The Clinical Data Cinema

The many roles of data visualization in clinical development

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Motivation

The „book“

- Data tables: what does it all mean?

Subject	Visit	AVAL	ID	TRT01PN	sex	age	BASE	ratio	pchg	chg
1001	0	10.505479	1	1	2	61	10.505479	1.0000000	0.000000	0.0000000
1001	3	19.016524	1	1	2	61	10.505479	1.8101529	81.015286	8.5110443
1001	778	9.443375	1	1	2	6				
1001	1	19.902487	1	1	2	6				
1001	2	19.471850	1	1	2	6				
1001	6	19.607682	1	1	2	6				
1002	1	21.048313	2	1	2	6				
1002	778	9.501440	2	1	2	6				
1002	0									
1002	3									
1002	6									
1002	2									
1003	778									
1003	6									

Visit	AVAL	ID	TRT01PN	sex	age	BASE	PASI100	PASI90	PASI75	PASI50	r
0	20.28729856	1	1	1	25	20.287299	N	N	N	N	
16	5.22783246	1	1	1	25	20.287299	N	N	N	Y	
8	-1.42217679	1	1	1	25	20.287299	Y	Y	Y	Y	-
1	19.73067642	1	1	1	25	20.287299	N	N	N	N	
3	-1.62338986	1	1	1	25	20.287299	Y	Y	Y	Y	-
4	-0.62258949	1	1	1	25	20.287299	Y	Y	Y	Y	-
12	2.34085618	1	1	1	25	20.287299	N	N	Y	Y	
2	10.86523212	1	1	1	25	20.287299	N	N	N	N	
1	19.36711571	2	1	2	53	25.967181	N	N	N	N	
8	0.79213767	2	1	2	53	25.967181	N	Y	Y	Y	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	

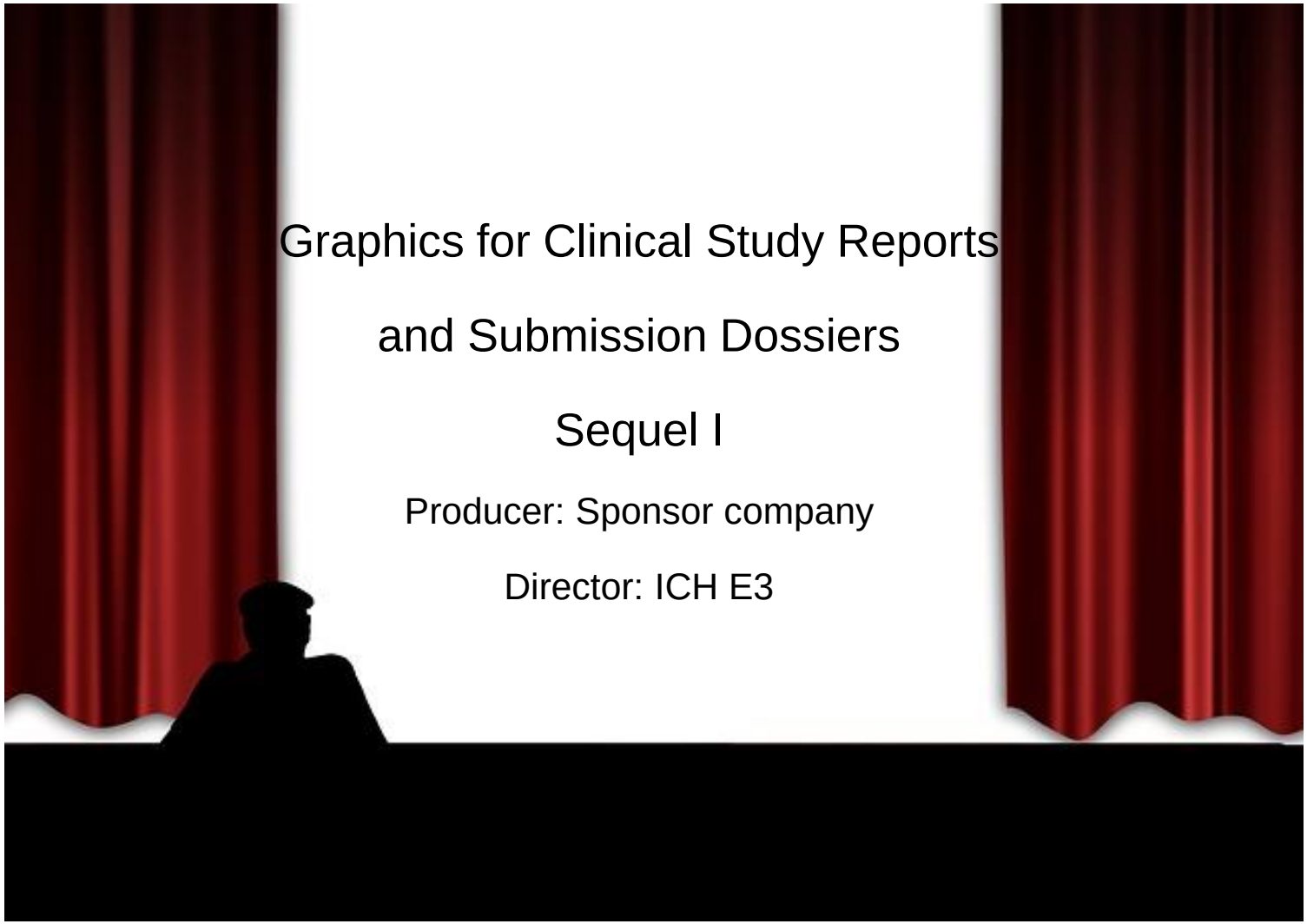
study	subgroup	n1	n2	parms										
X2301	>= 65 years	26	25	Adverse event										
X2301	< 65 years	89	85	Adverse event										
X2301	>= 65 years	26	25	Complete respo										
X2301	< 65 years	89	85	Complete respo										
X2301	>= 65 years	26	25	Partial response										
X2301	< 65 years	89	85	Partial response	0.55	0.41	48	32	NA	3.523692	174	32/ 85 (37.6%)	48/ 89 (53.9%)	1.9 (1.05, 3.52)	0.48
X2302	>= 65 years	58	57	Adverse event	0.20	0.10	18	5	NA	12.751994	115	5/ 57 (8.8%)	18/ 58 (31.0%)	4.4 (1.49, 12.75)	0.18
X2302	< 65 years	121	123	Adverse event	0.15	0.05	19	8	NA	6.158143	244	8/123 (6.5%)	19/121 (15.7%)	2.6 (1.09, 6.16)	0.12
X2302	>= 65 years	58	57	Complete response	0.36	0.25	25	13	NA	5.629105	115	13/ 57 (22.8%)	25/ 58 (43.1%)	2.5 (1.12, 5.63)	0.35
X2302	< 65 years	121	123	Complete response	0.40	0.25	37	35	NA	1.918399	244	35/123 (28.5%)	37/121 (30.6%)	1.1 (0.64, 1.92)	0.36
X2302	>= 65 years	58	57	Partial response	0.50	0.38	34	23	NA	4.348937	115	23/ 57 (40.4%)	34/ 58 (58.6%)	2.1 (0.98, 4.35)	0.53
X2302	< 65 years	121	123	Partial response	0.55	0.41	61	50	NA	2.454996	244	50/123 (40.7%)	61/121 (50.4%)	1.5 (0.89, 2.45)	0.49
X2303	>= 65 years	20	22	Adverse event	0.20	0.10	9	2	25	25.000000	42	2/ 22 (9.1%)	9/ 20 (45.0%)	6.8 (1.24, 37.07)	0.27
X2303	< 65 years	45	42	Adverse event	0.15	0.05	4	0	25	25.000000	87	0/ 42 (0.0%)	4/ 45 (8.9%)	9.2 (0.00, Inf)	0.08
X2303	>= 65 years	20	22	Complete response	0.36	0.25	7	7	NA	4.146928	42	7/ 22 (31.8%)	7/ 20 (35.0%)	1.1 (0.32, 4.15)	0.52

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



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Documentary

How CSRs and dossiers look like

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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?

Documentary

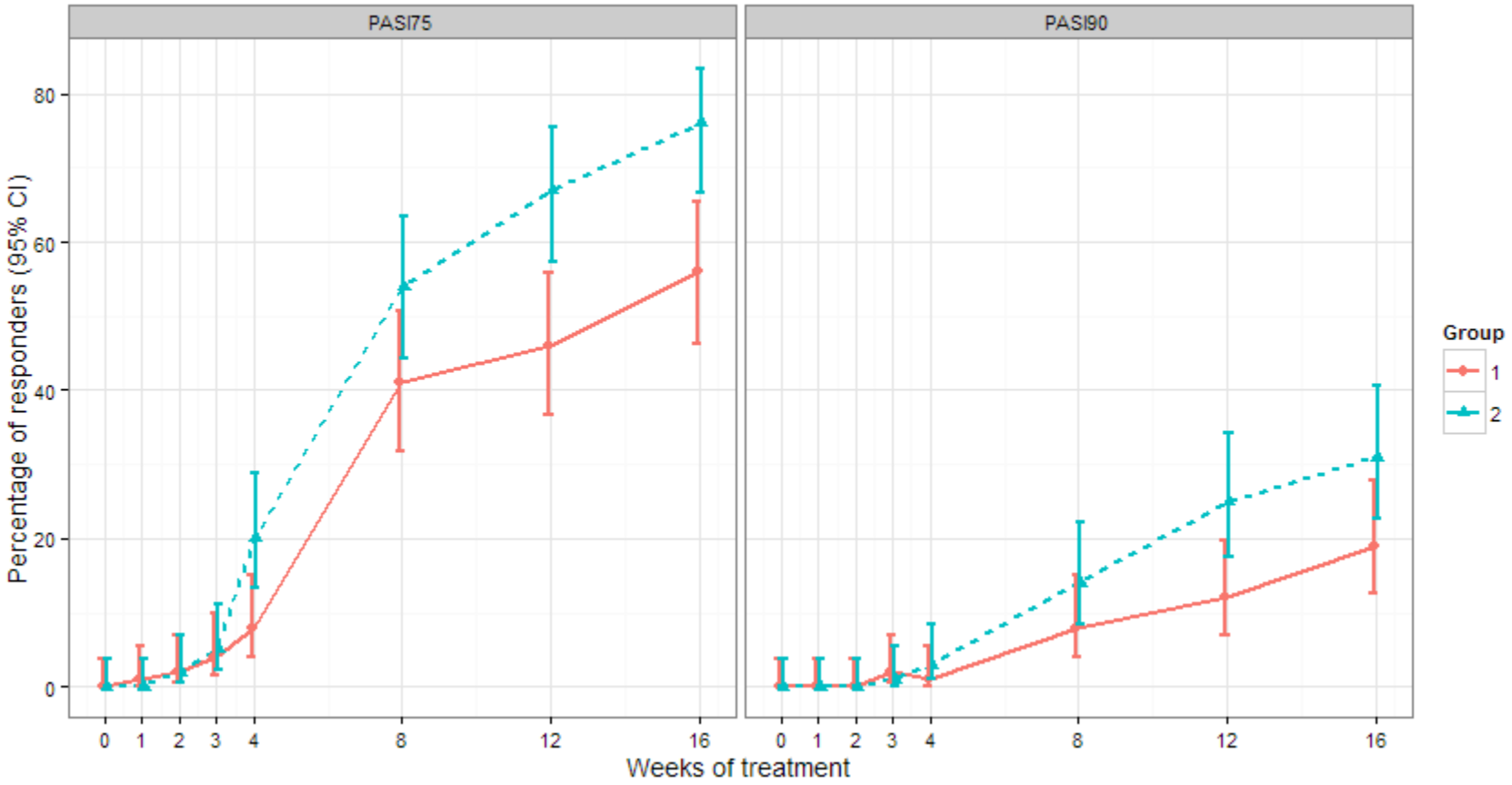
How figures (graphs) in CSRs and dossiers look like

- Post-text and in-text figures

Documentary

How figures (graphs) in CSRs and dossiers look like

- Post-text figure 1



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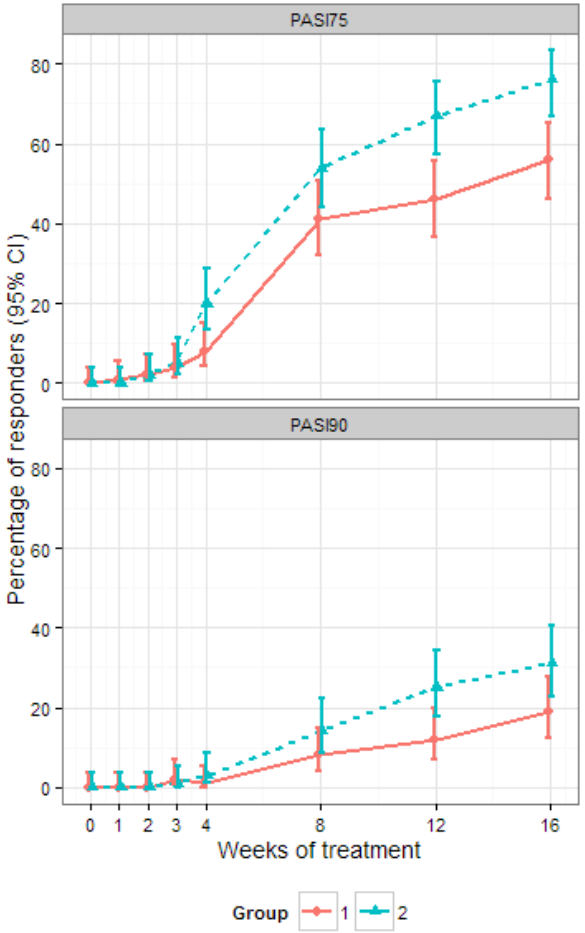
Documentary

How figures (graphs) in CSRs and dossiers look like

- In-text figure 1



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

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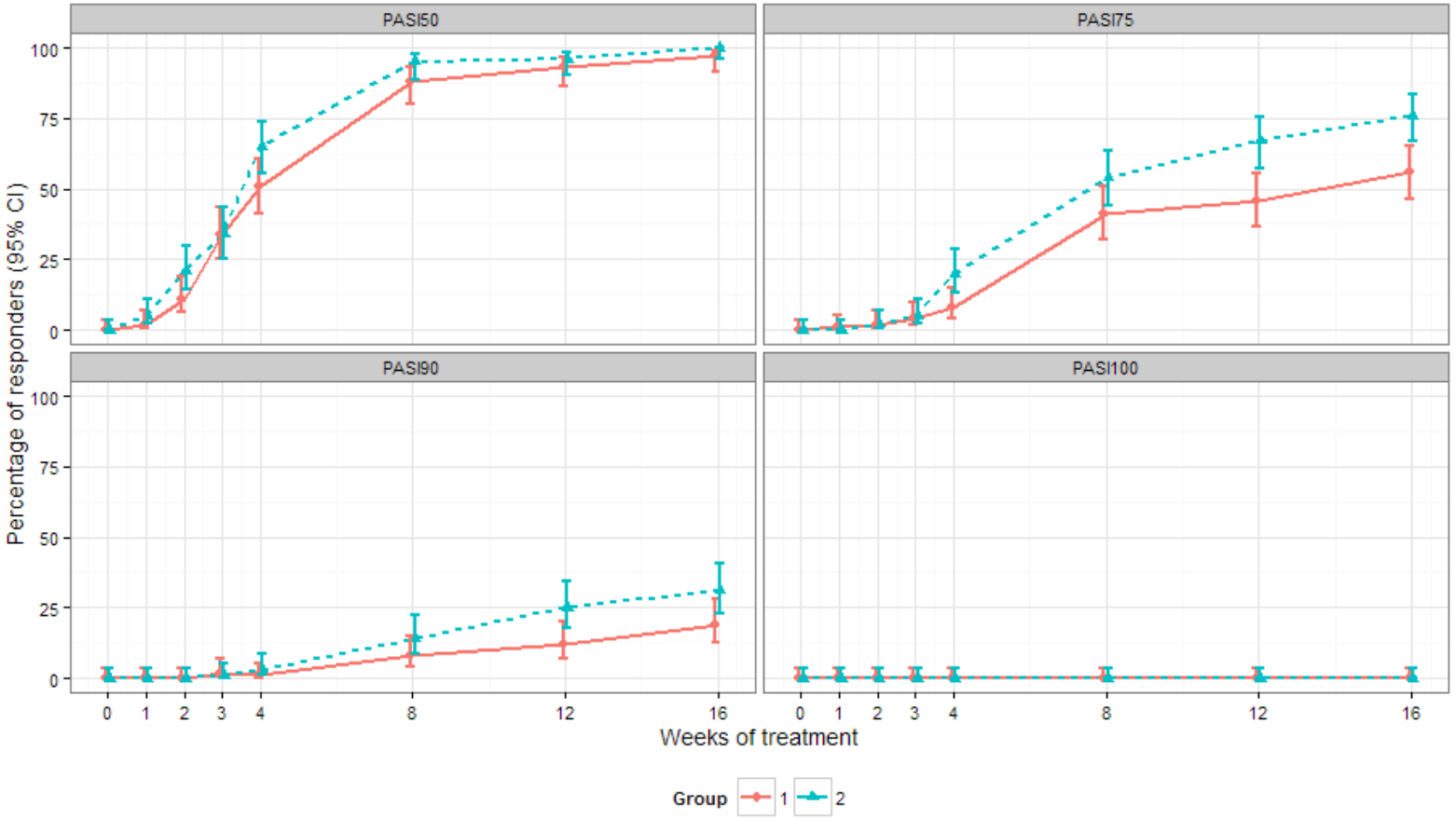
Documentary

How figures (graphs) in CSRs and dossiers look like

- Post-text figure 2



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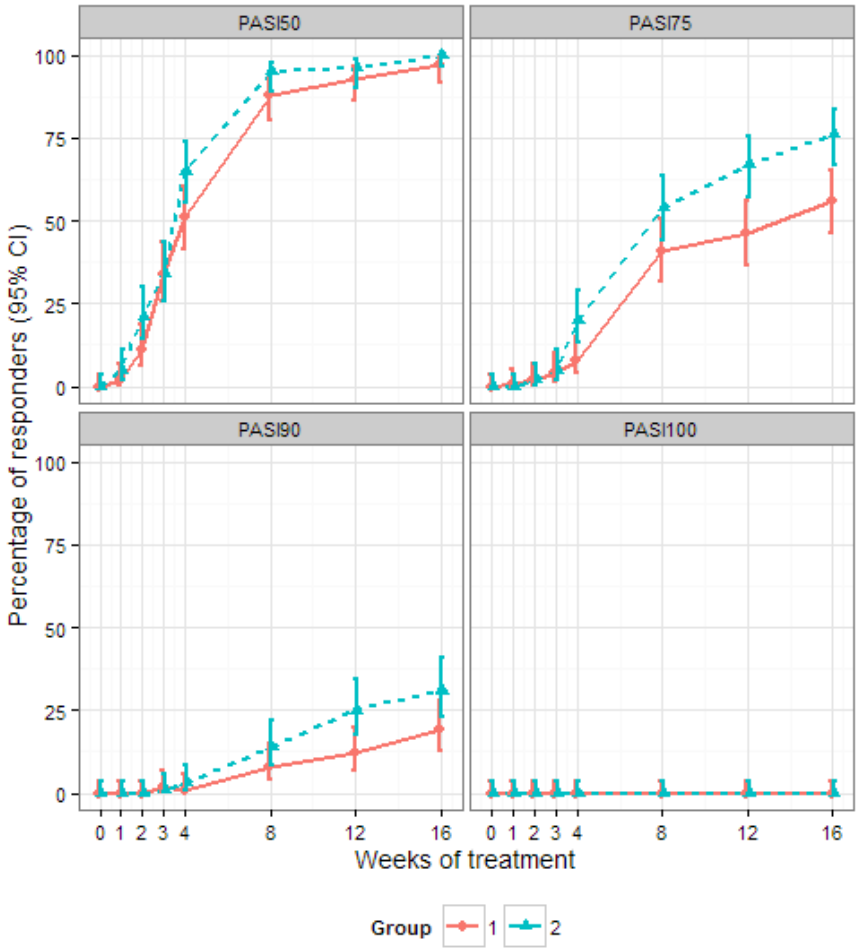
Documentary

How figures (graphs) in CSRs and dossiers look like

- In-text figure 2



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

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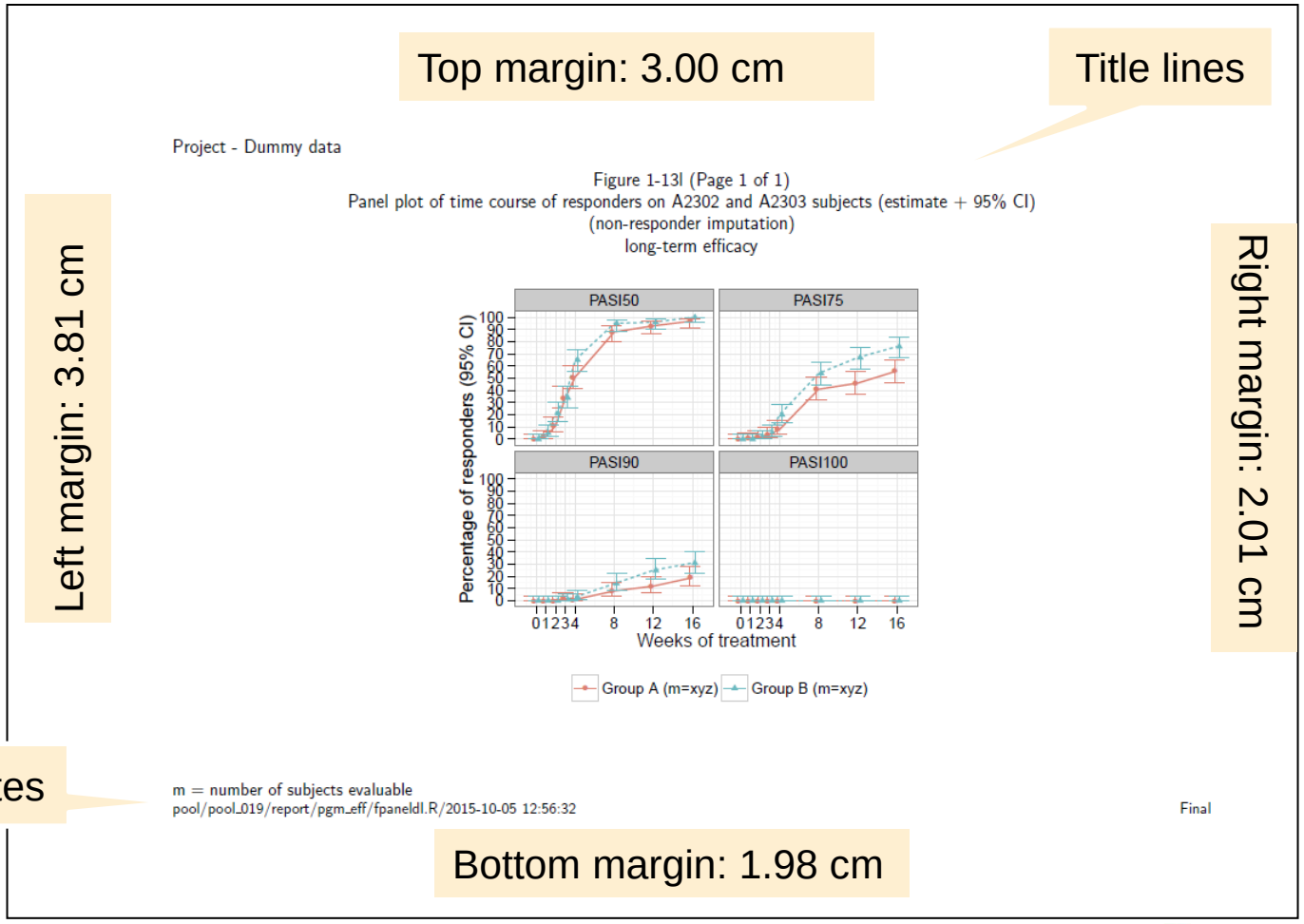
Documentary

Constraints for figures (graphs) in CSRs and dossiers

- Post-text



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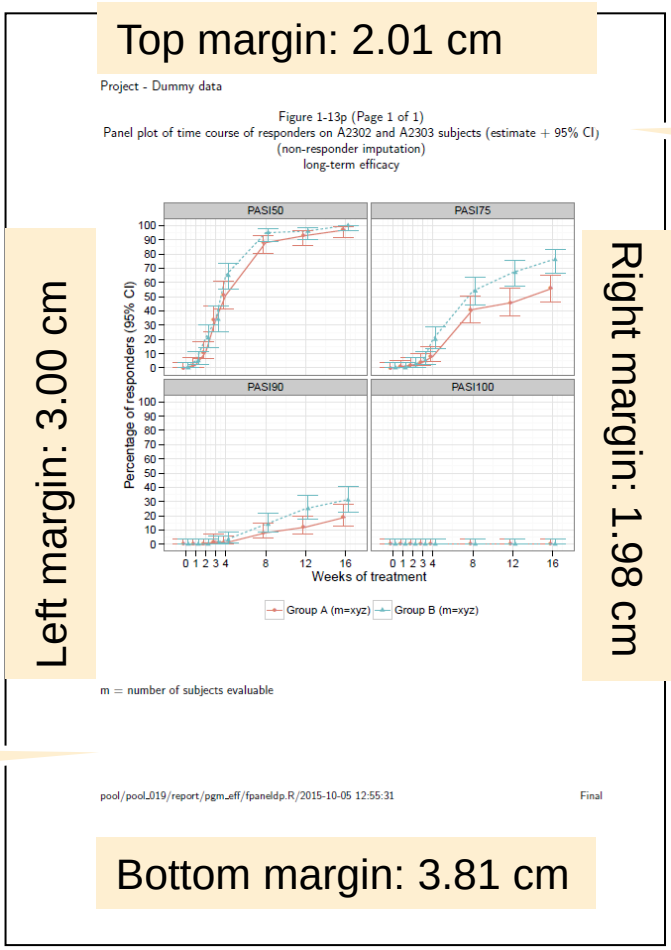
Documentary

Constraints for figures (graphs) in CSRs and dossiers

- In-text



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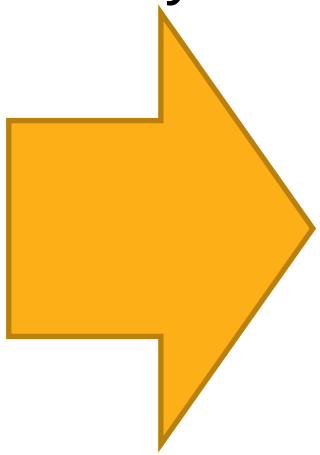
Documentary

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



Programmed

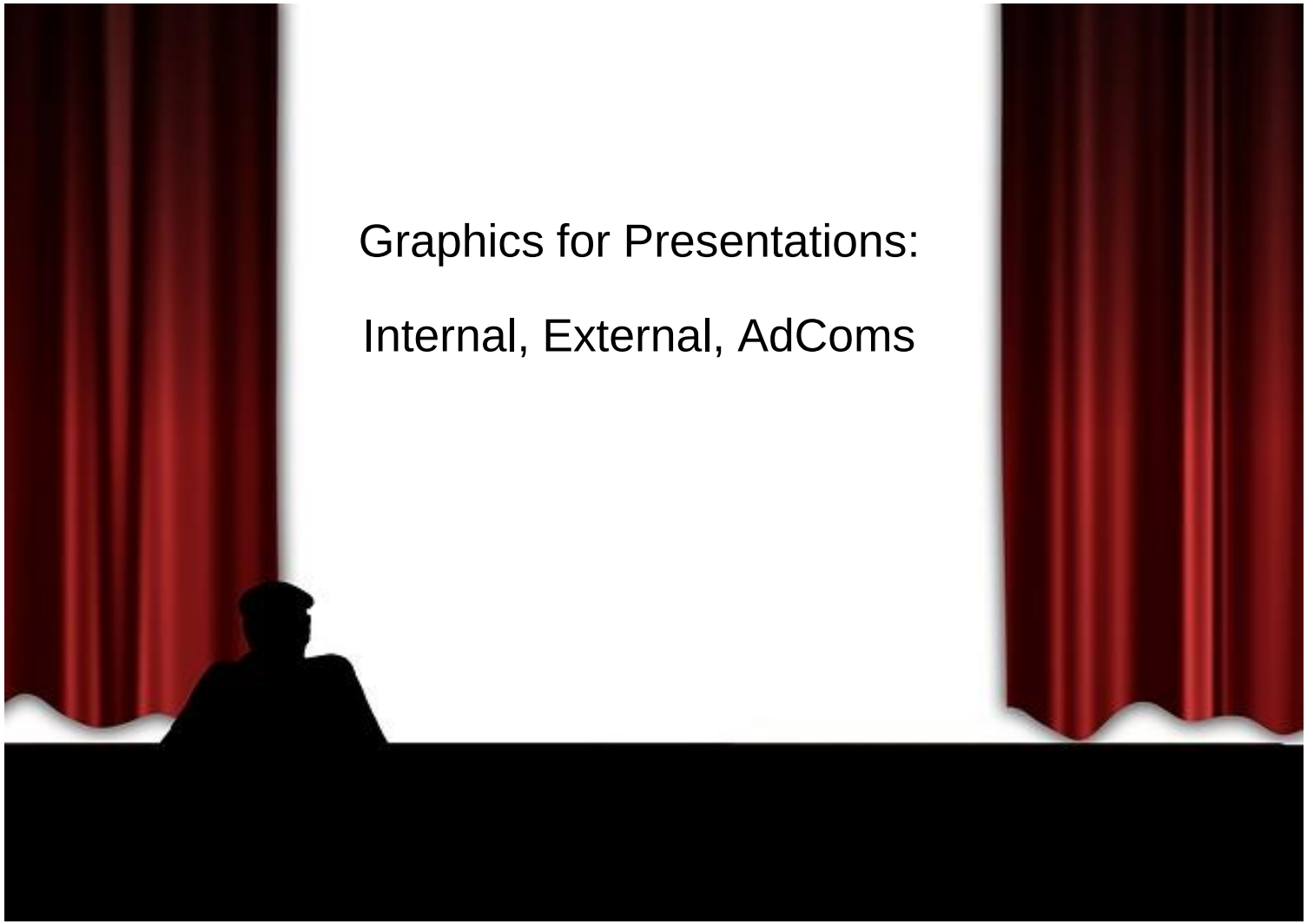
Documentary

Some reflections on in-text figures

- 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)
- Is there a better way?

Today‘s program

Drama / Comedy



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Drama, Comedy

Internal or external slide deck

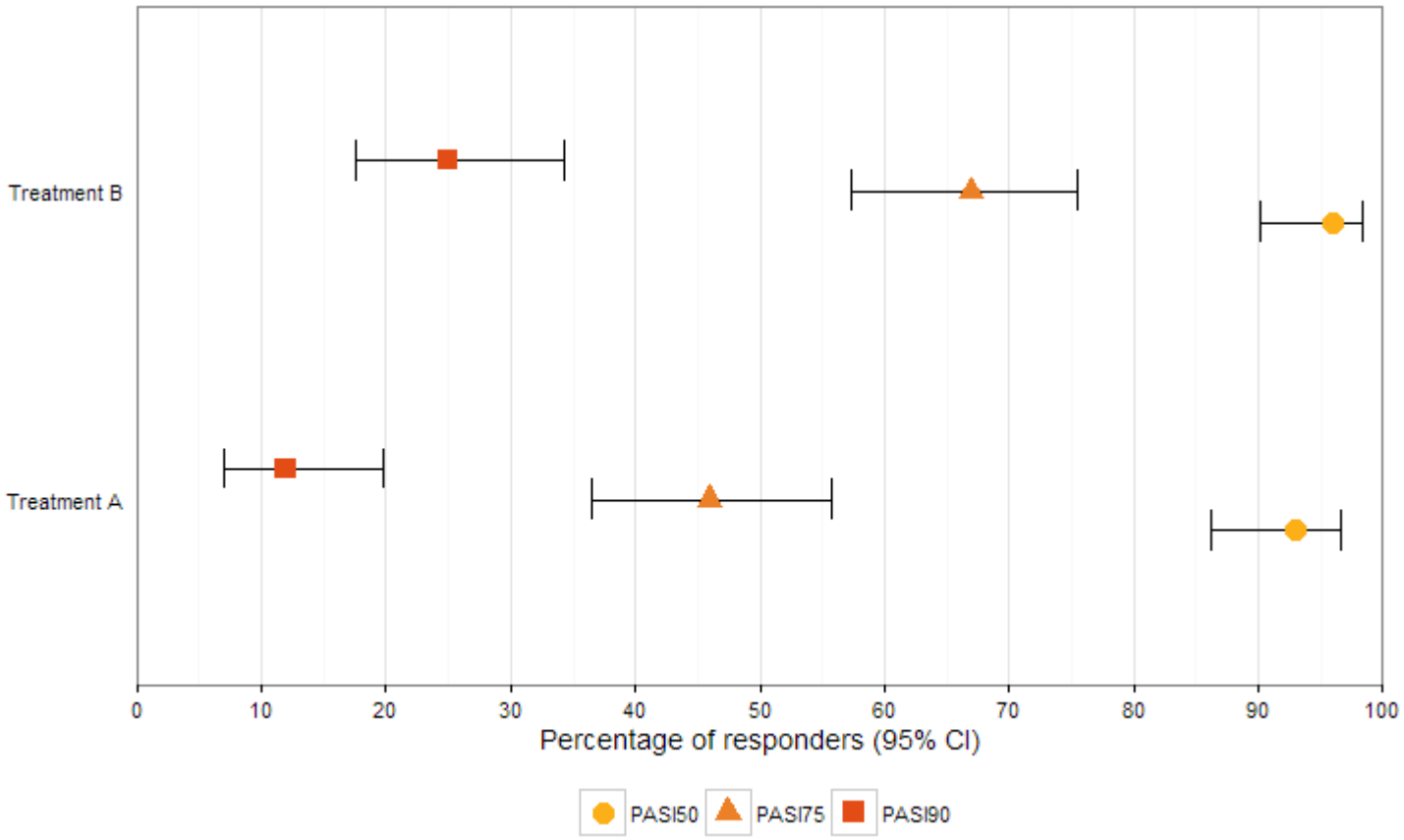
- Static, possibly animations
- Orientation: landscape
- Company colours

R	G	B	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)



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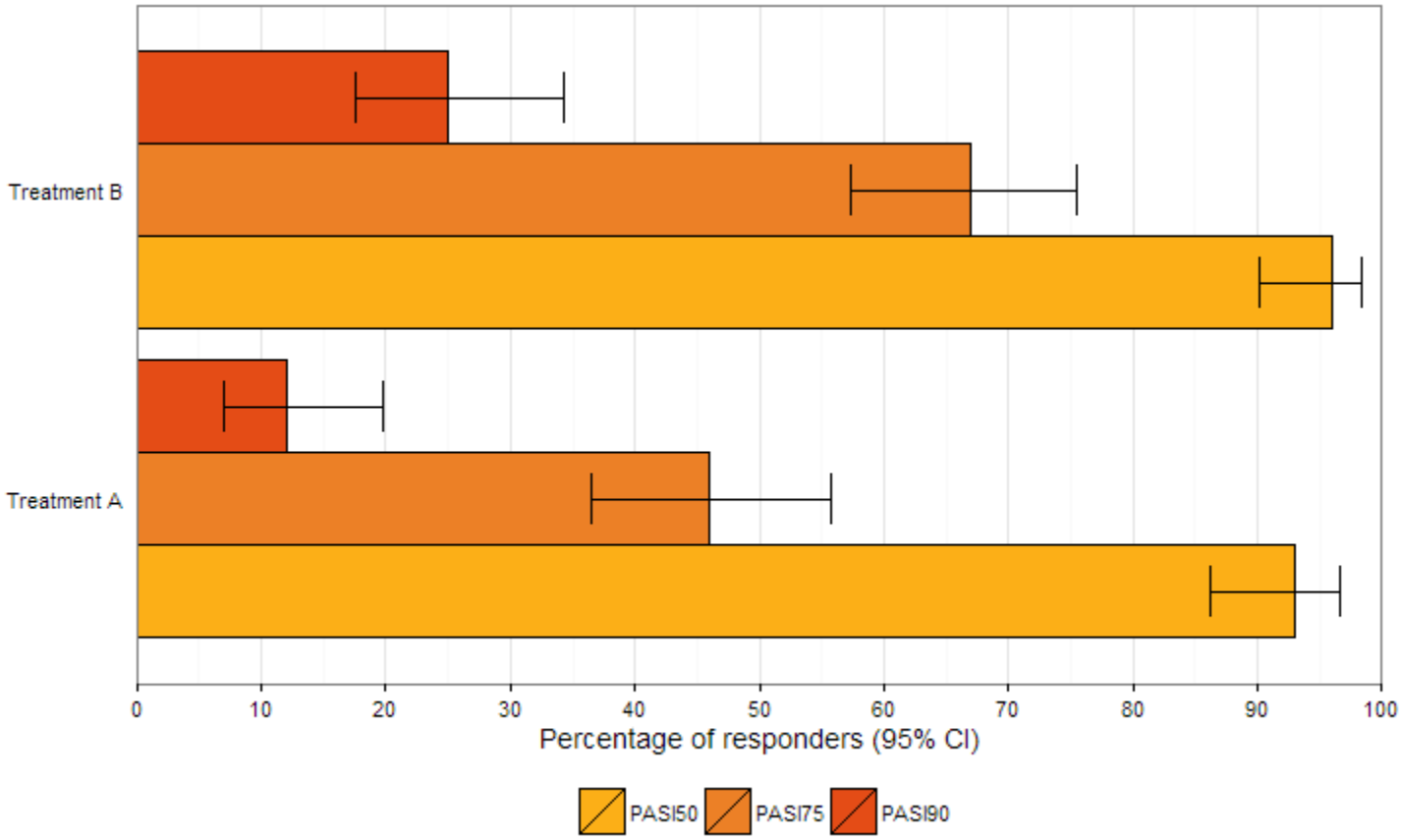
Drama, Comedy

Customers‘ preference (= simplicity or custom?)



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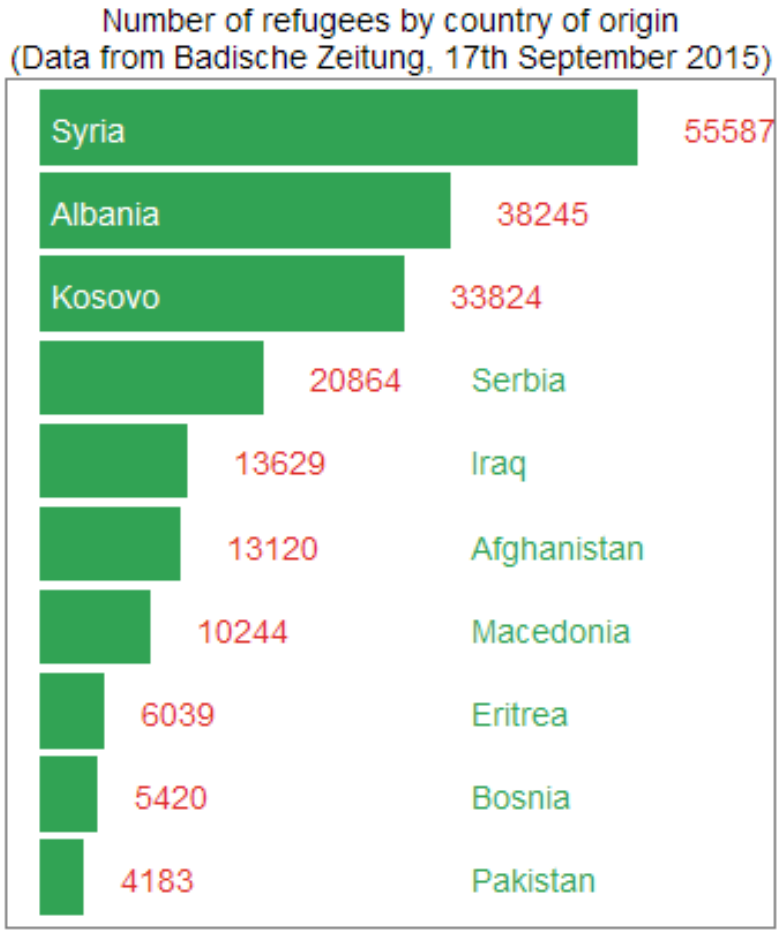
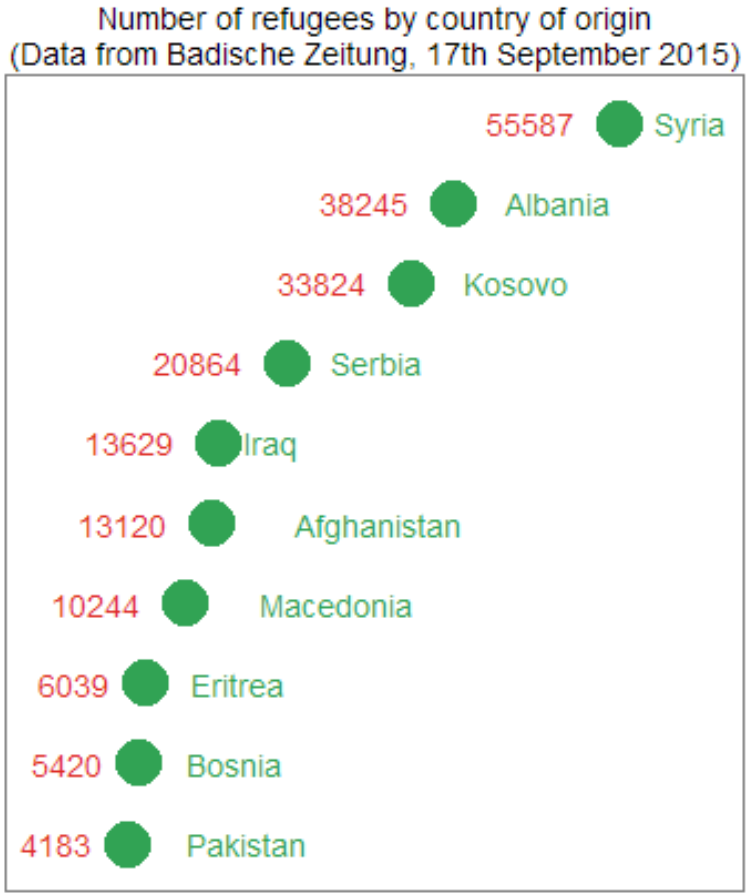
Drama, Comedy

My wife‘s preference?





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Drama, Comedy

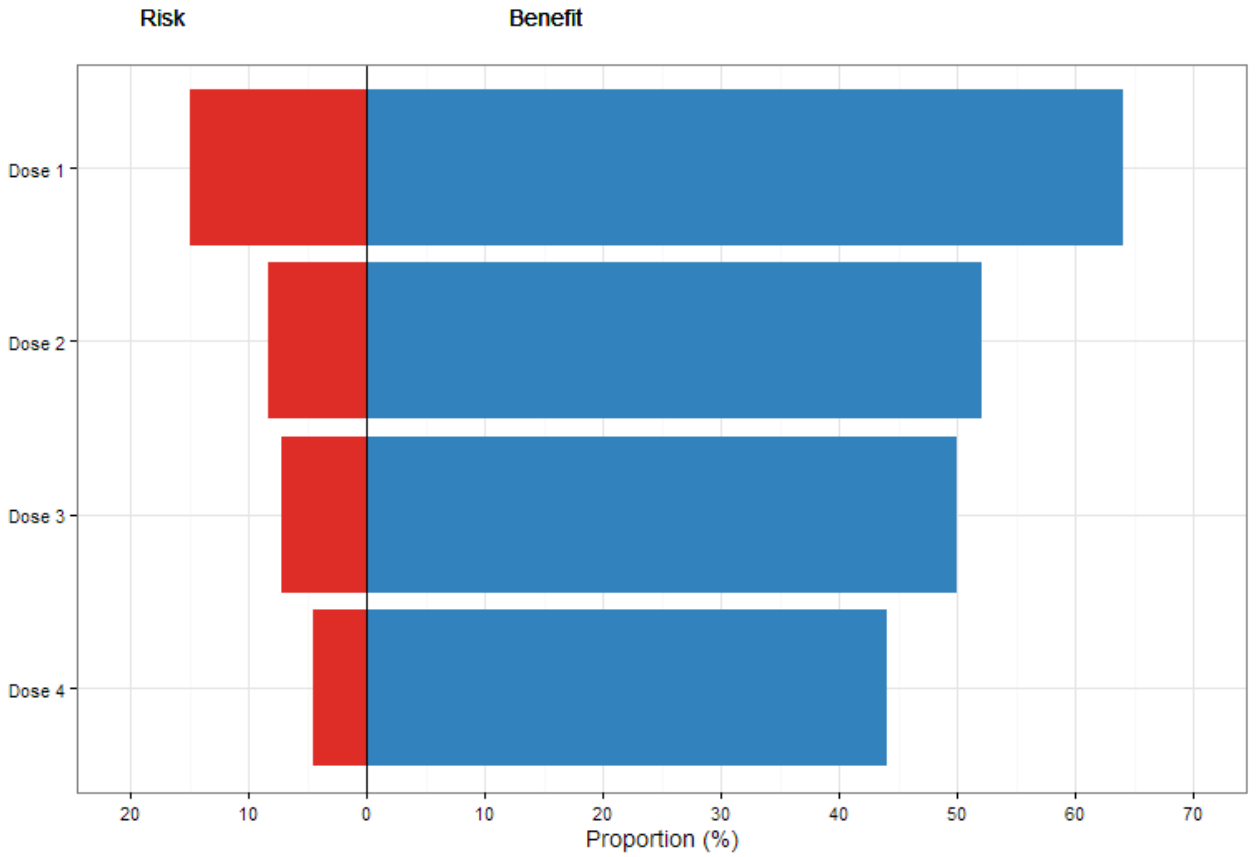
AdCom, HA presentation

- 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



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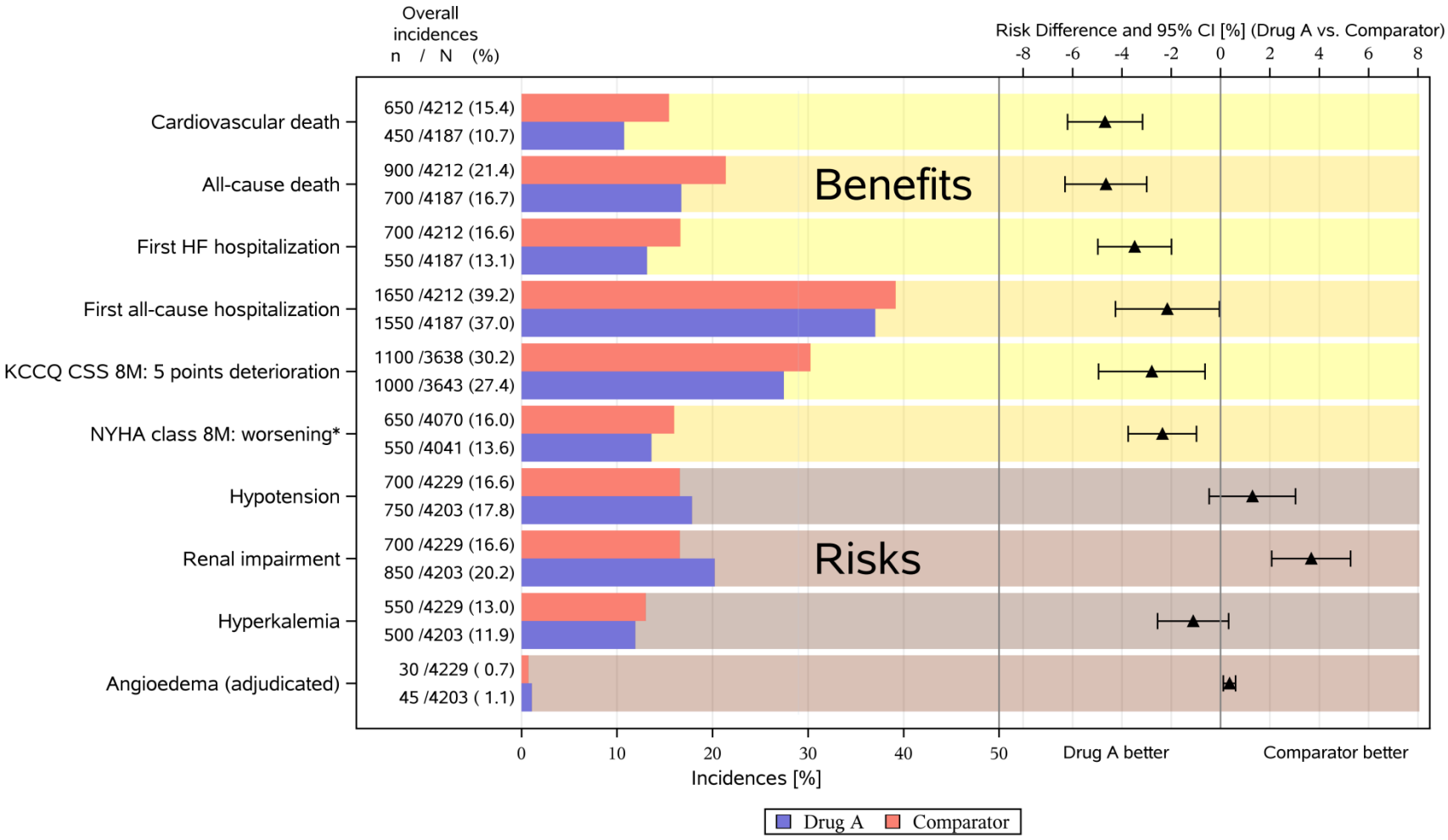
Drama, Comedy

Benefit-risk: more sophisticated



* death also counted as a worsening

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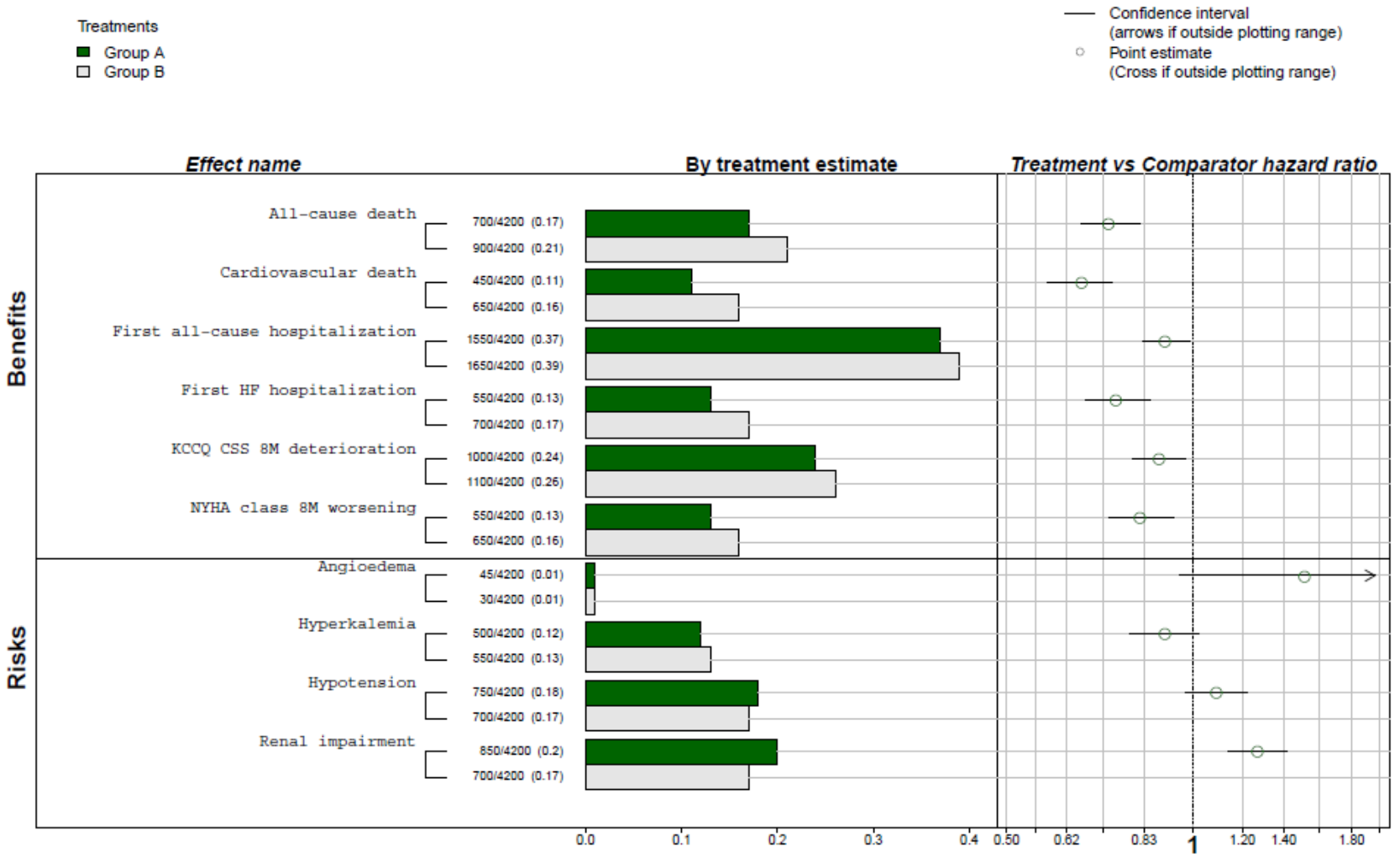
Drama, Comedy

Benefit-risk: more sophisticated (alternative version)



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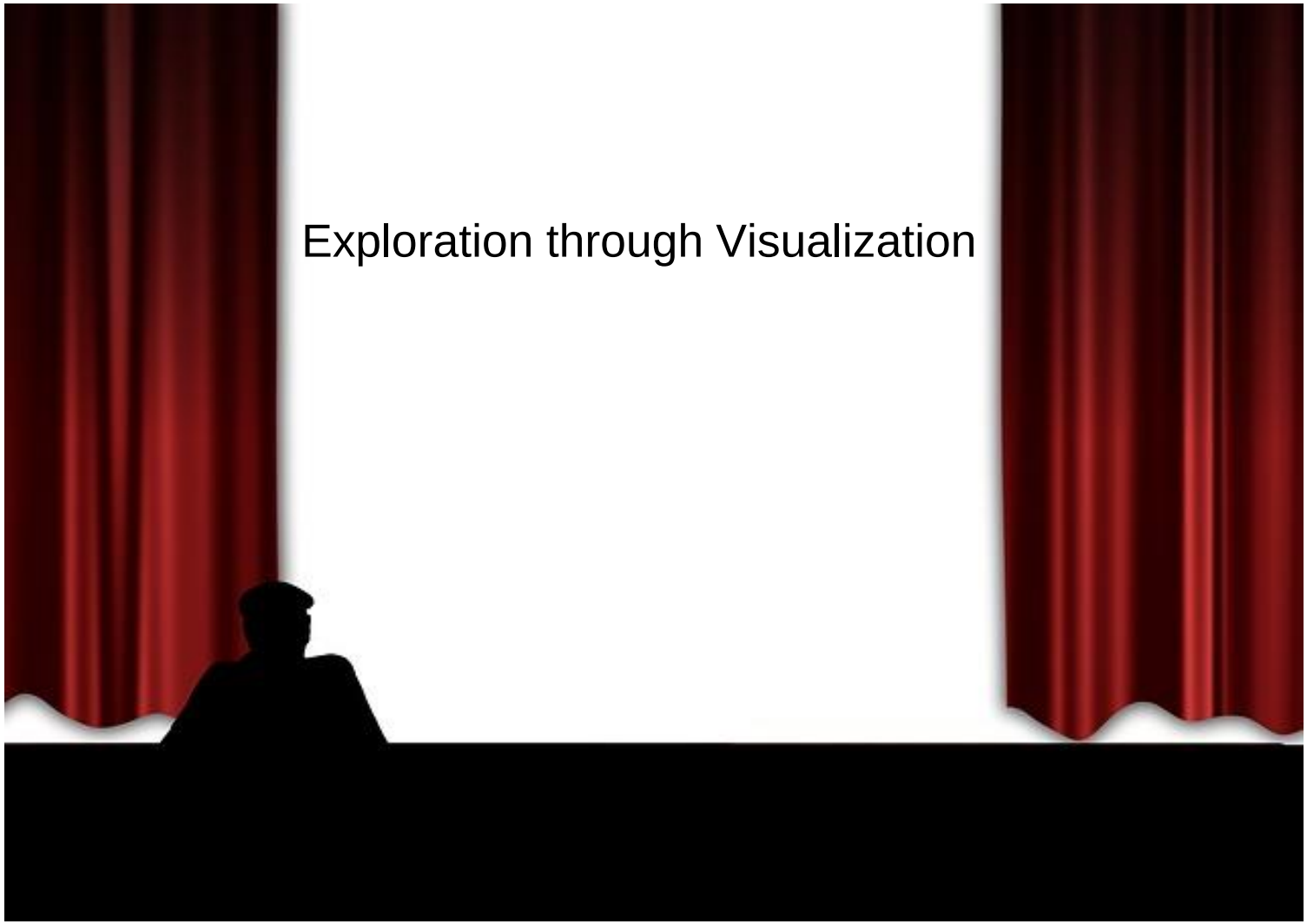
Today‘s program

Science



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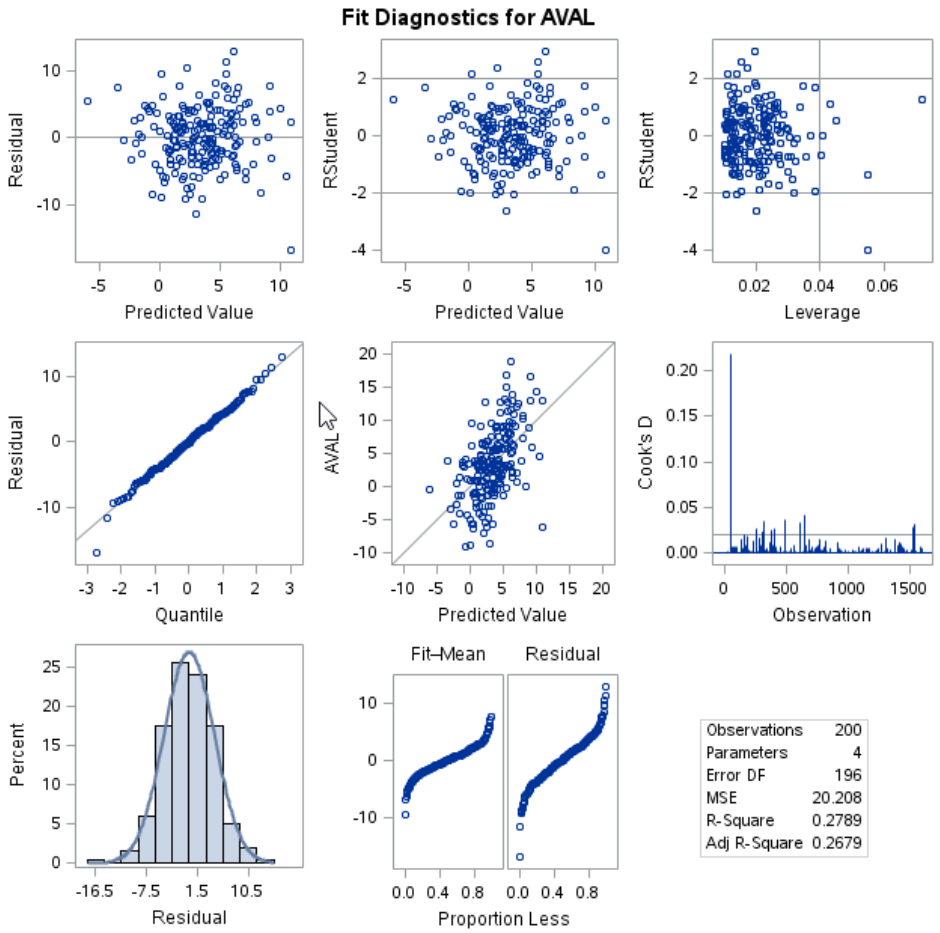
Science

Diagnostic plots

- E.g., ANCOVA



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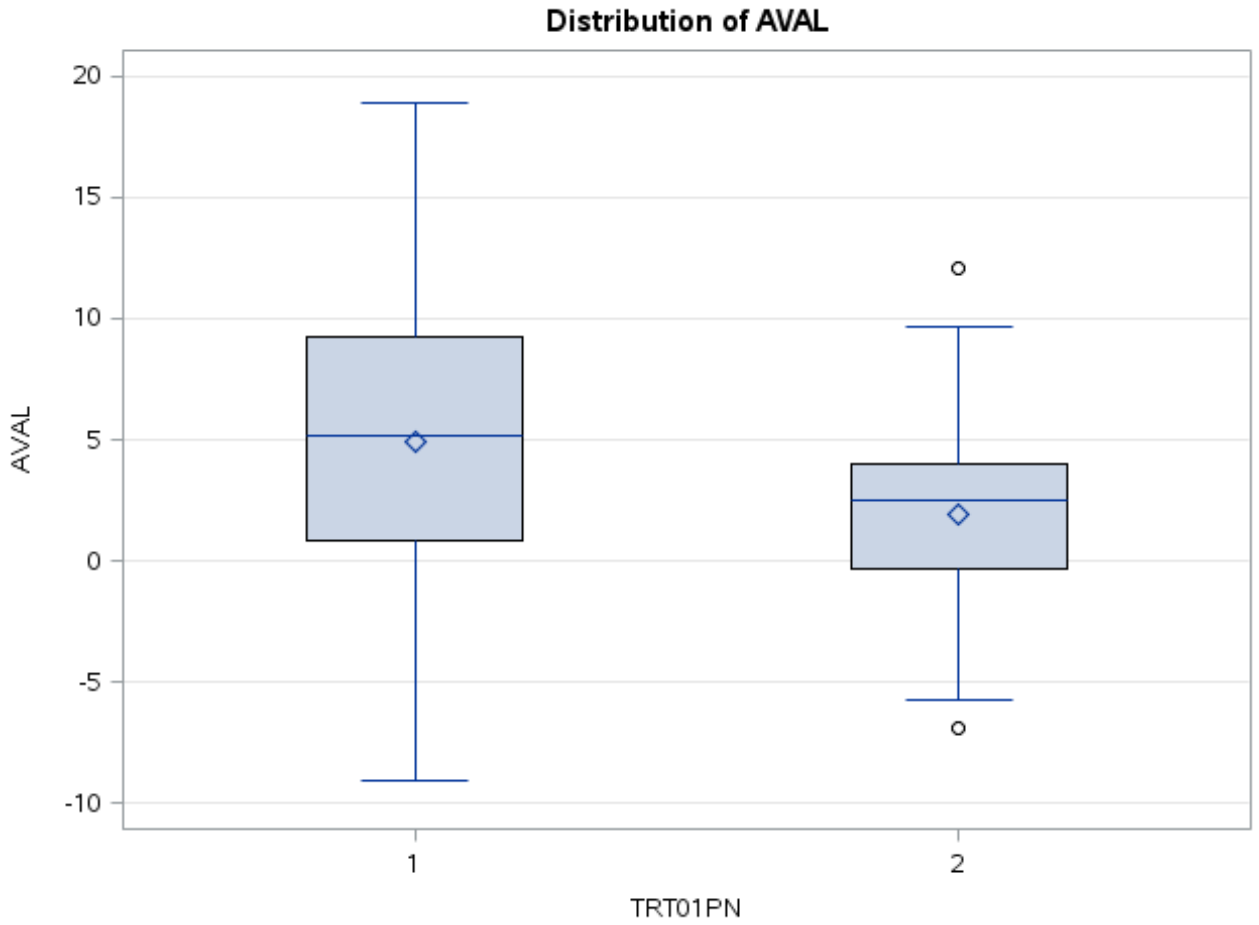
Science

Diagnostic plots

- E.g., ANCOVA



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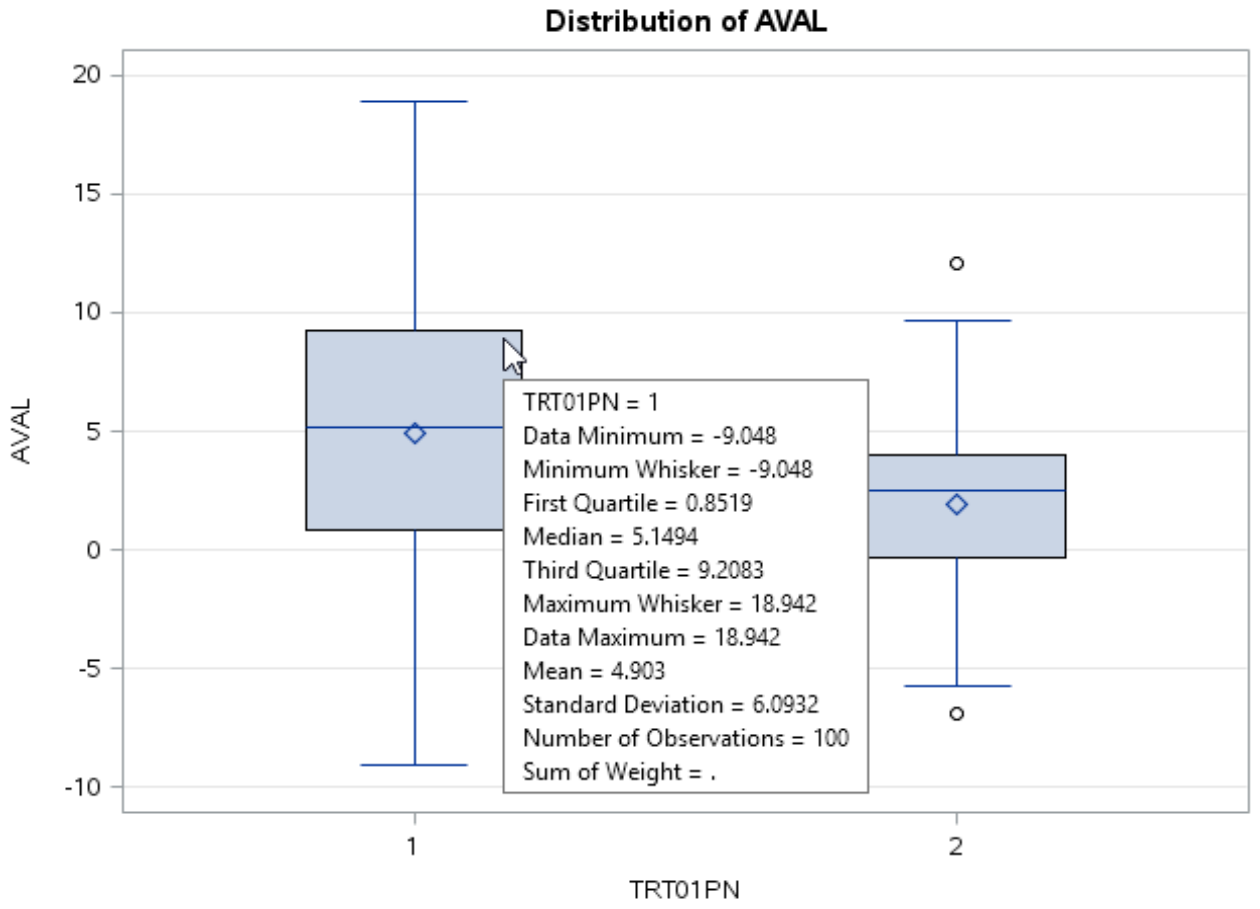
Science

Diagnostic plots

- E.g., ANCOVA



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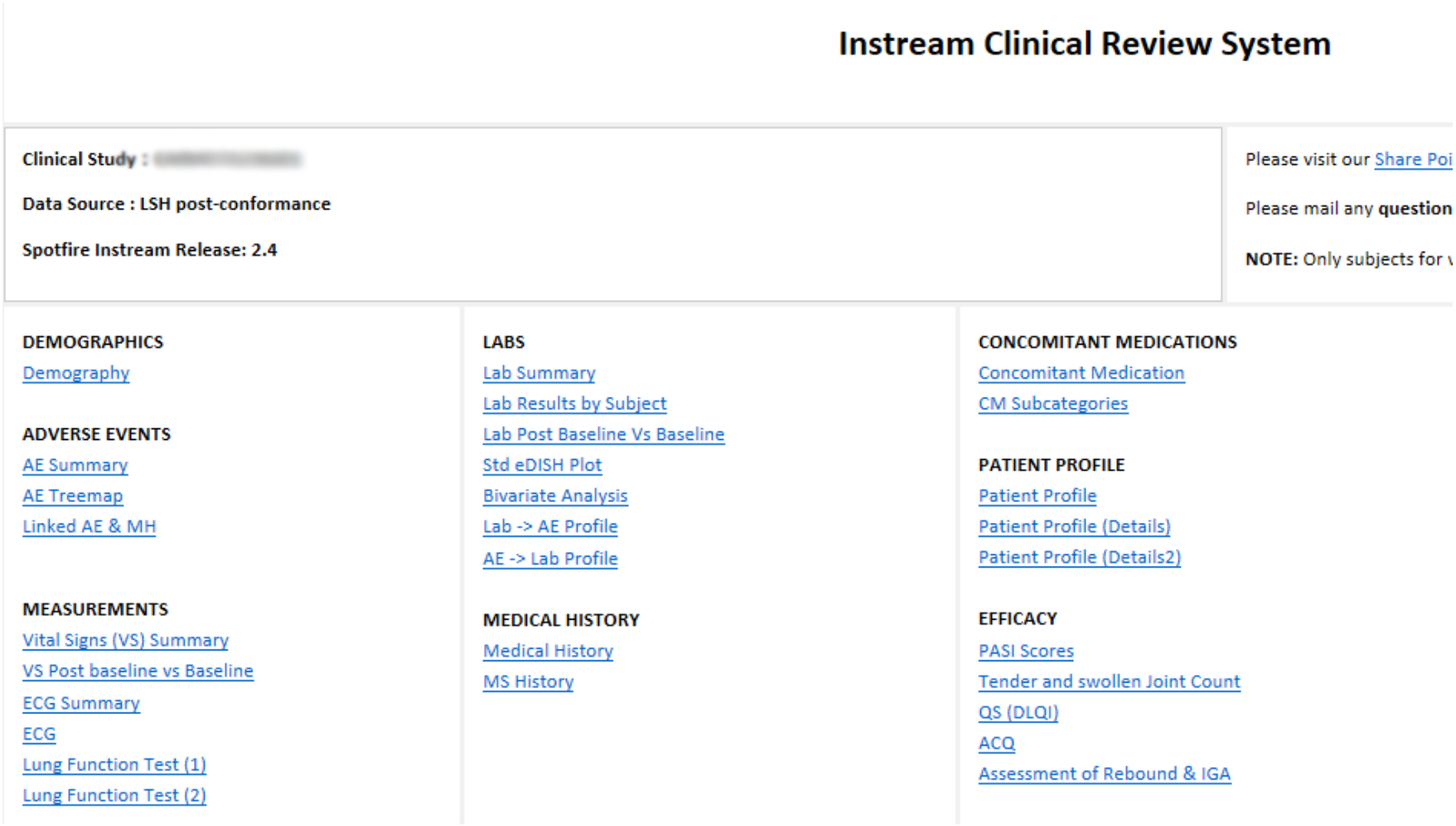
Science

Visual exploration

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

Science

Visual data review



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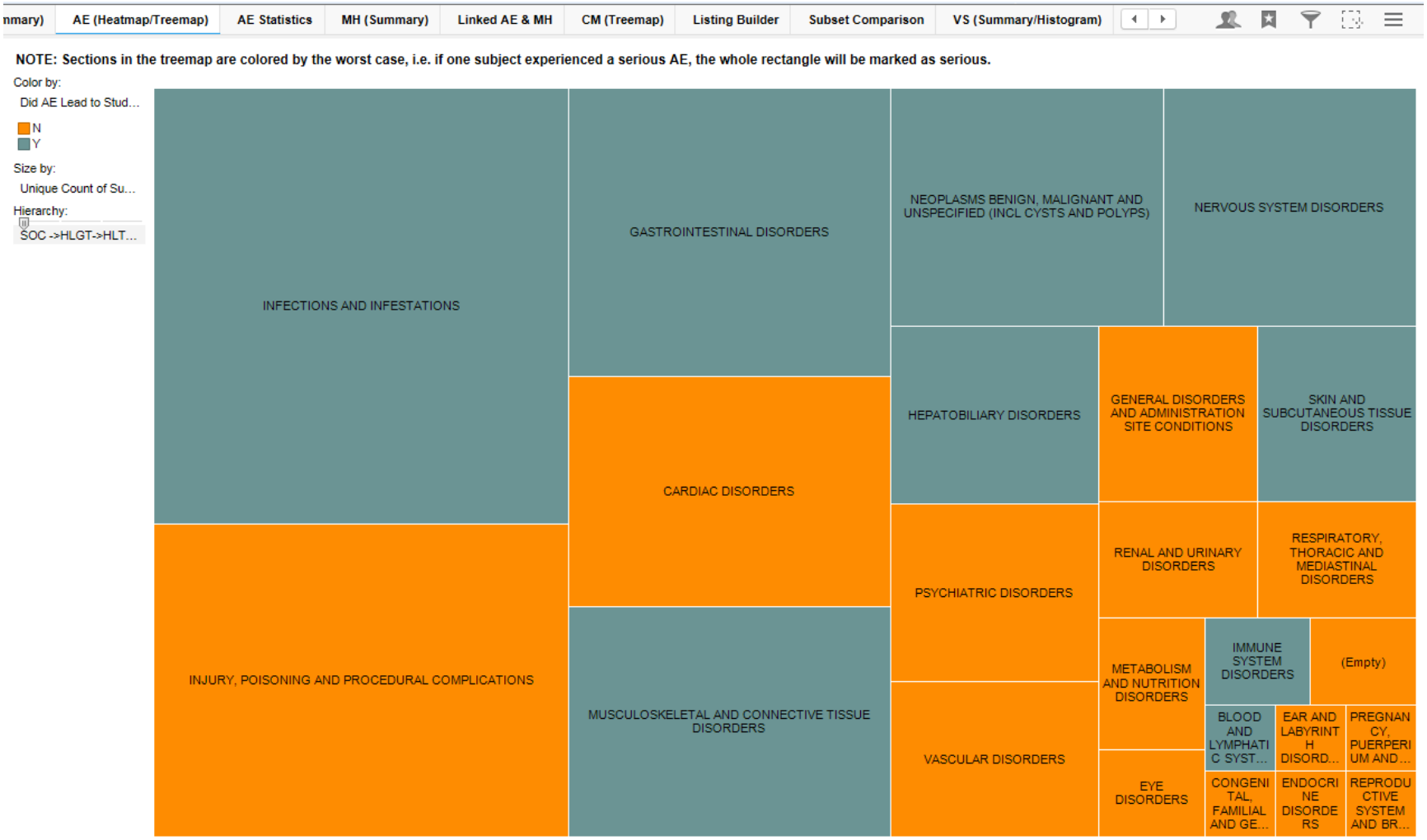
Science

Visual data review



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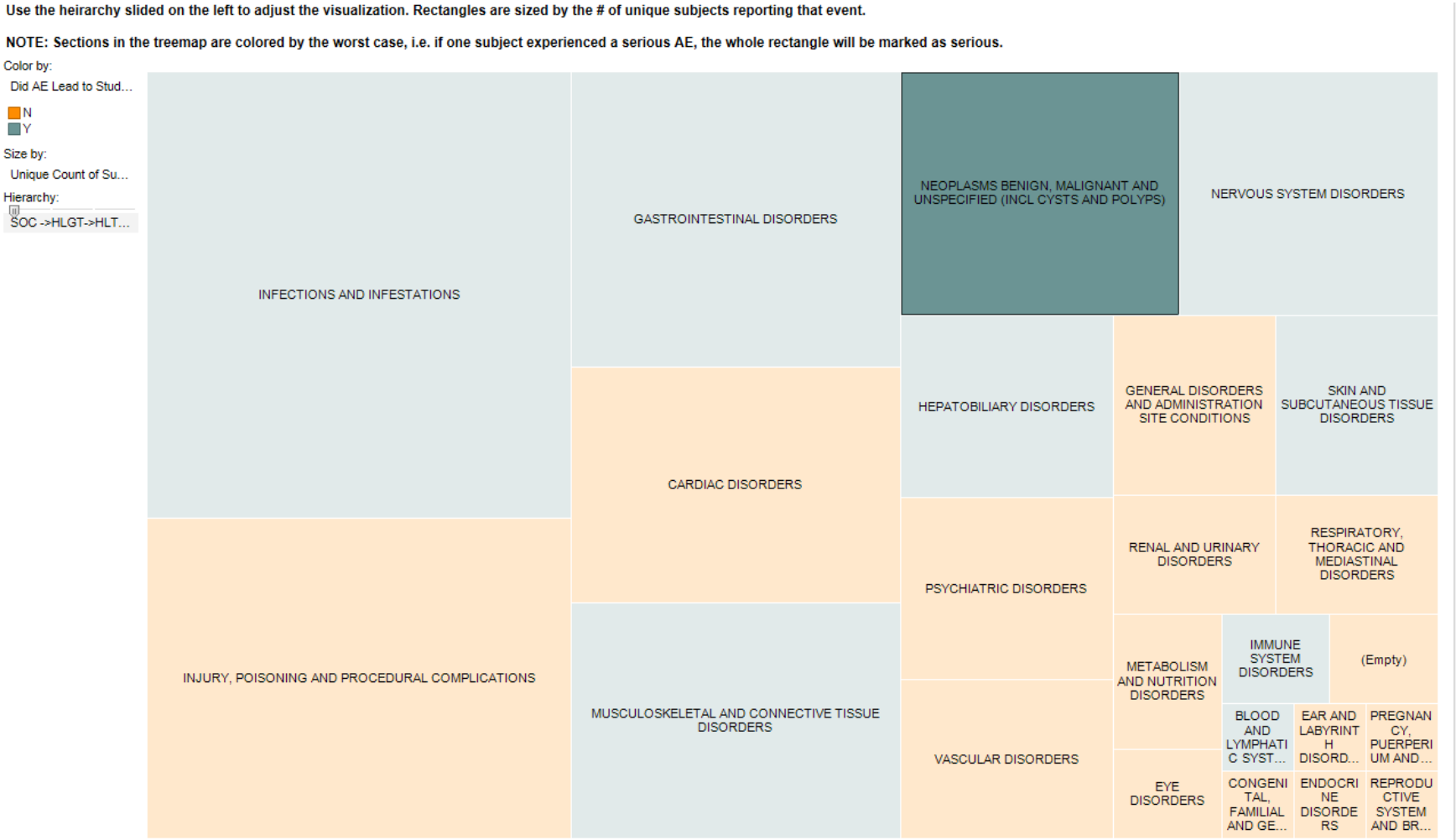
Science

Visual data review



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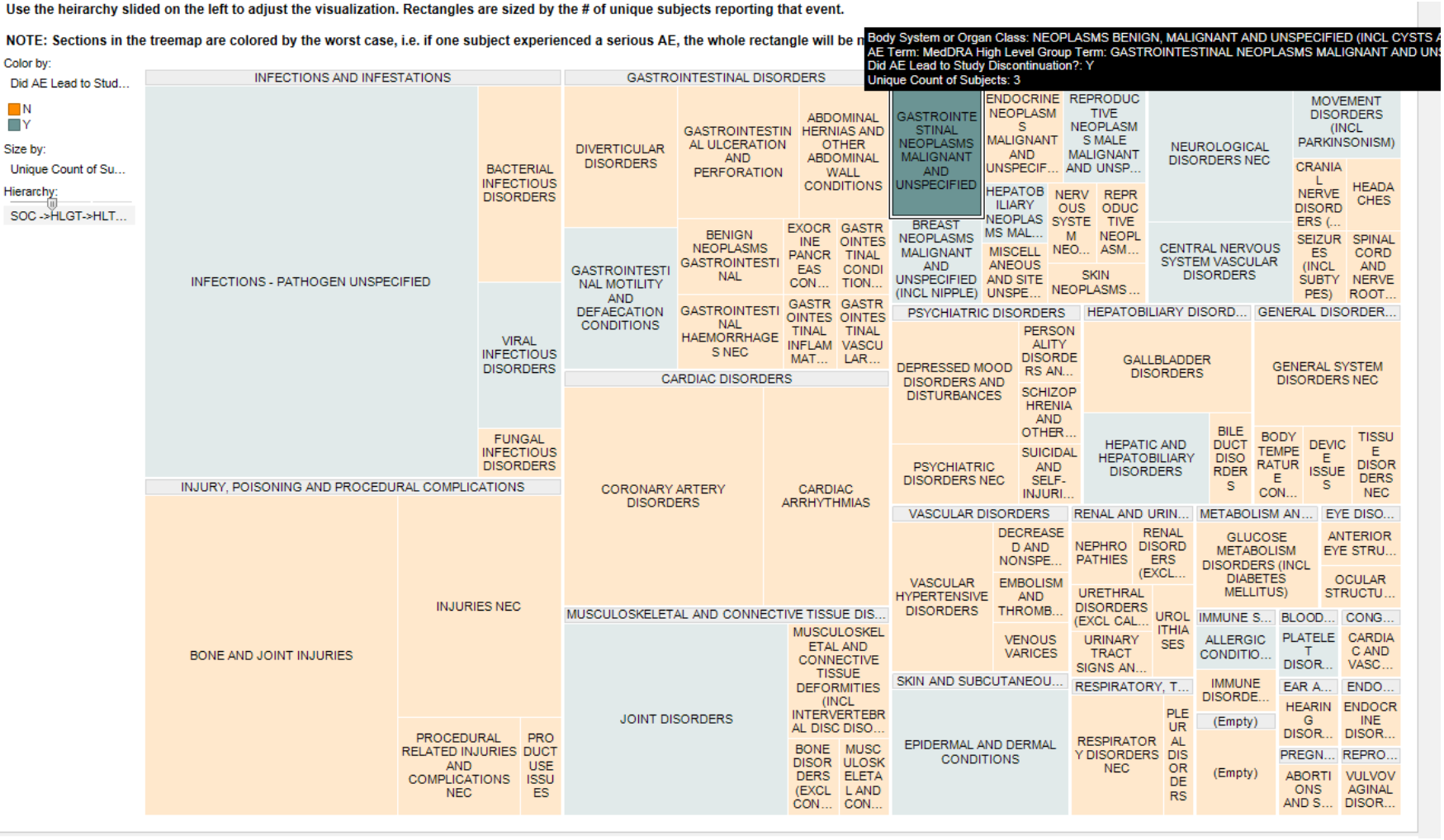
Science

Visual data review



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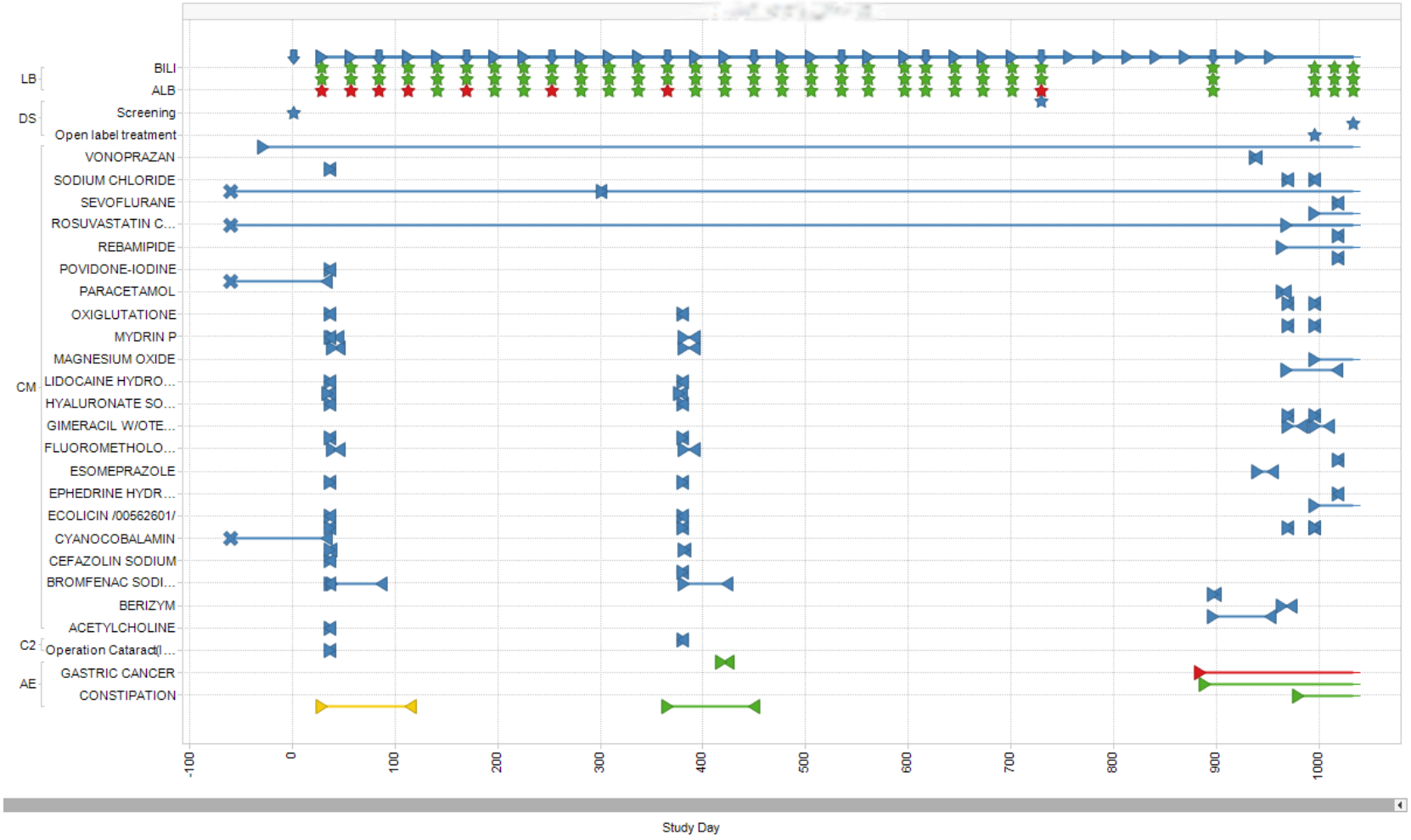
Science

Visual data review



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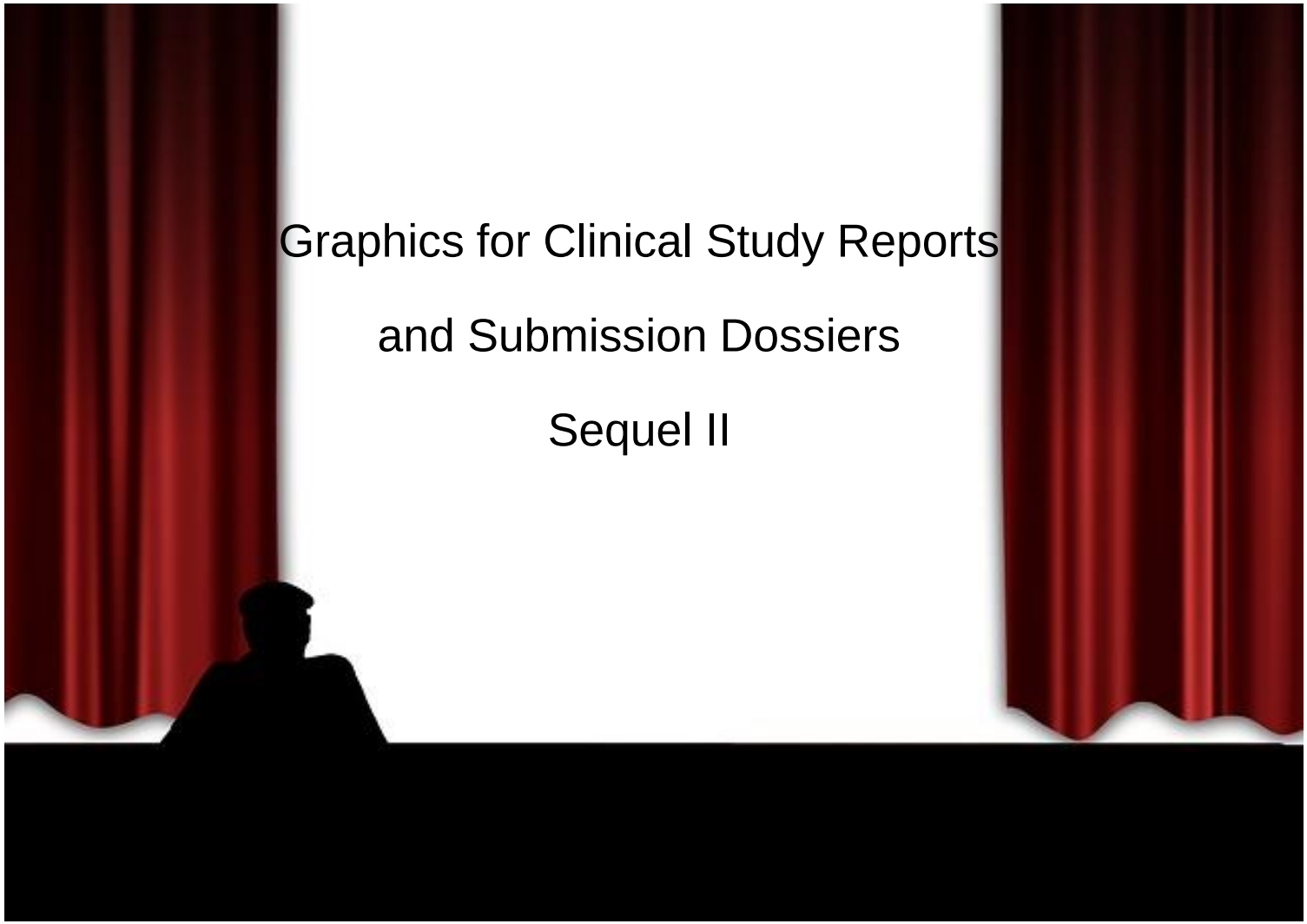
Today‘s program

Science Fiction



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Science fiction

The eCSR and eDossier

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

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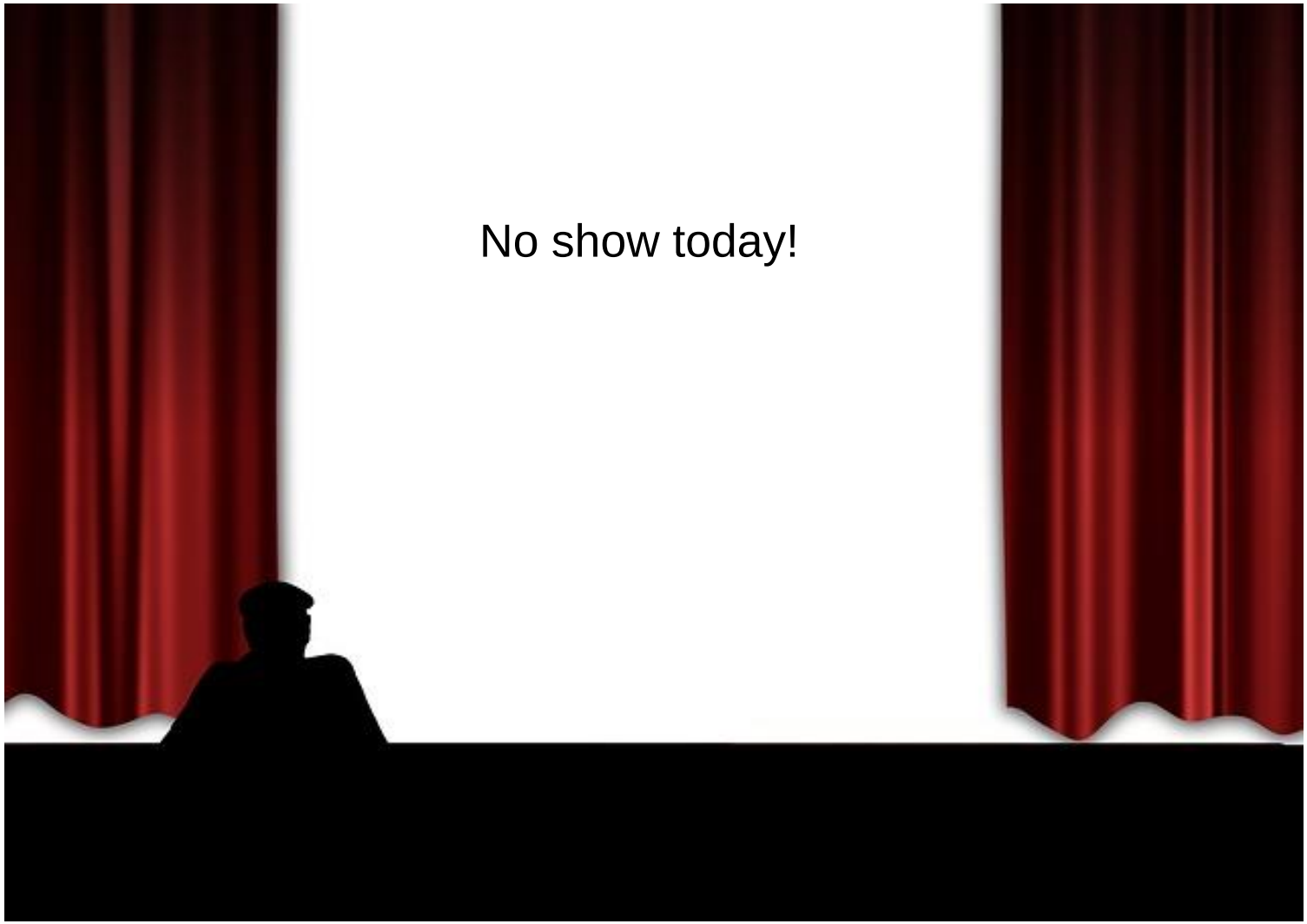
Science fiction

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



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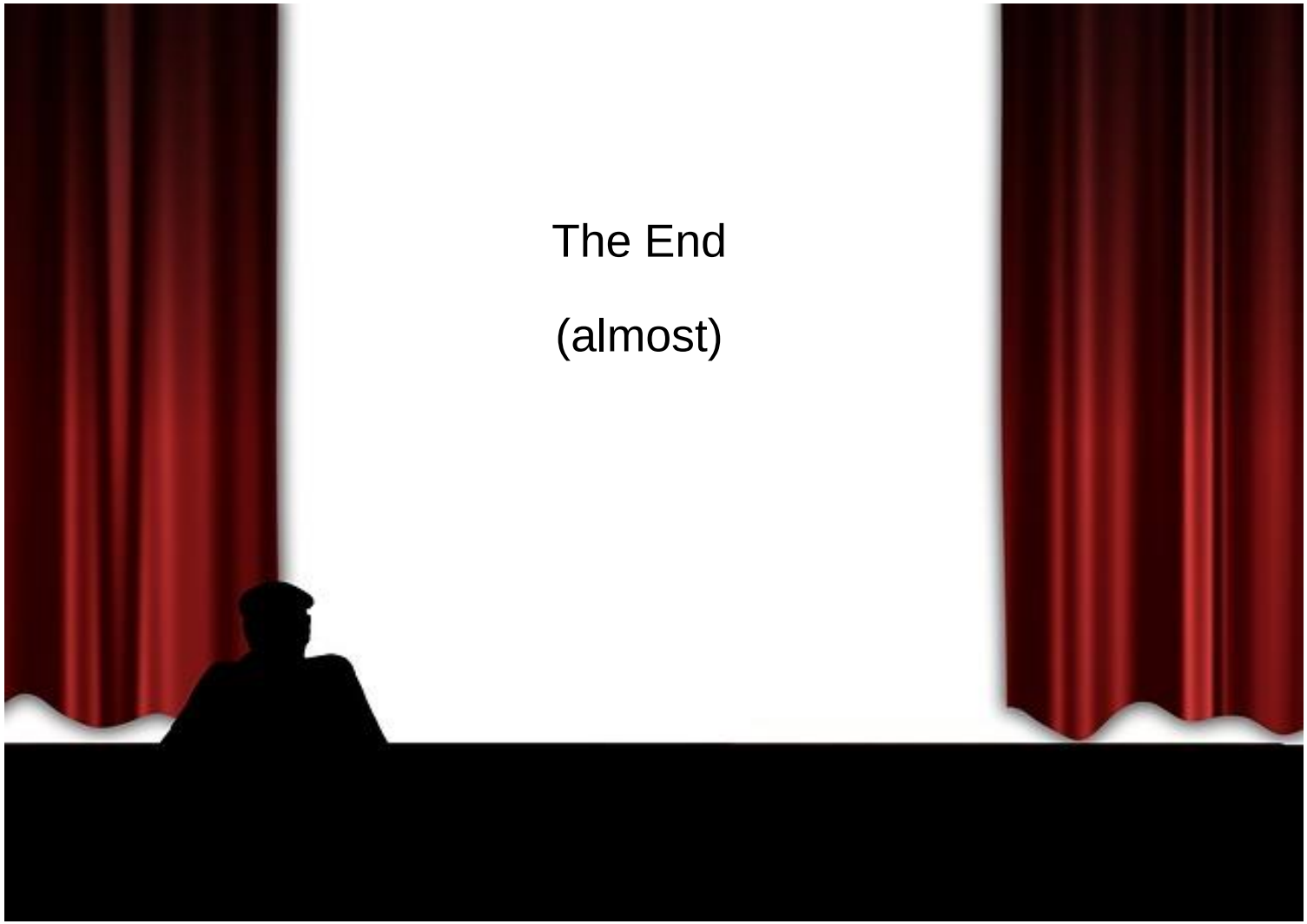
Advertisement

No show today!

- 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

The End



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Classification

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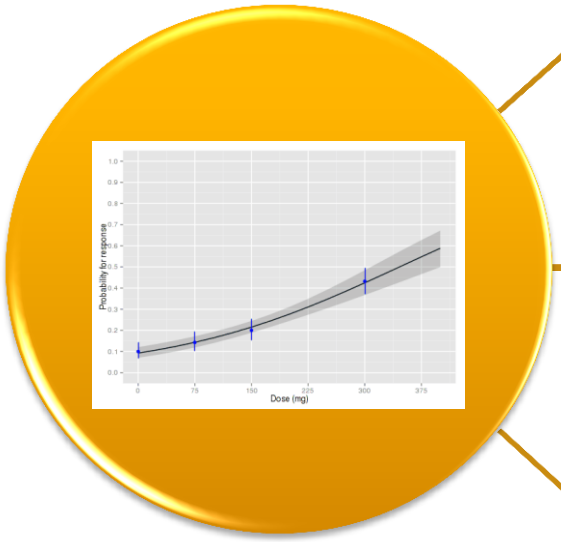
Classification



Target / purpose

- **CSR, submission dossier**
- **AdCom slide deck**
- **Publication**
- **Internal presentation**
- **Exploration**

Form / type

- **Static**
  - In-text
  - Post-text
  - Slide
- **Dynamic**
  - Web-based, interactive
  - Animated

Area / content

- **Results**
  - Efficacy
  - Safety
  - Demographics
  - PK
- **Benefit-risk**
- **Model checks**
- **Patient profiles**

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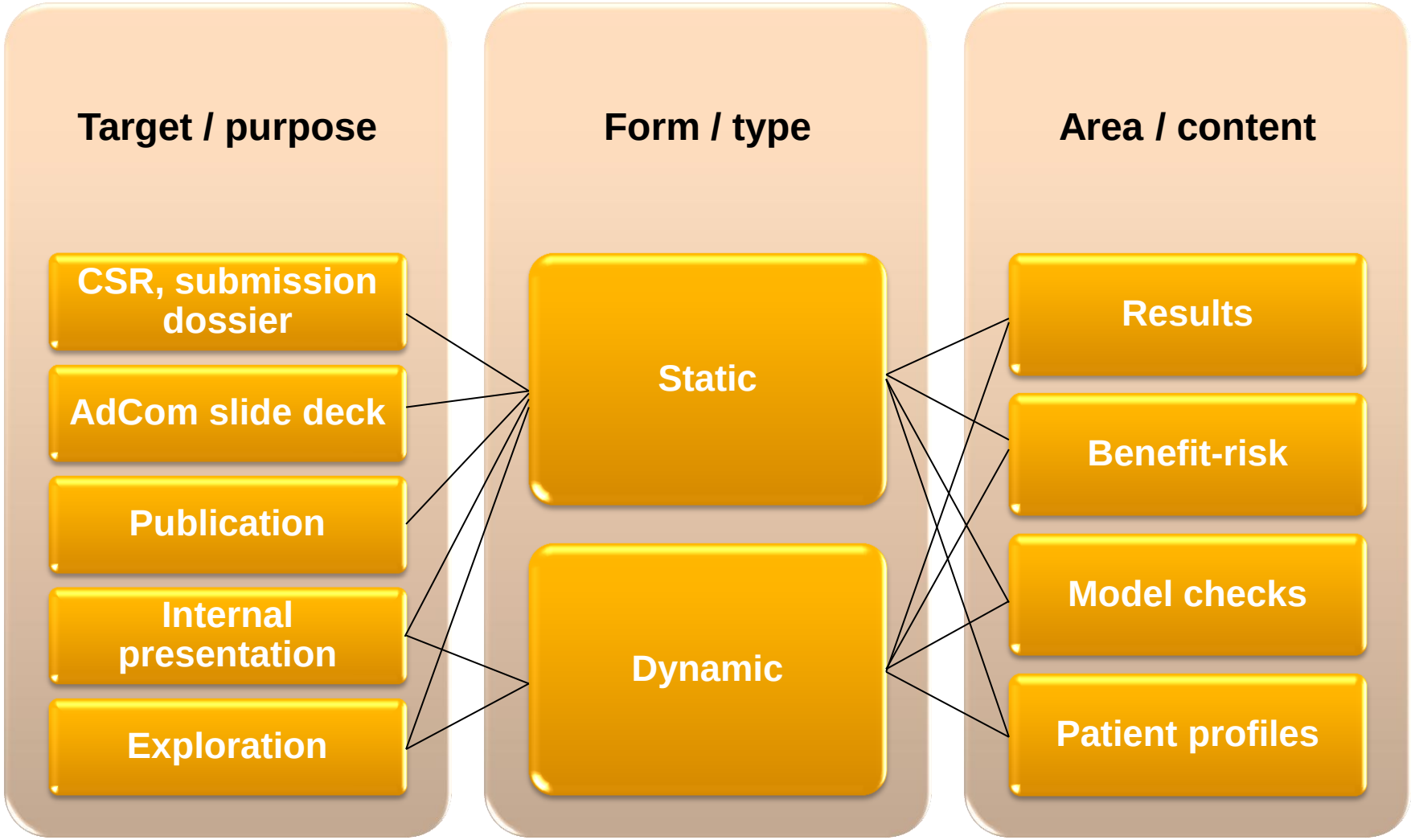
Classification



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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.
  - http://www.ctspedia.org/do/view/CTSpedia/SelectRightGraph

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“