HOW TO CHECK AND VERIFY THE DATA QUALITY FOR SUBMISSION

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DATA QUALITY

- Risk-Based Monitoring (RBM)
- Enrollment Pattern
- Fraud Detection

药物临床试验数据自查核查

食品药品审核查验中心

药物临床试验数据核查工作要求

4.药物临床机构抽查原则。多中心临床试验抽查2-3个临床试验机构，必要情况下，可扩大核查范围，适当增加抽查机构数。临床试验场点抽查风险考虑因素包括：

（1）有效性结果明显高于其他中心或者同类临床试验结果的临床试验中心； Efficacy

（2）安全性数据（不良事件、预期的严重不良事件）明显低于/高于其它中心或者同类临床试验结果的临床试验中心； Safety: AE and SAE

药物临床试验数据自查核查

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（3）试验入组速度明显快于其他中心的临床试验中心； Enrollment Speed

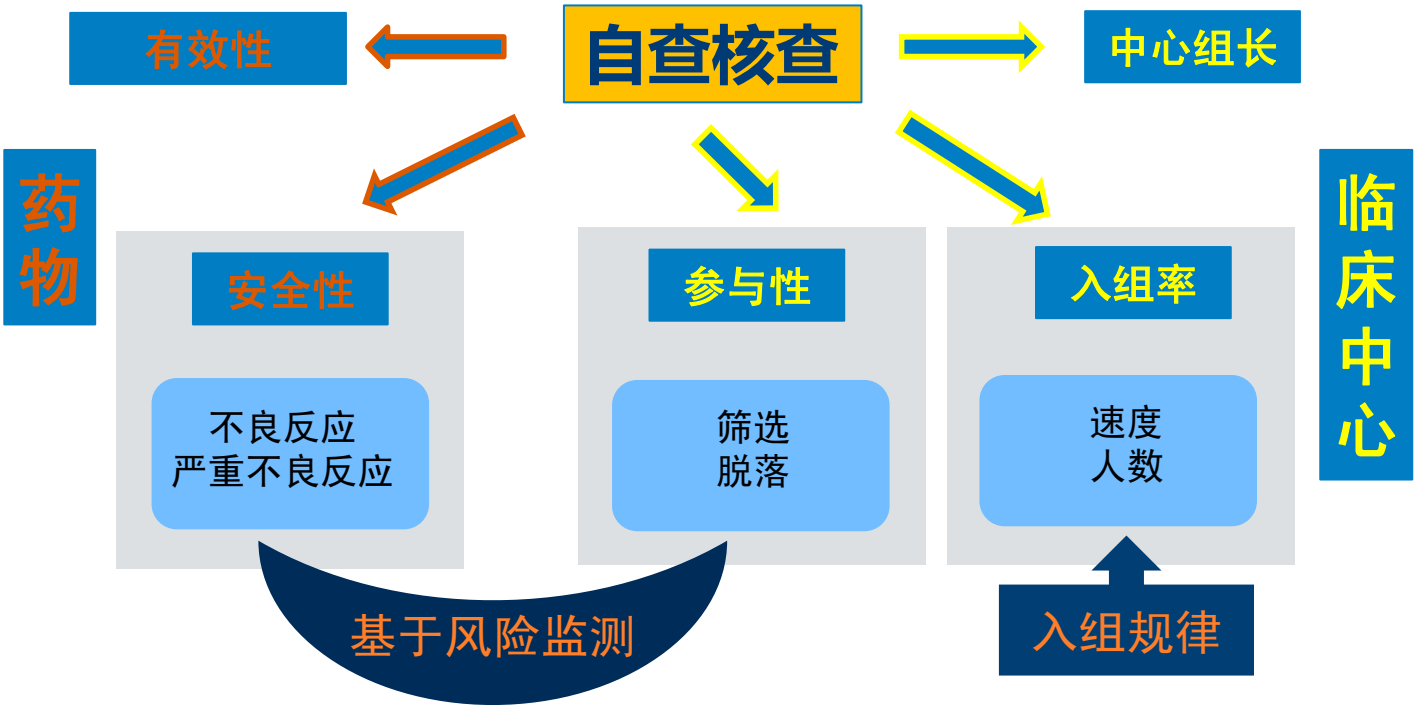
（4）试验筛选成功率明显高于常规的临床试验中心； Screen Success Rate

（5）试验脱落率明显高于常规的临床试验中心； Discontinued Rate

（6）试验入组人数最多的临床试验中心； # Enrollment

（7）担任组长单位的临床试验中心。Leader’s Site

药物临床自查核查



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RISK-BASED MONITORING (RBM)

TransCelerate BIOPHARMA INC.

ACCELERATING THE DEVELOPMENT OF NEW MEDICINES

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.

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RISK-BASED MONITORING (RBM)

风险指标

安全性
数据质量
入组和脱落
人员, 设施和用品
必备文件

风险域值

规则

+

CDISC域

AE (不良事件)
DM (人口学)
DS (处置)
SV (受试者随访)
EX (Exposure)
DV (分案偏离)
未达标内含/不含的阈值
ADSL

变量

→

风险评估

地图

交通红绿灯系统

分布图

结果

[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

国家和中心级的基于风险监查

安全性

- 不良反应
- 严重不良反应

参与性

- 脱落
- 筛选

Risk Indicators

- Overall Risk Indicator
- Overall Risk Indicator Adverse Events
- Overall Risk Indicator Disposition
- Overall Risk Indicator Enrollment
- Overall Risk Indicator Manually Entered
- AEs per PatientWeek
- Average AEs per Randomized Subject
- Average Computed Deviations per Randomized Subject
- Average Missing Pages per Randomized Subject
- Average Overdue Queries per Randomized Subject
- Average Queries per Randomized Subject
- Average SAEs per Randomized Subject
- CRF Entry Response Time
- Computed Deviations per PatientWeek
- Deaths per PatientWeek
- Missing Pages per PatientWeek
- Observed Minus Expected Randomized
- Overdue Queries per PatientWeek
- Percent Deaths of Randomized Subjects
- Percent Discontinued of Randomized Subjects
- Percent Screen Fail of Total Subjects
- Queries per PatientWeek
- Query Response Time
- Randomized per Week Active
- SAEs per PatientWeek

地图显示国家级的风险监查

不良反应 AES PER PATIENTWEEK

Output Description

Site-Level Data | Site-Level Distributions | Site-Level Map | Country-Level Data | Country-Level Distributions | Country-Level Map

Drill Downs

Risk Indicators

- Overall Risk Indicator
- Overall Risk Indicator Adverse Events
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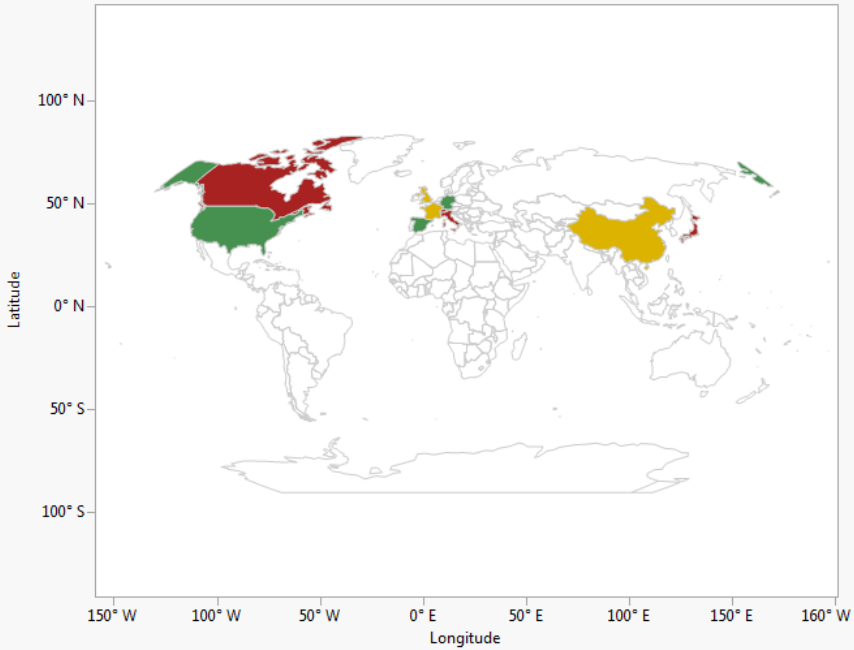
- SAEs per PatientWeek

Local Data Filter

Country-Level Data



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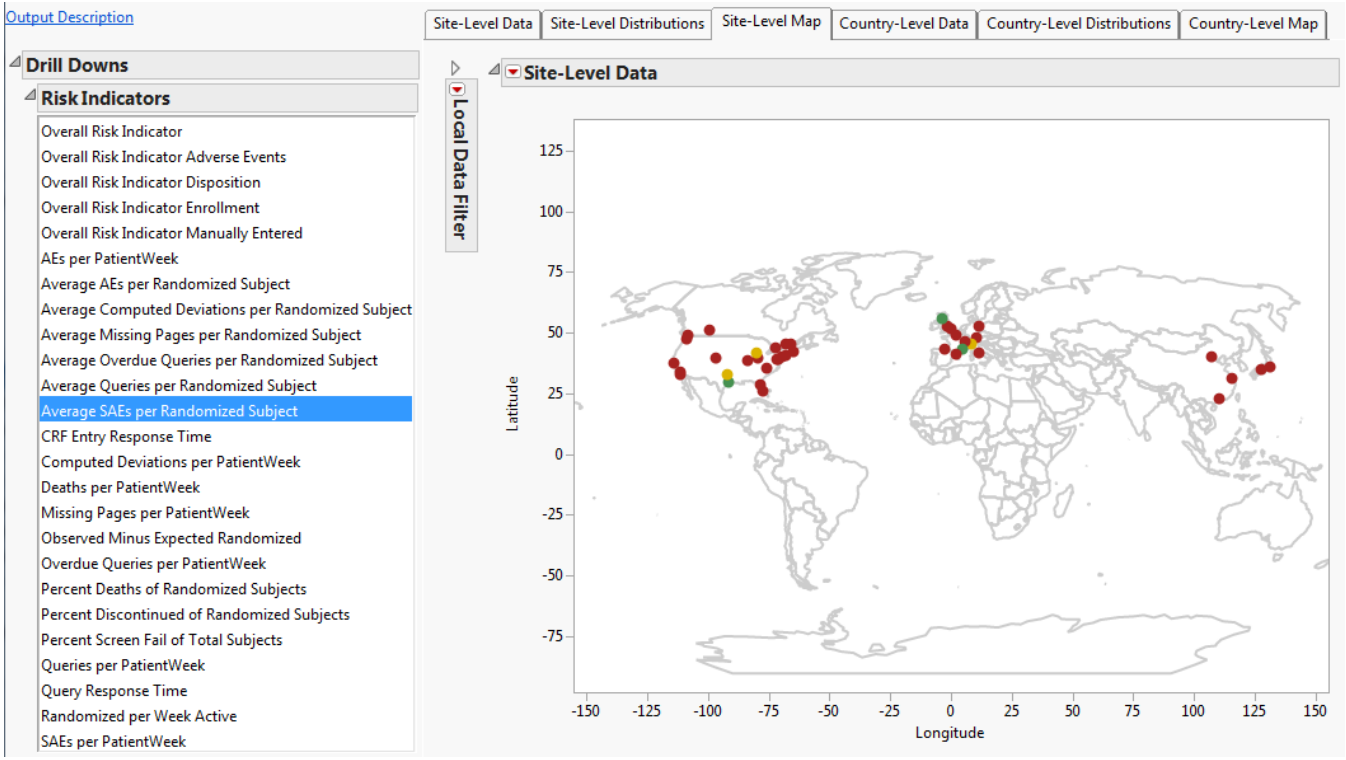
地图显示中心级的风险监查

中心级严重不良反应 AVE SAES PER RANDOMIZED SUBJECTS



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地图显示国家级风险监查

脱落： PERCENT DISCONTINUED OF RANDOMIZED SUBJECT

Output Description

Site-Level Data | Site-Level Distributions | Site-Level Map | Country-Level Data | Country-Level Distributions | Country-Level Map

Drill Downs

Risk Indicators

- Overall Risk Indicator
- Overall Risk Indicator Adverse Events
- Overall Risk Indicator Disposition
- Overall Risk Indicator Enrollment
- Overall Risk Indicator Manually Entered
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- Randomized per Week Active
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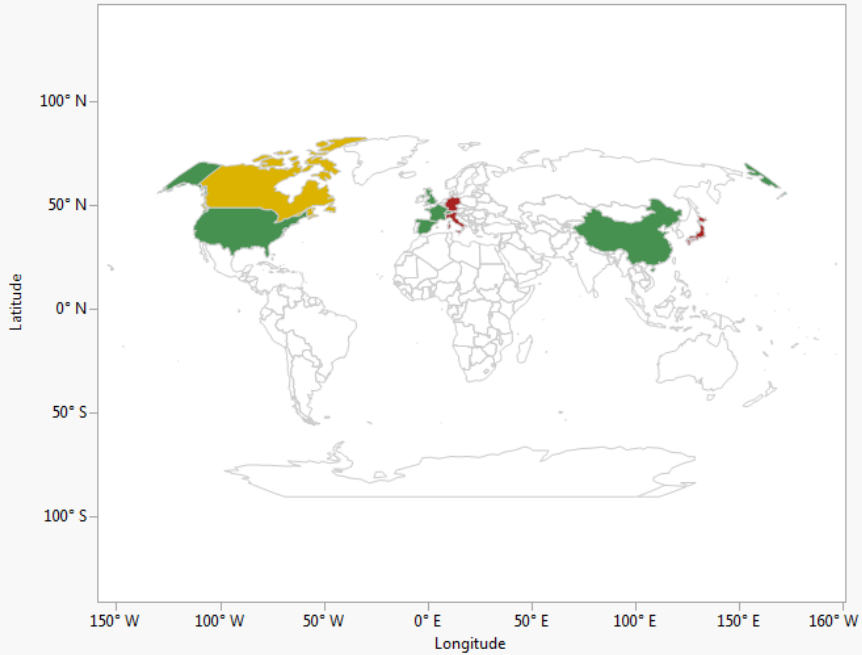
Local Data Filter

Country-Level Data



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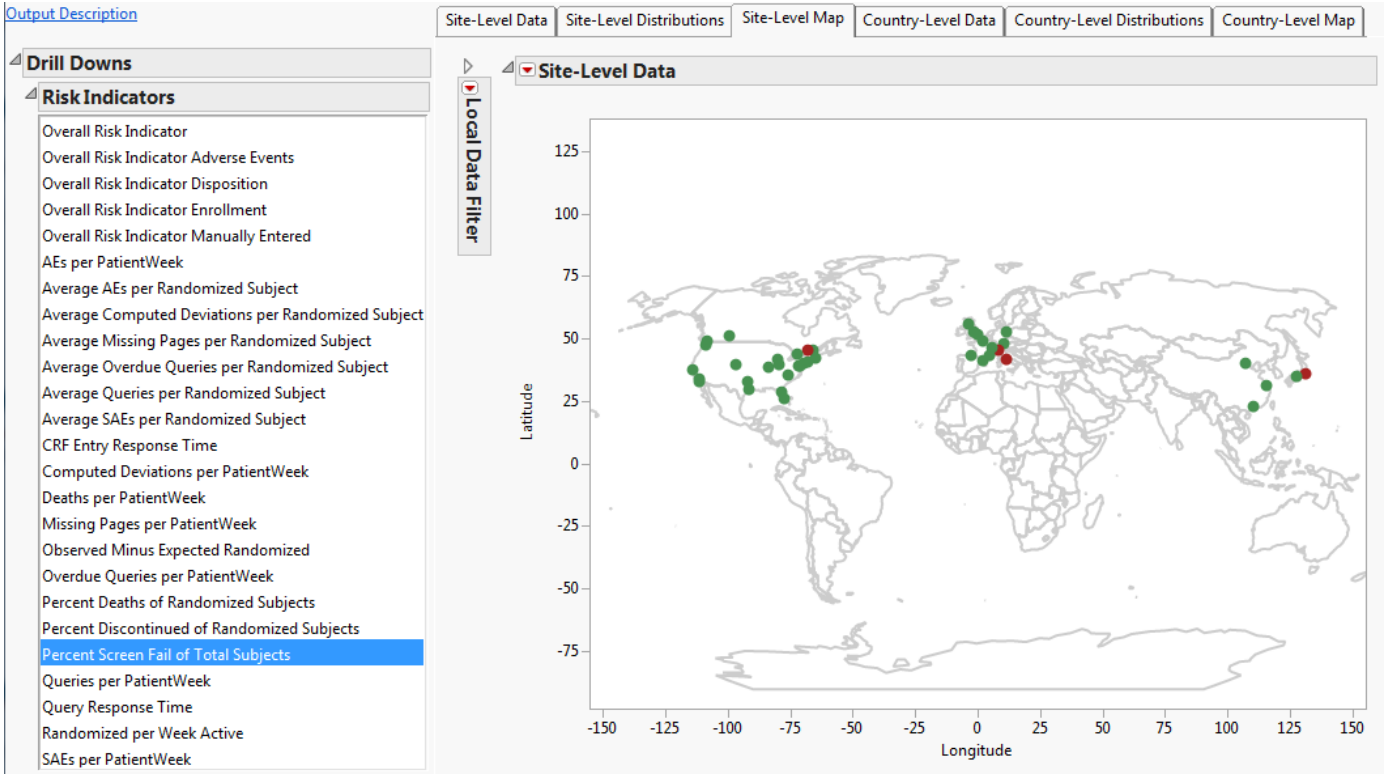
地图显示中心级的风险监查

筛选：PERCENT SCREEN FAIL OF TOTAL SUBJECTS



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红绿灯图显示国家级的风险监查

PERCENT DISCONTINUED OF RANDOMIZED SUBJECT

Output Description

Site-Level Data | Site-Level Distributions | Site-Level Map | Country-Level Data | Country-Level Distributions | Country-Level Map

Drill Downs

Risk Indicators

- Overall Risk Indicator
- Overall Risk Indicator Adverse Events
- Overall Risk Indicator Disposition
- Overall Risk Indicator Enrollment
- Overall Risk Indicator Manually Entered
- AEs per PatientWeek
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- Average Missing Pages per Randomized Subject
- Average Overdue Queries per Randomized Subject
- Average Queries per Randomized Subject
- Average SAEs per Randomized Subject

Applying risks defined in Default Risk Threshold.

51/0 Cols, 10/0 Rows

	Country	Overall Risk Indicator	Overall Risk Indicator Adverse	Overall Risk Indicator...	Overall Risk Indicator...	Overall Risk Indicator Manually	Total Sites	Total Subjects	Randomized	Screen Failure
1	CAN	0.283	0.388	0.267	0.897	0.029	5	221	221	1
2	CHE	0.202	0.482	0.023	0.185	0.098	1	24	24	0
3	CHN	0.307	0.415	0.181	0.000	0.376	3	33	33	0
4	DEU	0.360	0.213	0.724	0.000	0.493	2	24	24	0
5	ESP	0.171	0.193	0.032	0.000	0.240	2	23	23	0
6	FRA	0.317	0.430	0.045	0.000	0.412	2	44	44	0
7	GBR	0.315	0.112	0.060	0.322	0.457	3	81	81	0
8	ITA	1.766	2.028	2.915	1.595	1.501	2	10	10	2
9	JPN	0.628	1.421	0.711	0.443	0.280	2	43	43	1
10	USA	0.073	0.100	0.023	0.068	0.069	18	403	403	0

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红绿灯图显示中心级的风险监查

总风险评估

Drill Downs

Risk Indicators

- Overall Risk Indicator
- Overall Risk Indicator Adverse Events
- Overall Risk Indicator Disposition
- Overall Risk Indicator Enrollment
- Overall Risk Indicator Manually Entered
- AEs per PatientWeek
- Average AEs per Randomized Subject
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- Percent Deaths of Randomized Subjects
- Percent Discontinued of Randomized Subjects
- Percent Screen Fail of Total Subjects
- Queries per PatientWeek
- Query Response Time
- Randomized per Week Active
- SAEs per PatientWeek

Applying risks defined in Default Risk Threshold.

55/0 Cols
40/0 Rows

	Study Site Identifier	Country	City	State or Province	Monitor	Overall Risk Indicator	Overall Risk Indicator Adverse	Overall Risk Indicator...	Overall Risk Indicator...	Overall Risk Indicator Manually	Total Subjects	Rand
1	01	USA	New York	NY	Monitor G	0.518	0.441	0.056	0.607	0.603	51	
2	02	USA	Orlando	FL	Monitor F	0.257	0.637	0.448	0.218	0.047	32	
3	03	USA	Indianapolis	IN	Monitor E	0.127	0.205	0.497	0.000	0.069	23	
4	04	FRA	Paris	Ile-de-France	Monitor I	0.522	0.535	0.027	0.000	0.773	26	
5	05	ITA	Milano	Lombardia	Monitor H	1.729	1.288	3.660	2.120	1.498	5	
6	06	USA	Philadelphia	PA	Monitor G	1.443	2.481	1.289	0.000	1.431	7	
7	07	CHN	Guangzhou	Guangdong Sheng	Monitor K	1.367	1.682	1.107	0.000	1.709	5	
8	08	GBR	Birmingham	Birmingham	Monitor J	0.593	1.149	1.052	0.000	0.435	23	
9	09	CAN	Montreal	Quebec	Monitor A	0.301	0.400	0.629	0.356	0.178	40	
10	10	USA	Baltimore	MD	Monitor G	0.287	0.687	0.432	0.000	0.158	17	
11	12	DEU	Berlin	Berlin	Monitor H	0.483	0.881	1.346	0.008	0.299	16	
12	14	CAN	Toronto	Ontario	Monitor A	0.437	0.552	0.850	1.368	0.000	75	
13	16	USA	Seattle	WA	Monitor B	0.662	0.597	1.282	0.669	0.589	39	
14	17	USA	Los Angeles	CA	Monitor C	0.370	1.072	0.327	0.000	0.151	18	
15	18	JPN	Osaka	Osaka	Monitor L	0.529	0.548	1.155	0.109	0.556	22	
16	19	CAN	Ottawa	Ontario	Monitor A	0.721	0.368	0.682	1.178	0.752	9	
17	20	FRA	Marseille	Provence-Alpes-Co	Monitor I	0.152	0.286	0.382	0.027	0.088	18	
18	21	ESP	Barcelona	Cataluna	Monitor I	0.379	0.420	0.169	0.000	0.520	10	
19	22	CAN	Calgary	Alberta	Monitor B	0.508	1.209	0.058	0.067	0.381	23	
20	23	USA	Chicago	IL	Monitor E	0.174	0.136	0.095	0.225	0.188	29	
21	24	CHN	Shanghai	Shanghai Shi	Monitor K	0.243	0.221	0.838	0.002	0.235	21	
22	25	USA	Miami	FL	Monitor F	0.538	0.936	1.107	0.000	0.424	15	
23	26	DEU	Muenchen	Bayern	Monitor H	0.623	0.633	0.648	0.000	0.822	8	
24	27	CHE	Geneve	Geneve	Monitor I	0.201	0.249	0.116	0.176	0.200	24	
25	28	CAN	Vancouver	British Columbia	Monitor B	0.460	0.073	0.669	1.334	0.326	74	

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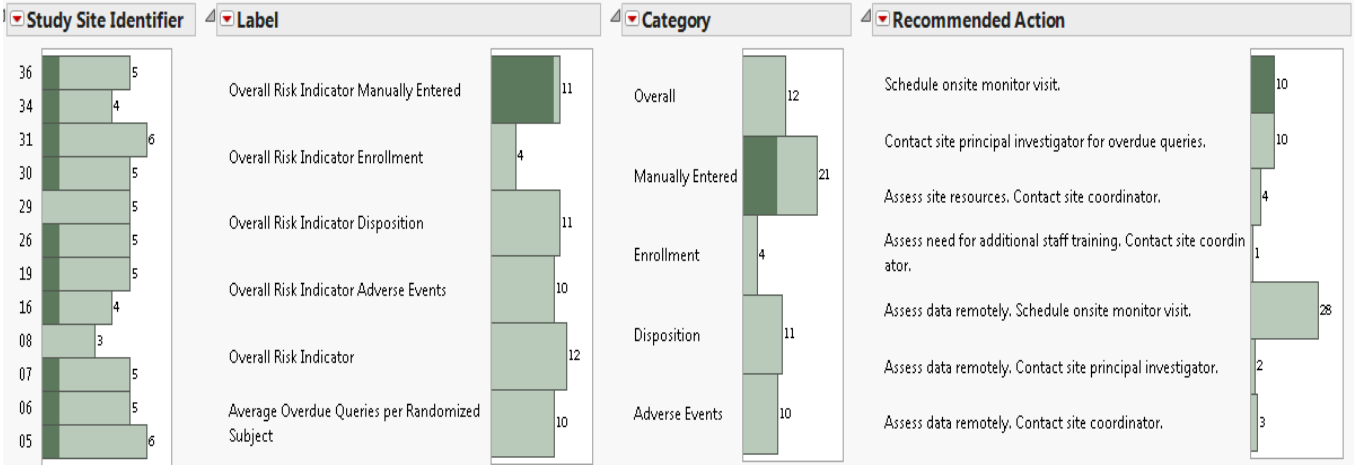
基于风险监查 (RBM)

RISK INDICATORS: SUGGESTION ACTION



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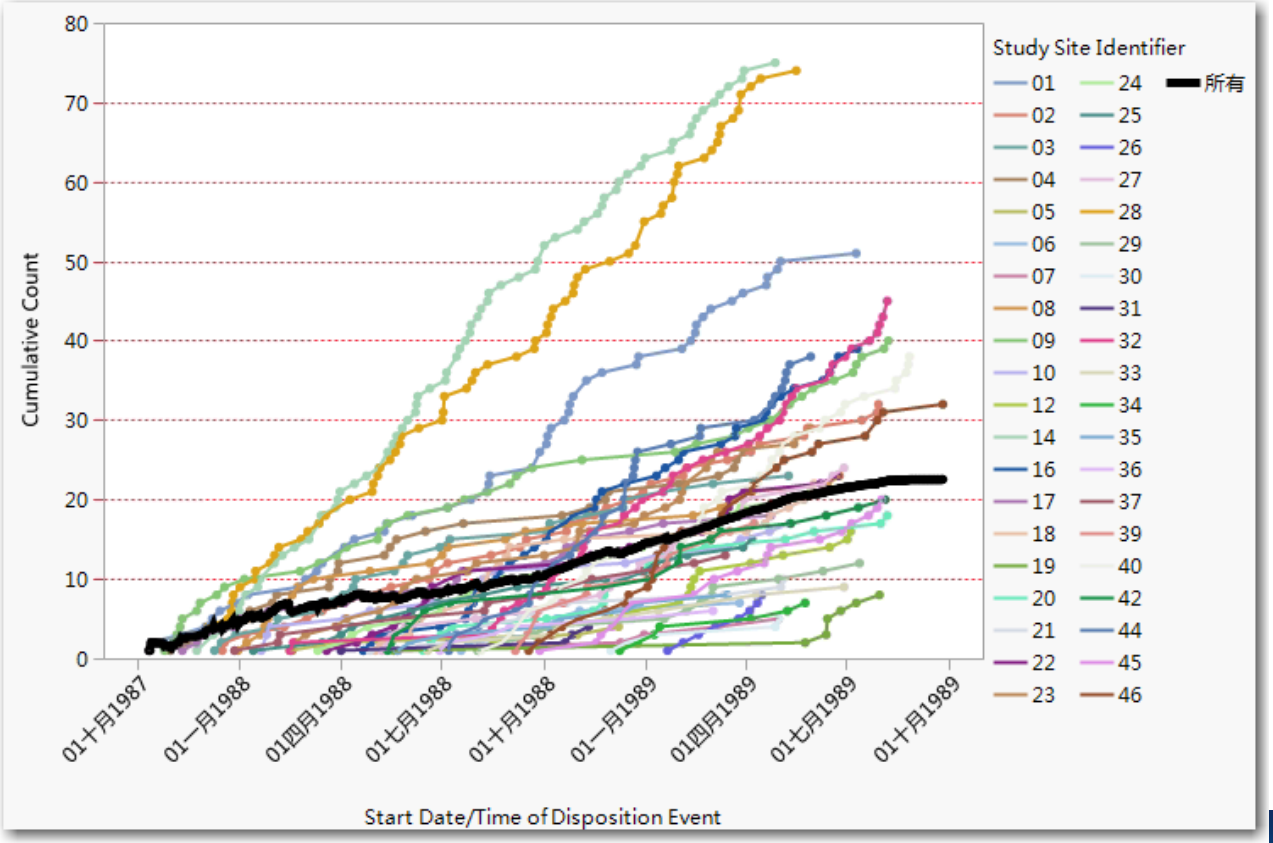
入组

各中心入组速度及人数



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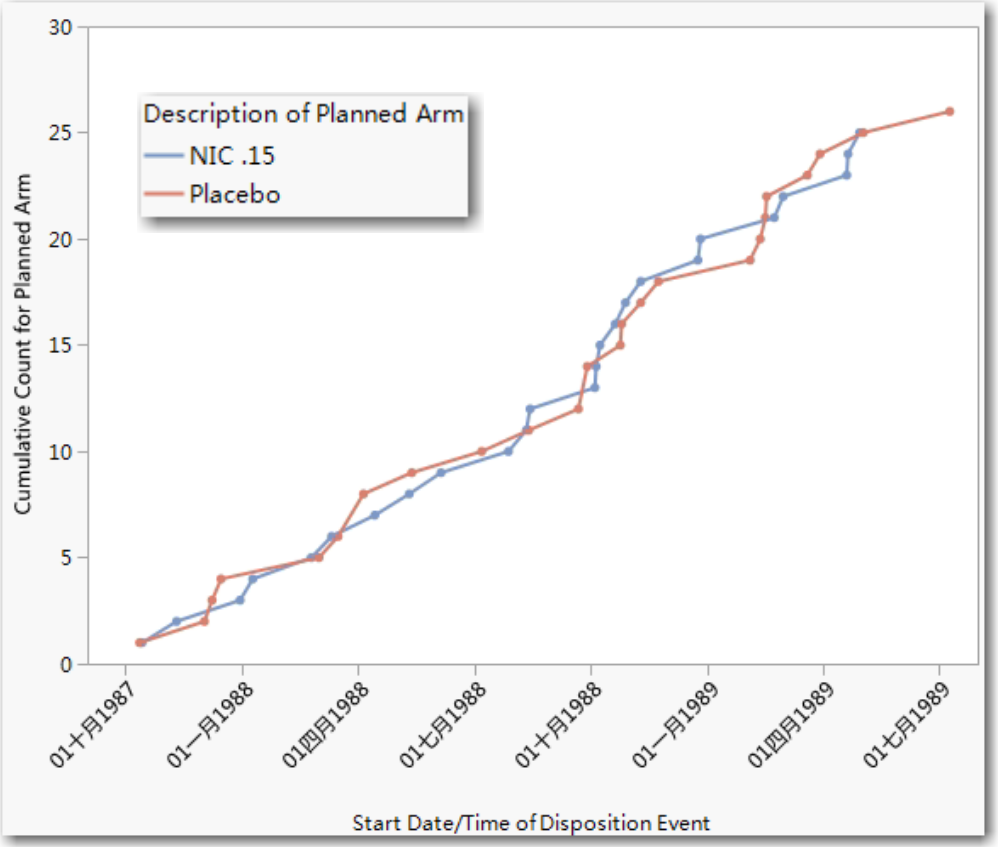
入组

某中心治疗和对照组入组速度及人数



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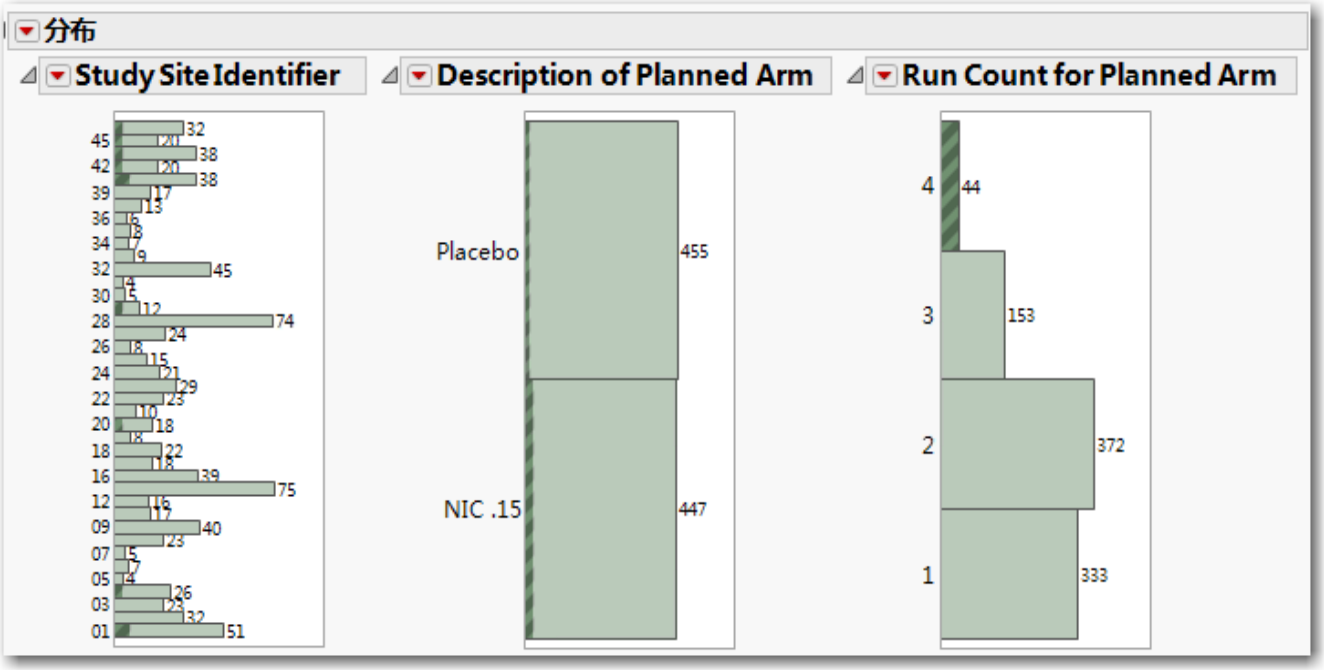
入组

各中心入组的随机性



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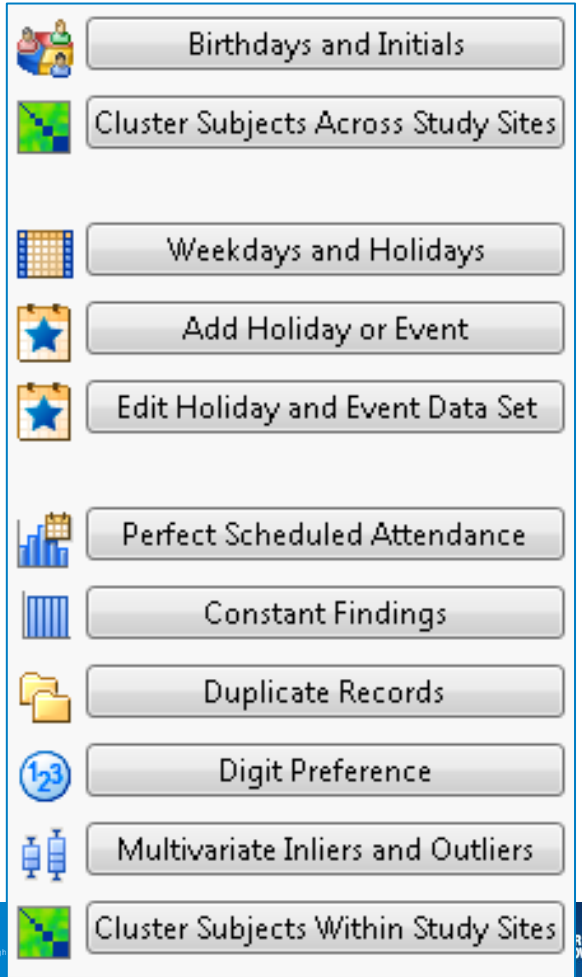
FRAUD DETECTION



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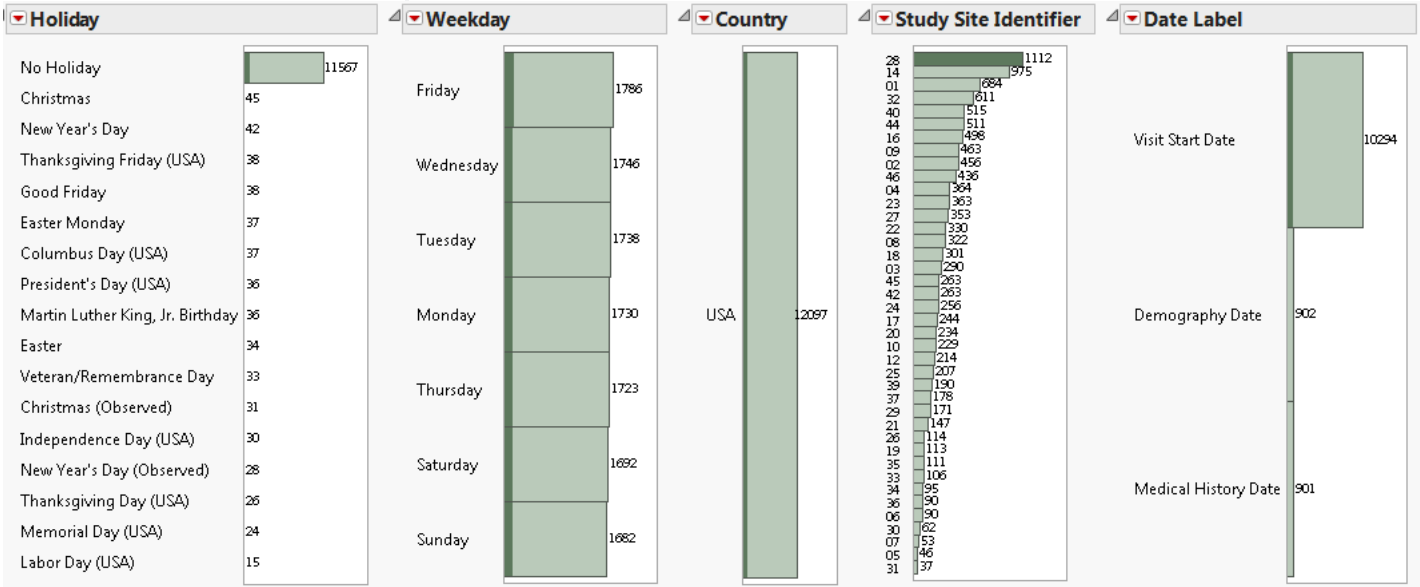
FRAUD DETECTION

HOLIDAYS AND WEEKENDS



Subset of weekhol_001

Source

Columns (10/0)

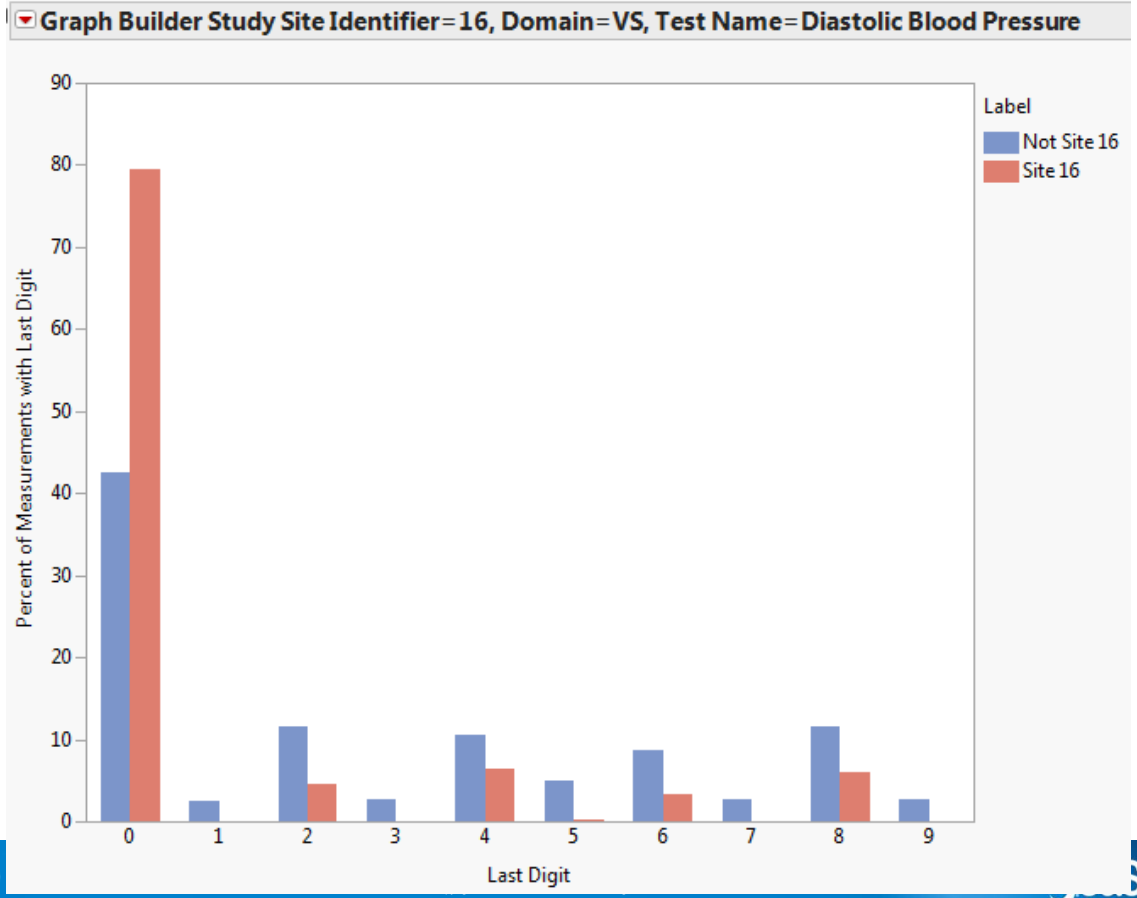
- Holiday
- Holiday Flag
- Weekday *
- Unique Subject Identifier
- Study Site Identifier
- Country
- Date Label
- Date
- d9partial_DMDTC
- Visit Number

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

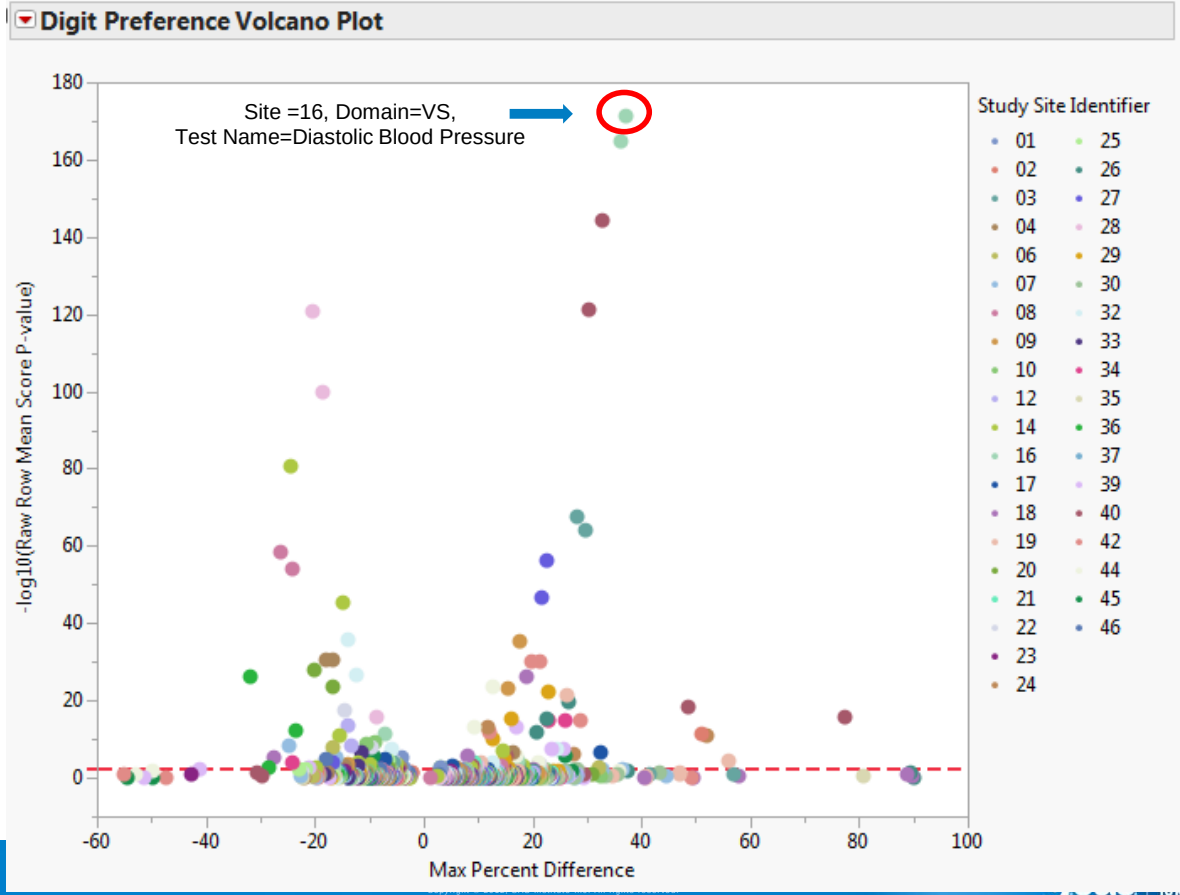
FRAUD DETECTION

DIGIT PREFERENCE

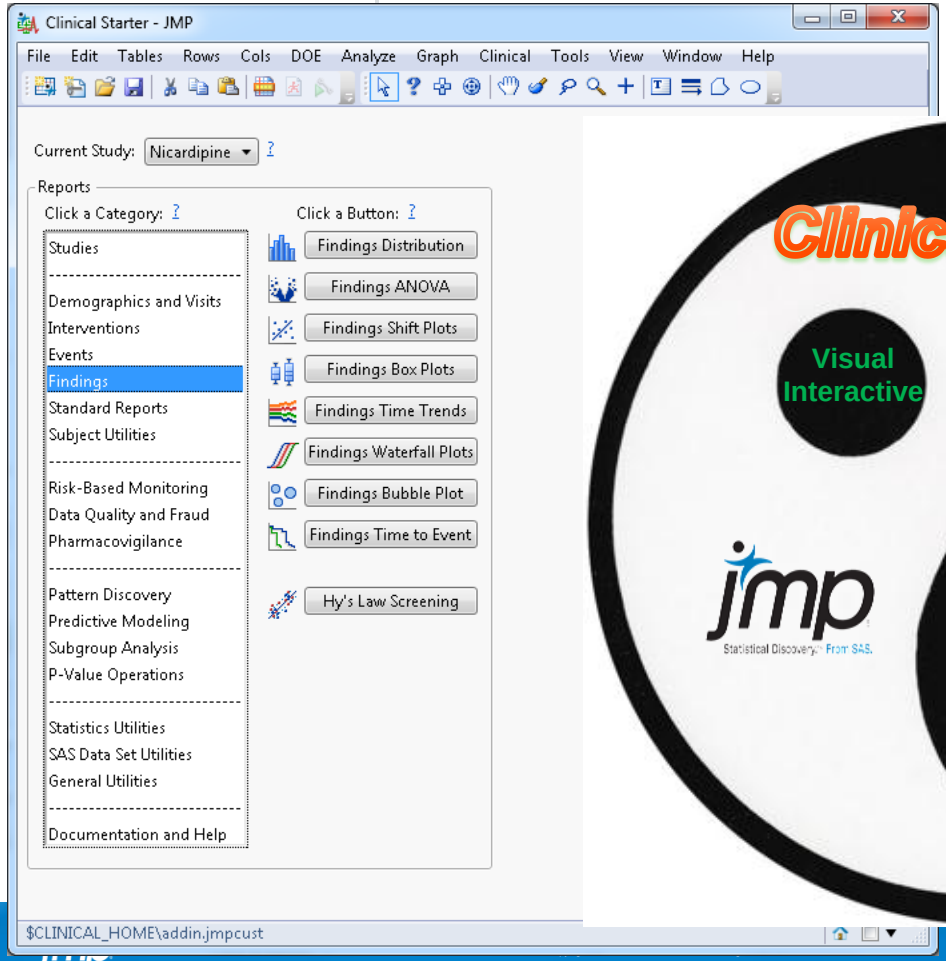


FRAUD DETECTION

DIGIT PREFERENCE



JMP CLINICAL: CLINICAL TRIAL STUDY SOLUTION



Thank You!!

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