



# Clinical Trials Graphical Reporting: A Rescue From Tables

Frank E Harrell Jr

Department of Biostatistics, Vanderbilt University School of Medicine  
Nashville, Tennessee USA

STATISTICAL METHODS IN BIOPHARMACY

EMERGING TOPICS FOR STATISTICAL METHODOLOGY IN CLINICAL DRUG

DEVELOPMENT

Biopharmacie et Sante

Société Française de Statistique

SFdS

Paris, France

17 September 2013



- Miscellaneous interim analyses
- Repeated DMC and final reports
- Reviewers need help
- Make patterns and signals apparent
- Handling multiple dimensions
- Tables often require categorization of continuous variables



# What are Tables Good For?

## Inducing Sleep!

	Growth (n = 5,218)		Mature (n = 5,226)		Stagnant (n = 5,262)		Full (n = 26,243)	
	MED	SD	MED	SD	MED	SD	MED	SD
R	0.10	1.06	0.33	1.38	0.21	1.40	0.23	1.36
BM	0.57	1.37	0.69	1.47	0.80	1.10	0.75	1.57
BETA	0.72	2.02	1.01	1.06	1.12	1.60	0.89	5.60
SIZE	3.26	2.32	5.07	2.47	5.60	2.25	4.92	2.37
LEV	0.19	0.28	0.17	0.27	0.14	0.19	0.17	0.24
ΔSG	0.06	2.24	0.01	0.24	-0.00	0.08	0.03	1.07
ΔCE	0.05	0.78	0.03	0.82	-0.00	0.18	0.04	1.02
ΔCFO	0.00	0.37	0.03	1.09	-0.00	0.85	0.02	1.51
ΔROS	1.21	30.08	2.20	50.23	-0.57	21.46	1.17	59.47
ΔNI	0.10	1.05	0.33	1.38	-0.00	1.40	0.04	1.02
SG	0.61	4.13	0.26	3.28	-0.07	0.25	0.39	3.38
CAP	0.12	0.31	0.08	0.15	0.02	0.03	0.06	0.21
DIV	0.00	0.25	0.07	0.39	1.21	1.74	0.31	8.02
AGE	16	10.55	39	27.3	74	22.6	45	27.5





# What are Tables Good For?

Clinical Trials  
Graphical  
Reporting

RCT  
Reporting

Tables

Guidelines

General  
Examples

Safety  
Displays:  
Many AEs

Mixing Tables  
and Graphics

Suggested  
Model

References

- Summarizing categorical variables
- Information look-up
- Pretending there is more precision in estimates than actually exists
- Providing denominators (sample sizes)



- 1 Display data values using position or length.
- 2 Use horizontal lengths in preference to vertical lengths.
- 3 Watch your data-ink ratio.
- 4 Think very carefully before using color to represent data values.
- 5 Do *not* use areas to represent data values.
- 6 *Please* do not use angles or slopes to represent data values.
- 7 *Please, please* do not use volumes to represent data values.



# Guidelines for High Information Graphics

- Exclude unneeded dimensions and chartjunk
- Graphics don't need to be “dumbed down” or “sexy”
- Keep continuous variables continuous
- Use graphical perception research
  - Emphasize position along a common scale
- Don't choose a graphic requiring an arbitrary choice
  - E.g., rotation of pie chart
- Avoid bar charts
- Choose *descriptive* descriptive statistics
- *Show* differences
- Use real estate to show useful information, not Table 1



# Classic Books

Clinical Trials  
Graphical  
Reporting

RCT  
Reporting

Tables

Guidelines

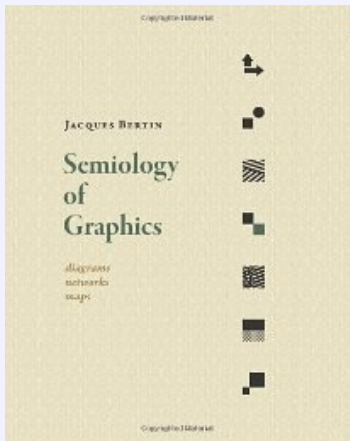
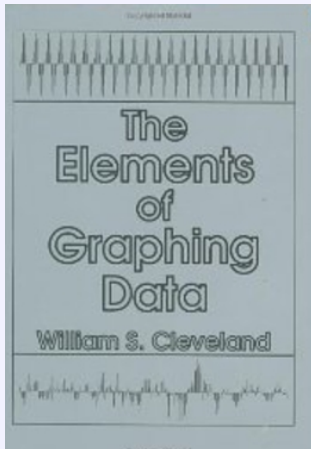
General  
Examples

Safety  
Displays:  
Many AEs

Mixing Tables  
and Graphics

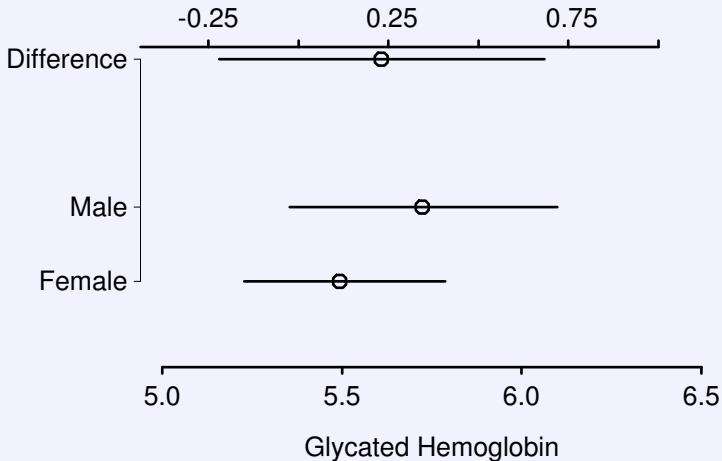
Suggested  
Model

References





# Showing the Difference







# Not This

Clinical Trials  
Graphical  
Reporting

RCT  
Reporting

Tables

Guidelines

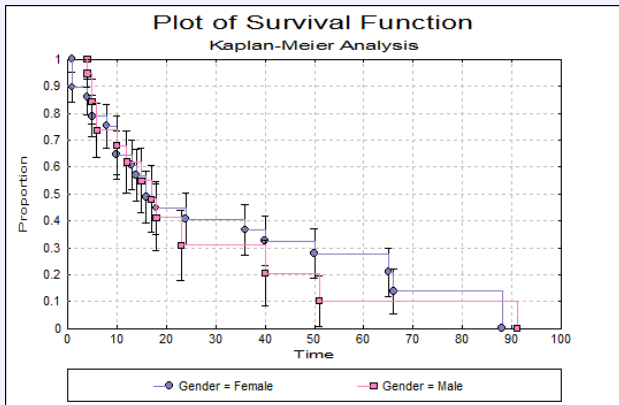
General  
Examples

Safety  
Displays:  
Many AEs

Mixing Tables  
and Graphics

Suggested  
Model

References





# Showing Differences: Two Kaplan-Meier Curves

Clinical Trials  
Graphical  
Reporting

RCT  
Reporting

Tables

Guidelines

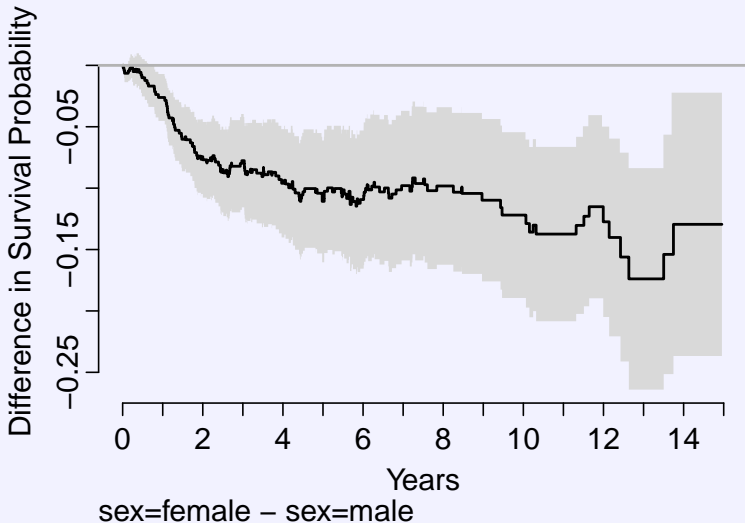
General  
Examples

Safety  
Displays:  
Many AEs

Mixing Tables  
and Graphics

Suggested  
Model

References





# Depicting Uncertainty

Clinical Trials  
Graphical  
Reporting

RCT  
Reporting

Tables

Guidelines

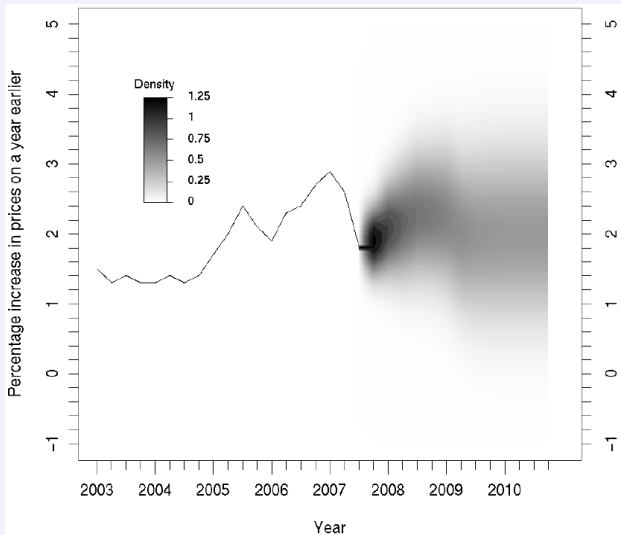
General  
Examples

Safety  
Displays:  
Many AEs

Mixing Tables  
and Graphics

Suggested  
Model

References



Jackson [2008]



# General Examples: Dropouts

Clinical Trials  
Graphical  
Reporting

RCT  
Reporting

Tables

Guidelines

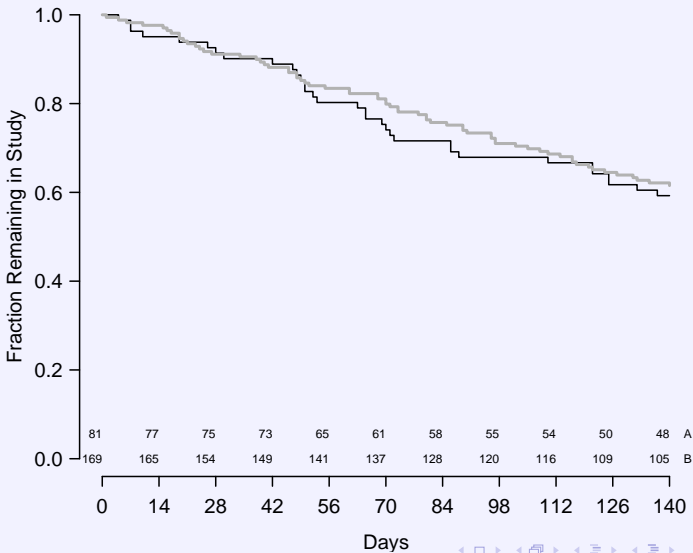
**General  
Examples**

Safety  
Displays:  
Many AEs

Mixing Tables  
and Graphics

Suggested  
Model

References





# Safety Variable Clustering

Clinical Trials  
Graphical  
Reporting

RCT  
Reporting

Tables

Guidelines

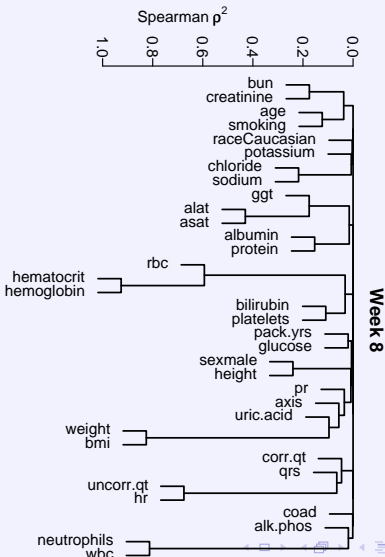
General  
Examples

Safety  
Displays:  
Many AEs

Mixing Tables  
and Graphics

Suggested  
Model

References





# Cumulative Incidence of AEs

Clinical Trials  
Graphical  
Reporting

RCT  
Reporting

Tables

Guidelines

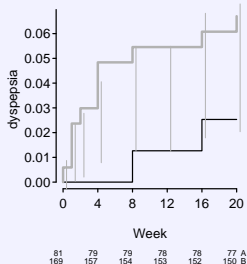
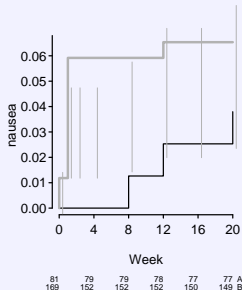
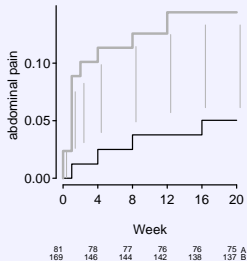
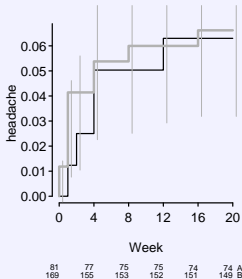
General  
Examples

Safety  
Displays:  
Many AEs

Mixing Tables  
and Graphics

Suggested  
Model

References





# Empirical CDFs

Clinical Trials  
Graphical  
Reporting

RCT  
Reporting

Tables

Guidelines

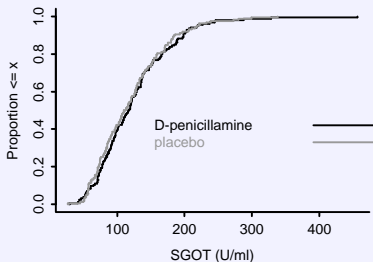
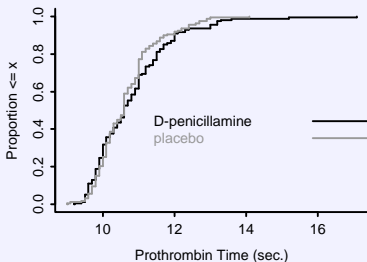
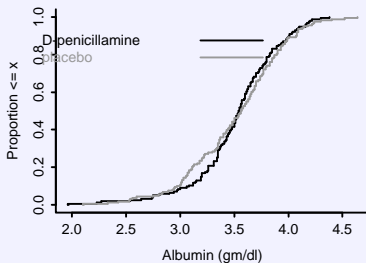
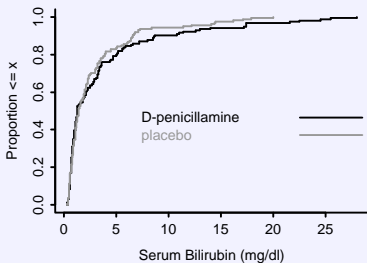
General  
Examples

Safety  
Displays:  
Many AEs

Mixing Tables  
and Graphics

Suggested  
Model

References





# Extended Box Plots

Clinical Trials  
Graphical  
Reporting

RCT  
Reporting

Tables

Guidelines

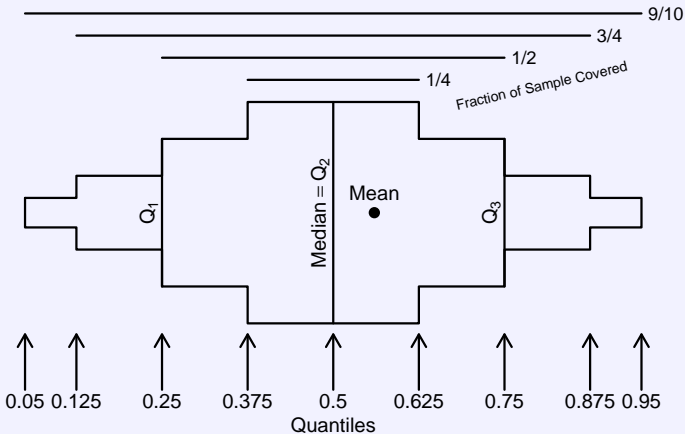
General  
Examples

Safety  
Displays:  
Many AEs

Mixing Tables  
and Graphics

Suggested  
Model

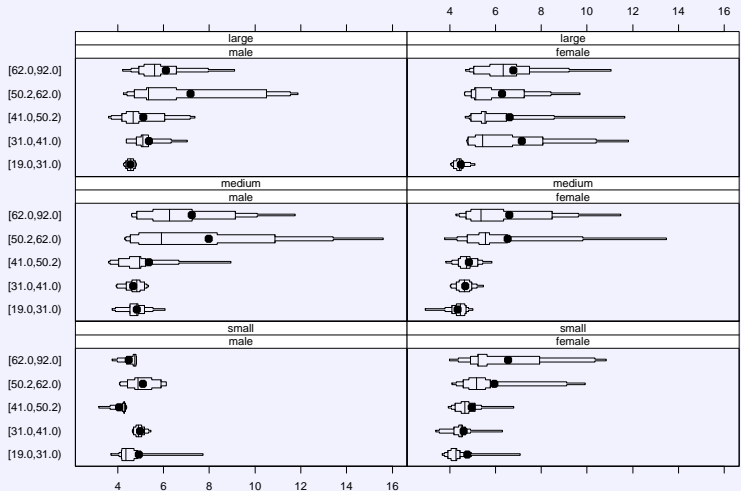
References







# Multi-Panel Extended Box Plots





# Instead of Table 1: Baseline Variables vs. Outcome

Clinical Trials  
Graphical  
Reporting

RCT  
Reporting

Tables

Guidelines

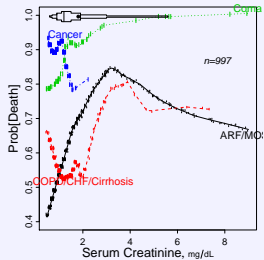
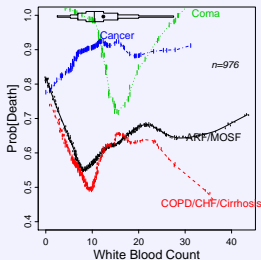
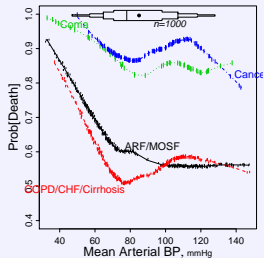
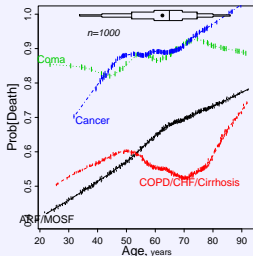
General  
Examples

Safety  
Displays:  
Many AEs

Mixing Tables  
and Graphics

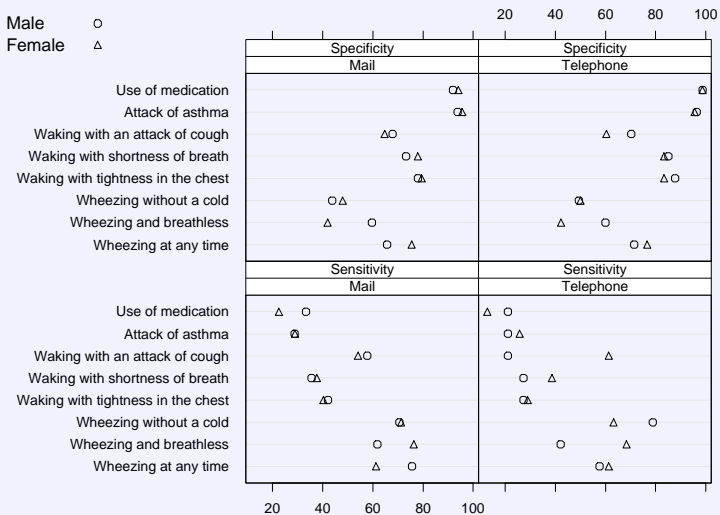
Suggested  
Model

References



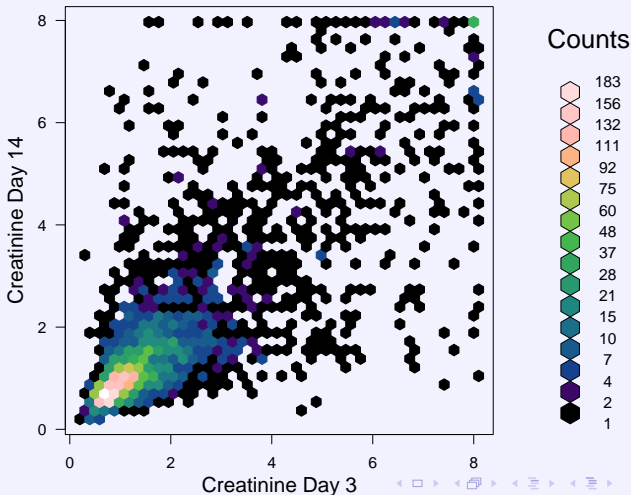


# Multi-Panel Dot Plots



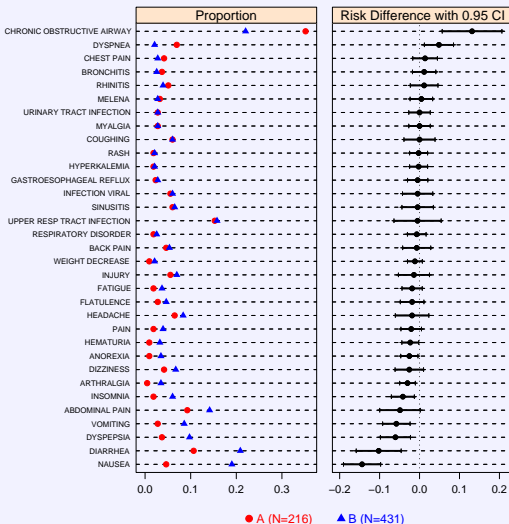


# Dispense with Lab Parameter Change Tables





### Most Frequent On-Therapy Adverse Events Sorted by Risk Difference





# SAEs by Body System and Preferred Term

Clinical Trials  
Graphical  
Reporting

RCT  
Reporting

Tables

Guidelines

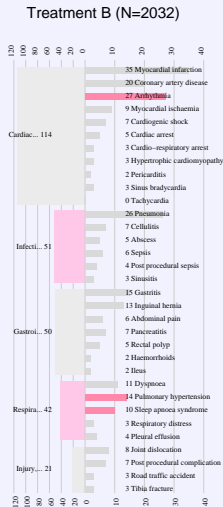
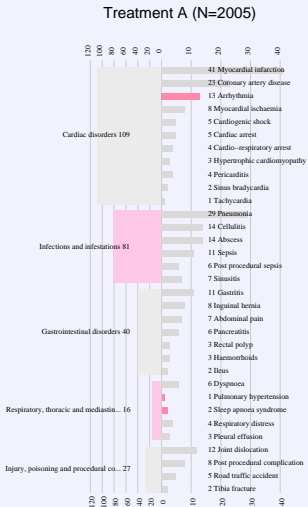
General  
Examples

Safety  
Displays:  
Many AEs

Mixing Tables  
and Graphics

Suggested  
Model

References





# Mixing Tables and Graphics

		D-penicillamine <i>N</i> = 154		placebo <i>N</i> = 158		Test Statistic		
Serum Bilirubin	mg/dl	0.725	<b>1.300</b>	3.600	0.800	<b>1.400</b>	3.200	$F_{1,310} = 0.04, P = 0.842^1$
Albumin	gm/dl	3.34	<b>3.54</b>	3.78	3.21	<b>3.56</b>	3.83	$F_{1,310} = 0, P = 0.951^1$
Histologic Stage Ludwig Criteria								
1			3%	$\frac{4}{154}$		8%	$\frac{12}{158}$	
2			21%	$\frac{32}{154}$		22%	$\frac{35}{158}$	
3			42%	$\frac{64}{154}$		35%	$\frac{56}{158}$	
4			35%	$\frac{54}{154}$		35%	$\frac{55}{158}$	
Prothrombin Time	sec.	10.0	<b>10.6</b>	11.4	10.0	<b>10.6</b>	11.0	$F_{1,310} = 0.29, P = 0.589^1$
sex								
female			90%	$\frac{139}{154}$		87%	$\frac{137}{158}$	
Age		41.4	<b>48.1</b>	55.8	43.0	<b>51.9</b>	58.9	$F_{1,310} = 5.52, P = 0.019^1$
spiders			29%	$\frac{45}{154}$		28%	$\frac{45}{158}$	$\chi^2_1 = 0.02, P = 0.885^2$

*a b c* represent the lower quartile *a*, the median *b*, and the upper quartile *c* for continuous variables.

Tests used: <sup>1</sup>Wilcoxon test; <sup>2</sup>Pearson test



# Mixing Tables and Graphics, *continued*

$$\chi_3^2 = 4.63, P = 0.201^2$$



$$F_{1,310} = 0.29, P = 0.589^1$$

$$\chi_1^2 = 0.96, P = 0.326^2$$







# Suggested Model for Reports

- Primary presentation completely graphical
- pdf hyperlink to dense tables for value look-ups
- Alternative 1: table pop-up when hover over graphics
- Alternative 2: micrographics inside tables (limiting, difficult)
- **Better:** supplement graphics with denominators, %, etc.
- R,  $\LaTeX$ , knitr, Markdown, RStudio



[ctspedia.org/StatGraphHome](http://ctspedia.org/StatGraphHome)

FDA/Industry/Academia Safety Graphics Working Group



## References

- O. Amit, R. M. Heiberger, and P. W. Lane. Graphical approaches to the analysis of safety data from clinical trials. *Pharm Stat*, 7:20–35, 2008. URL <http://www3.interscience.wiley.com/journal/114129388/abstract>.
- C. H. Jackson. Displaying uncertainty with shading. *Am Statistician*, 62(4):340–347, 2008.
- P. Murrell. Infovis and statistical graphics: Comment. *J Comp Graph Stat*, 22(1):33–37, 2013. doi: 10.1080/10618600.2012.751875. URL <http://www.tandfonline.com/doi/abs/10.1080/10618600.2012.751875>.