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The Clinical Data Cinema

The many roles of data visualization in clinical development Jürgen Löffler, Novartis Pharma AG, Basel London, 9th October 2015



Motivation

Data tables: what does it all mean?

Subject $^{\diamond}$	Visit 🍦	AVAL	† ID †	TRTO	LPN ÷	sex 🔅	age 🔅	BASE	÷	ratio	pchg	÷	chg	÷								
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Today's program

Documentary

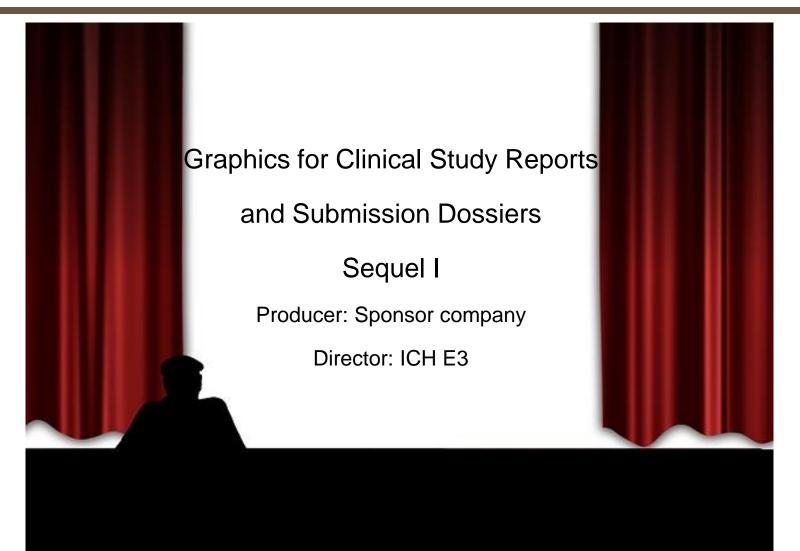
- Graphics for Clinical Study Reports and Submission Dossiers I
- Drama / Comedy
 - Presentations (all sorts of)
- Science
 - Data exploration and other interesting things

Science fiction

- Graphics for Clinical Study Reports and Submission Dossiers II
- Wrap up (not a film)



Today's program Documentary





Documentary How CSRs and dossiers look like





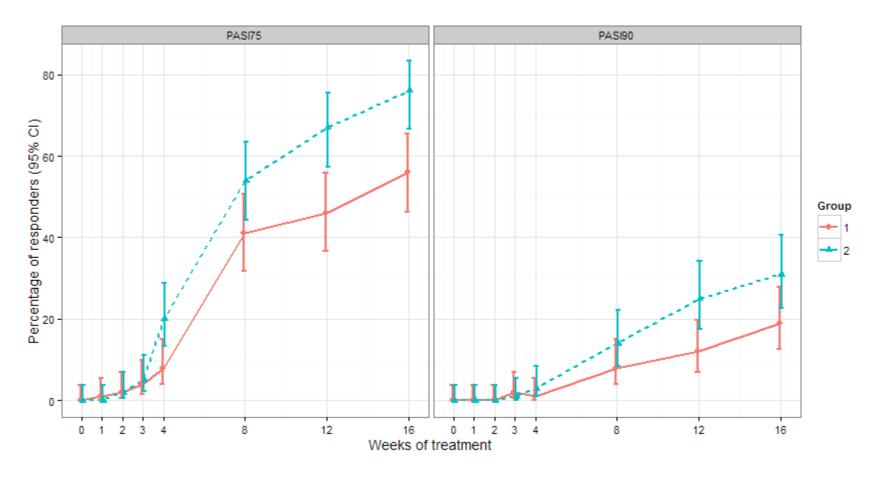
Documentary How CSRs and dossiers look like

- A recent Novartis submission
 - Paper copy for Australia
 - 1485 Folders in 375 boxes for a total weight of 4152 KG
- Thousands of pages of tables, listings and (some) graphs
- How does anyone view pieces of information that belong together but are separated by meters?

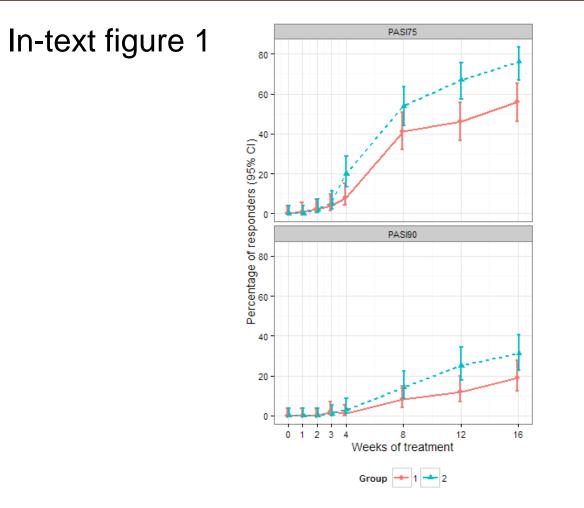
Post-text and in-text figures



Post-text figure 1



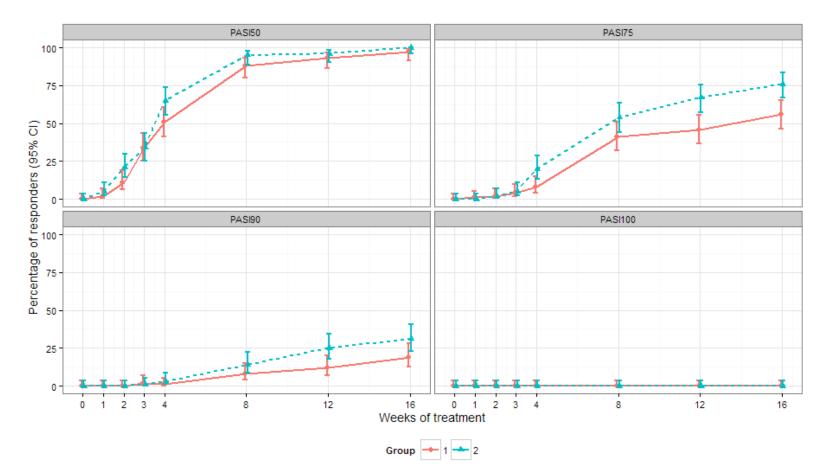
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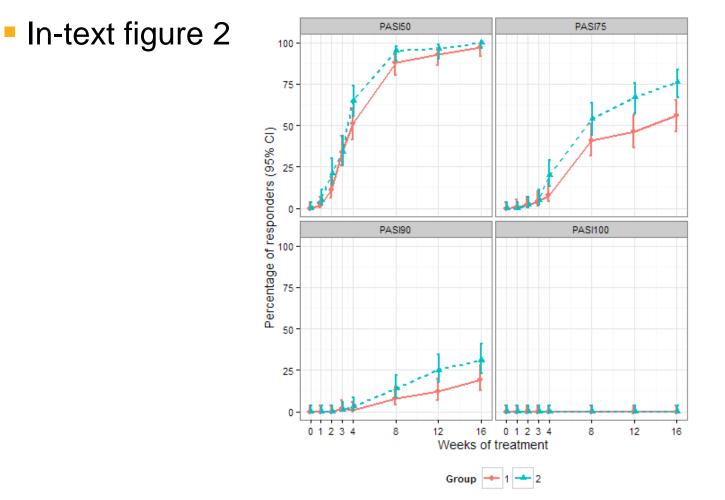


• (at least the aspect ratio in each cell is maintained)

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Post-text figure 2



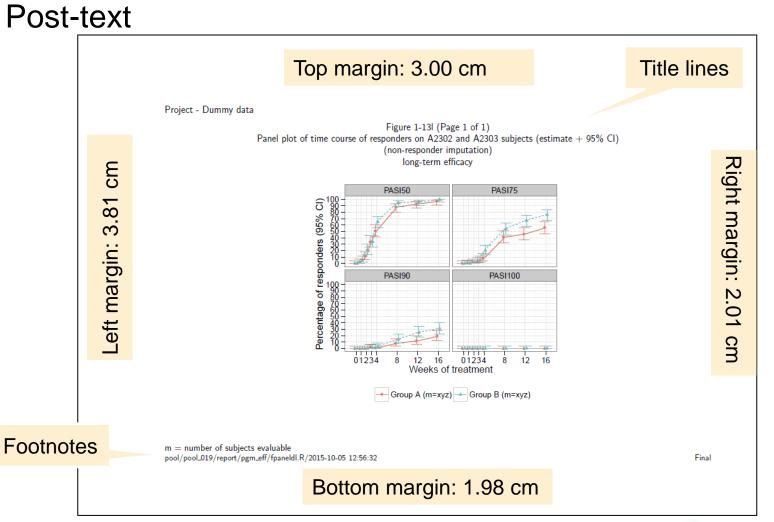


• (aspect ratio now sacrificed due to portrait: different message?)

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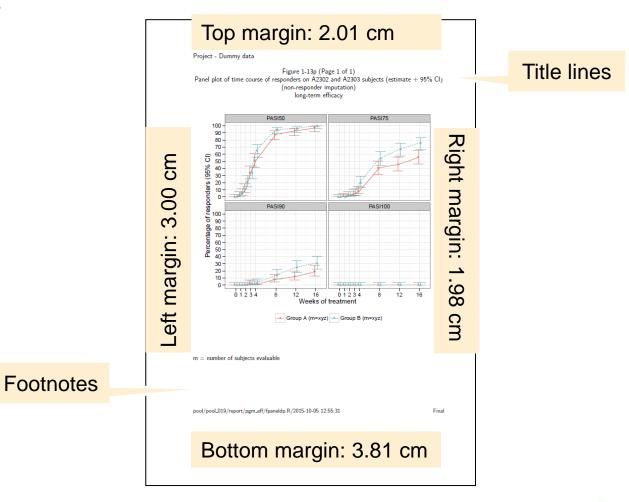
Documentary *Constraints for figures (graphs) in CSRs and dossiers*





Documentary *Constraints for figures (graphs) in CSRs and dossiers*

In-text





Documentary *Limitations and constraints*

- Static
- Limited use of colour (black and white safe)
- Limited size (page margins!)
- Only certain image file formats, no transparency (?)
- Orientation defined by document (not graphical principles)
- Audit trail
- Reproducible
- Validated



NOVARTIS

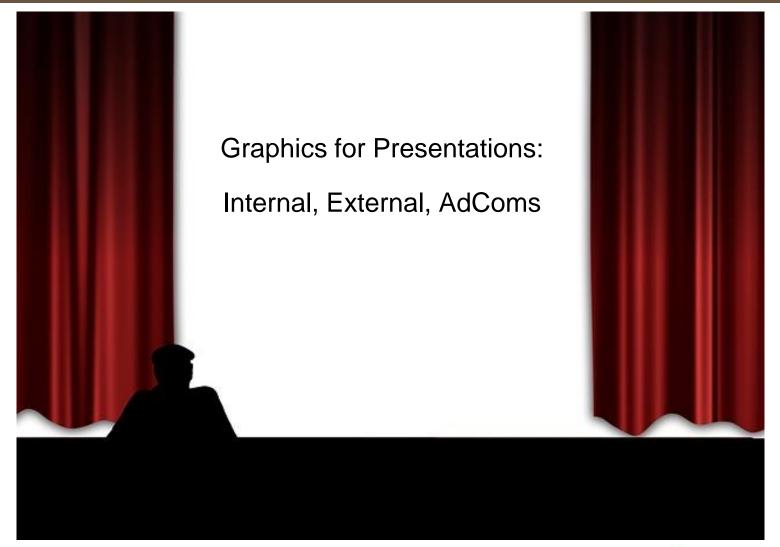
- We produce them as RTF and render to PDF
- The PDF is stored in the document management system (along with the RTF source)
- The medical writer extracts the image (copy or screenshot) and pastes into Word document, resizes as needed (a bitmap file!)
- For convenience, an image file (PNG) may be directly used
 - Produced as a "side product" in SAS (not formally validated, audit trailed, stored)

NOVARTIS

Is there a better way?

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Today's program Drama / Comedy





Drama, Comedy Internal or external slide deck

- Static, possibly animations
- Orientation: landscape
- Company colours

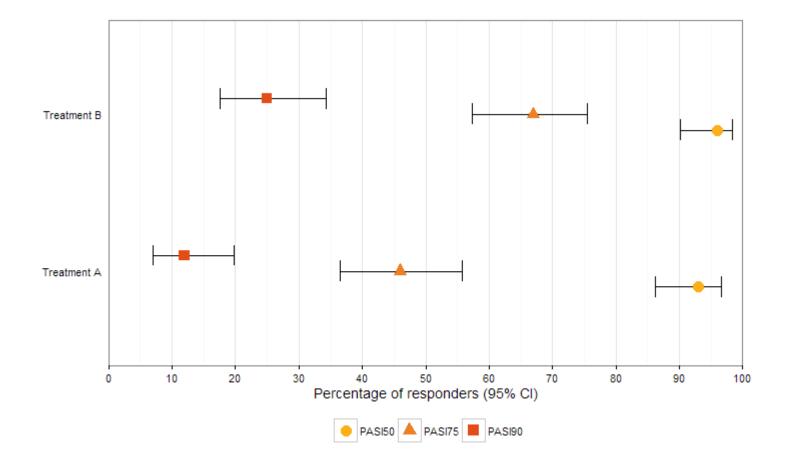
R	G	В	Hex	Preview
252	175	23	FCAF17	
236	128	38	EC8026	
228	76	22	E44C16	
146	50	34	923222	
99	67	41	634329	

Simplicity

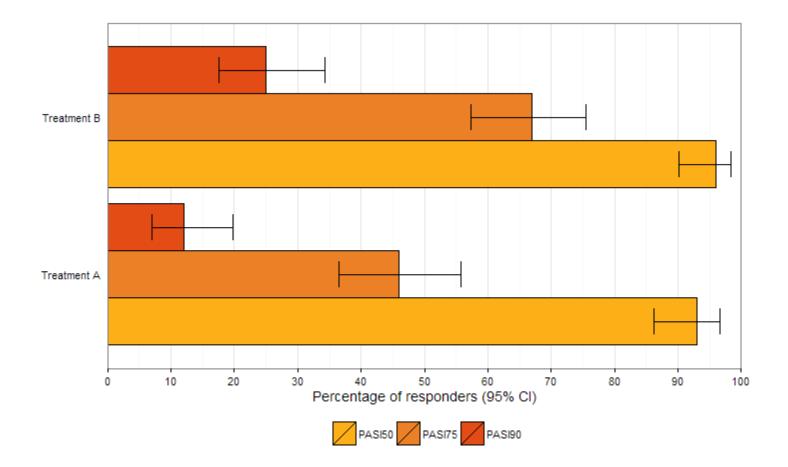
Chart types that audience is used to



Drama, Comedy Statisticians' preference (minimize ink)



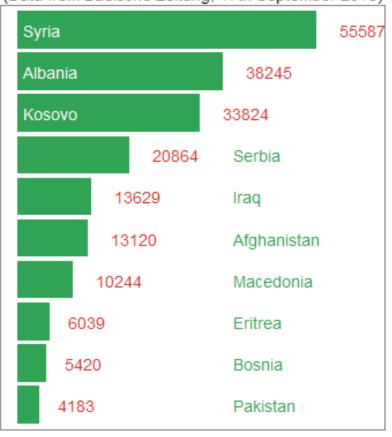
Drama, Comedy Customers' preference (= simplicity or custom?)

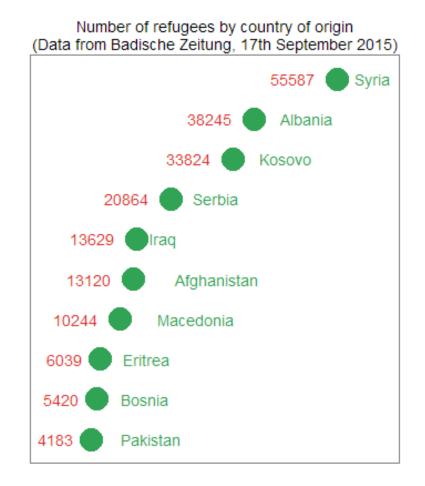




Drama, Comedy My wife's preference?

Number of refugees by country of origin (Data from Badische Zeitung, 17th September 2015)





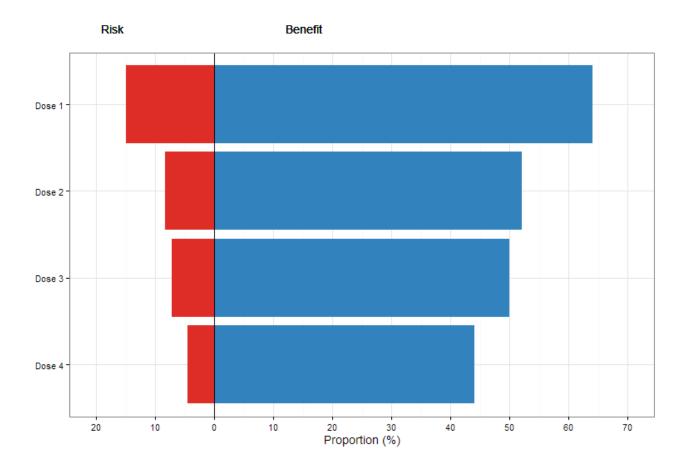
Drama, Comedy AdCom, HA presentation

- Static
- Orientation landscape
- "FDA colours" (not respected here)
- Simplicity
 - Charts that audience is used to: "laypersons"
- Benefit-risk



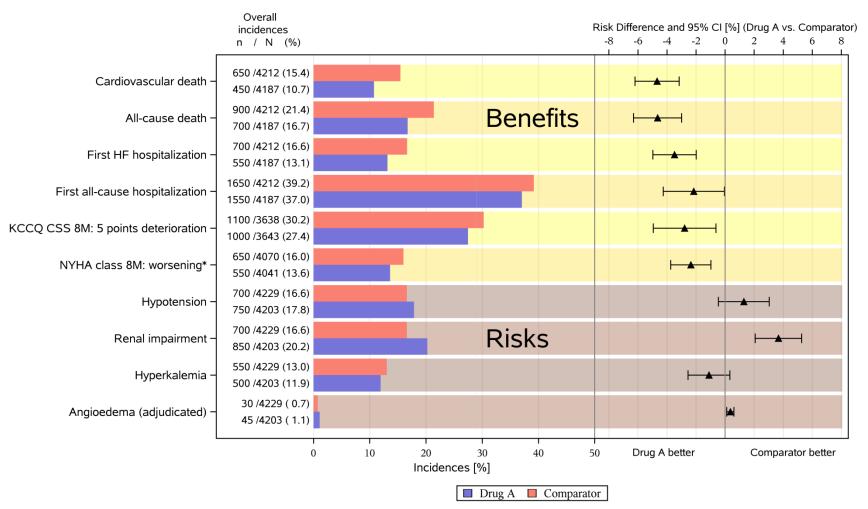
Drama, Comedy Benefit-risk: FDA

FDA presentation at AdCom





Drama, Comedy Benefit-risk: more sophisticated



* death also counted as a worsening

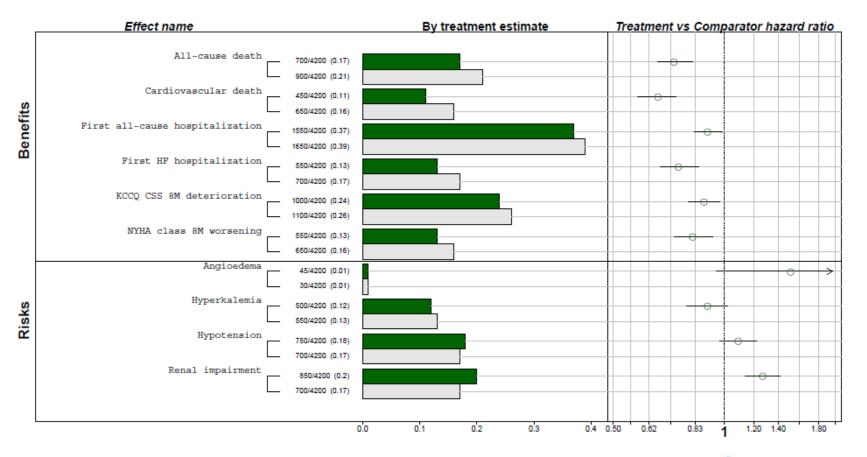
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Drama, Comedy Benefit-risk: more sophisticated (alternative version)

Confidence interval

(arrows if outside plotting range) Point estimate

(Cross if outside plotting range)



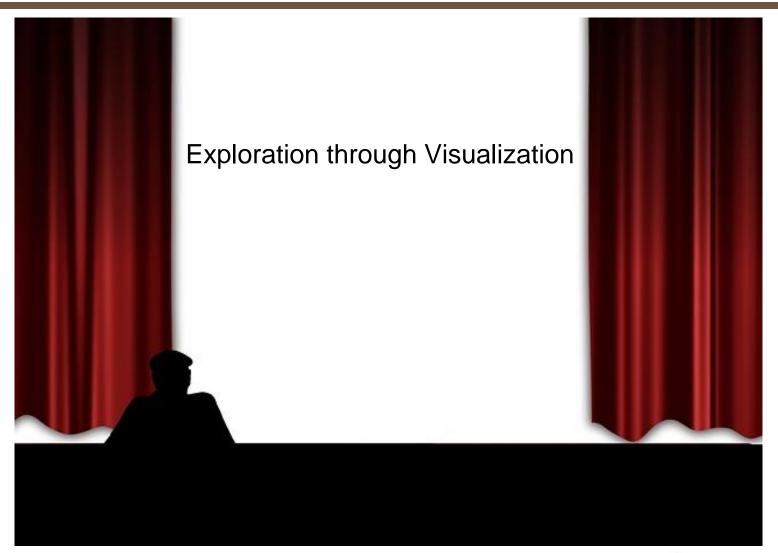


Treatments

Group A

Group B

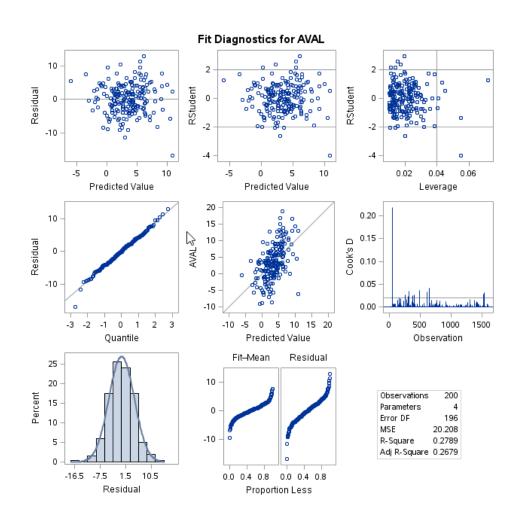
Today's program Science





Science Diagnostic plots

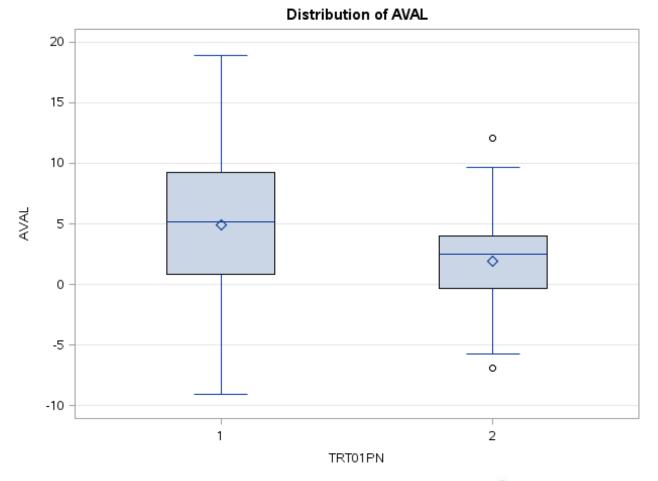
E.g., ANCOVA





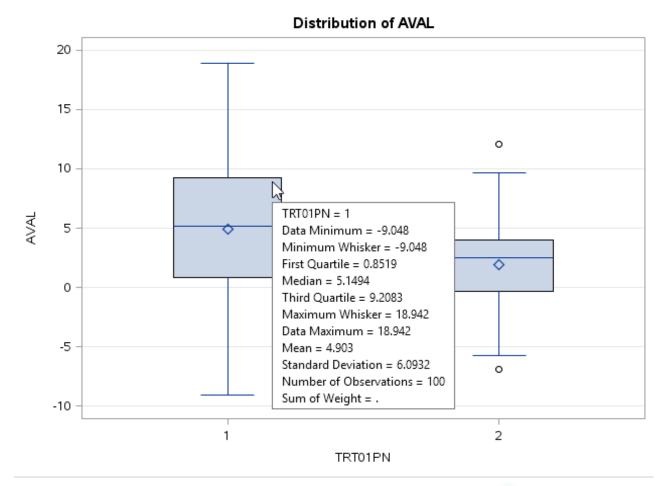
Science Diagnostic plots

E.g., ANCOVA



Science Diagnostic plots

E.g., ANCOVA



- Static
 - Quick, perhaps using "point and click" software
- Interactive
 - Provide pre-made "templates"
 - Let the user decide what to look at (and how)
 - <u>https://loeffju1.shinyapps.io/Histogram</u>
 - <u>https://loeffju1.shinyapps.io/Boxplot</u>



	I	Instream Clinical Review System
Clinical Study Data Source : LSH post-conformance Spotfire Instream Release: 2.4		Please visit our <u>Share Poi</u> Please mail any question NOTE: Only subjects for v
DEMOGRAPHICS Demography ADVERSE EVENTS AE Summary AE Treemap Linked AE & MH	LABS Lab Summary Lab Results by Subject Lab Post Baseline Vs Baseline Std eDISH Plot Bivariate Analysis Lab -> AE Profile AE -> Lab Profile	CONCOMITANT MEDICATIONS Concomitant Medication CM Subcategories PATIENT PROFILE Patient Profile Patient Profile (Details) Patient Profile (Details2)
MEASUREMENTS <u>Vital Signs (VS) Summary</u> <u>VS Post baseline vs Baseline</u> <u>ECG Summary</u> <u>ECG</u> <u>Lung Function Test (1)</u> <u>Lung Function Test (2)</u>	MEDICAL HISTORY Medical History MS History	EFFICACY <u>PASI Scores</u> <u>Tender and swollen Joint Count</u> <u>QS (DLQI)</u> <u>ACQ</u> <u>Assessment of Rebound & IGA</u>



nmary)	AE (Heatmap/Tre	eemap) /	AE Statistics	MH (Summary)	Linked AE & MH	CM (Treemap)	Listing Builder	Subset Comp	arison V	S (Summary/Histogram)		1	*	Y [3 ≡
NOTE: S	ections in the tr	reemap are (colored by the	e worst case, i.e. if	f one subject experi	enced a serious A	AE, the whole recta	ngle will be ma	irked as seri	ous.					
Color by: Did AE Lead to Stud N Y Size by: Unique Count of Su Hierarchy: SOC ->HLGT->HLT			INFECTION	IS AND INFESTATIO	INS	GASTR	DINTESTINAL DISOF	DERS	NEOPLAS UNSPECIF	SMS BENIGN, MALIGNA IED (INCL CYSTS AND	NT AND POLYPS)	S SYSTEM DISORDERS			
							ARDIAC DISORDERS	;	HEPATOBILIARY DISORDERS		GENERAL DIS AND ADMINIS SITE COND	TRATION	RATION SUBCUTANEOU		US TISSUE
									PSYCHIA	ATRIC DISORDERS	RENAL AND URINARY DISORDERS		RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS		C AND TINAL
		INJURY, I	RY, POISONING AND	ND PROCEDURAL COM	OMPLICATIONS						METABOLISM AND NUTRITIC	SYS	IUNE TEM RDERS	EM (Empty)	
						MUSCULOSKE	LETAL AND CONNEC DISORDERS	TIVE TISSUE	VASOU	ILAR DISORDERS	DISORDERS	BLOOI AND LYMPHA C SYST		BYRINT H	PREGNAN CY, PUERPERI UM AND
									VASCO	DAT DISURDERS	EYE DISORDERS	CONGE TAL, FAMILIA AND GE		IDOCRI NE SORDE RS	REPRODU CTIVE SYSTEM AND BR

Science Visual data review

Use the heirarchy slided on the left to adjust the visualization. Rectangles are sized by the # of unique subjects reporting that event.

NOTE: Sections in the treemap are colored by the worst case, i.e. if one subject experienced a serious AE, the whole rectangle will be marked as serious.

Color by:								
Did AE Lead to Stud N Y Size by: Unique Count of Su Hierarchy: SOC ->HLGT->HLT	INFECTIONS AND INFESTATIONS	GASTROINTESTINAL DISORDERS	NEOPLASMS BENIGN, MALIGNA UNSPECIFIED (INCL CYSTS AND		TEM DISORDE	EM DISORDERS		
		CARDIAC DISORDERS	HEPATOBILIARY DISORDERS	GENERAL DISO AND ADMINISTE SITE CONDIT	RATION SUI	SKIN AND BCUTANEOUS DISORDER	TISSUE	
			PSYCHIATRIC DISORDERS	RENAL AND UR DISORDEF		RESPIRATOR THORACIC A MEDIASTINA DISORDER	AND AL	
	INJURY, POISONING AND PROCEDURAL COMPLICATIONS			METABOLISM AND NUTRITION	IMMUNE SYSTEM DISORDEF	(Emp	pty)	
		MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	VASCULAR DISORDERS	DISORDERS	AND LYMPHATI	EAR AND PR LABYRINT H PU DISORD UN	CY, JERPERI	
			VASUULAR DISORDERS	EYE DISORDERS	CONGENI TAL,	ENDOCRI RE NE (DISORDE S)		

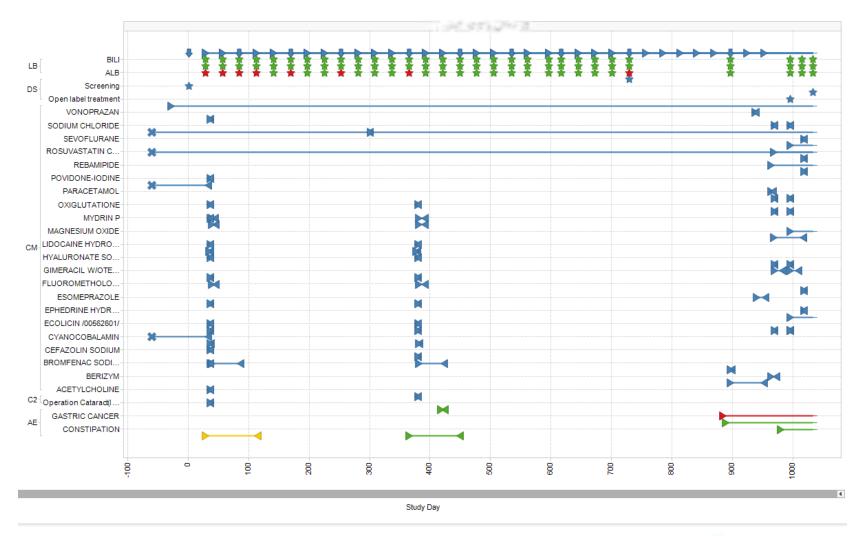


Science Visual data review

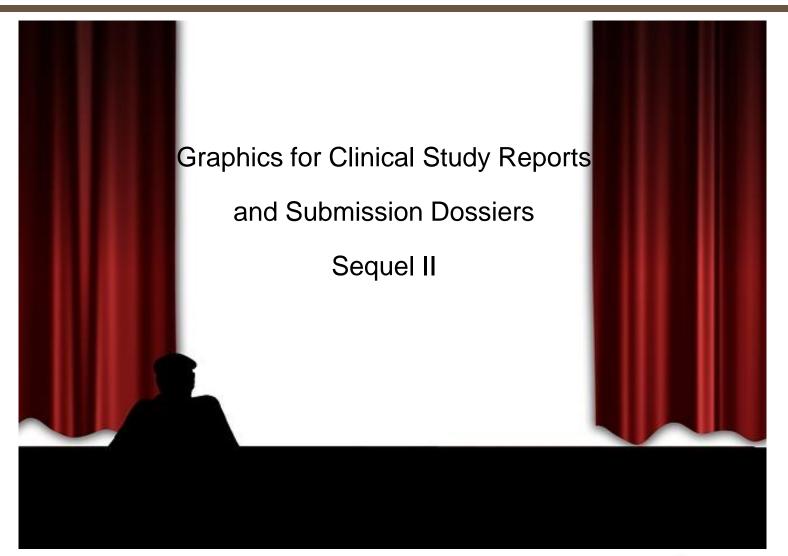
Use the heirarchy slided on the left to adjust the visualization. Rectangles are sized by the # of unique subjects reporting that event.

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E Lead to Stud	INFECTIONS AND INFEST	GASTRO	DINTESTINAL DI	SORDERS	S Unio	que Count of Subje	ects: 3																	
y: ue Count of Su chy: 		INFECTIO		BACTERIAL INFECTIOUS DISORDERS		INFECTIOUS		INFECTIOUS		DIVERTICULAR DISORDERS	GASTROINTE AL ULCERATI AND PERFORATI	STIN HEF ION AB ON	DOMINAL RNIAS AND OTHER DOMINAL WALL NDITIONS	GASTROINTE STINAL NEOPLASMS MALIGNANT AND UNSPECIFIED	HEPATOB NE	TIVE NEOPLASM S MALE MALIGNANT AND UNSP ERV REPR US ODUC		ROLOGICA RDERS NE	DIS AL PARK C CRAN L NERV DISOR	E HEADA CHES				
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	INJURY, POISONING AND PROCEDUR	DISORDERS RAL COMPLICATIONS		IRAL COMPLICATIONS		RAL COMPLICATIONS								CORONARY DISORD			IDIAC THMIAS	PSYCHIATRIC DISORDERS N		-		RDER	CON	JE DISOR DERS NEC
												DISORD	ERS	ARREIT	THMIAS	VASCULAR DI	SORDERS	RENAL AND U	JRIN	METABOLI	ISM AN E	YE DISO		
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			ES NEC	MUSCULOSKELET	AL AND CONNE	CTIVE TIS	SUE DIS	DISORDERS	THROMB	DISORDERS (EXCL CAL	UROL	IMMUNE S	BLOOD.	CONG										
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							E MUSC	EPIDERMAL AN		RESPIRATOR Y DISORDER	R AL			DISOR REPRO										
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Science Visual data review



Today's program Science Fiction





Science fiction The eCSR and eDossier

- Recent Novartis submission:
 - US Electronic dossier was about 200 GB of data

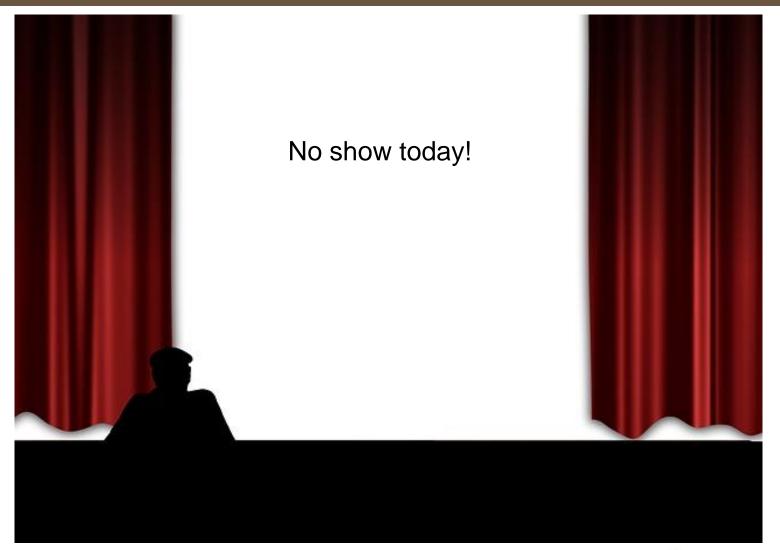




Science fiction A vision: the CSR of the future

- What will the eCSR and eDossier in the (near) future look like?
- Minimum: hyperlinked PDF
- Vision: hyperlinked, dynamic web format
 - The graphical CSR?
- Interactive Report Example

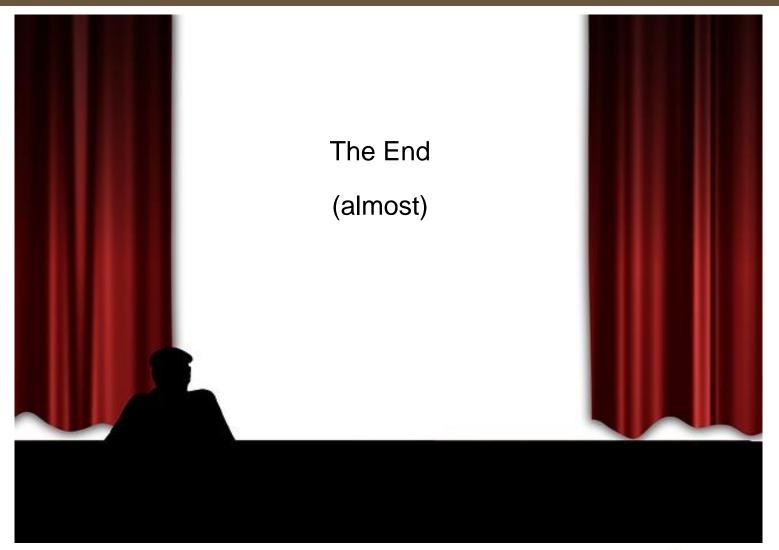
Today's program Advertisement





- But what you might have seen:
- Graphics for commercial material, sometimes publications
 - Paper (brochure), internet or sceenshow, TV
 - Fancy infographics
 - Static, animated, interactive
 - Video?

Today's program



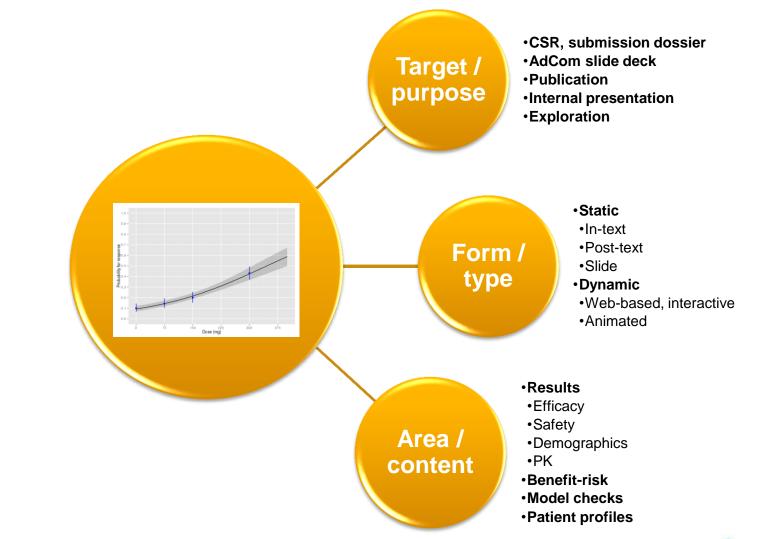


Classification



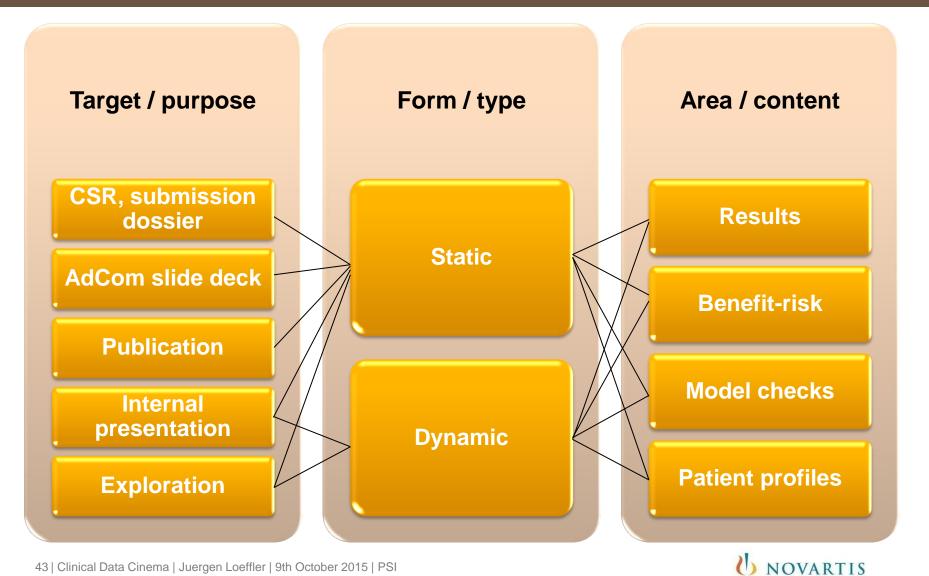


Classification



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Classification



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Structured approach

- How do we best design an individual graph (be it static or dynamic)?
- Follow graphical principles
- A structured approach has recently been published:
 - Duke SP, Bancken F, Crowe B, Soukup M, Botsis T, Forshee R. (2015) Seeing is believing: Good graphic design principles for medical research. Statist. Med., 34: 3040-3059.
 - <u>http://www.ctspedia.org/do/view/CTSpedia/SelectRightGraph</u>



Summary

- Data visualization is used in many areas of clinical development
- The type of visualization depends on the target and the content (but also the audience)
- Most importantly, visualizations can be static or dynamic
- Restrictions and limitations mainly imposed by target
- The future will hopefully be more dynamic
- By the way:
 - All data shown are dummy data (unless noted otherwise)



Acknowledgements

- David Carr
 - For programming the BR plot alternative 1
- Oumaima Fdil, Richard Nixon & Dieter Haering
 - For programming the shiny app creating BR plot alternative 2
- Fabrice Bancken, David Carr & Baldur Magnusson
 - For various discussions and ideas
- Achim Guettner
 - For the photographs of the "submission package"

