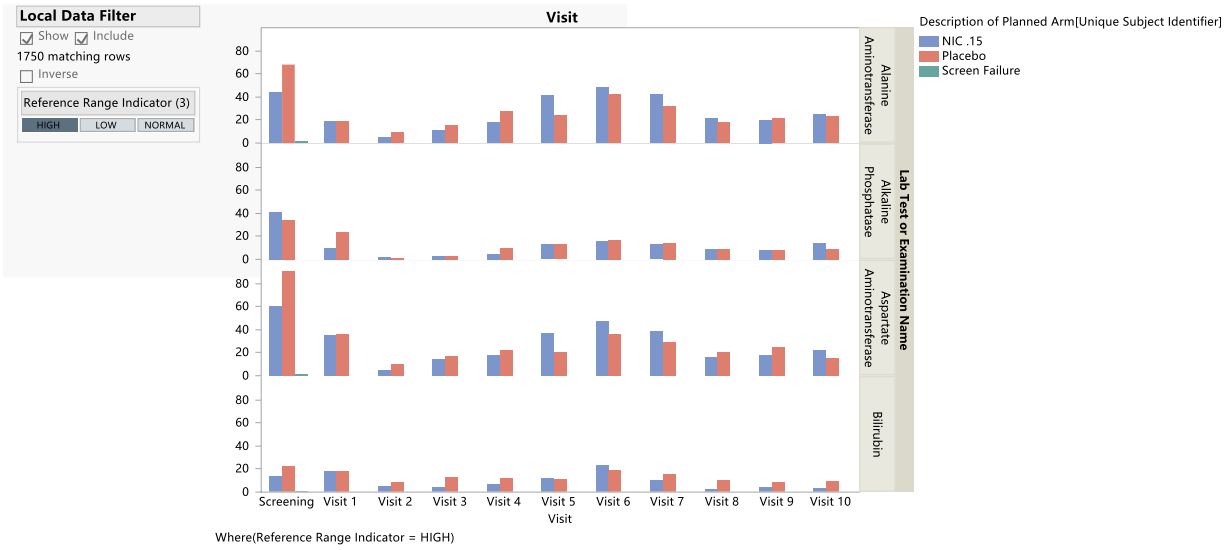


Figure 18. Trend chart of changes in visit count and follow-up time in different treatment groups

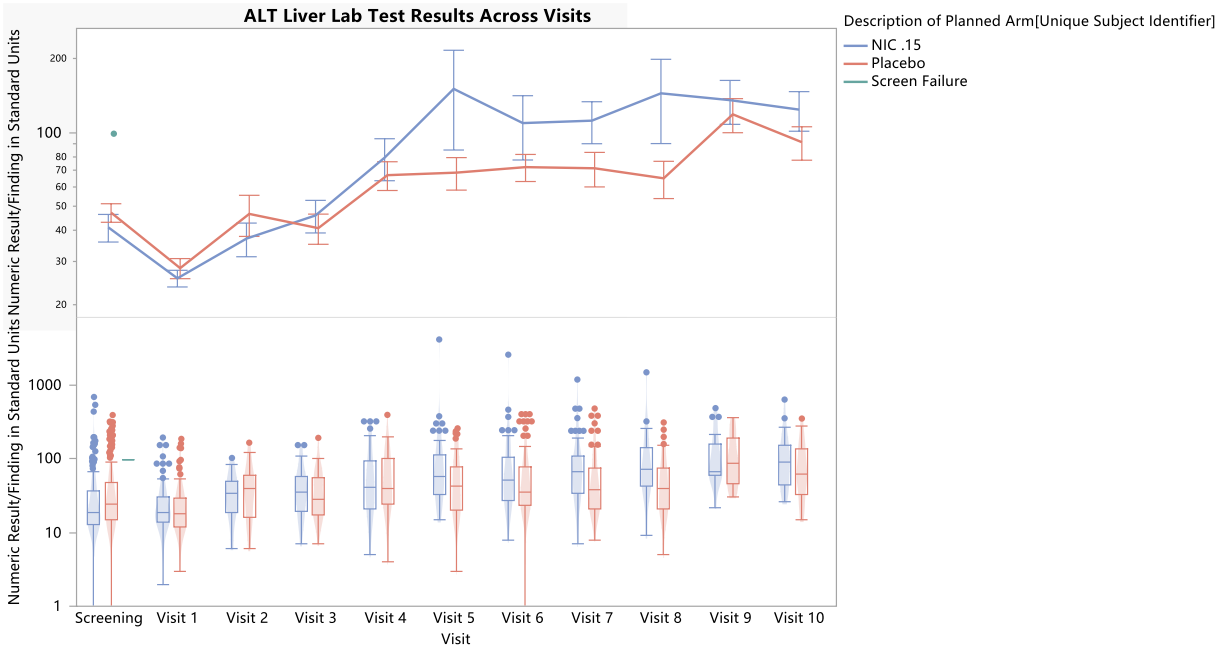


Figure 19. Trend chart of changes in follow-up time of laboratory test results in different treatment groups

If researchers want to view the distribution of subjects of different ages in different research centers, the information in data table DM is sufficient. However, if it is necessary to display the information of subjects with laboratory indicators above the limit and serious adverse reactions in the graph, they need to use the information in data table AE and data table LB through the "scheduling" function of the virtual link, It can display the information contained in data table AE and data table LB in the graph generated by data table DM.

Figure 20. Schematic diagram for generating distribution maps of subjects of different ages in different research centers including laboratory abnormal results and SAE

Finally, the dashboard function can also be used to merge and interactively display multiple graphs generated from multiple data tables, facilitating multi-dimensional viewing of information and comprehensively understanding the safety of drugs.

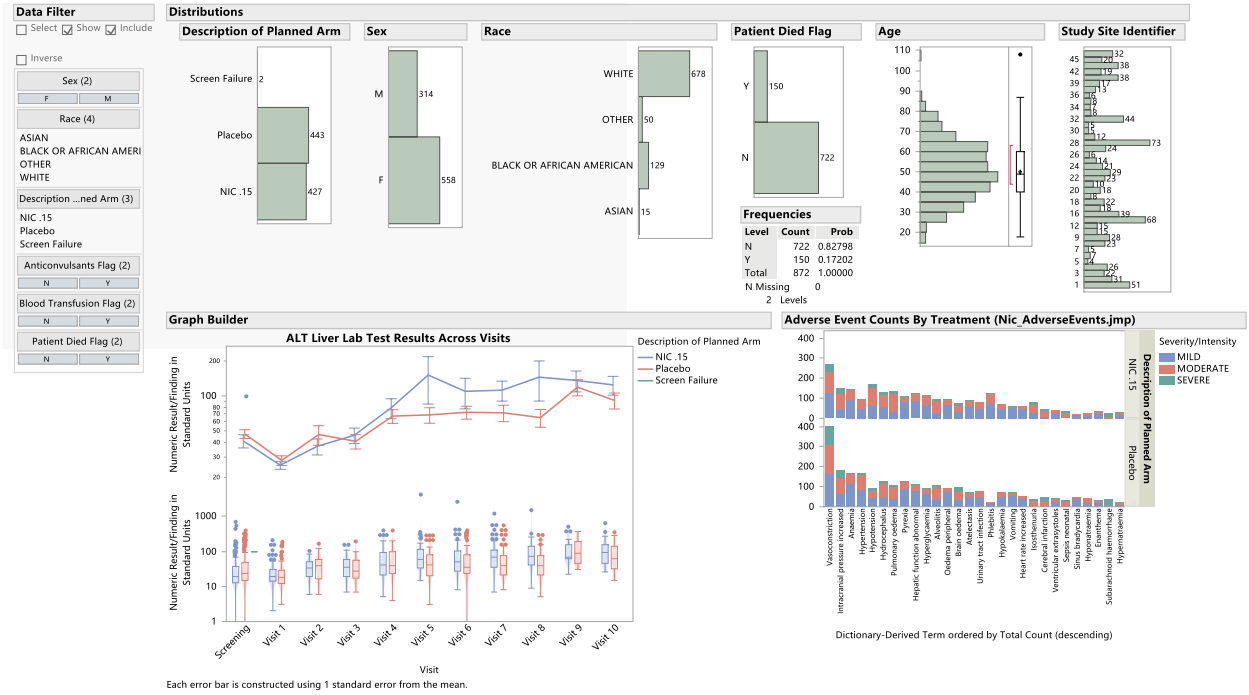


Figure 21. A comprehensive visual dashboard containing multi-dimensional information

CONCLUSION

The safety and effectiveness evaluation of drugs is a very important step in the development process of new drugs. With the help of visual statistical analysis software JMP Clinical, efficient safety and effectiveness can be achieved. Based on standard CDISC format clinical data, JMP Clinical can automatically generate over 60 clinically relevant analysis output reports with one click. For non-standard EDC, manual source data can also be generated through simple selection to generate specified clinical data interactive visualization reports, without any programming operations. Therefore, whether it is a clinical researcher, clinical data scientist, medical editor, data management team member and biostatisticians can easily master it, making clinical data analysis easy, enjoyable, and effective.

CONTACT INFORMATION

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