VISUALIZATION OF STANDARD TLFS FOR CLINICAL TRIAL DATA ANALYSIS

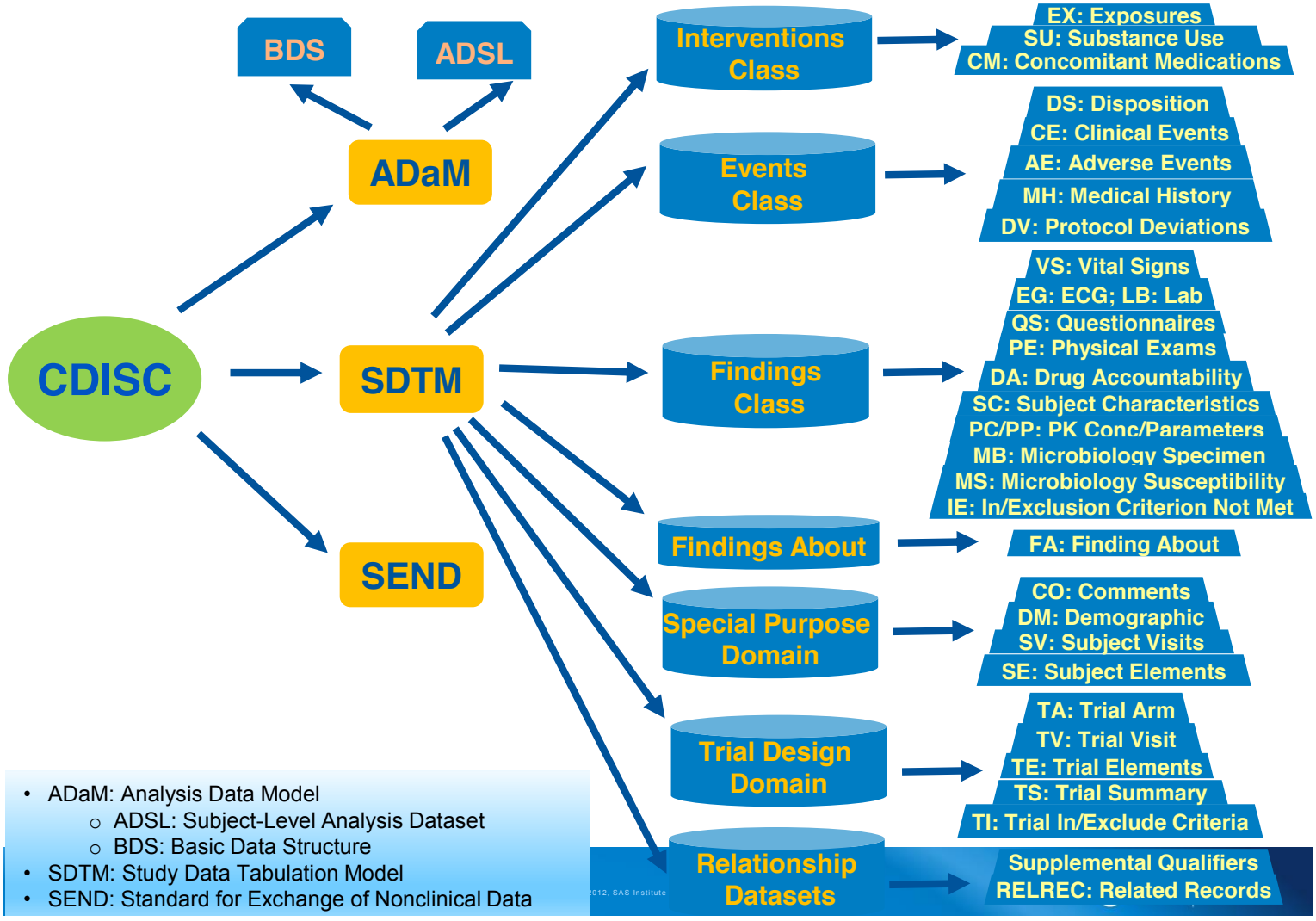
WENJUN BAO AND JASON CHEN
JMP, SAS INC.

PHUSE, SHANGHAI, NOV 28, 2014

OUTLINES:

- **CDISC Standard**
  - SDTM
  - ADaM
- **Interactive Standardized TLFs**
  - Tables
  - Lists
  - Figures
- **Conclusion**

CDISC: CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM



- ADaM: Analysis Data Model
  - ADSL: Subject-Level Analysis Dataset
  - BDS: Basic Data Structure
- SDTM: Study Data Tabulation Model
- SEND: Standard for Exchange of Nonclinical Data

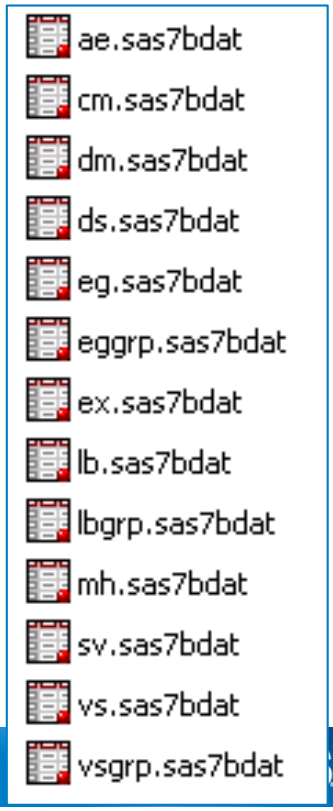
BASIC RULES FOR CDISC VARIABLES

- The *Variable Name* 8 characters
- The *Variable Label* 40 characters
- The data *Type*

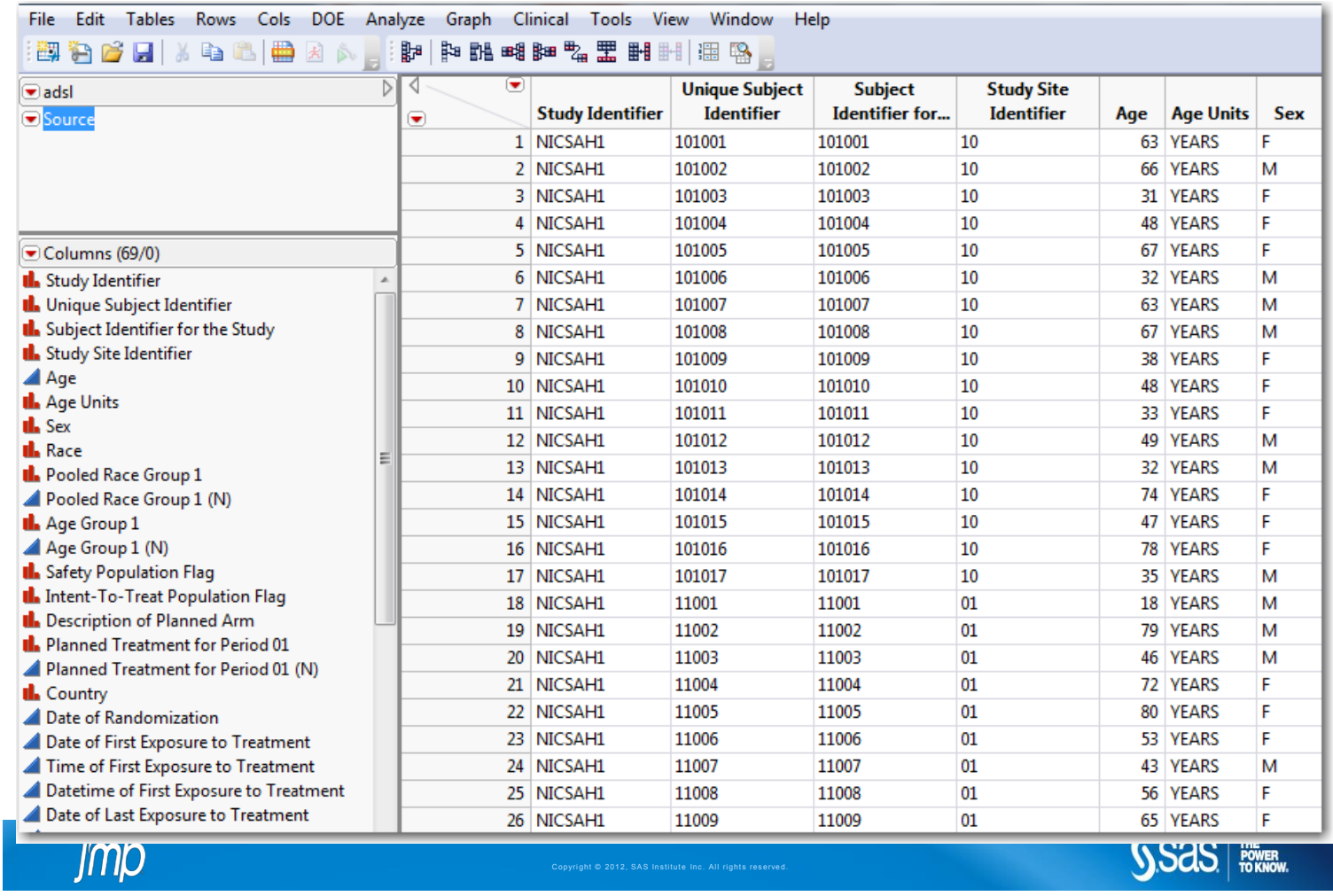
SDTM AND ADAM

ADaM

SDTM

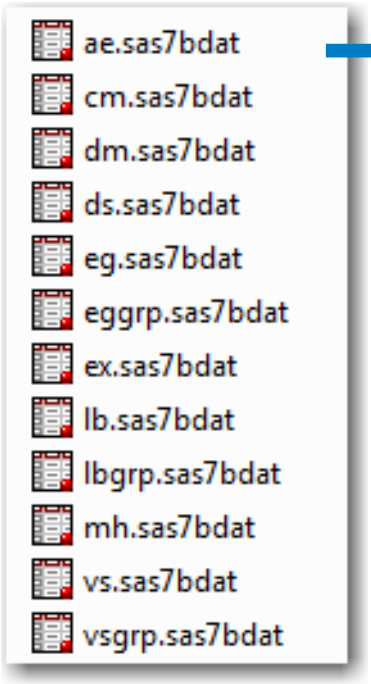


ADAM: ANALYSIS DATA MODEL



	Study Identifier	Unique Subject Identifier	Subject Identifier for...	Study Site Identifier	Age	Age Units	Sex
1	NICSAH1	101001	101001	10	63	YEARS	F
2	NICSAH1	101002	101002	10	66	YEARS	M
3	NICSAH1	101003	101003	10	31	YEARS	F
4	NICSAH1	101004	101004	10	48	YEARS	F
5	NICSAH1	101005	101005	10	67	YEARS	F
6	NICSAH1	101006	101006	10	32	YEARS	M
7	NICSAH1	101007	101007	10	63	YEARS	M
8	NICSAH1	101008	101008	10	67	YEARS	M
9	NICSAH1	101009	101009	10	38	YEARS	F
10	NICSAH1	101010	101010	10	48	YEARS	F
11	NICSAH1	101011	101011	10	33	YEARS	F
12	NICSAH1	101012	101012	10	49	YEARS	M
13	NICSAH1	101013	101013	10	32	YEARS	M
14	NICSAH1	101014	101014	10	74	YEARS	F
15	NICSAH1	101015	101015	10	47	YEARS	F
16	NICSAH1	101016	101016	10	78	YEARS	F
17	NICSAH1	101017	101017	10	35	YEARS	M
18	NICSAH1	11001	11001	01	18	YEARS	M
19	NICSAH1	11002	11002	01	79	YEARS	M
20	NICSAH1	11003	11003	01	46	YEARS	M
21	NICSAH1	11004	11004	01	72	YEARS	F
22	NICSAH1	11005	11005	01	80	YEARS	F
23	NICSAH1	11006	11006	01	53	YEARS	F
24	NICSAH1	11007	11007	01	43	YEARS	M
25	NICSAH1	11008	11008	01	56	YEARS	F
26	NICSAH1	11009	11009	01	65	YEARS	F

SDTM: STUDY DATA TABULATION MODEL



Study Identifier	Domain Abbreviation	Unique Subject Identifier	Sequence Number	Reported Term for the Adverse..	Dictionary-Derived Term	Body System or Organ Class	Severity/Intensity	Serious Event	Action Taken with	Causality	Outcome of
NICSAH1	AE	101001	1	Hydrocephalus	Hydrocephalus	NERVOUS SYSTEM DISORDERS	MILD	N	DRUG WIT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101001	2	Pyrexia	Pyrexia	GENERAL DISORDERS AND ADMINISTR	MILD	N	DOSE NOT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101001	3	Vasoconstriction	Vasoconstriction	VASCULAR DISORDERS	MODERATE	N	DOSE NOT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101001	4	Vomiting	Vomiting	GASTROINTESTINAL DISORDERS	MILD	N	DOSE NOT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101002	1	Alveolitis	Alveolitis	RESPIRATORY, THORACIC AND MEDIAS	MODERATE	N	UNKNOWN	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101002	2	Hydrocephalus	Hydrocephalus	NERVOUS SYSTEM DISORDERS	MODERATE	N	UNKNOWN	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101002	3	Hyperglycaemia	Hyperglycaemia	METABOLISM AND NUTRITION DISORDE	MODERATE	N	UNKNOWN	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101002	4	Pulmonary oede...	Pulmonary oedema	RESPIRATORY, THORACIC AND MEDIAS	MODERATE	N	UNKNOWN	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101002	5	Urinary tract infecti	Urinary tract infection	INFECTIONS AND INFESTATIONS	MODERATE	N	UNKNOWN	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101002	6	Vasoconstriction	Vasoconstriction	VASCULAR DISORDERS	MILD	N	UNKNOWN	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101002	7	Ventricular extrasy	Ventricular extrasystole	CARDIAC DISORDERS	MODERATE	N	UNKNOWN	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101004	1	Brain oedema	Brain oedema	NERVOUS SYSTEM DISORDERS	MILD	N	UNKNOWN	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101004	2	Coma	Coma	NERVOUS SYSTEM DISORDERS	SEVERE	Y	DRUG WIT	RELATED	RECOVERED/RESO
NICSAH1	AE	101004	3	Hydrocephalus	Hydrocephalus	NERVOUS SYSTEM DISORDERS	SEVERE	Y	DRUG WIT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101004	4	Hyperglycaemia	Hyperglycaemia	METABOLISM AND NUTRITION DISORDE	MILD	N	DRUG WIT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101004	5	Hypotension	Hypotension	VASCULAR DISORDERS	SEVERE	Y	DRUG WIT	RELATED	RECOVERED/RESO
NICSAH1	AE	101004	6	Intracranial press	Intracranial pressure in	NERVOUS SYSTEM DISORDERS	SEVERE	Y	DRUG WIT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101004	7	Subarachnoid ha	Subarachnoid haemorr	NERVOUS SYSTEM DISORDERS	SEVERE	Y	DRUG WIT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101004	8	Vasoconstriction	Vasoconstriction	VASCULAR DISORDERS	SEVERE	Y	DRUG WIT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101005	1	Alveolitis	Alveolitis	RESPIRATORY, THORACIC AND MEDIAS	MODERATE	N	DRUG WIT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101005	2	Anaemia	Anaemia	BLOOD AND LYMPHATIC SYSTEM DISOR	MILD	N	DRUG WIT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101005	3	Heart rate increas	Heart rate increased	INVESTIGATIONS	MILD	N	DRUG WIT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101005	4	Hydrocephalus	Hydrocephalus	NERVOUS SYSTEM DISORDERS	MILD	N	DRUG WIT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101005	5	Hyperglycaemia	Hyperglycaemia	METABOLISM AND NUTRITION DISORDE	MODERATE	N	DRUG WIT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101005	6	Hypertension	Hypertension	VASCULAR DISORDERS	MODERATE	N	DRUG WIT	NOT RELATE	RECOVERED/RESO
NICSAH1	AE	101005	7	Hypokalaemia	Hypokalaemia	METABOLISM AND NUTRITION DISORDE	MILD	N	DRUG WIT	NOT RELATE	RECOVERED/RESO

CDISC: Clinical Data Interchange Standards Consortium

CLASSIC DEMOGRAPHICS TABLE REPORT:

Contains Nonbinding Recommendations

7.2.1.2 Demographics

The reviewer should include appendix tables in a format similar to that illustrated in Table 7.2.1.2.1 (showing percent distribution within treatments of patients by age, gender, and race as well as weight in various groups), providing overall demographic information for phase 1 and phase 2 to 3 study pools separately. It may be appropriate to provide demographic displays for subsets within these larger pools at other points in the review.

FDA Reviewer Guidance 2005

Patient Population By Age Group
Table 7.2.1.2.1 of the GRP

	Description of Planned Arm				All	
	NIC .15		Placebo			
	N	%	N	%	N	%
AgeGroup						
39 or less	114	12.58	108	11.92	222	24.50
40-64	267	29.47	286	31.57	553	61.04
65 & older	68	7.51	63	6.95	131	14.46
All	449	49.56	457	50.44	906	100.00

Patient Population By Gender
Table 7.2.1.2.1 of the GRP

	Description of Planned Arm				All	
	NIC .15		Placebo			
	N	%	N	%	N	%
Gender						
Female	281	31.02	297	32.78	578	63.80
Male	168	18.54	160	17.66	328	36.20
All	449	49.56	457	50.44	906	100.00

Patient Population By Race
Table 7.2.1.2.1 of the GRP

	Description of Planned Arm				All	
	NIC .15		Placebo			
	N	%	N	%	N	%
Race						
ASIAN	8	0.88	7	0.77	15	1.66
BLACK	79	8.72	60	6.62	139	15.34
OTHER	21	2.32	30	3.31	51	5.63
WHITE	341	37.64	360	39.74	701	77.37
All	449	49.56	457	50.44	906	100.00

MODERN DEMOGRAPHICS TABLE REPORT: SAME

Subject Population by Age Group

	Planned Treatment for Period 01					
	NIC .15		Placebo			
Age Group	Count	Column %	Count	Column %	Count	% of Total
Age 39 or younger	113	25.3%	107	23.5%	220	24.39%
Age 65 and older	68	15.2%	63	13.8%	131	14.52%
Age between 40 and 64	266	59.5%	285	62.6%	551	61.09%
All	447	100.0%	455	100.0%	902	100.00%

Subject Population by Sex

	Planned Treatment for Period 01					
	NIC .15		Placebo			
Sex	Count	Column %	Count	Column %	Count	% of Total
F	281	62.9%	297	65.3%	578	64.08%
M	166	37.1%	158	34.7%	324	35.92%
All	447	100.0%	455	100.0%	902	100.00%

Subject Population by Race

	Planned Treatment for Period 01					
	NIC .15		Placebo			
Race	Count	Column %	Count	Column %	Count	% of Total
ASIAN	8	1.8%	7	1.5%	15	1.66%
BLACK OR AFRICAN AMERICAN	78	17.4%	60	13.2%	138	15.30%
OTHER	21	4.7%	29	6.4%	50	5.54%
WHITE	340	76.1%	359	78.9%	699	77.49%
All	447	100.0%	455	100.0%	902	100.00%

MODERN DEMOGRAPHICS TABLE REPORT: NEW

Subject Population by Age

		Planned Treatment for Period 01		
		NIC .15	Placebo	All
Age	N	447	455	902
	Mean	49.70	50.25	49.98
	Std Dev	13.92	13.75	13.83
	Min	18	18	18
	Quantiles25	39	40	40
	Median	49	50	50
	Quantiles75	60	60	60
	Max	86	108	108

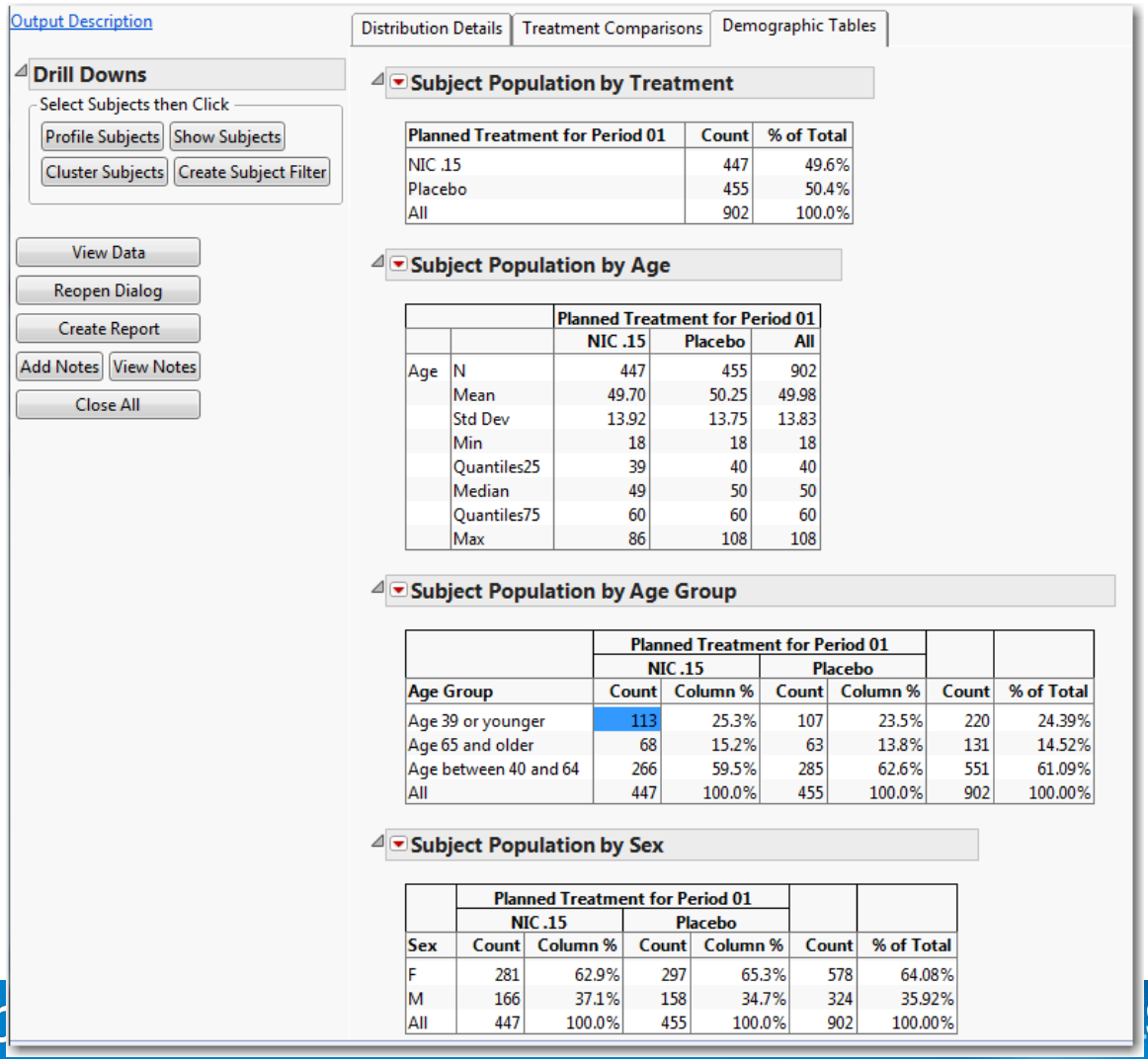
Subject Population by Treatment

Planned Treatment for Period 01	Count	% of Total
NIC .15	447	49.6%
Placebo	455	50.4%
All	902	100.0%

Subject Population by Study Site

		Planned Treatment for Period 01					
		NIC .15		Placebo			
Country	Study Site Identifier	Count	Column %	Count	Column %	Count	% of Total
USA	01	25	5.6%	26	5.7%	51	5.65%
	02	16	3.6%	16	3.5%	32	3.55%
	03	11	2.5%	12	2.6%	23	2.55%
	04	14	3.1%	12	2.6%	26	2.88%
	05	2	0.4%	2	0.4%	4	0.44%
	06	3	0.7%	4	0.9%	7	0.78%

INTERACTIVE MODERN DEMOGRAPHICS TABLE REPORT



Output Description

Distribution Details | Treatment Comparisons | Demographic Tables

Drill Downs

Select Subjects then Click

Profile Subjects | Show Subjects | Cluster Subjects | Create Subject Filter

View Data | Reopen Dialog | Create Report | Add Notes | View Notes | Close All

Subject Population by Treatment

Planned Treatment for Period 01	Count	% of Total
NIC .15	447	49.6%
Placebo	455	50.4%
All	902	100.0%

Subject Population by Age

		Planned Treatment for Period 01		
		NIC .15	Placebo	All
Age	N	447	455	902
	Mean	49.70	50.25	49.98
	Std Dev	13.92	13.75	13.83
	Min	18	18	18
	Quantiles25	39	40	40
	Median	49	50	50
	Quantiles75	60	60	60
	Max	86	108	108

Subject Population by Age Group

	Planned Treatment for Period 01					
	NIC .15		Placebo			
Age Group	Count	Column %	Count	Column %	Count	% of Total
Age 39 or younger	113	25.3%	107	23.5%	220	24.39%
Age 65 and older	68	15.2%	63	13.8%	131	14.52%
Age between 40 and 64	266	59.5%	285	62.6%	551	61.09%
All	447	100.0%	455	100.0%	902	100.00%

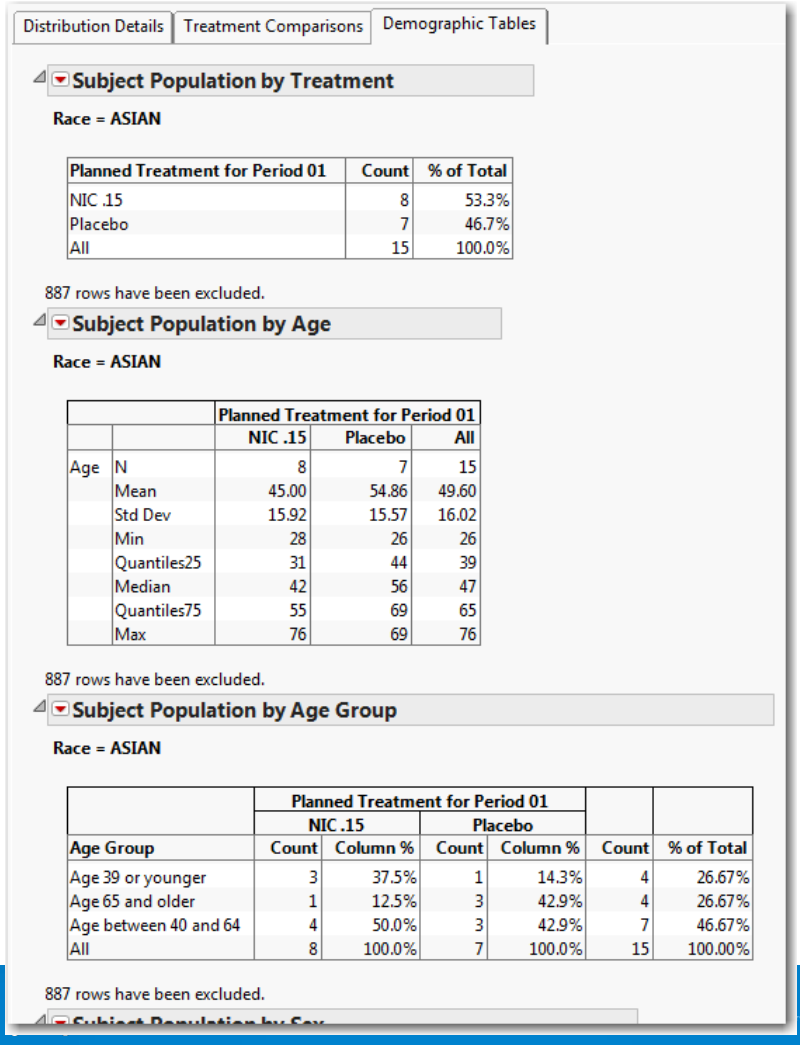
Subject Population by Sex

	Planned Treatment for Period 01					
	NIC .15		Placebo			
Sex	Count	Column %	Count	Column %	Count	% of Total
F	281	62.9%	297	65.3%	578	64.08%
M	166	37.1%	158	34.7%	324	35.92%
All	447	100.0%	455	100.0%	902	100.00%

REPORT LISTS: INDIVIDUAL INFORMATION LIST

PATIENT PROFILES

INTERACTIVE MODERN DEMOGRAPHICS TABLE REPORT



Distribution Details | Treatment Comparisons | Demographic Tables

Subject Population by Treatment

Race = ASIAN

Planned Treatment for Period 01	Count	% of Total
NIC .15	8	53.3%
Placebo	7	46.7%
All	15	100.0%

887 rows have been excluded.

Subject Population by Age

Race = ASIAN

		Planned Treatment for Period 01		
		NIC .15	Placebo	All
Age	N	8	7	15
	Mean	45.00	54.86	49.60
	Std Dev	15.92	15.57	16.02
	Min	28	26	26
	Quantiles25	31	44	39
	Median	42	56	47
	Quantiles75	55	69	65
	Max	76	69	76

887 rows have been excluded.

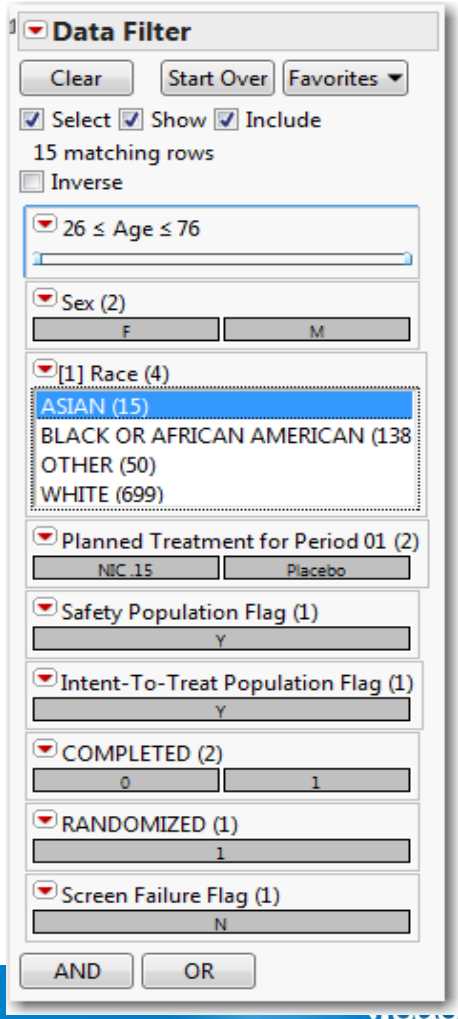
Subject Population by Age Group

Race = ASIAN

	Planned Treatment for Period 01					
	NIC .15		Placebo			
Age Group	Count	Column %	Count	Column %	Count	% of Total
Age 39 or younger	3	37.5%	1	14.3%	4	26.67%
Age 65 and older	1	12.5%	3	42.9%	4	26.67%
Age between 40 and 64	4	50.0%	3	42.9%	7	46.67%
All	8	100.0%	7	100.0%	15	100.00%

887 rows have been excluded.

Subject Population by Sex



Data Filter

Clear | Start Over | Favorites

Select | Show | Include

15 matching rows

Inverse

26 ≤ Age ≤ 76

Sex (2)

F | M

[1] Race (4)

ASIAN (15)
BLACK OR AFRICAN AMERICAN (138
OTHER (50)
WHITE (699)

Planned Treatment for Period 01 (2)

NIC .15 | Placebo

Safety Population Flag (1)

Y

Intent-To-Treat Population Flag (1)

Y

COMPLETED (2)

0 | 1

RANDOMIZED (1)

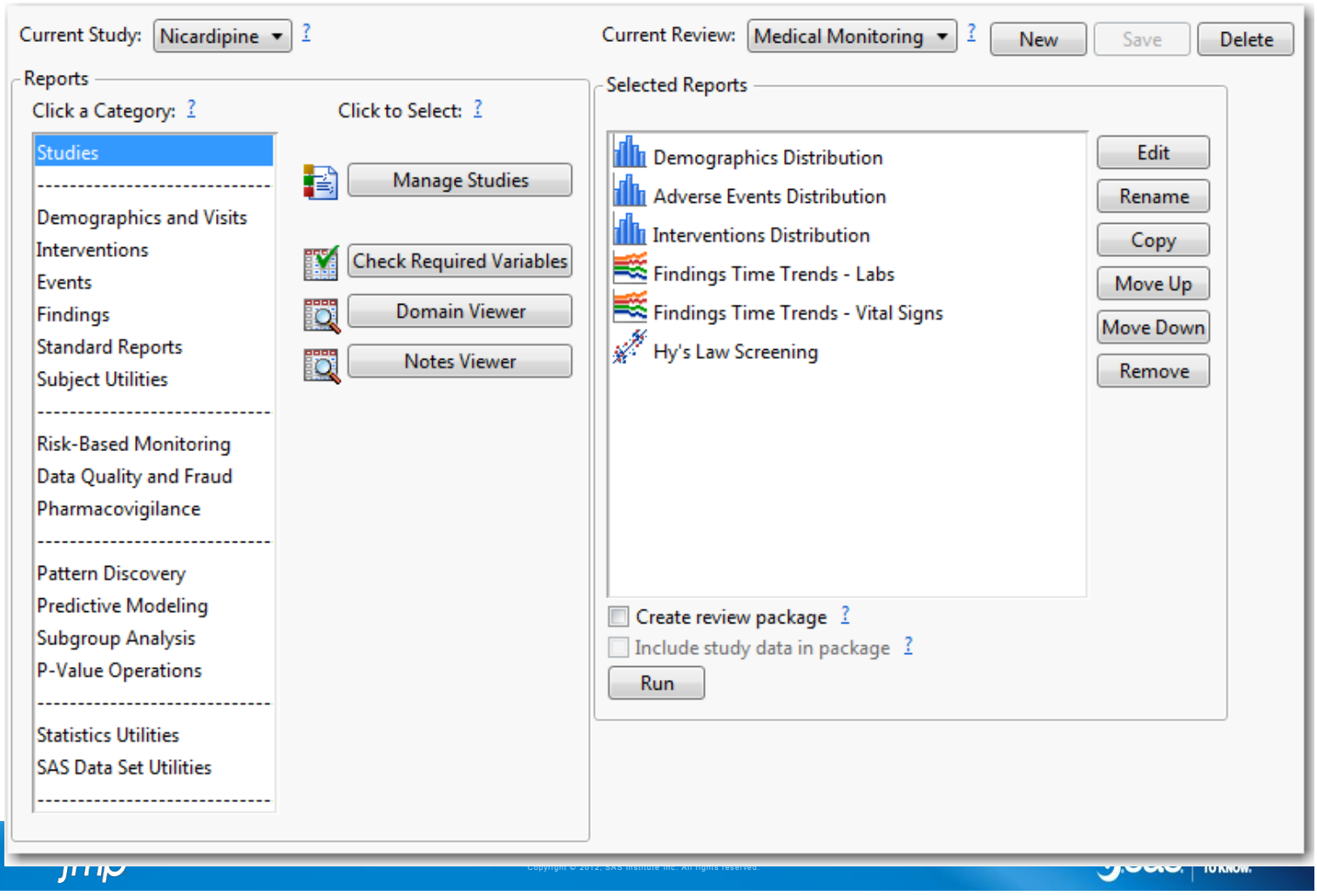
1

Screen Failure Flag (1)

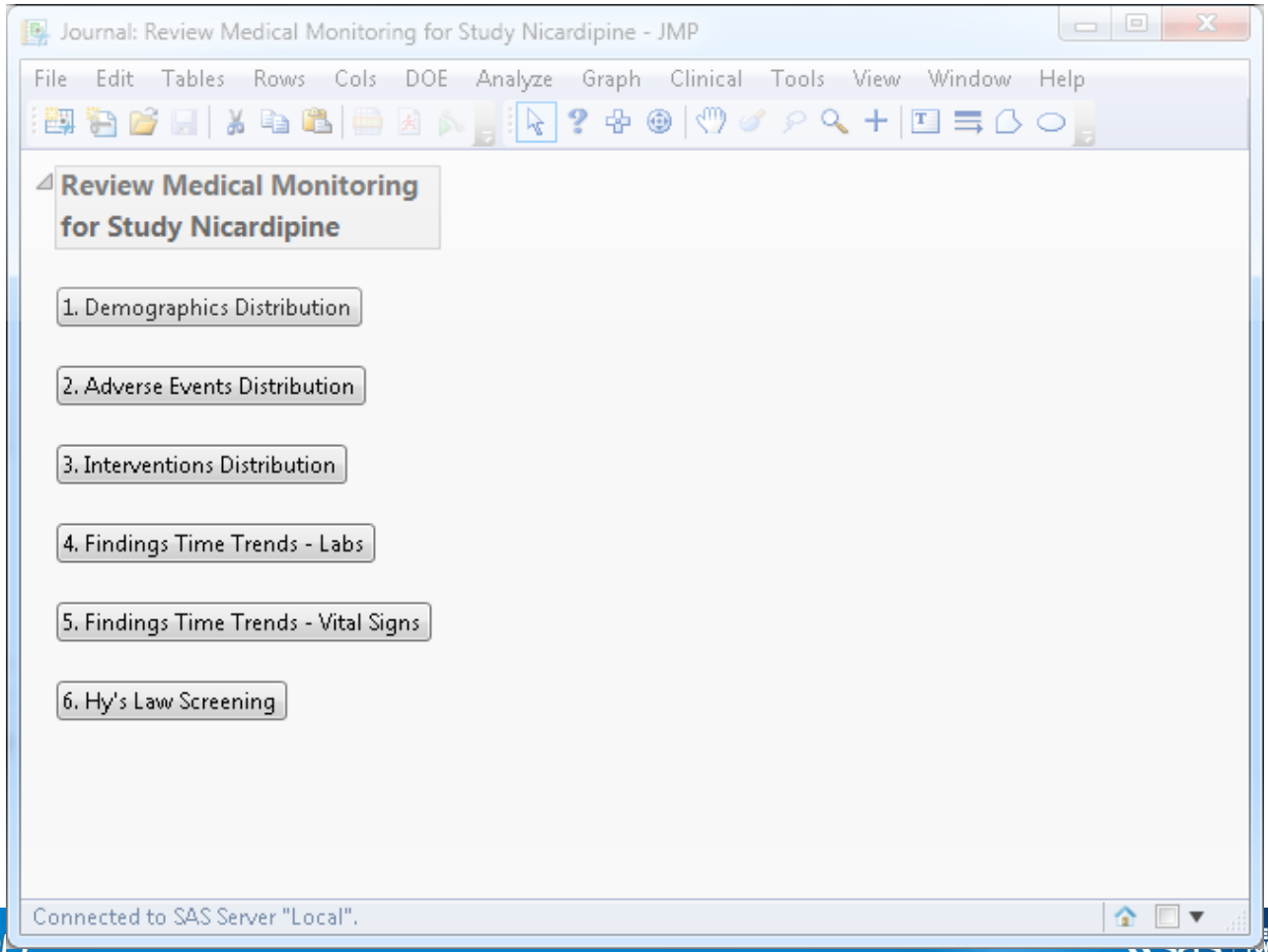
N

AND | OR

REPORT LISTS: STANDARDIZED WHAT TO ANALYSIS



REPORT LISTS: STANDARDIZED WHAT THE RESULTS ARE



REPORT LISTS: INDIVIDUAL INFORMATION LIST

PATIENT PROFILES

REPORT LISTS: INDIVIDUAL INFORMATION LIST

PATIENT AE NARRATIVE

Subject: 101004
Randomized Arm: NIC .15
Investigator Name: 101A
Drugs and Doses on Day of Event: On Treatment

Serious Adverse Event (coded term [reported term]): COMA [COMA]

Subject 101004 was a 48-year-old white female. Her medical history included focal deficit associated with sah (1988), headache associated with sah (1988), loss of consciousness associated with sah (1988), vomiting associated with sah (1988), other medical condition (1977), and allergies (start date unknown). The subject discontinued the trial on 31JAN1988 (Day 4) due to death.

On 28JAN1988 (Day 1) the subject experienced a coma (severe) which was considered a serious adverse event (SAE). Though the event was considered serious, no reasons were provided on the case report form. The subject was on treatment when the event occurred. It is not known from the case report form if therapeutic measures were administered to treat the event.

Adverse events that occurred within a +/- 3-day window of the onset of the SAE included brain oedema (mild), hydrocephalus (severe), hyperglycaemia (mild), hypotension (severe), intracranial pressure increased (severe), subarachnoid haemorrhage (severe), and vasoconstriction (severe). Concomitant medications taken at the onset of the SAE included: docusate sodium, phenobarbital, potassium supplements, and ranitidine.

The investigator considered the AE to be related to study medication. The event ended on 31JAN1988 (Day 4) with a final outcome of recovered/resolved.

RISK BASED MONITORING (RBM)

TransCelerate BIOPHARMA INC.

Position Paper: Risk-Based Monitoring Methodology

1. Abstract

Current On-site Monitoring practices are frequency-based, conform to a prescribed monitoring visit schedule, and provide generalized quality control at investigational sites. Although this practice does provide a level of control, advances in risk-based approaches and technology provide an opportunity for a more holistic and proactive approach through Off-site and Central Monitoring and a targeted approach to On-site Monito
operational cor
entirely. Trans
processes fron
monitoring. Th
mechanisms to
further support site processes, subject safety, and data quality.

RBM employs Centralized and Off-site mechanisms to monitor important study parameters holistically and uses adaptive On-site Monitoring to further support site processes, subject safety, and data quality.

1 Position Paper: Risk-Based Monitoring Methodology. TransCelerate Biopharma Inc, 2013
2 Risk-based Monitoring and fraud detection in clinical trials using JMP and SAS. Richard Zink 2014

jmp

sas THE POWER TO KNOW.

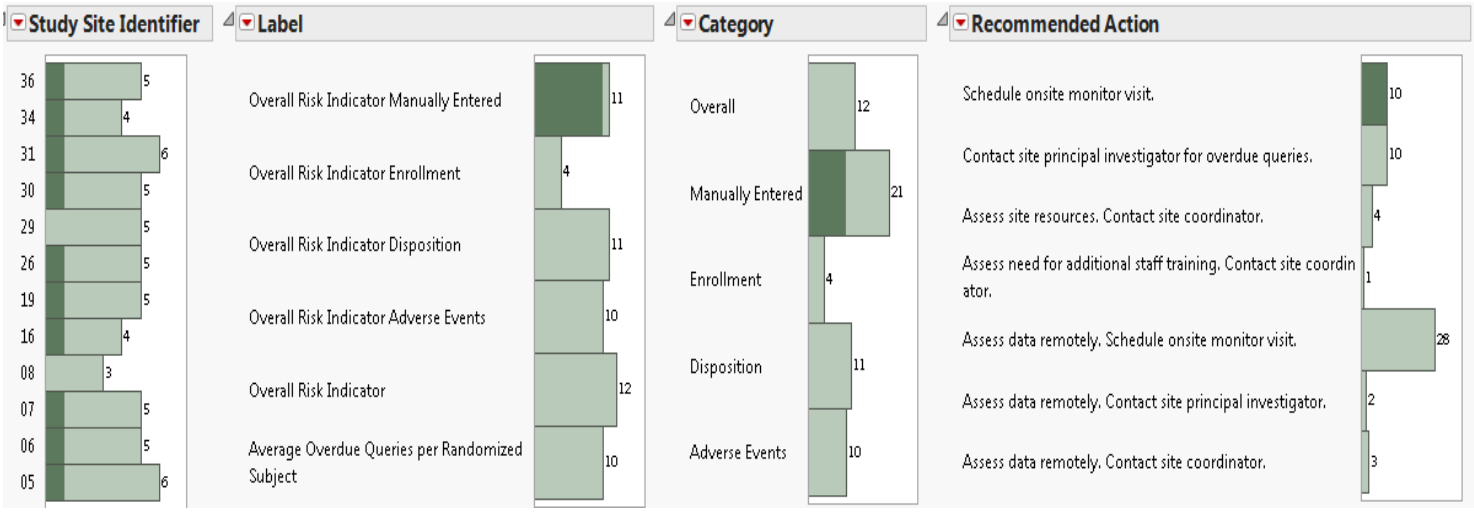
INTERACTIVE GRAPHICS: RBM

RISK INDICATORS: TRAFFIC-LIGHT SYSTEM AT SITE (OR COUNTRY) LEVEL

55/0 Cols	Study Site Identifier	Country	City	State or...	Monitor	Overall Risk Indicator	Overall Risk Indicator...	Overall Risk Indicator...	Overall Risk Indicator...	Overall Risk Indicator...
1	01	USA	New York	NY	Monitor G	0.518	0.441	0.056	0.607	0.603
2	02	USA	Orlando	FL	Monitor F	0.257	0.637	0.448	0.218	0.047
3	03	USA	Indianapolis	IN	Monitor E	0.127	0.205	0.497	0.000	0.069
4	04	FRA	Paris	Ile-de	Monitor I	0.522	0.535	0.027	0.000	0.773
5	05	ITA	Milano	Lomb	Monitor H	1.729	1.288	3.660	2.120	1.498
6	06	USA	Philadelphia	PA	Monitor G	1.443	2.481	1.289	0.000	1.431
7	07	CHN	Guangzhou	Guan	Monitor K	1.367	1.682	1.107	0.000	1.709
8	08	GBR	Birmingham	Birmi	Monitor J	0.593	1.149	1.052	0.000	0.435
9	09	CAN	Montreal	Queb	Monitor A	0.301	0.400	0.629	0.356	0.178
10	10	USA	Baltimore	MD	Monitor G	0.287	0.687	0.432	0.000	0.158
11	12	DEU	Berlin	Berlin	Monitor H	0.483	0.881	1.346	0.008	0.299
12	14	CAN	Toronto	Ontar	Monitor A	0.437	0.552	0.850	1.368	0.000
13	16	USA	Seattle	WA	Monitor B	0.662	0.597	1.282	0.669	0.589
14	17	USA	Los Angeles	CA	Monitor C	0.370	1.072	0.327	0.000	0.151
15	18	JPN	Osaka	Osak	Monitor L	0.529	0.548	1.155	0.109	0.556
16	19	CAN	Ottawa	Ontar	Monitor A	0.721	0.368	0.682	1.178	0.752
17	20	FRA	Marseille	Prove	Monitor I	0.152	0.286	0.382	0.027	0.088
18	21	ESP	Barcelona	Catal	Monitor I	0.379	0.420	0.169	0.000	0.520
19	22	CAN	Calgary	Alber	Monitor B	0.508	1.209	0.058	0.067	0.381
20	23	USA	Chicago	IL	Monitor E	0.174	0.136	0.095	0.225	0.188

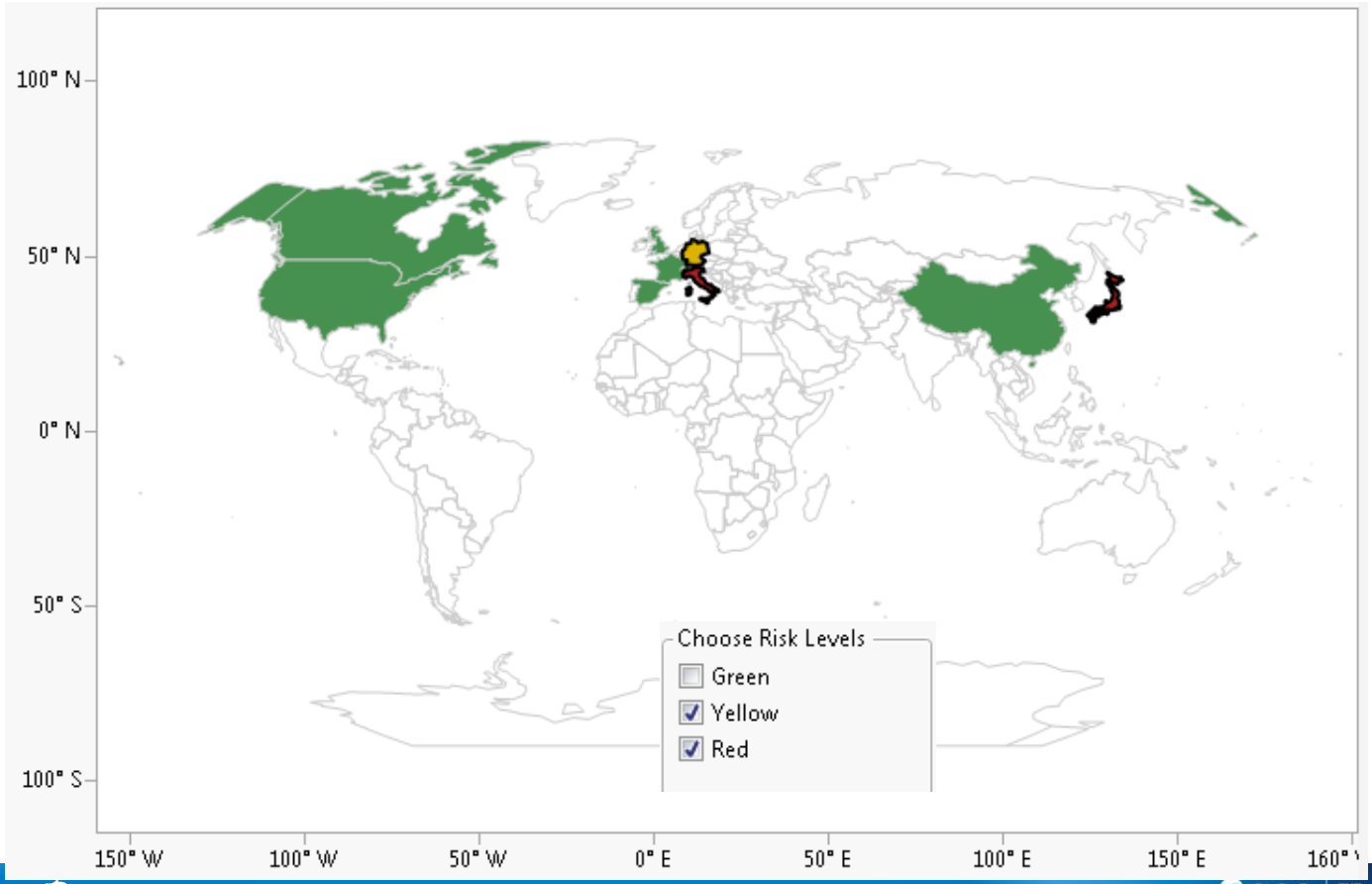
INTERACTIVE GRAPHICS: RBM

RISK INDICATORS: SUGGESTION ACTION

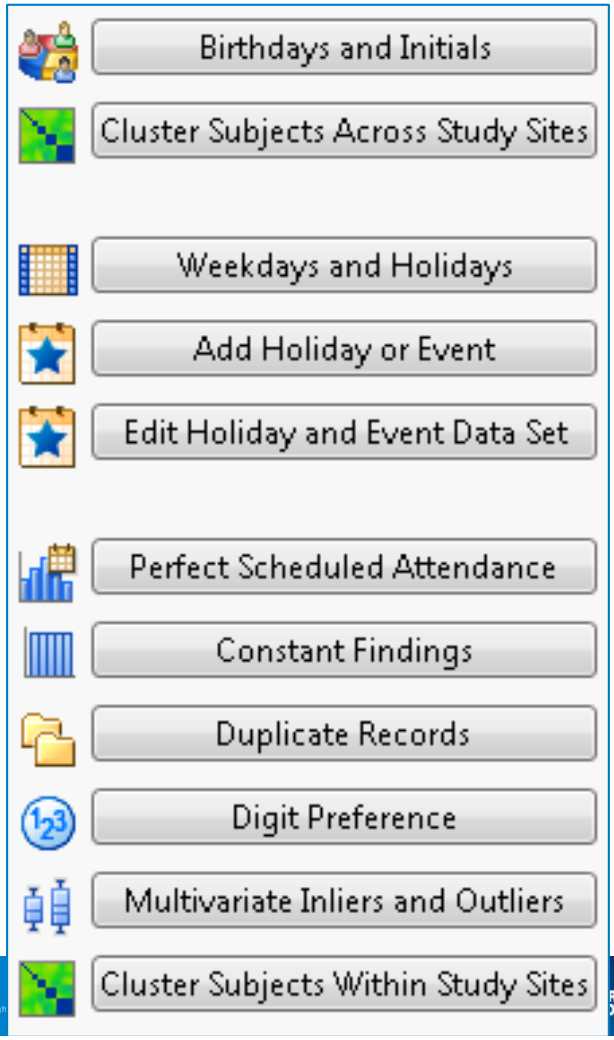


INTERACTIVE GRAPHICS: RBM

RISK INDICATORS: MAPS

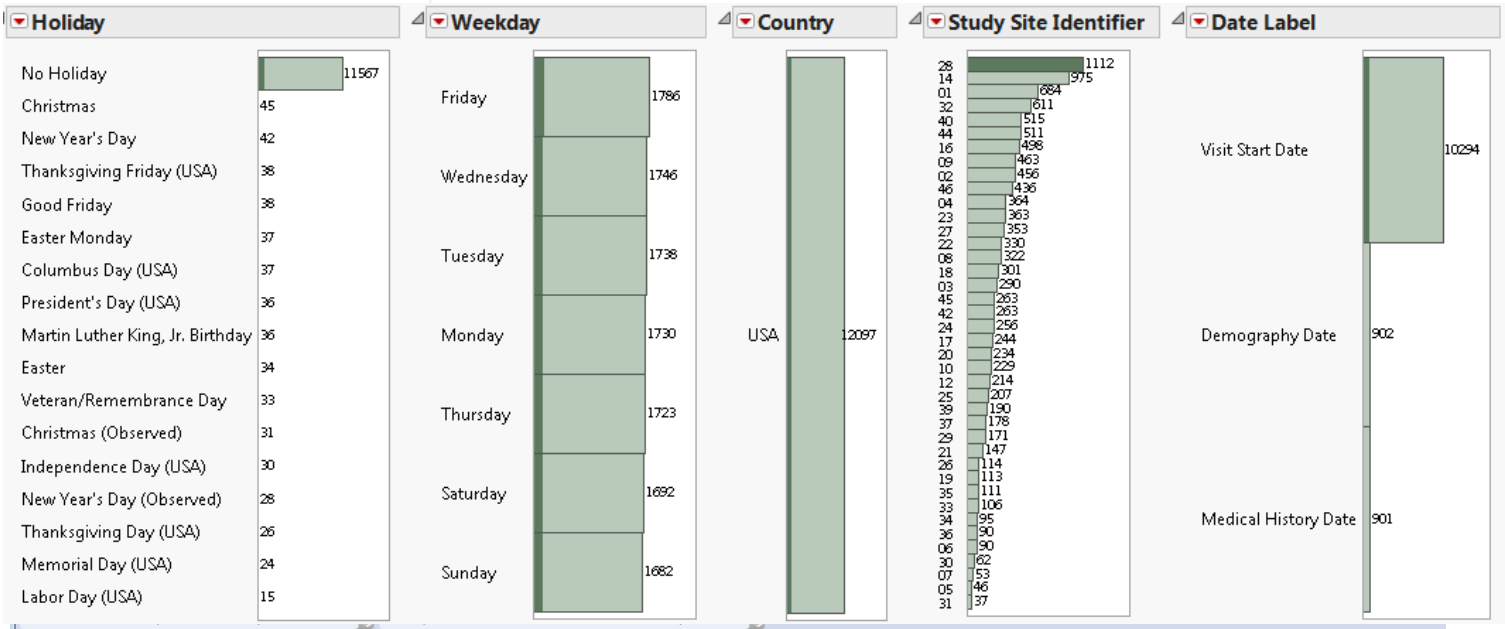


INTERACTIVE GRAPHICS: FRAUD DETECTION



INTERACTIVE GRAPHICS: FRAUD DETECTION

HOLIDAYS AND WEEKENDS



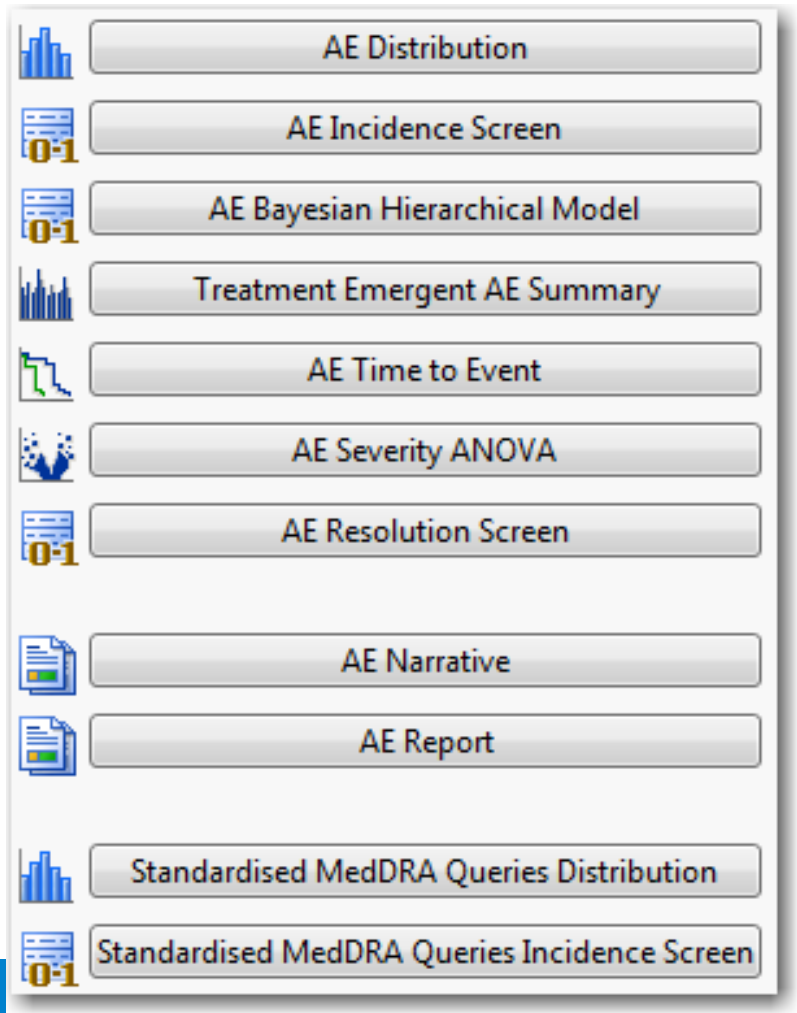
Subset of weekhol_001
Source

Columns (10/0)
- Holiday
- Holiday Flag
- Weekday *
- Unique Subject Identifier
- Study Site Identifier
- Country
- Date Label
- Date
- d9partial_DMDTC
- Visit Number

Rows

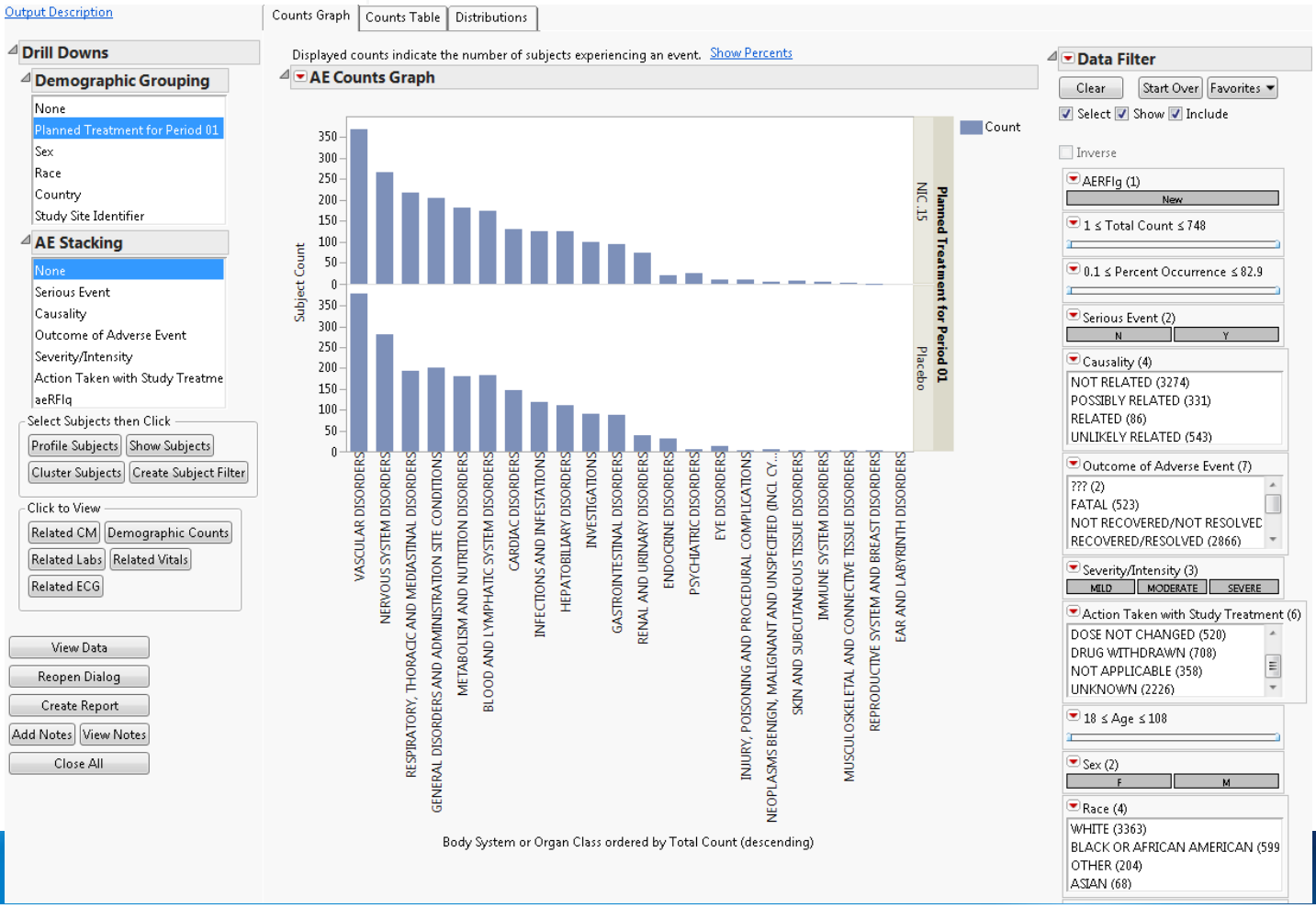
	Holiday	Holiday Flag	Weekday	Unique Subject Identifier	Study Site Identifier	Country	Date Label	Date
1	No Holiday	No Holiday	Thursday	281001	28	USA	Demography Date	24Dec1987
2	No Holiday	No Holiday	Thursday	281001	28	USA	Medical History Date	24Dec1987
3	No Holiday	No Holiday	Sunday	281001	28	USA	Visit Start Date	27Dec1987
4	No Holiday	No Holiday	Monday	281001	28	USA	Visit Start Date	28Dec1987
5	No Holiday	No Holiday	Tuesday	281001	28	USA	Visit Start Date	29Dec1987
6	No Holiday	No Holiday	Wednesday	281001	28	USA	Visit Start Date	30Dec1987
7	No Holiday	No Holiday	Thursday	281001	28	USA	Visit Start Date	31Dec1987
8	New Year's Day	Holiday	Friday	281001	28	USA	Visit Start Date	01Jan1988
9	No Holiday	No Holiday	Saturday	281001	28	USA	Visit Start Date	02Jan1988
10	No Holiday	No Holiday	Sunday	281001	28	USA	Visit Start Date	03Jan1988
11	No Holiday	No Holiday	Monday	281001	28	USA	Visit Start Date	04Jan1988
12	No Holiday	No Holiday	Tuesday	281001	28	USA	Visit Start Date	05Jan1988
13	No Holiday	No Holiday	Thursday	281001	28	USA	Visit Start Date	07Jan1988
14	No Holiday	No Holiday	Friday	281001	28	USA	Visit Start Date	08Jan1988
15	New Year's Day	Holiday	Friday	281002	28	USA	Demography Date	01Jan1988

INTERACTIVE GRAPHICS: ADVERSE EVENTS



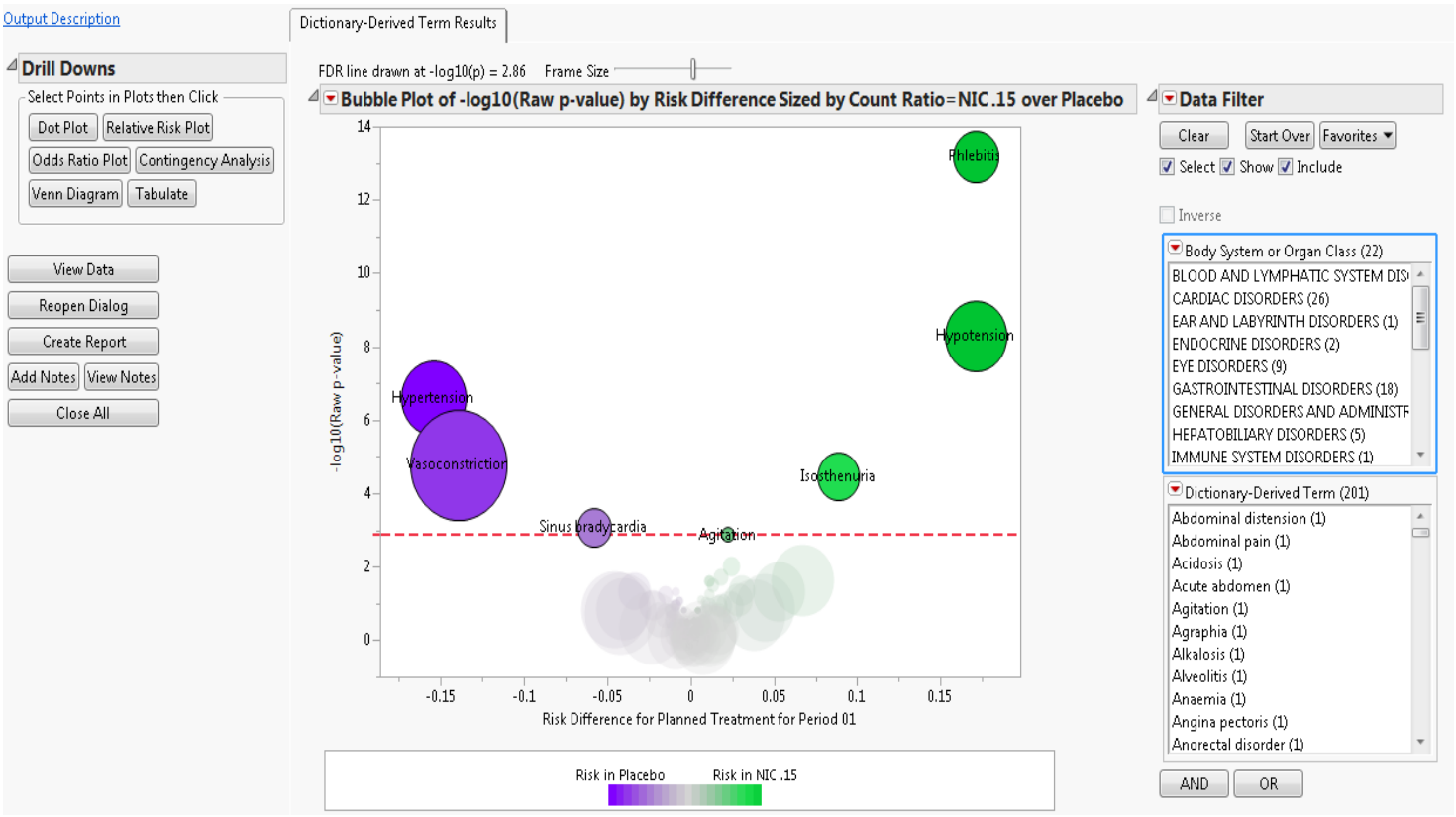
INTERACTIVE GRAPHICS: ADVERSE EVENTS

AE DISTRIBUTION

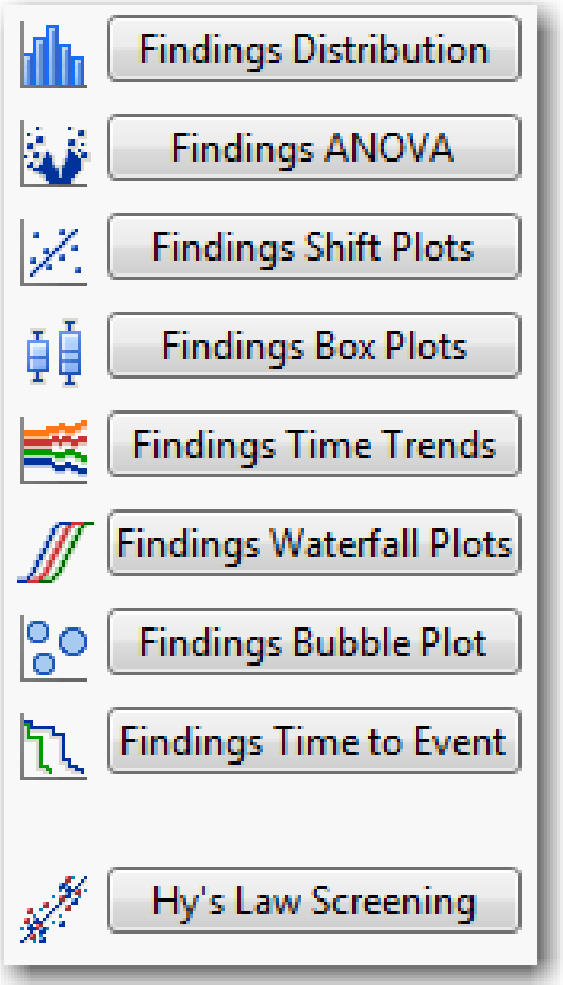


INTERACTIVE GRAPHICS: ADVERSE EVENTS

AE INCIDENCE SCREEN BUBBLE PLOT

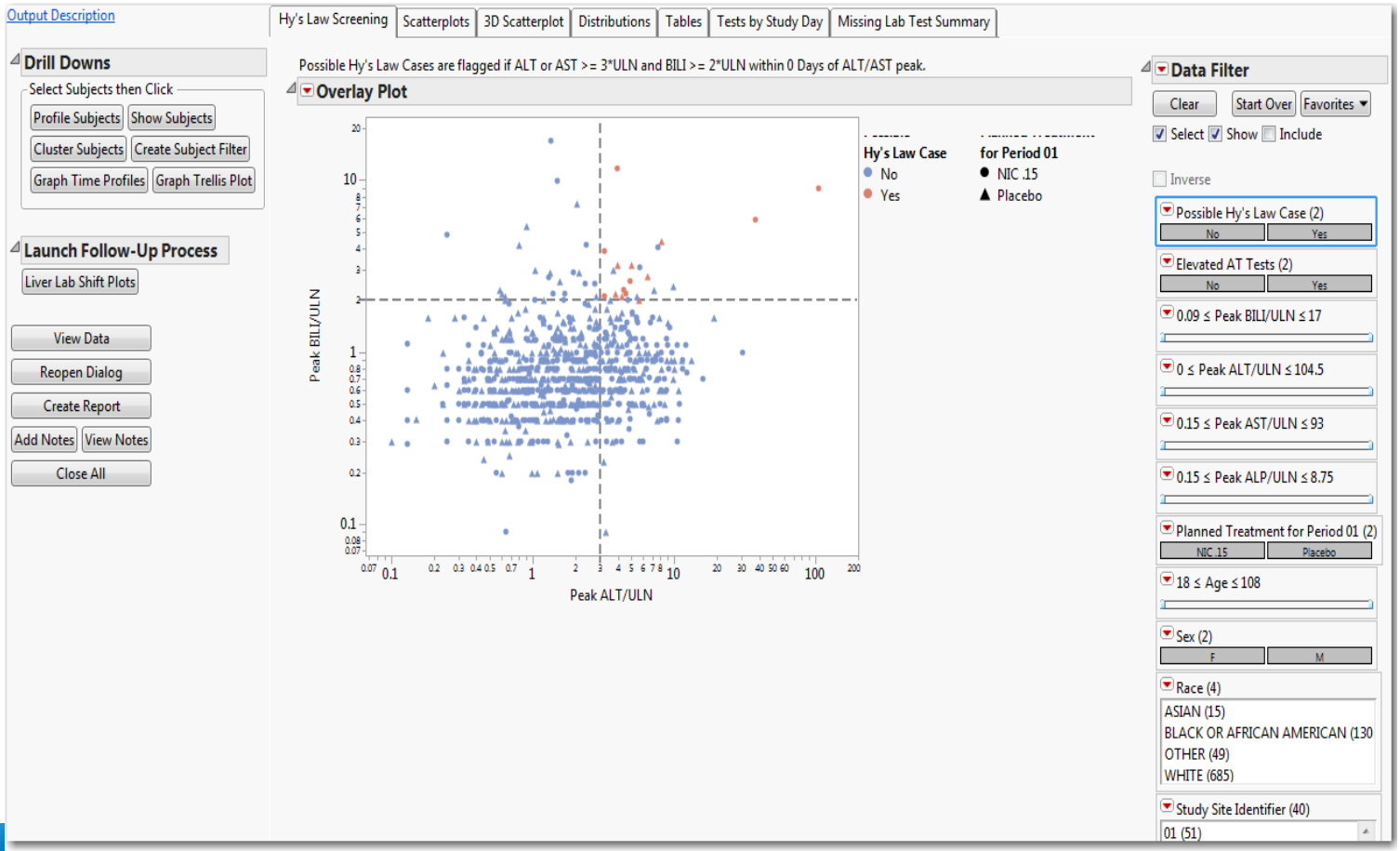


INTERACTIVE GRAPHICS: FINDINGS

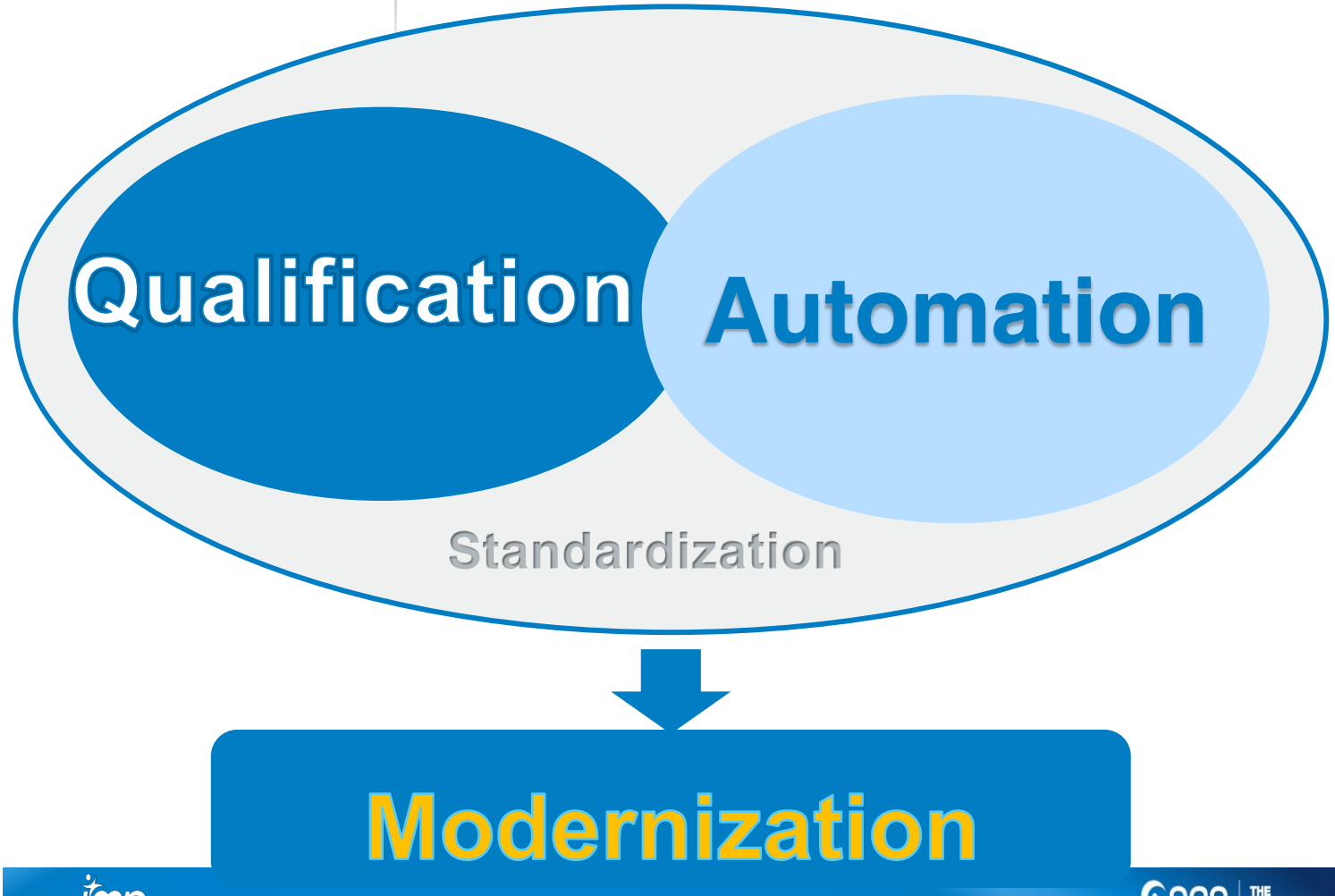


INTERACTIVE GRAPHICS: FINDINGS

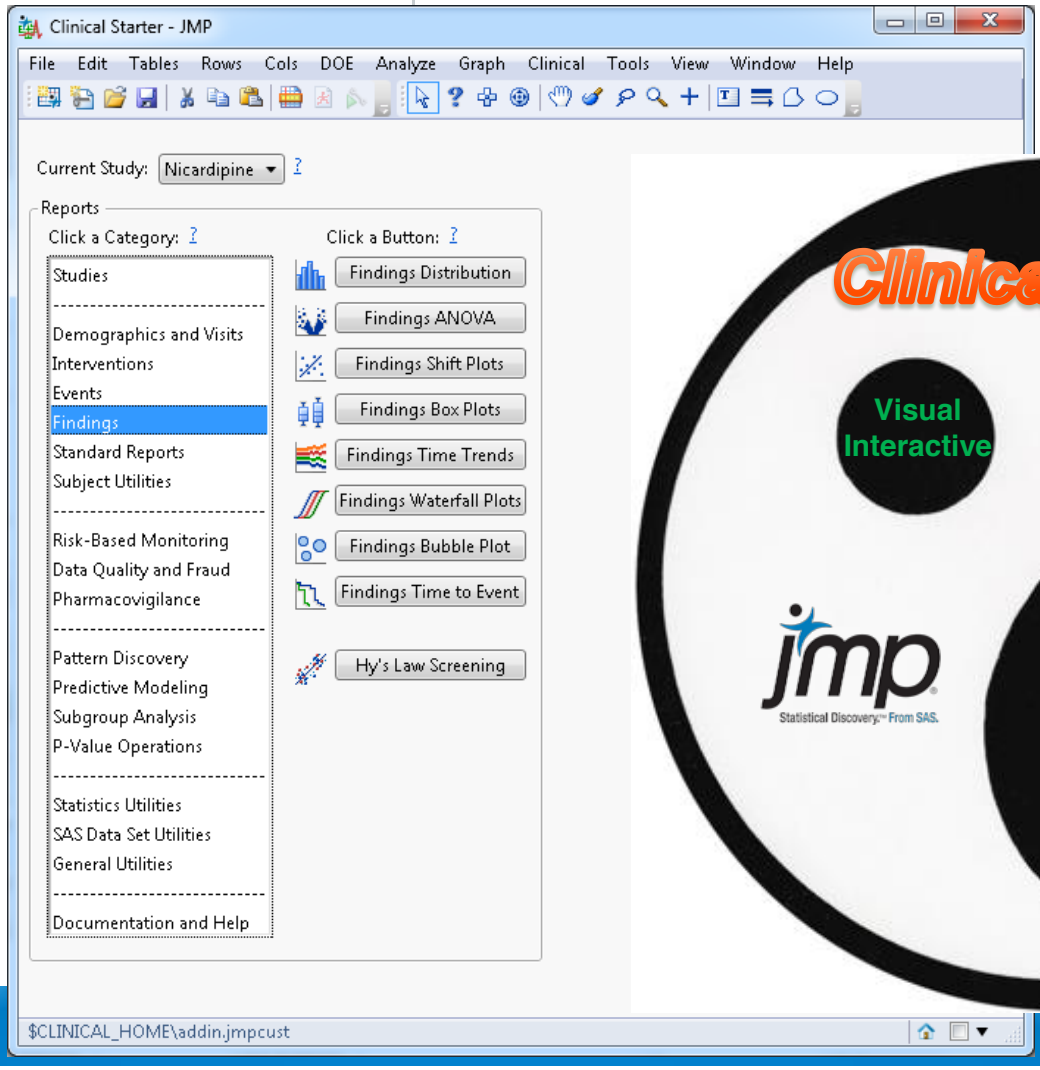
HY'S LAWS



CONCLUSIONS



JMP CLINICAL: CLINICAL TRIAL STUDY SOLUTION

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wenjun.bao@jmp.com
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