



# Today's Session

<b>Statistical Graphics for Analysis of Drug Safety and Efficacy</b>	
<b>Section on Statistical Graphics</b> , Section on Risk Analysis, WNAR	
<i>Organizer(s): Michael O'Connell, Insightful Corporation</i>	
<i>Chair(s): Stephen Kaluzny, Insightful Corporation</i>	
2:05 PM	<a href="#"><u>Statistical Graphics for Analysis and Reporting of Clinical Trials</u></a> Michael O'Connell, Insightful Corporation
2:25 PM	<a href="#"><u>Using Graphics To Discover and Explore</u></a> Julia Wang, Johnson & Johnson PRD
2:45 PM	<a href="#"><u>Statistical Graphics for the Analysis of Safety and Efficacy Data from Clinical Trials</u></a> William Bushnell, GlaxoSmithKline
3:05 PM	<a href="#"><u>Graphical Analyses of Clinical Trial Safety Data</u></a> Haijun Ma, Amgen Inc.; Kefei Zhou, Amgen Inc.; Hong A. Xia, Amgen Inc.; Matthew Austin, Amgen Inc.; George Li, Amgen Inc.; Michael O'Connell, Insightful Corporation
3:25 PM	<a href="#"><u>Design of Statistical Graphics for Clinical Data</u></a> Richard M. Heiberger, Temple University
3:45 PM	Floor Discussion

## Michael O'Connell

+ Statistical Graphics Principles – Functional Areas, Software

## Julia Wang

+ Graphs for Exploratory Data Analysis

## William Bushnell

+ Graphs for Safety - Labs, AEs, patient profile, ...

## Haijun Ma

+ Graphs for Safety - Labs, AEs, patient profile, ...

## Rich Heiberger

+ Graphs / Design for Vitals, Labs, AEs, ...



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## Statistical Graphics for Analysis and Reporting of Clinical Data

Michael O'Connell

July, 2007





## Business Problem

- + Clinical Drug Development – Use of Graphics

## Statistical Graphics

- + Graphics Principles, Elements, Types and Patterns

## Graphics in Functional Areas

- + Design, Review, Report

## Software

- + Graphics breakdown and mashup

# Clinical Drug Development

Pharma Milestones

Candidate Selection

First in Human

Proof of Concept

Confirmation

Marketing

Compound Evaluation  
Pharmaceutical /  
Chemical  
Development

Healthy Volunteer  
Safety  
ADME

Diseased Patient  
Dosing  
M & S

Large Population  
Safety  
Efficacy

Real World  
Outcomes  
Epidemiology

*Need to go faster, better/safer and cheaper !! [\$1B/yr drug = \$3M/day]*

IND Filing

End of Phase 2 Mtg

NDA Filing

LSSS ?

FDA - Pharma Interactions

Pre-Clinical

Phase I

Phase II

Phase III

Phase IV

Drug Development



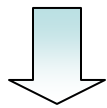
# Clinical Trial Environment – Use Cases, Actors

**Trial Design** → **EDA / Review** → **Report: Submission, Publication**



**Statistics**  
**Clinical**  
**Management**

**Design**

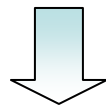


**Protocol**  
**SAP**



**Monitors**  
**Data Mgt**

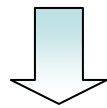
**Instream**



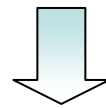
**Data**  
**Cleaning**



**Clinical**  
**Statistics**



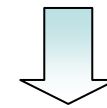
**Safety**



**Instream**  
**Clinical**  
**Review**



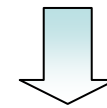
**Statistics**  
**Programming**



**CSR**  
**NDA**  
**Labeling**



**Publishing**  
**Medical**  
**Writing**



**Journals**  
**Scientific**  
**Meetings**

*Statistical Graphics drive faster and better decisions*

Speed the analysis and reporting process

- + Faster registrational documents

Improve the quality of decisions

- + Rapid and clear information from data

Increase likelihood of discerning safety and efficacy signals

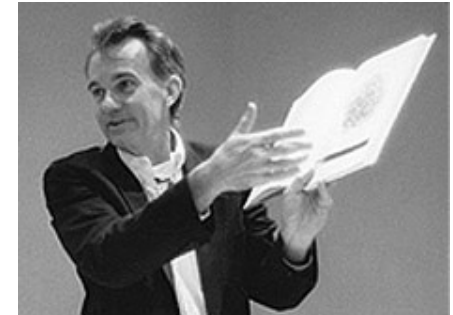
- + Comparative graphical analysis on all safety and efficacy data

Provide consistent form of communication across organization, cultures and functional areas

Improve interactions between sponsors and FDA

- + FDA wants transparency and clear analysis / presentation

***Excellence in statistical graphics consists of complex ideas communicated with clarity, precision and efficiency***



- + Show all the data when possible
  - Multivariate data and metadata
- + Induce the viewer to think about the substance rather than the graphic design – maximize the data-to-ink ratio
- + Encourage the eye to compare different pieces of data – leverage reader ' s investment by showing multiple plots of same type
- + Reveal the data at several levels of detail, from a broad overview to the fine structure
- + Serve a clear purpose: description, exploration, tabulation
- + Be closely integrated with the statistical and verbal descriptions of a data set
- + Use gray scale and color sparingly

## Variable Grouping

- + Symbols, colors for groups – *compare pieces of data*
- + **Treatment v Placebo**

## Trellis Plots and Conditioning

- + Panels for subjects, sub-groups – *principle of small multiples*
- + **Adverse Event groups**

## Matrix Plots

- + Plots for individual variables together – *multivariate data*
- + **Lab panels**

## Metadata – Margins and Axes

- + Use of ticks, color-regions, margins around plots – *multivariate metadata*
- + **Safety and Efficacy combination graphics**

## Brushing, Drilldown

- + Data browsing – *levels of detail*
- + **Population Lab -> Subject Lab -> AE -> demographics**

## Summary stats – univariate categorical

- + Dotplot
- + Barchart [low data-to-ink ratio]
- + Pie chart [poor perception]
- + Forest Plot

## Distributions – univariate continuous

- + Boxplot
- + Empirical CDF
- + Density Plot
- + Histogram

## Relations and trends

- + Line plot
- + Scatter plot
- + Scatter plot matrix
- + Surface, contour and image (heatmap) plots
- + Kaplan Meier Plot

## Figures convey trial designs and expected trial behavior

- + Data analyst produces for clinician and management
- + Multiple trial options are compared – operations (e.g. accrual) and potential outcomes for variety of scenarios

## Examples

- + Protocol
- + SAP

## Color and Format

- + Needs to be clear and easy to interpret and compare designs
- + Statistical (e.g. # events) and calendar information need to be clearly communicated

***Illustrate today with survival trials***

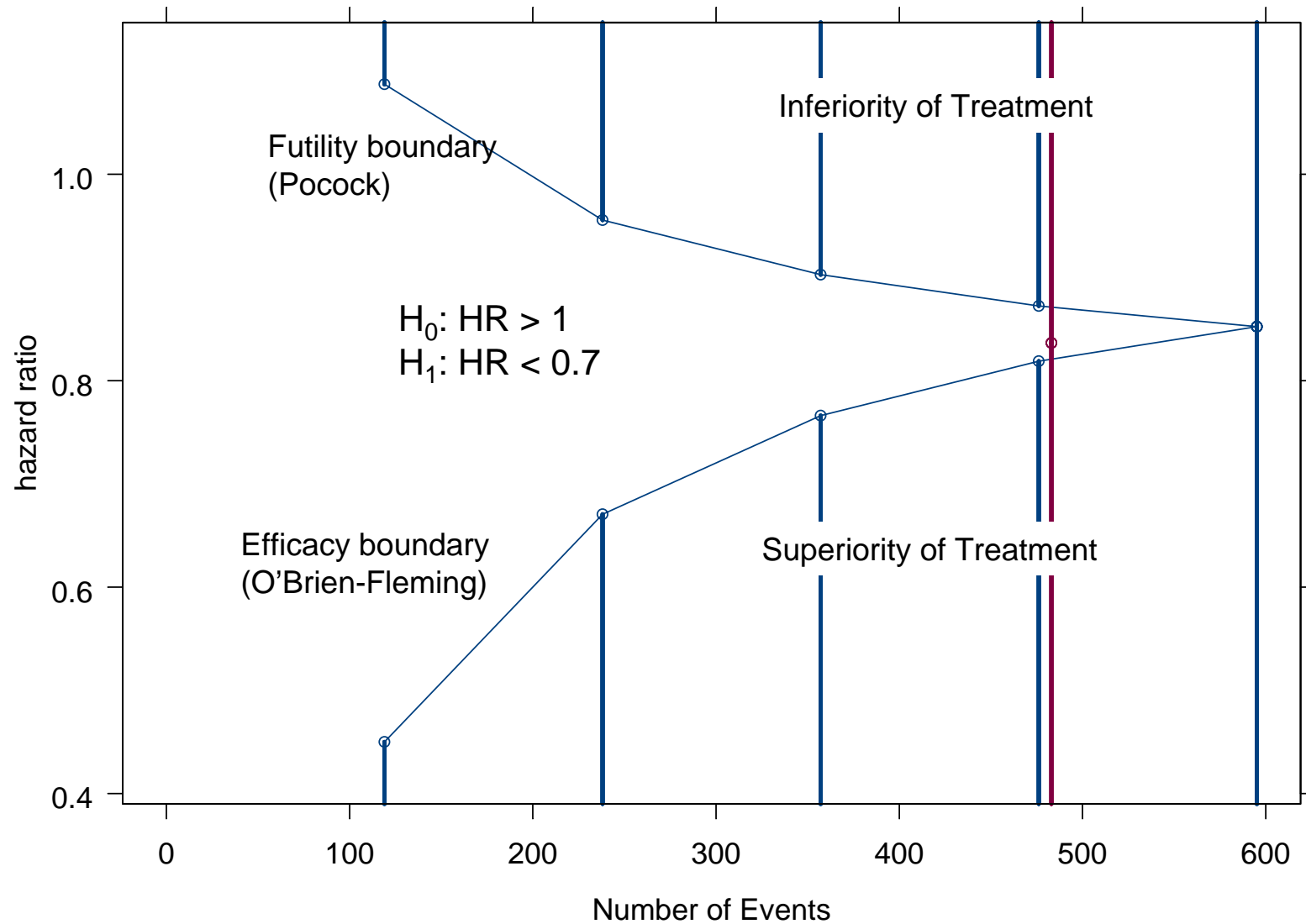


# Trial Design Graphic: Sequential HR Design

Line Plot | Group

Design

○ — dsnA11  
○ — Fixed

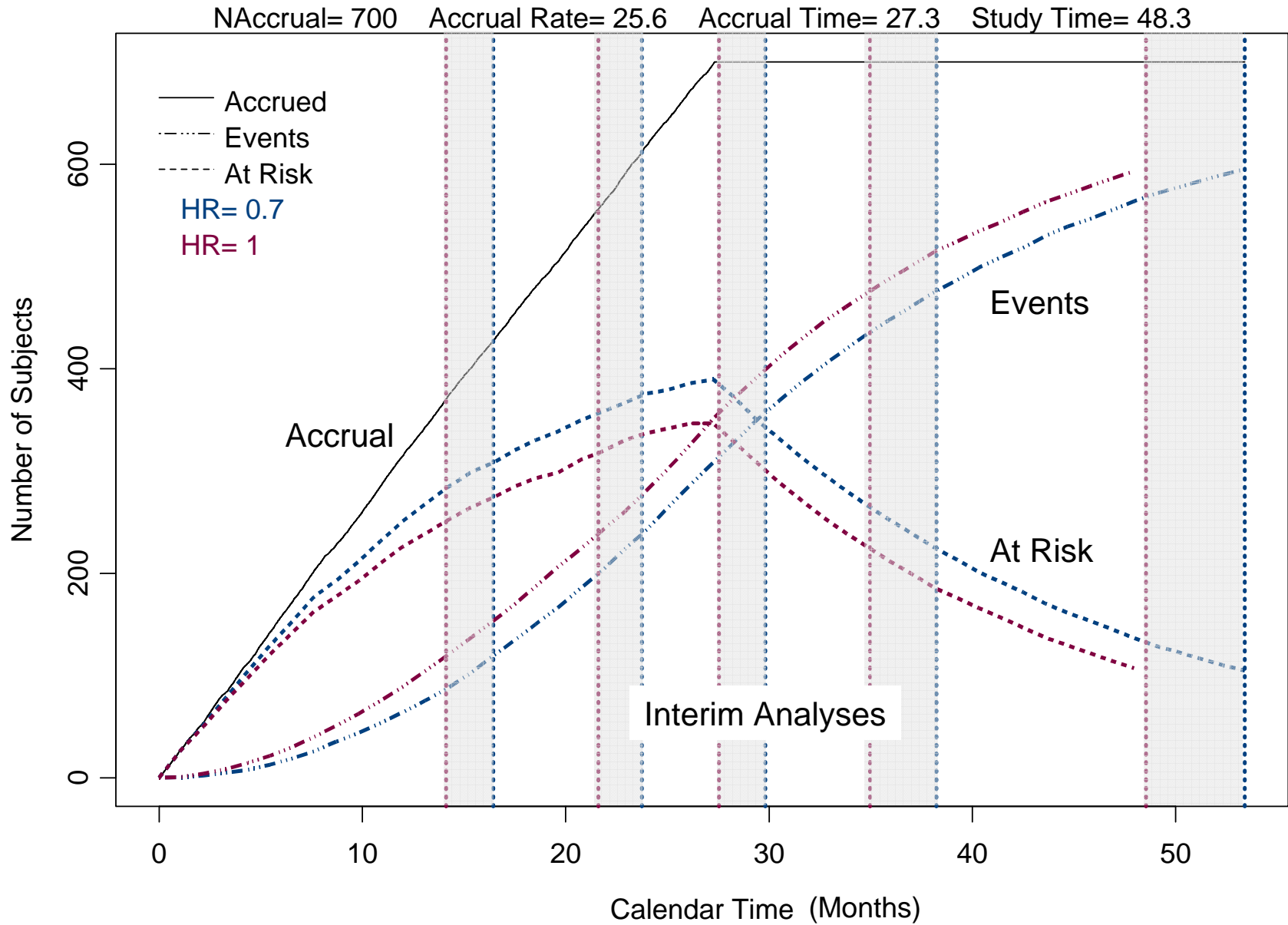




# Trial Design Graphic: Sequential HR Design

Line Plot | Group

Design

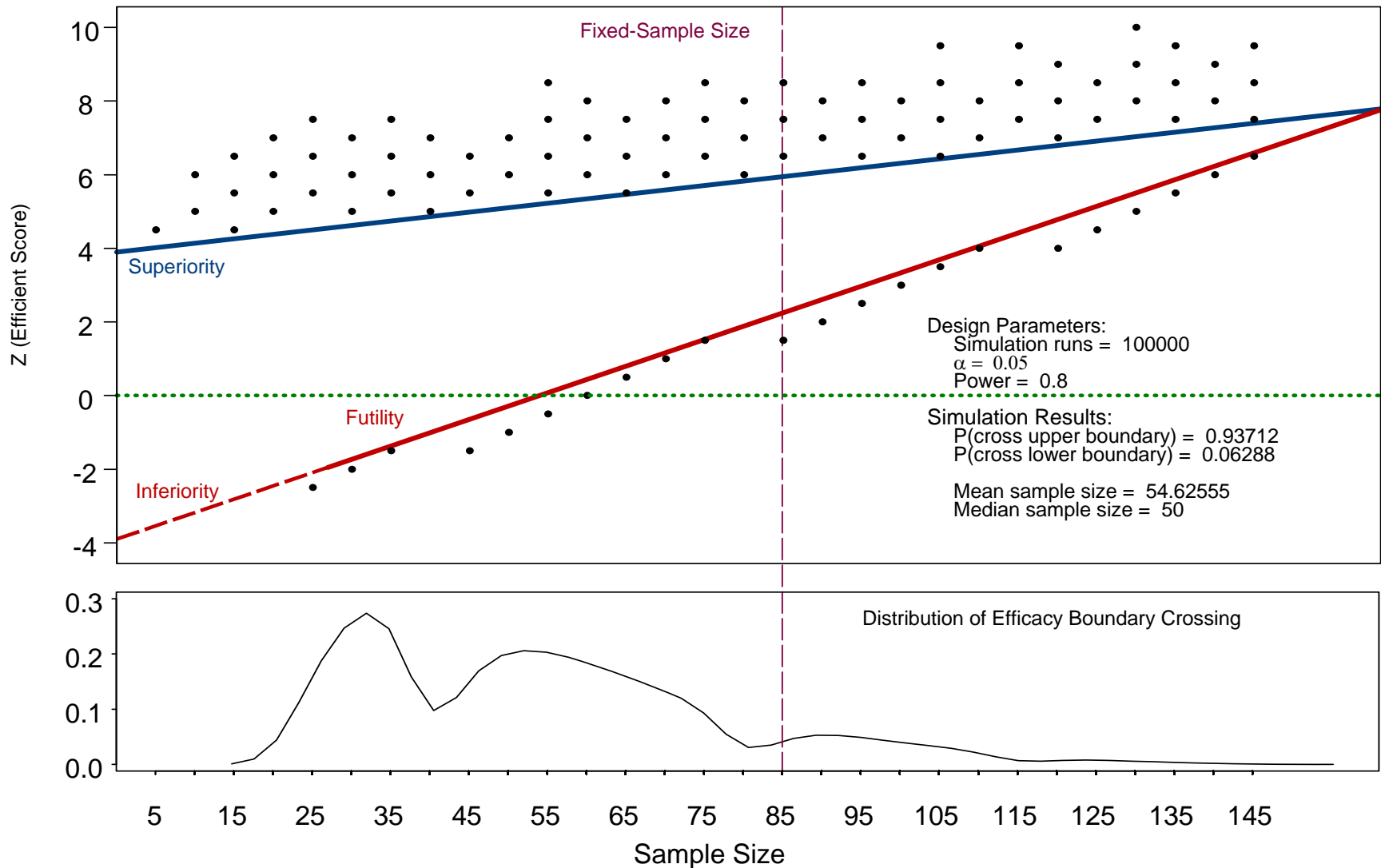




# Trial Design Graphic: Adaptive Design

Line Plot | Matrix

Design



### Figure not necessarily self-contained

- + Data analyst produces for detailed review with clinician
- + Data analyst produces for the data analyst

### Examples

- + Clinical data review by/with clinician
- + Viewing all data – data cleaning
- + Residual diagnostics - identification of functional form of relationship, assessing model assumptions

### Color and Format

- + Few pre-defined rules
- + Just make it clear and easy to interpret

## ***Adverse Events - Interpretive Goals***

Which adverse events are elevated in treatment vs. placebo?

How rapid is onset in treatment vs. placebo?

*Population level analysis is important*

## ***Labs - Interpretive Goals***

Which subjects have elevated (liver) labs?

Are there subjects with elevation on multiple labs?

*Subject Level analysis is important*



## Adverse Events with Severity and Time

	Baseline		Week 12	
	Active ( <i>N</i> = 1000)	Vehicle ( <i>N</i> = 500)	Active ( <i>N</i> = 900)	Vehicle ( <i>N</i> = 400)
<b>Erythema</b>				
Absent (0)	550 (55)	250 (50)	600 (67)	375 (94)
Mild (1)	350 (35)	220 (44)	250 (29)	20 (5)
Moderate (2)	80 (8)	25 (5)	45 (5)	5 (1)
Severe (3)	20 (2)	5 (1)	5 (1)	0 (0)
<b>Burning</b>				
Absent (0)	800 (80)	380 (76)	750 (83)	325 (82)
Mild (1)	190 (19)	100 (20)	135 (15)	70 (17)
Moderate (2)	10 (1)	20 (4)	15 (2)	5 (1)
Severe (3)	0 (0)	0 (0)	0 (0)	0 (0)
<b>Itching</b>				
⋮	⋮	⋮	⋮	⋮

Data Courtesy Mat Soukup, FDA

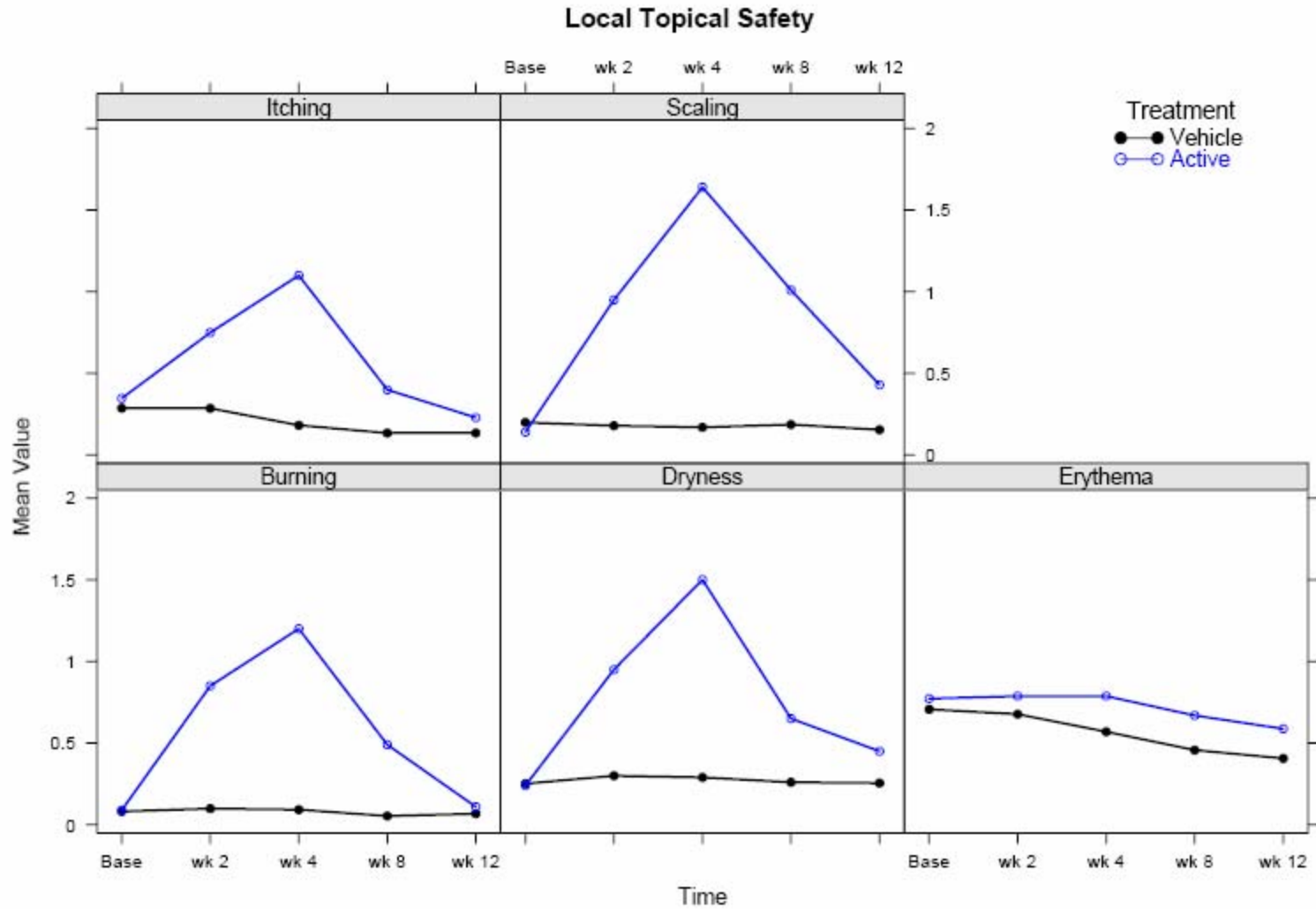


# Adverse Event Review Graphic

Line Plot | Group, Trellis



Review



# Adverse Events Counts

PT	SOC	TRT.A/214	TRT.B/428
Abdominal distension	Gastrointestinal disorder	5	0
Abdominal pain	Gastrointestinal disorder	11	11
Abdominal pain lower	Gastrointestinal disorder	2	0
Abdominal pain upper	Gastrointestinal disorder	5	2
Acne	Skin and subcutaneous tis	2	7
Ageusia	Nervous system disorders	2	1
Alanine aminotransferase	Investigations	8	22
Alopecia	Skin and subcutaneous tis	4	4
Anaemia	Blood and lymphatic syste	5	1
Anorexia	Metabolism and nutrition	9	10
Anxiety	Psychiatric disorders	4	3
Arthralgia	Musculoskeletal and conne	9	8
Aspartate aminotransfera	Investigations	32	3
Asthenia	General disorders and adm	7	2
Back pain	Musculoskeletal and conne	5	3
Blood alkaline phosphata	Investigations	3	1
Blood creatinine increas	Investigations	3	0
Burning sensation	Nervous system disorders	2	2
Cancer pain	Neoplasms benign, maligna	3	2
Chest pain	General disorders and adm	1	1
Chills	General disorders and adm	7	0
... ..	... ..		

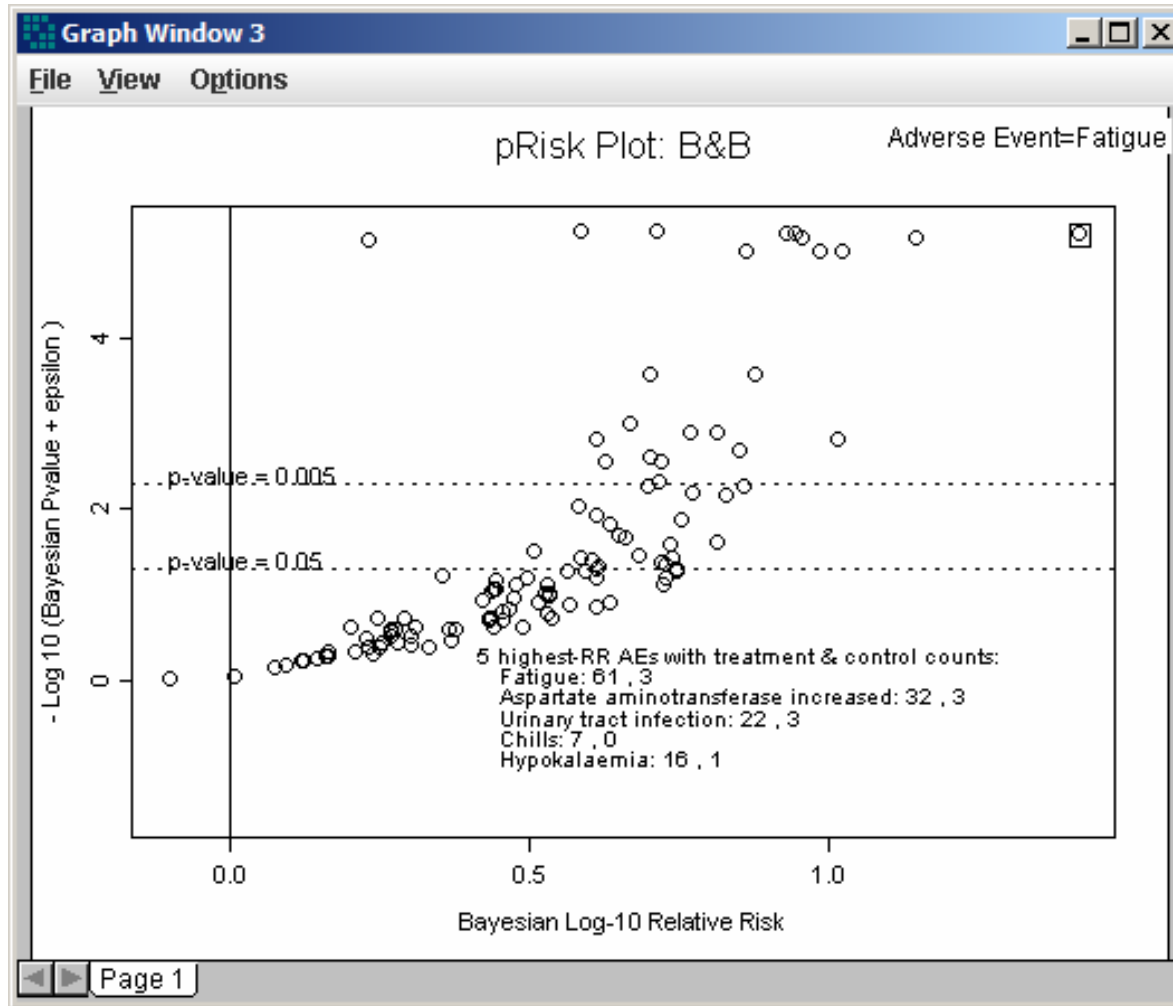
Data Courtesy Mike Durante, GSK

# Adverse Event Review Graphic: B&B Model

Scatter / pRisk Plot | Brush, Drill

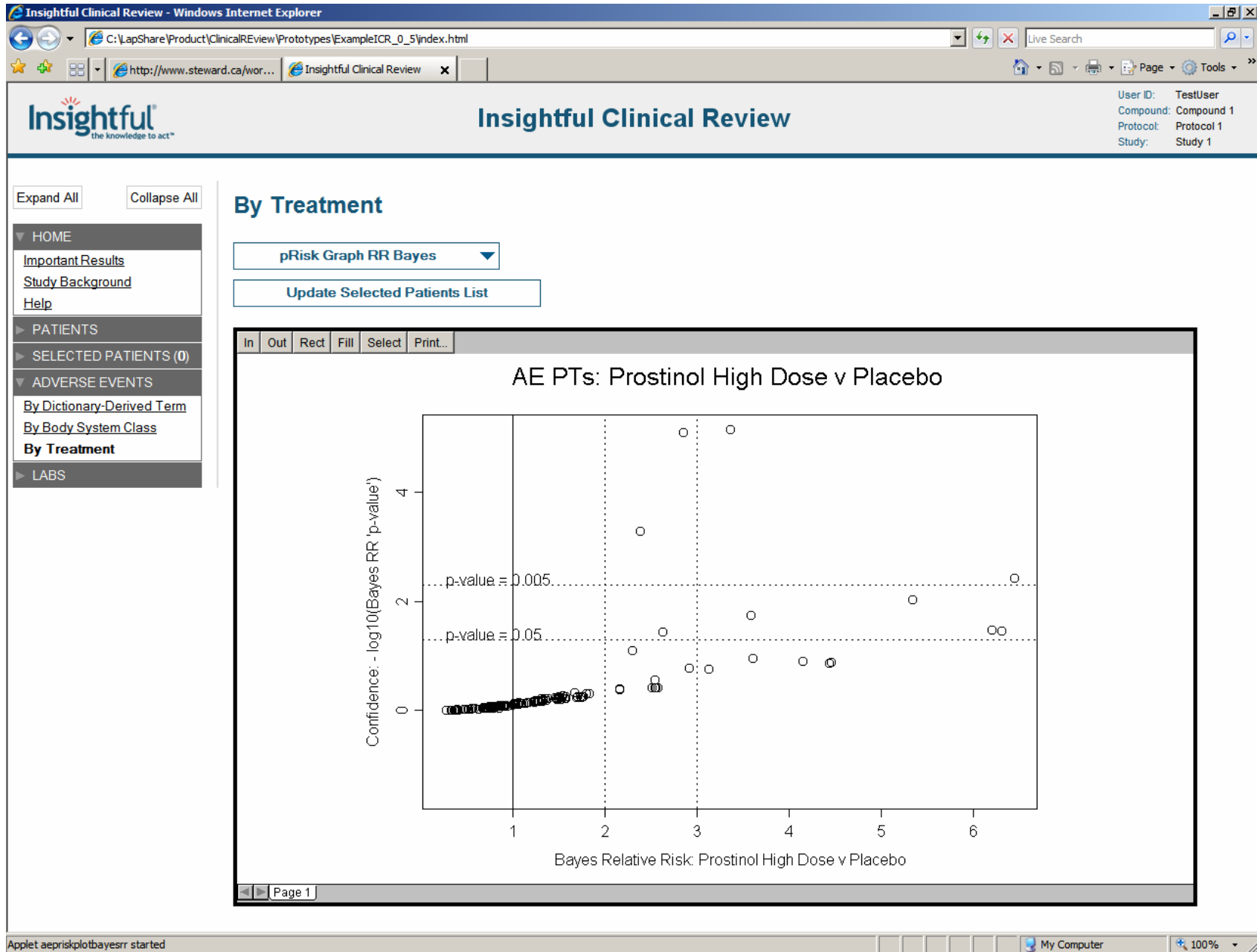


Review

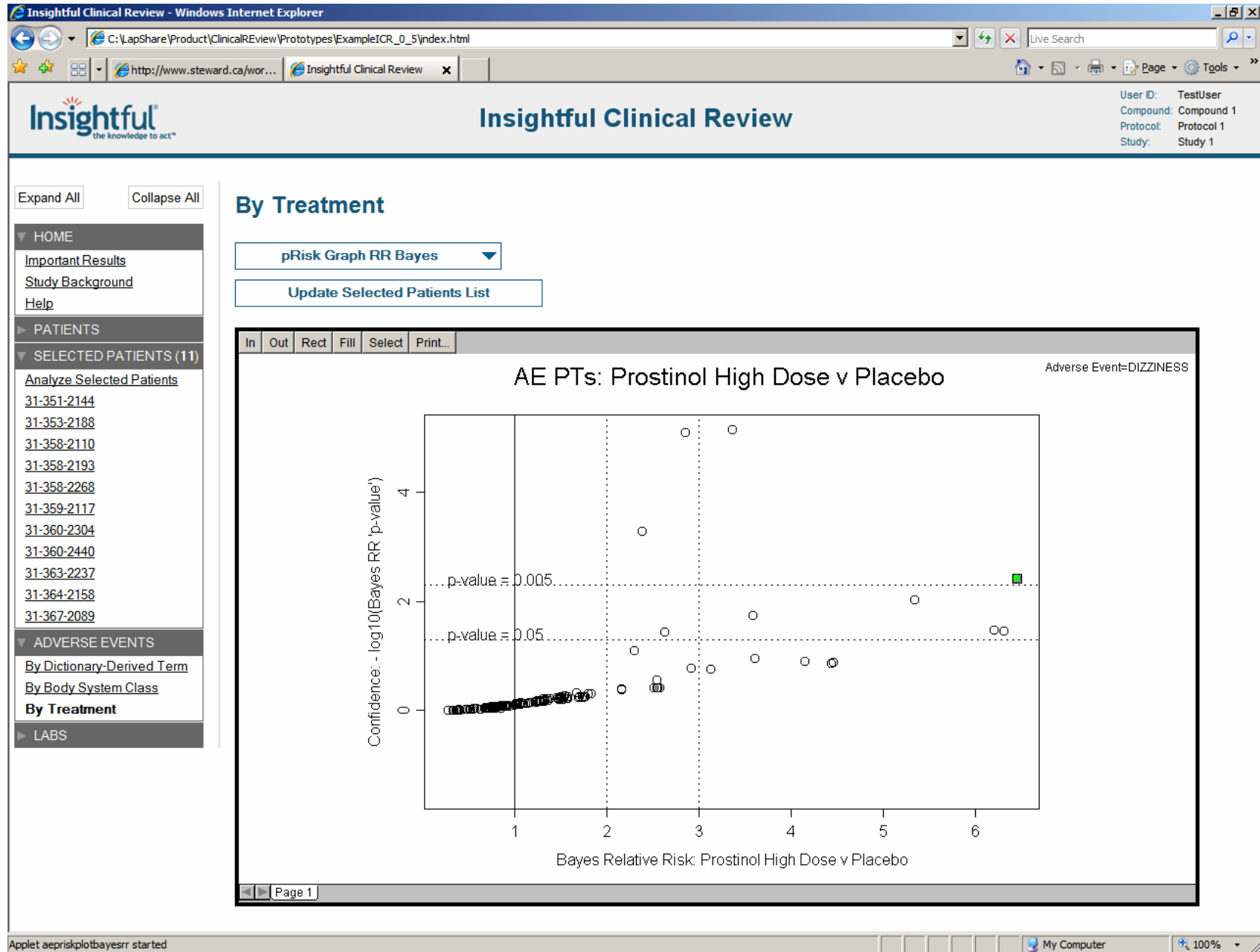


$$\text{B\&B Model: } \theta_{ij} \sim \pi_i I\{0\} + (1-\pi_i) N(\mu_{\theta_i}, \sigma_{\theta_i}^2)$$

# Insightful Clinical Review



# Insightful Clinical Review



# Insightful Clinical Review

Insightful Clinical Review - Windows Internet Explorer

C:\LapShare\Product\ClinicalReview\Prototypes\ExampleICR\_0\_5\index.html

Live Search

http://www.steward.ca/wor... Insightful Clinical Review

User ID: TestUser  
Compound: Compound 1  
Protocol: Protocol 1  
Study: Study 1

Insightful  
the knowledge to act™

Insightful Clinical Review

Expand All Collapse All

HOME

- Important Results
- Study Background
- Help

PATIENTS

SELECTED PATIENTS (11)

Analyze Selected Patients

- 31-351-2144
- 31-353-2188
- 31-358-2110
- 31-358-2193
- 31-358-2268
- 31-359-2117
- 31-358-2193
- 31-358-2268
- 31-359-2117
- 31-360-2304
- 31-360-2440
- 31-363-2237
- 31-364-2158
- 31-367-2089

ADVERSE EVENTS

- By Dictionary-Derived Term
- By Body System Class
- By Treatment

LABS

## Analyze Selected Patients

By Demographics

### Demographics

Subject ID	Treatment Group	Treatment Start Date	Age	Sex	Ethnicity	Height (cm)	Weight (kg)	BMI (kg/m <sup>2</sup> )
31-351-2144	Prostinol High Dose	01/28/2005	61	M	CAUCASIAN	177.8	82.56	26.12
31-353-2188	Prostinol High Dose	12/20/2003	78	F	CAUCASIAN	154.94	61.69	25.7
31-358-2110	Prostinol High Dose	05/08/2004	73	M	CAUCASIAN	190.5	85.28	23.5
31-358-2193	Placebo	10/06/2004	61	M	CAUCASIAN	185.42	78.02	22.69
31-358-2268	Prostinol High Dose	05/30/2005	77	F	AFRICAN DESCENT (NEGRO, BLACK)	165.1	63.05	23.13
31-359-2117	Prostinol High Dose	01/14/2005	70	M	CAUCASIAN	170.18	NA	NA
31-360-2304	Prostinol High Dose	03/03/2004	76	F	CAUCASIAN	152.4	57.61	24.8
31-360-2440	Prostinol High Dose	07/12/2004	77	M	CAUCASIAN	170.18	71.22	24.59
31-363-2237	Prostinol High Dose	10/26/2004	77	F	CAUCASIAN	165.1	52.16	19.14
31-364-2158	Prostinol High Dose	05/05/2005	77	M	AFRICAN DESCENT (NEGRO, BLACK)	162.56	50.35	19.05
31-367-2089	Prostinol High Dose	09/30/2004	77	M	CAUCASIAN	181.61	83.01	25.17

Applet aepriskplotbayesrr started

My Computer 100%

# Insightful Clinical Review

Insightful Clinical Review - Windows Internet Explorer

C:\LapShare\Product\ClinicalReview\Prototypes\ExampleICR\_0\_5\index.html

http://www.steward.ca/wor... Insightful Clinical Review

User ID: TestUser  
Compound: Compound 1  
Protocol: Protocol 1  
Study: Study 1

**Insightful** the knowledge to act™ **Insightful Clinical Review**

Expand All Collapse All

HOME  
[Important Results](#)  
[Study Background](#)  
[Help](#)

PATIENTS

SELECTED PATIENTS (1)  
[Analyze Selected Patients](#)  
 31-353-2188

ADVERSE EVENTS  
[By Dictionary-Derived Term](#)  
[By Body System Class](#)  
[By Treatment](#)

LABS

**Patient 31-353-2188: Adverse Events**

Dictionary-Derived Term	Body System or Organ Class	Serious Event	Severity	Assessed Causality	Adverse Event Start Date	Adverse Event End Date
DIZZINESS	NERVOUS SYSTEM DISORDERS	N	MODERATE	NONE	06/02/1992	NA
DIZZINESS	NERVOUS SYSTEM DISORDERS	N	MILD	NONE	06/02/1992	NA
UPPER RESPIRATORY TRACT INFECTION	INFECTIONS AND INFESTATIONS	N	MILD	NONE	01/11/2004	01/19/2004
UPPER RESPIRATORY TRACT INFECTION	INFECTIONS AND INFESTATIONS	N	MILD	NONE	01/11/2004	01/19/2004
NAUSEA	GASTROINTESTINAL DISORDERS	N	MILD	PROBABLE	02/04/2004	06/26/2004
NAUSEA	GASTROINTESTINAL DISORDERS	N	MODERATE	PROBABLE	02/04/2004	06/26/2004
NAUSEA	GASTROINTESTINAL DISORDERS	N	MILD	PROBABLE	02/04/2004	06/26/2004

**Patient 31-353-2188: Liver Function Tests**

Visit	Date	Alanine Aminotransferase	Alkaline Phosphatase	Aspartate Aminotransferase	Gamma Glutamyl Transferase	Albumin	Bilirubin	Protein
LAB BASELINE	12/10/2003	42.96	77.98	35.97	32.91	40	10.2	66.06
WEEK 2	12/31/2003	39.09	78.05	29.06	35.18	40.01	10.38	69.05
WEEK 4	01/17/2004	38.13	90.01	33.08	29.27	37.01	10.44	67.01
WEEK 6	02/04/2004	24.22	84.11	23.14	19.45	43.02	10.56	73.04
WEEK 8	02/14/2004	25.26	83.14	25.17	21.54	41.02	10.62	71.09
WEEK 12	03/10/2004	21.3	71.16	20.19	22.63	44.02	7.26	70.07
WEEK 16	04/06/2004	27.35	79.18	27.22	26.72	43.03	12.45	75.1
WEEK 20	05/04/2004	19.39	68.21	19.25	19.81	43.03	9.09	72.01
WEEK 24	06/01/2004	19.43	70.23	18.28	18.9	43.03	12.57	73.07

**Key: Lab Data**  
 Above Upper Limit of Normal  
 Below Lower Limit of Normal

Applet aeprispilotbayesrr started

My Computer 100%

## Figure must be self-contained

- + In-text figures should have an explanation in the caption

## Figure must be documented

- + Log file
- + Time stamp
- + Source data and output file references

## Examples

- + NDA Submission
- + Scientific Publication
- + Clinical Study Report and Presentation

## Color / Format

- + Must be interpretable when copied in black and white
- + Compatible with Microsoft Word
- + Resizable



# Adverse Event Report Graphic

Dot Plot | Group

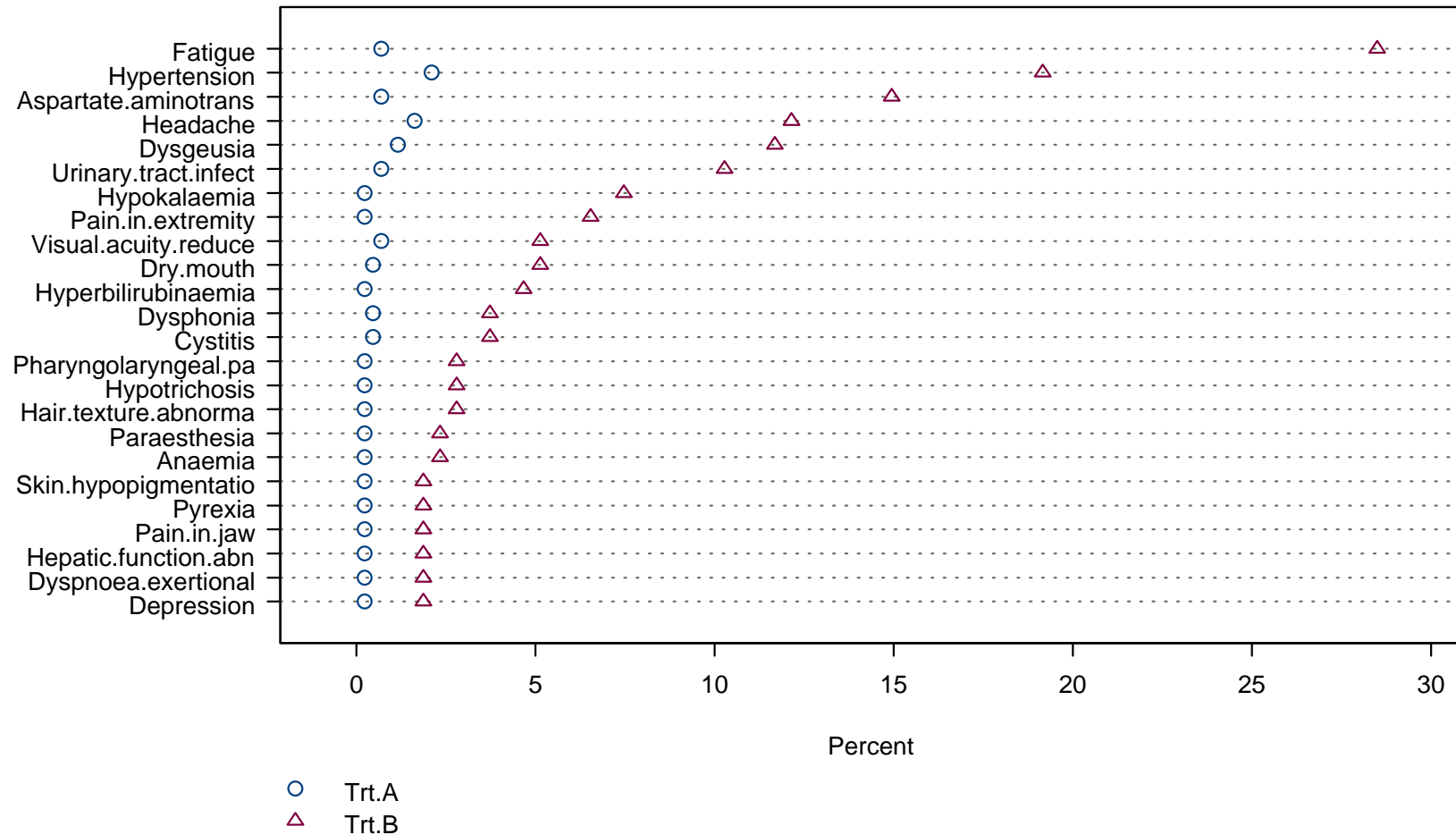


Report

Protocol: 38-316  
Candidate: Oncology 38-316-001

Page 1 of 1

AE Dotplot: Percent by PT



Run: M O'Connell  
Time: March 21, 2007; 10.06pm ET  
Data Source: H:/Oncology/P38316/Report1/AEterm.sas7bdat  
Output: H:/Oncology/P38316/Report1/AEterm.pdf



# Adverse Event Report Graphic

Dot Plot | Group

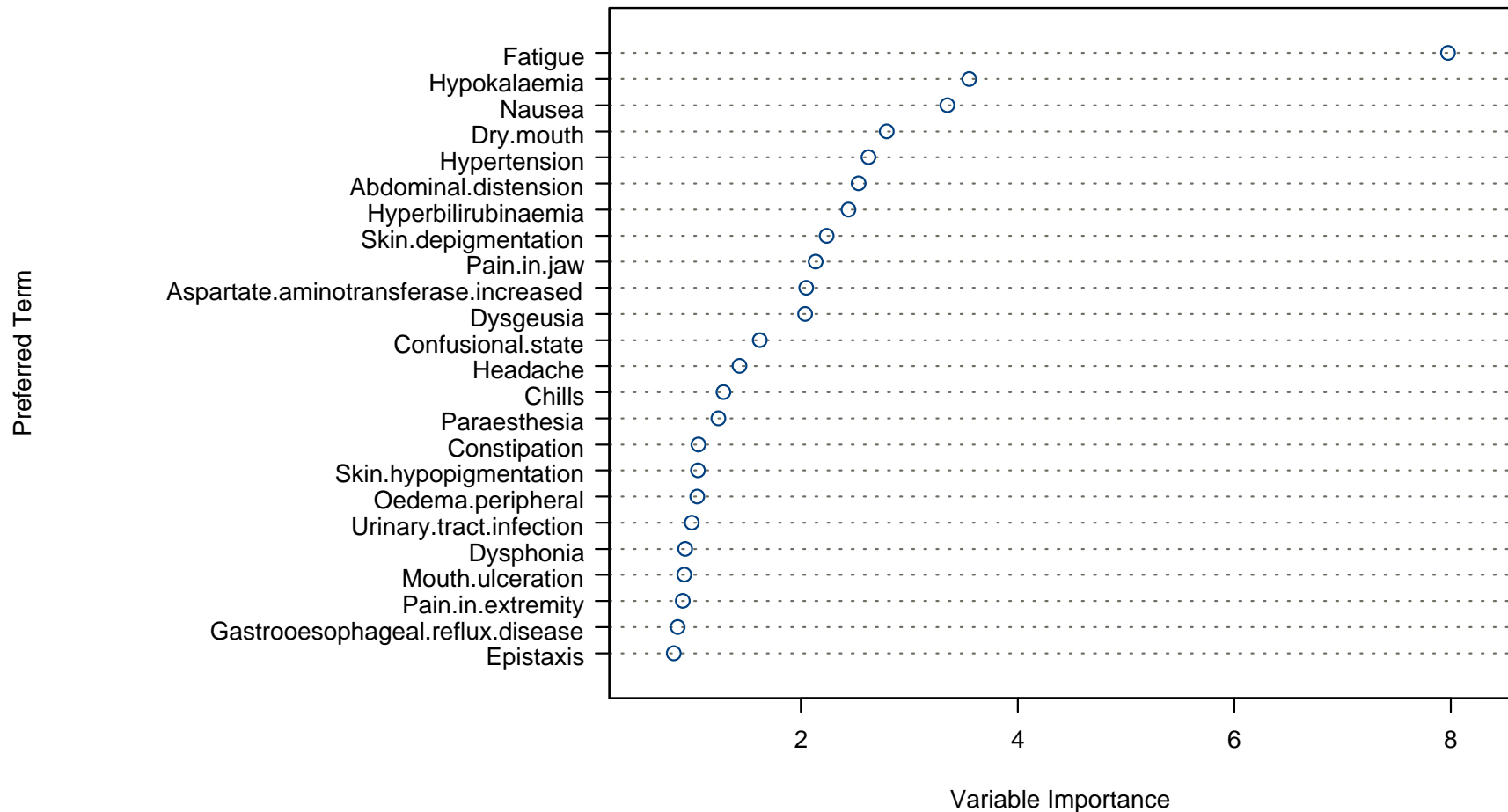


Report

Protocol: 38-316  
Candidate: Oncology 38-316-001

Page 1 of 1

Dotplot of Variable Importance  
Random Forest Inside-Out Model



Run: M O'Connell  
Time: March 27, 9.04pm  
Data Source: H:/Oncology/P3816/Report/AEterm.sas7bdat

$Trt_{ij} = f(PT_j) + e_{ij}$   
 $i = 1, \dots, 642$  subjects,  $j = 1, \dots, 111$  AEs

Easy creation of (information-rich) statistical graphics for clinical data analysis

- + Dot plot, box plot, line plot, etc...

Easy re-purposing of graphs across studies and functional areas

- + Graph standards – layering on (CDISC) data standards

Use of same graphs in exploratory and validated areas

- + Windows/UNIX exploratory and UNIX compliant

Consistent use of graphs across organization

- + Graphic language for effective communication

# Graphics System Mashup

**Design**



**Review**



**Report**



## **Statistics**

Specify Graph  
From Type Palette

Create/Add Graph  
Pattern to Store

Select Graph  
Pattern from Store

Add Type to Palette

## **Monitors**

### **Data Mgt**

Apply Pattern  
to Data

## **Clinical**

### **Statistics**

Apply Pattern  
to Bound Data

## **Statistics**

### **Programming**

Run  
Bound Pattern  
for NDA

## **Publishing**

Apply CSS  
Style to  
Bound Pattern

**Instream**

**Unblinded**

## **Clinical Graphics Store**

**Persisted  
Graph Types,  
Patterns, Styles &  
Metadata  
(WEBDAV)**

**S-PLUS  
Script Files  
(SSC)**

## *Graph Types*

## *Graph Patterns*

### Summary stats – univariate categorical

- + Dotplot
- + Barchart [low data-to-ink ratio]
- + Pie chart [poor perception]

- + Forest Plot
- + My AE Dotplot with Intervals

### Distributions – univariate continuous

- + Boxplot
- + Empirical CDF
- + Density Plot
- + Histogram

- + My Boxplot

### Relations and trends

- + Line plot
- + Scatter plot
- + Scatter plot matrix
- + Surface, contour and image plots

- + Kaplan Meier Plot
- + My Patient Profile Liver Plot
- + My Liver Lab Shift Plot
- + My Liver Lab Scatter Plot Matrix

# Software Interface

Prostinol Phase III - Insightful Fuji System

File Edit View Insert Format Graph Data Window Help

New Graph... Import Graphs... Find Graphs... Saved Graphs

Annotation History Metadata Arial 12pt. B I U [List Icons]

**New Graph - Graph Type**

Start with Graph Type  Start with Data Source Themes... Selected Theme: CSR

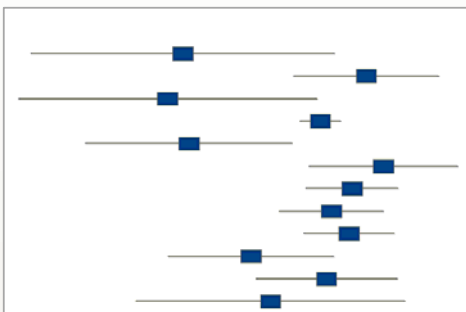
All Graphs My Recent

View by: Graph Type

- Line Plot
- Kaplan Meier
- Bar Chart
- Scatter Plot
- Empirical CDF
- Dot Plot
- Histogram
- Pie Chart
- QQ Plot
- Box Plot
- Forest Plot

Base Dot Plot  
Dot Plot with Interval  
AE Incidence Double Dot Plot  
AE Relative Risk Dot Plot  
AE Incidence and Relative Risk Dot Plot

**Dot Plot with Interval**  
(Preview)



< Previous Data Source > Cancel

**Saved Graphs**

Sort by: My most recent Show: All

- LET\_ScatterPlotMatrix
- SOC\_DotPlot
- End\_LinePlot
- ate\_LinePlot
- rom\_Base\_LinePlot
- \_Response\_KM
- nue\_KM
- \_Change\_BarPlot

Send to...

# Software Interface

Prostinol Phase III - Insightful Fuji System

File Edit View Insert Format Graph Data Window Help

New Graph... Import Graphs... Find Graphs... Saved Graphs

Annotation History Metadata Arial 12pt. B I U [Text Alignment] [Color] [Line Style] [Grid]

DotPlotWithInterval1

Scrolling view  Page-by-page view 100%  Before & After View

Header1

### Title1

Page 1 of 1

Study Name	n	logOR (approx.)	CI (approx.)
Bach(a)	NaN	-2.2	[-3.5, -0.9]
Bach(b)	8	-2.2	[-3.5, -0.9]
Ciresi	17	-0.5	[-1.8, 0.8]
Collins	8	-2.2	[-3.5, -0.9]
Combined	61	-0.8	[-2.1, 0.5]
George	12	-2.2	[-3.5, -0.9]
Hannan	17	-0.2	[-1.5, 1.1]
Heard	27	-0.5	[-1.8, 0.8]
Maki	24	-0.8	[-2.1, 0.5]
Ramsay	27	-0.8	[-2.1, 0.5]
Tennenberg	15	-1.5	[-2.8, -0.2]
Trazzera	18	-0.8	[-2.1, 0.5]
vanHeerden	9	-1.3	[-2.6, 0.0]

names

logOR

Footer1

**Saved Graphs**

**Annotation**

**History**

Create Graph

**Metadata**

File Descriptive Production Status Comments

**Graph Type:**  
Dot Plot with Interval

**Data Source Path:**  
...\\RE-ISO\Data\mdf.sas7bdat

**Graph File Path:**  
--

**Author:**  
--

**Created:**  
--

**Last Modified:**  
--

**Latest Version:**  
--

**Production:**  
--

Edit Metadata...

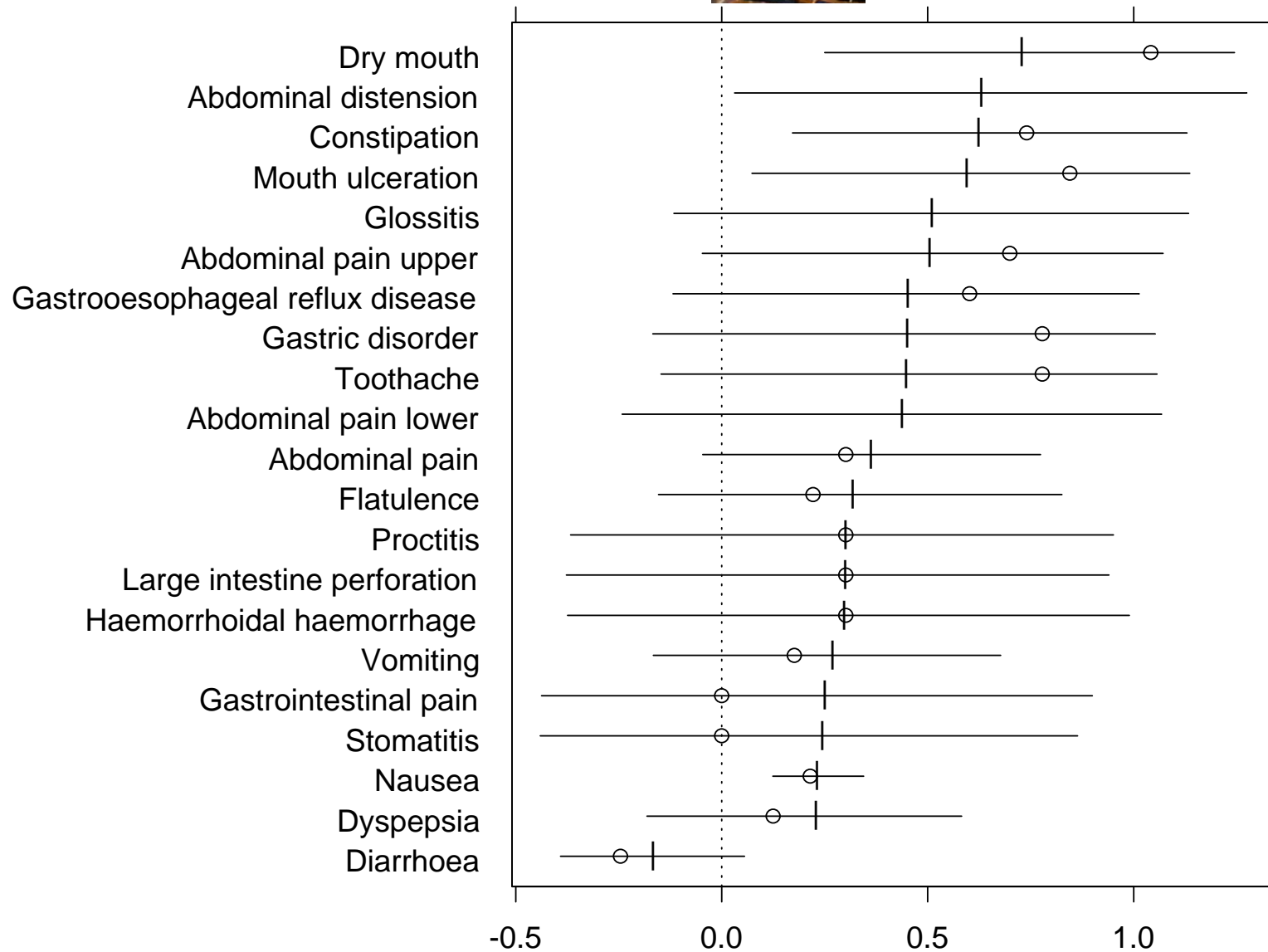


# My AE Dot Plot with Interval Pattern

Dot Plot



Review



○ log-10 Empirical RR

+ Bayes Posterior Mean of Log Relative Risk with 99% BCI



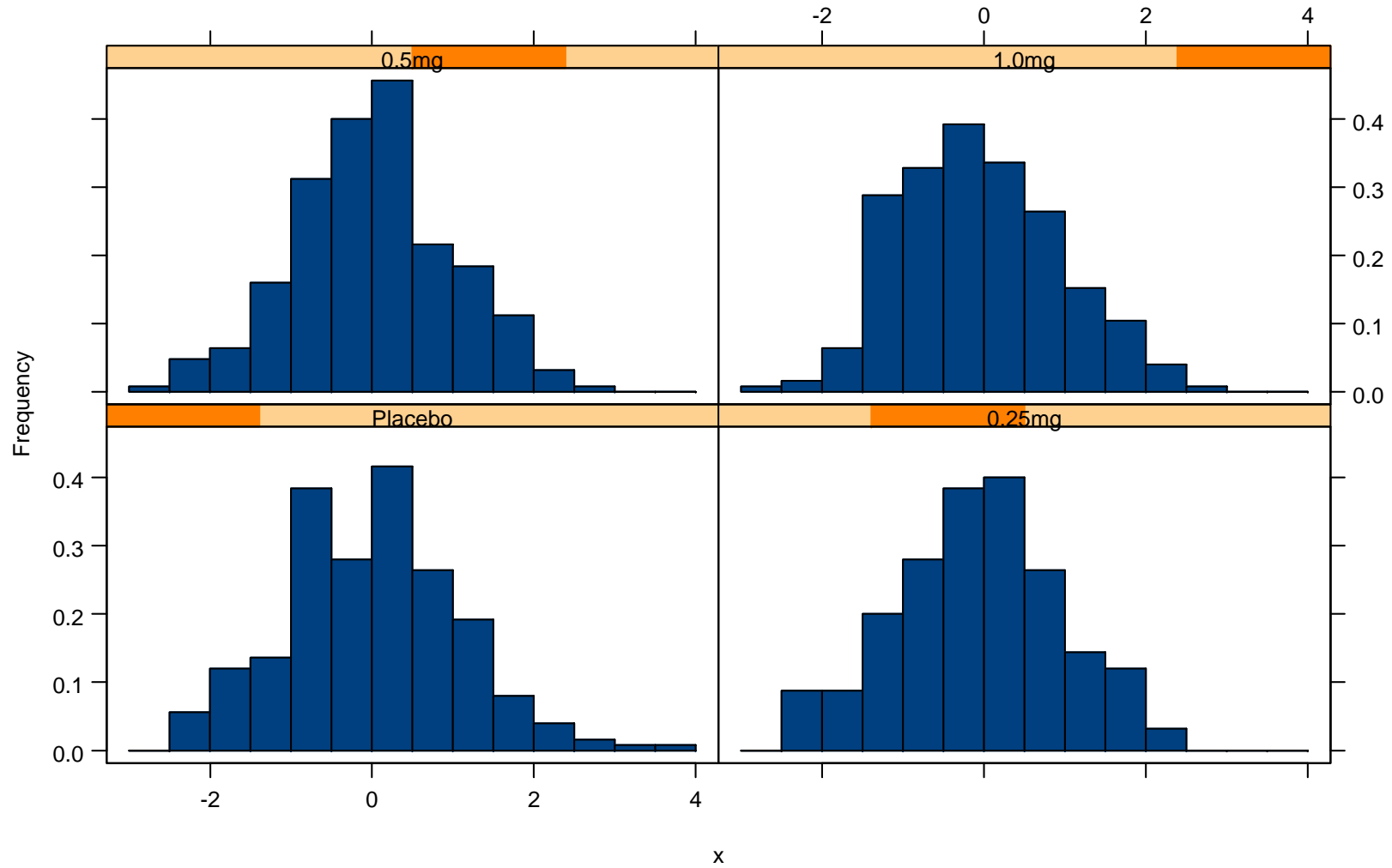
# My Histogram for Internal Power Point Pattern

Histogram | Trellis



Report

Page 1 of 1





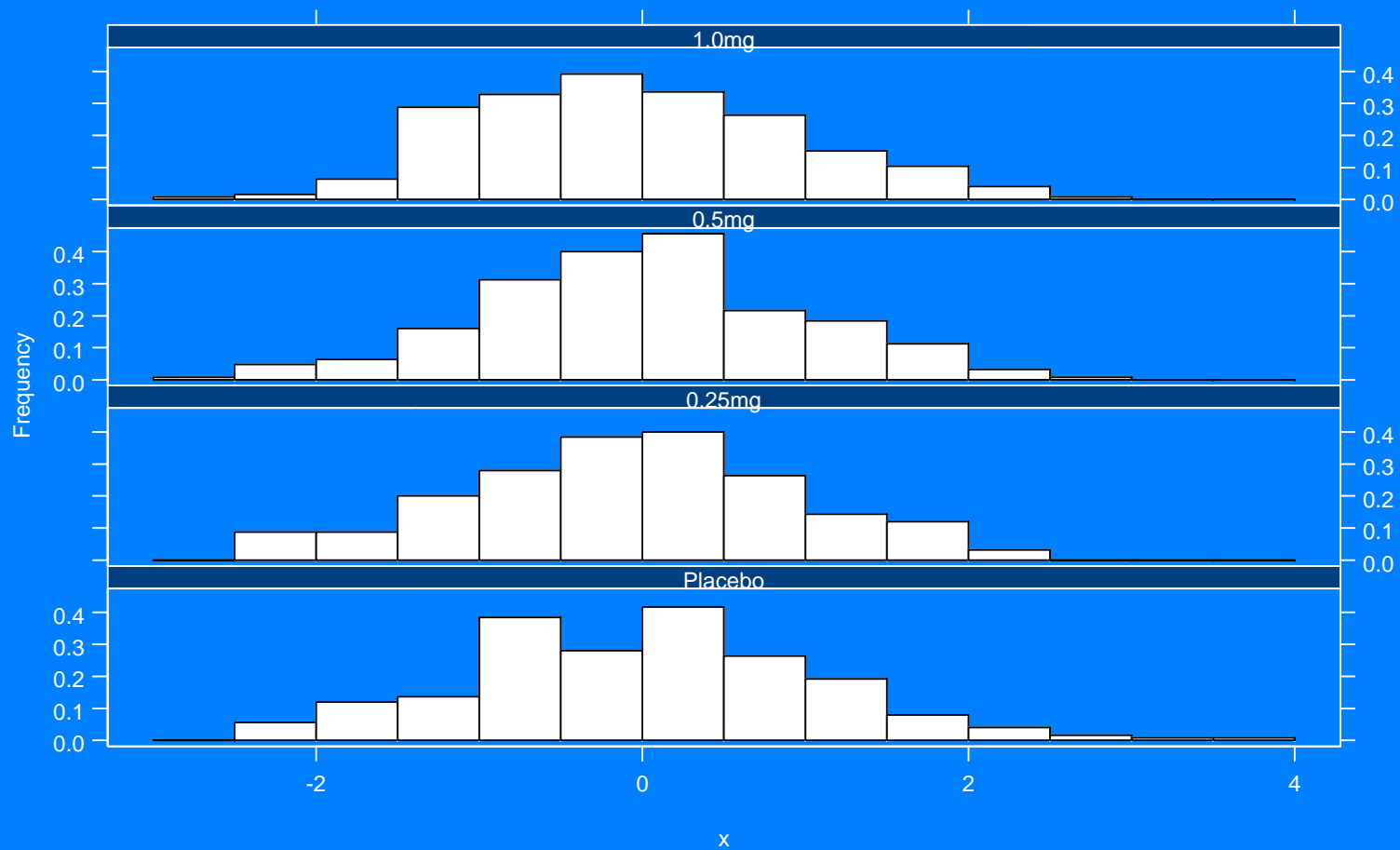
# My Histogram for Internal Power Point Pattern

Histogram | Trellis



Report

Page 1 of 1



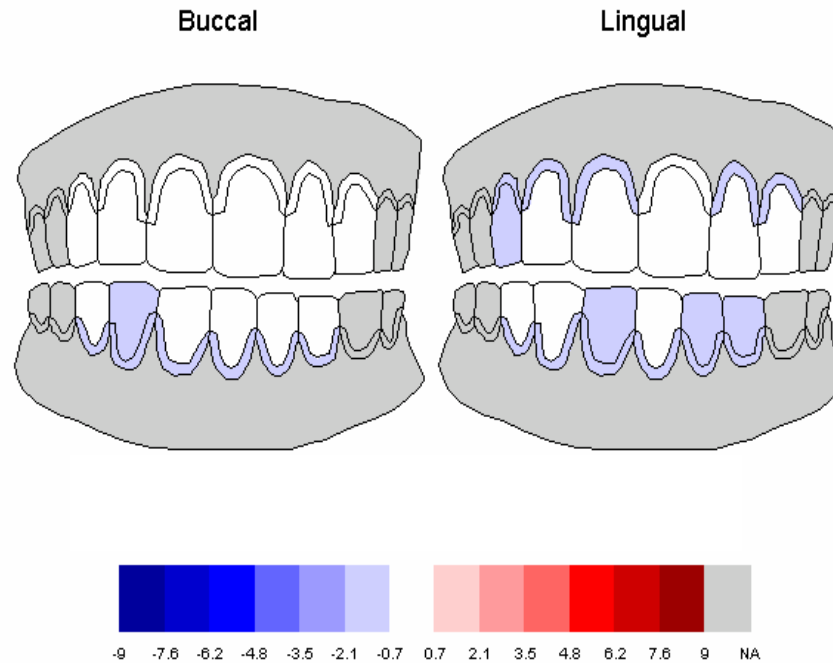


# Combined Graphical and Tabular Reports

Body Plot



Review



Treatment Minus Placebo Stain at Week 4

# Insightful Clinical Review

Insightful Clinical Review - Windows Internet Explorer

C:\LapShare\Product\ClinicalREview\Prototypes\ExampleICR\_0\_5\index.html

http://www.steward.ca/wor... Insightful Clinical Review

User ID: TestUser  
Compound: Compound 1  
Protocol: Protocol 1  
Study: Study 1

Expand All Collapse All

HOME  
Important Results  
Study Background  
Help

PATIENTS  
SELECTED PATIENTS (0)

ADVERSE EVENTS  
By Dictionary-Derived Term  
By Body System Class  
By Treatment

LABS

## By Dictionary-Derived Term

Graph (All Causes)

Update Selected Patients List

In Out Rect Fill Select Print...

Placebo N=72 ProstHigh N=71 ProstLow N=69 31-351-2002,31-351-2159,31-351-2171,31-360-2440

Adverse Event	Placebo N=72 (%)	ProstHigh N=71 (%)	ProstLow N=69 (%)
DIARRHOEA	20	35	35
ABDOMINAL PAIN	10	35	40
PRURITUS	10	30	30
NAUSEA	10	15	15
RASH	5	15	15
DIZZINESS	5	15	15
VOMITING	5	10	10
SKIN IRRITATION	5	10	10
SINUS BRADYCARDIA	5	10	10
FATIGUE	5	10	10
COUGH	5	10	10
UPPER RESPIRATORY TRACT INFECTION	5	10	10
NASOPHARYNGITIS	5	10	10
HYPERHIDROSIS	5	10	10
HEADACHE	5	10	10
MYOCARDIAL INFARCTION	5	10	10
SYNCOPE	5	10	10
NASAL CONGESTION	5	10	10
OEDEMA PERIPHERAL	5	10	10
ELECTROCARDIOGRAM ST SEGMENT DEPRESSION	5	10	10
ATRIOVENTRICULAR BLOCK SECOND DEGREE	5	10	10
ATRIAL FIBRILLATION	5	10	10
SOMNOLENCE	5	10	10
SALIVARY HYPERSECRETION	5	10	10

Page 1

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My Computer 100%

# Insightful Clinical Review

Insightful Clinical Review - Windows Internet Explorer

C:\LapShare\Product\ClinicalReview\Prototypes\ExampleICR\_0\_4\ExampleICR\index.html

Microsoft Outlook Web Access Insightful Clinical Review

Insightful the knowledge to act™

Insightful Clinical Review

User ID: TestUser  
Compound: Compound 1  
Protocol: Protocol 1  
Study: Study 1

Expand All Collapse All

HOME

Important Results  
Study Background  
Help

PATIENTS

SELECTED PATIENTS (1)

Analyze Selected Patients  
31-351-2207

ADVERSE EVENTS

By Dictionary-Derived Term  
By Body System Class

LABS

Liver Function Tests  
Lipids  
Renal Function  
Electrolytes  
Other Biochemistry  
Muscle

DOSE OPTIMIZATION

Dose: MCPMod

### Patient 31-351-2207: Adverse Events

Dictionary-Derived Term	Body System or Organ Class	Serious Event	Severity	Assessed Causality	Adverse Event Start Date	Adverse Event End Date
DIARRHOEA	GASTROINTESTINAL DISORDERS	N	MILD	POSSIBLE	06/13/2005	NA
DIARRHOEA	GASTROINTESTINAL DISORDERS	N	MODERATE	POSSIBLE	06/13/2005	NA
SKIN ODOUR ABNORMAL	SKIN AND SUBCUTANEOUS TISSUE DISORDERS	N	MILD	REMOTE	06/13/2005	NA
PRURITUS	SKIN AND SUBCUTANEOUS TISSUE DISORDERS	N	MILD	POSSIBLE	06/14/2005	NA
ABDOMINAL PAIN	GASTROINTESTINAL DISORDERS	N	MILD	PROBABLE	06/21/2005	07/10/2005
ABDOMINAL PAIN	GASTROINTESTINAL DISORDERS	N	MILD	PROBABLE	06/21/2005	07/10/2005
UPPER RESPIRATORY TRACT INFECTION	INFECTIONS AND INFESTATIONS	N	MILD	NONE	07/22/2005	08/11/2005
UPPER RESPIRATORY TRACT INFECTION	INFECTIONS AND INFESTATIONS	N	MILD	NONE	07/22/2005	08/11/2005
FATIGUE	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	N	MILD	REMOTE	07/31/2005	NA
HORDEOLUM	INFECTIONS AND INFESTATIONS	N	MILD	NONE	08/31/2005	NA

### Patient 31-351-2207: Liver Function Tests

Visit	Date	Alanine Aminotransferase	Alkaline Phosphatase	Aspartate Aminotransferase	Gamma Glutamyl Transferase	Albumin	Bilirubin	Protein
LAB BASELINE	05/29/2005	63.94	81.97	37.98	67.95	41	39.27	71.07
UNSCHEDULED	06/07/2005	60.94	79.98	35.98	69.95	42	34.15	77.03
WEEK 2	06/26/2005	47.12	95.05	26.05	66.1	40.01	18.93	71.1
WEEK 4	07/10/2005	61.18	89.08	43.07	59.15	42.01	34.38	75.07
WEEK 6	07/21/2005	60.31	89.13	32.11	51.26	41.02	25.95	72.05
WEEK 8	08/05/2005	71.37	77.15	35.14	71.31	38	24.3	75.03
WEEK 12	09/01/2005	70.43	90.18	35.16	60.36	40.03	15.81	75.03
WEEK 16	10/01/2005	35.49	75.2	26.18	47.41	38.04	24.42	71.07
WEEK 20	10/27/2005	35.56	83.23	23.2	49.46	43.04	26.19	75.07
WEEK 24	11/26/2005	43.62	71.25	28.23	53.51	41.05	31.38	76.06
WEEK 26	12/10/2005	39.68	73.28	23.25	48.56	41.05	19.47	75.03

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My Computer 100%

# Futures: Interactive Clinical Review on the iPhone

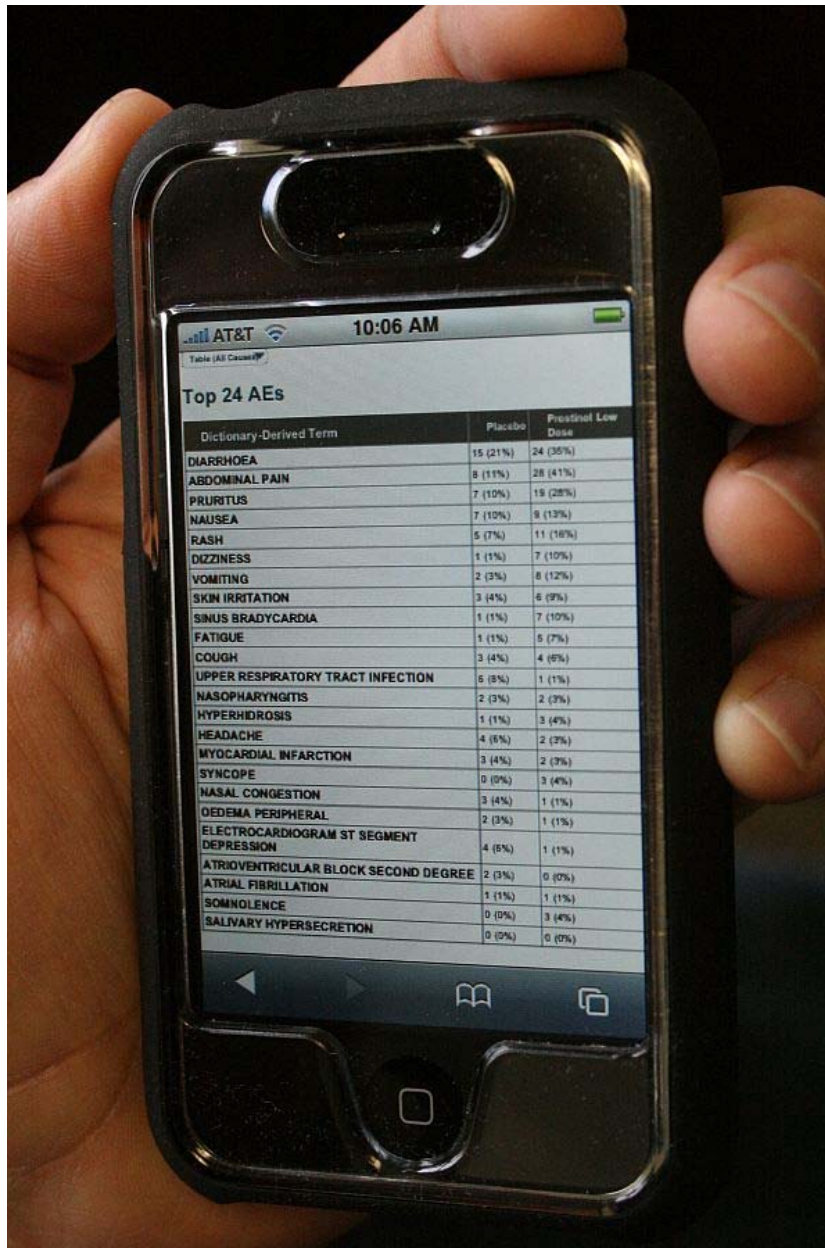


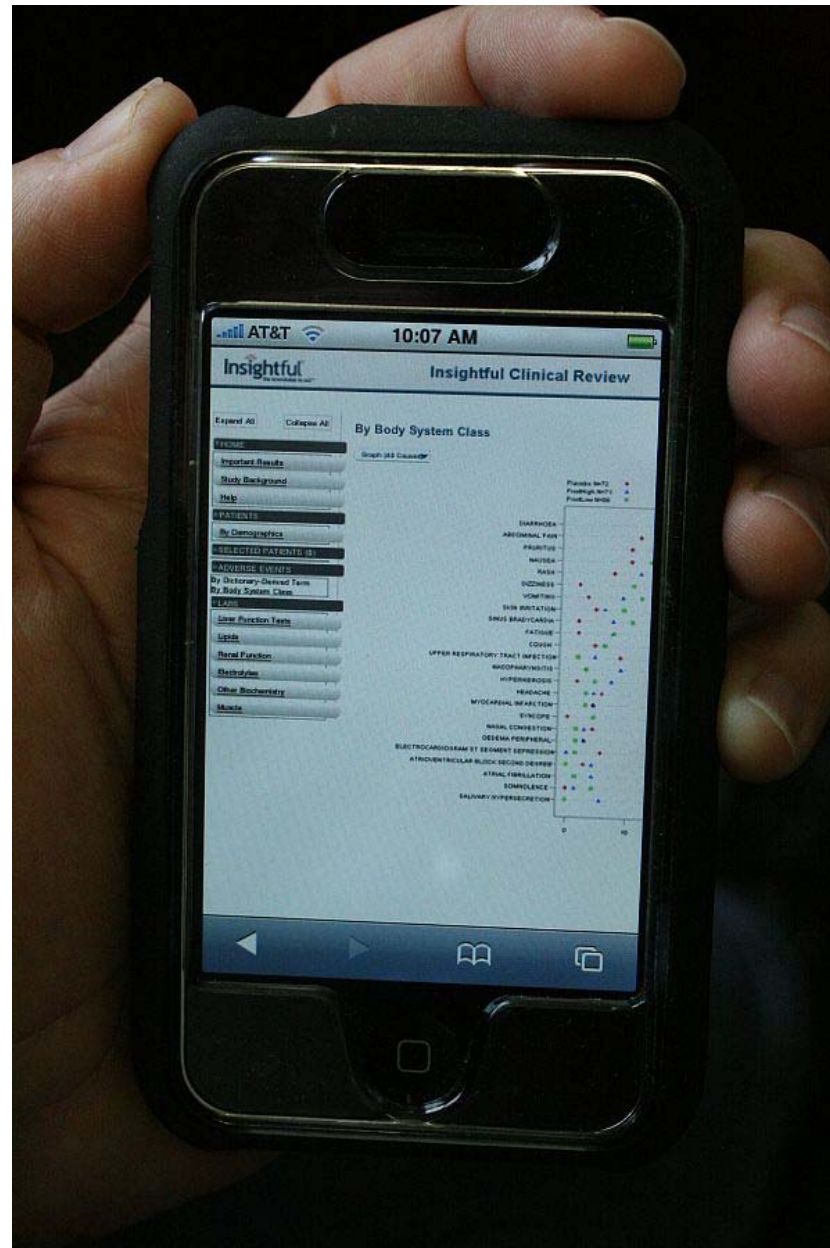
Table (All Causes)

### Top 24 AEs

Dictionary-Derived Term	Placebo	Proximal Low Dose
DIARRHOEA	15 (21%)	24 (35%)
ABDOMINAL PAIN	9 (11%)	28 (41%)
PRURITUS	7 (10%)	19 (28%)
NAUSEA	7 (10%)	9 (13%)
RASH	5 (7%)	11 (16%)
DIZZINESS	1 (1%)	7 (10%)
VOMITING	2 (3%)	8 (12%)
SKIN IRRITATION	3 (4%)	6 (9%)
SINUS BRADYCARDIA	1 (1%)	7 (10%)
FATIGUE	1 (1%)	5 (7%)
COUGH	3 (4%)	4 (6%)
UPPER RESPIRATORY TRACT INFECTION	6 (8%)	1 (1%)
NASOPHARYNGITIS	2 (3%)	2 (3%)
HYPERHDROSIS	1 (1%)	3 (4%)
HEADACHE	4 (6%)	2 (3%)
MYOCARDIAL INFARCTION	3 (4%)	2 (3%)
SYNCOPE	0 (0%)	3 (4%)
NASAL CONGESTION	3 (4%)	1 (1%)
OEDEMA PERIPHERAL	2 (3%)	1 (1%)
ELECTROCARDIOGRAM ST SEGMENT DEPRESSION	4 (6%)	1 (1%)
ATRIOVENTRICULAR BLOCK SECOND DEGREE	2 (3%)	0 (0%)
ATRIAL FIBRILLATION	1 (1%)	1 (1%)
SOMNOLENCE	0 (0%)	3 (4%)
SALIVARY HYPERSECRETION	0 (0%)	0 (0%)



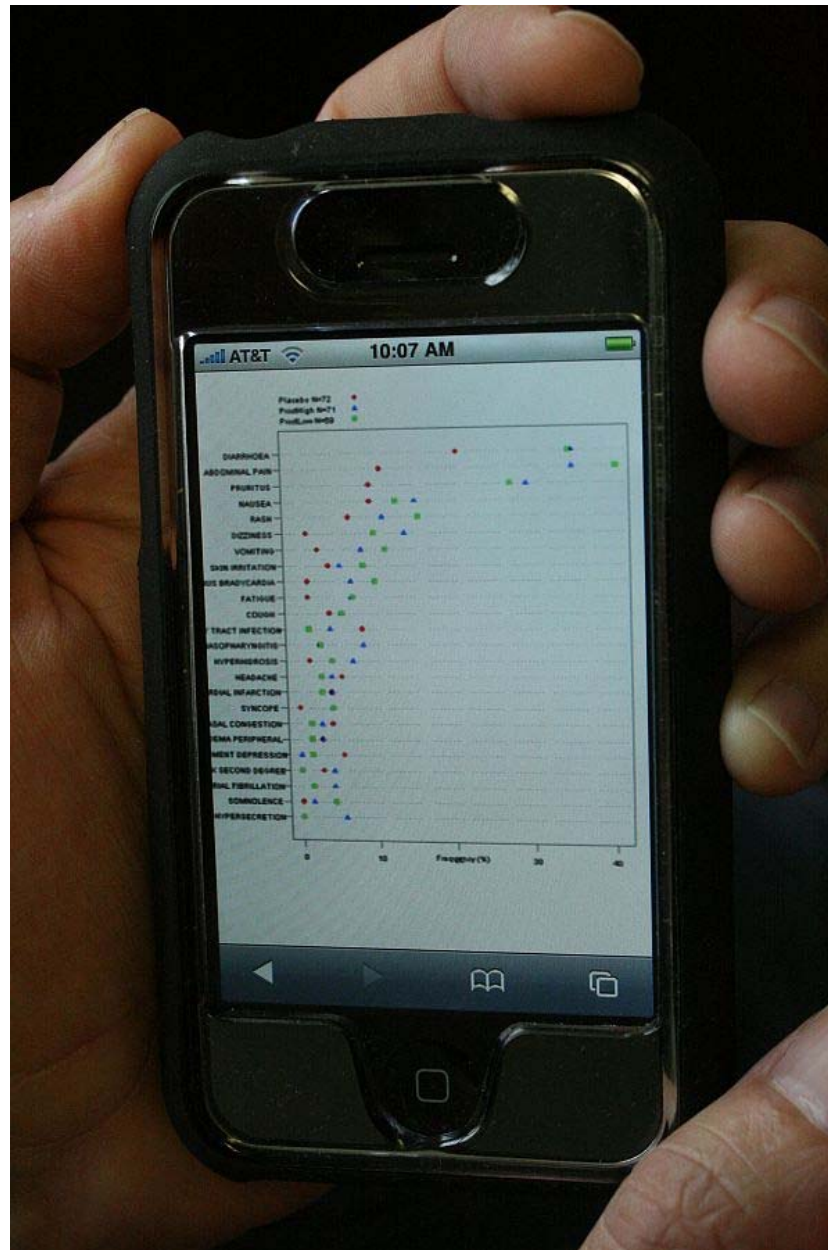
# Interactive Clinical Review on the iPhone







# Interactive Clinical Review on the iPhone





## Key Clinical Graphics Use Cases – Mashups

### Point-click specification of statistical graphics (stats, programming)

- + Easy to create informative statistical graphics (point-click)
- + Comprehensive palette of graph types: dot plot, box plot, line plot, ...

### Create / save a graph pattern for re-use on bound or new data

- + Instream clinical data review / cleaning (data refresh)
- + Analysis of different trial/endpoint by different person/TA (CDISC helps)

### System creation of script to be run in validated environment

- + Oracle / SAS and submission reporting

### Graph styling and presentation with bound data (publishing)

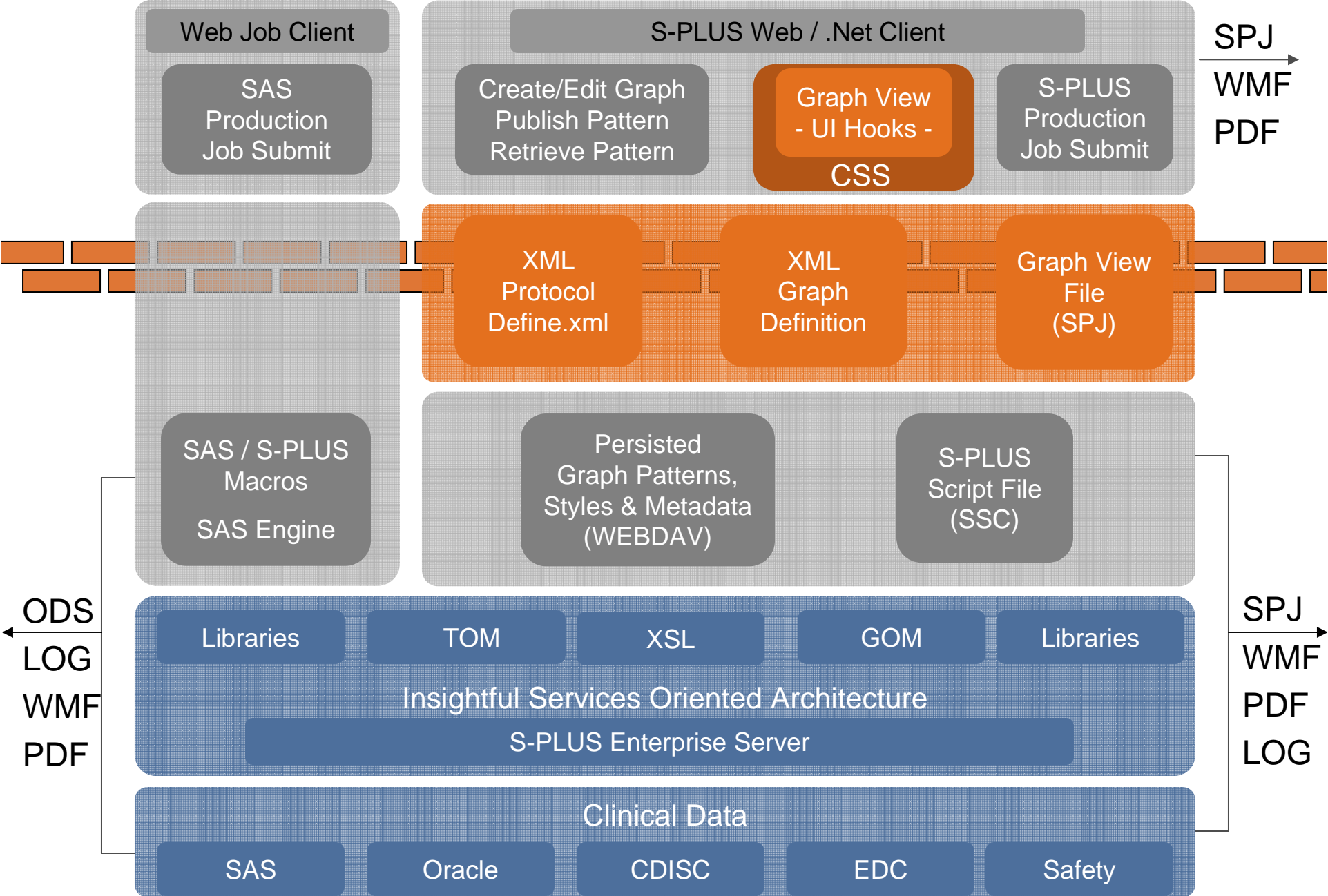
- + Graph in to company power point style e.g. b&w <-> color
- + Graph in to journal style
- + No change to scientific graph content

### Create / add new graph type (stats)

- + New statistical graphics added by statistics for use throughout

### *Permissioned re-purposing of complex statistical graphics*

# Insightful Clinical Graphics



## Statistical Graphics are at the core in the analysis and interpretation of clinical / safety data

- + *Comparative analysis of treatment effects*
- + Exploratory – understand the data, cleaning and outliers
- + Review – all components of population and patient level data
- + Submission – clinical study reports
- + Presentation – scientific and marketing applications

## Consistency in statistical graphics principles/standards is key

- + S-PLUS Trellis™ and S-PLUS Graphlets™ provide consistency across graph types and environments
- + Same graphs in reports and exploratory data browsing
- + Graphical language across organizations and industry

This is widely recognized by industry and the FDA

*In the not too distant future..... I see a world where*

Statistical Graphics are widely used to anchor the messaging from clinical studies

+ Group and Trellis / Metadata / Drill-down

Statistical Graphics are mashed up within pharma companies for rapid design, analysis, review, submission, publication and presentation

+ Using the clinical graphics taxonomy – types and patterns

A standard Statistical Graphics palette with rich APIs for repurposing is used across industry and the FDA

+ Simple interactions between industry and the FDA

*Safety and the critical path are making this reality*

**Michael O'Connell**

**[moconnell@insightful.com](mailto:moconnell@insightful.com)**

**Today's presentation will be available on our website soon**

**[http://www.insightful.com/news\\_events](http://www.insightful.com/news_events)**

**Insightful's 10<sup>th</sup> User Conference in Atlantic City**

**Insightful Impact 2007**

**October 10-11, 2007, Tropicana Hotel, Atlantic City**

**[http://www.insightful.com/news\\_events/impact2007/default.asp](http://www.insightful.com/news_events/impact2007/default.asp)**