

# Comparison of four visual analytics techniques for the visualization of adverse drug event rates in clinical trials

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# Introduction

## 📌 Drugs are evaluated during clinical trials

◆ Observed adverse drug events are recorded

● Lots of data is available on trial registries such as ClinicalTrials.gov

◆ But this data is little used, due to its tabular presentation

▼ Serious Adverse Events ⓘ				
	Placebo	Pregabalin 300 mg	Pregabalin 450 mg	Pregabalin 600 mg
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	4/184 (2.17%)	2/184 (1.09%)	8/182 (4.40%)	4/186 (2.15%)
Blood and lymphatic system disorders				
Anaemia * 1	0/184 (0.00%)	1/184 (0.54%)	0/182 (0.00%)	0/186 (0.00%)
General disorders				
Chest pain * 1	0/184 (0.00%)	0/184 (0.00%)	1/182 (0.55%)	0/186 (0.00%)
Hepatobiliary disorders				
Cholelithiasis * 1	0/184 (0.00%)	0/184 (0.00%)	0/182 (0.00%)	1/186 (0.54%)
Infections and infestations				
Bronchopneumonia * 1	0/184 (0.00%)	0/184 (0.00%)	1/182 (0.55%)	0/186 (0.00%)
Cellulitis * 1	0/184 (0.00%)	0/184 (0.00%)	1/182 (0.55%)	0/186 (0.00%)
Gastroenteritis salmonella * 1	1/184 (0.54%)	0/184 (0.00%)	0/182 (0.00%)	0/186 (0.00%)
Herpes zoster * 1	0/184 (0.00%)	0/184 (0.00%)	0/182 (0.00%)	1/186 (0.54%)
Pneumonia * 1	0/184 (0.00%)	0/184 (0.00%)	0/182 (0.00%)	1/186 (0.54%)
Injury, poisoning and				

# Introduction

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**Which visual analytics for comparing adverse event rates in various categories (e.g. digestive, cardiovascular,...) ?**

## ➤ In this study, we test and compare four visual analytics for this task

# Data preparation













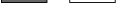
## ➤ We defined 13 categories of adverse drug events

- ◆ Each event is classified in 1 or 2 categories
- ◆ Using the MedDRA standard terminology
  - (Medical Dictionary for Regulatory Activities)
- ◆ One color per category
  - Colors are hints when possible

## ➤ We considered two levels of event seriousness

- ◆ Serious vs non-serious
  - Data is present in ClinicalTrials.gov

### The 13 categories of events:

	Psychology and psychiatry
	Nervous system
	Sensory system
	Musculo-skeletal system
	Skin and subcutaneous tissue
	Digestive system
	Genital system and reproduction
	Urinary system
	Endocrine system, metabolism and nutrition
	Blood and immune system
	Cardiovascular system
	Respiratory system
	Unclassified

# Data preparation

## Dataset:

- ◆ A comparative clinical trial includes 2 or more patient groups
- ◆ Each patient group is a 26-dimensional point
  - 13 categories x 2 seriousness levels

## Example: Randomized, double-blind, placebo-controlled trial of pregabalin in patients with fibromyalgia

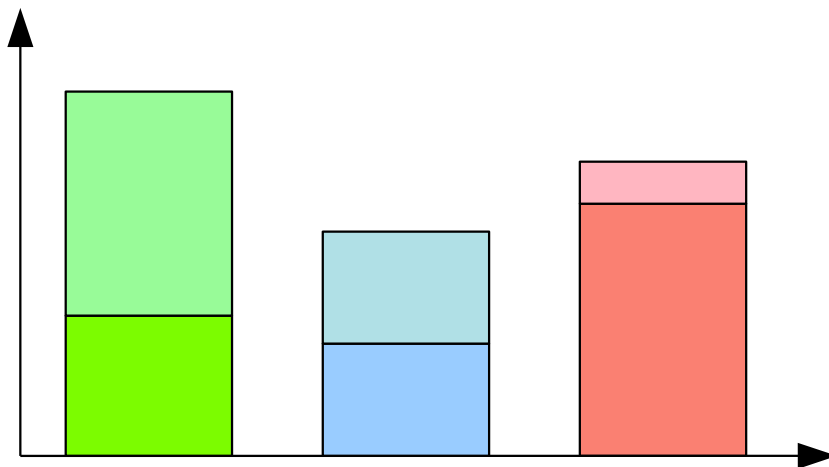
- ◆ NCTID: NCT00333866, 4 patient groups

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# Related works

➤ Many visual analytics have been proposed for visualizing  $n$ -dimensional points

◆ Simple diagrams : **stacked bar charts**

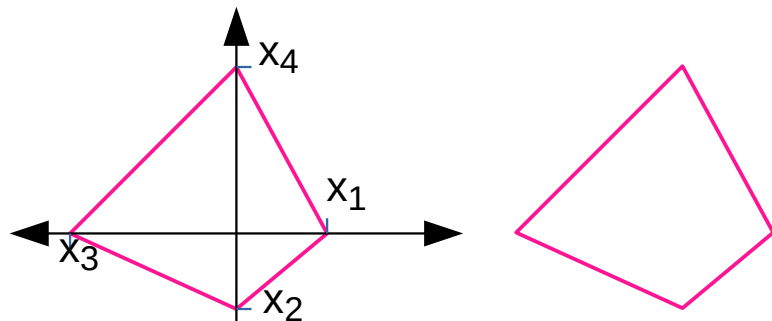


# Related works

➤ **Glyphs:** each data point is represented by a small icon called **glyph**

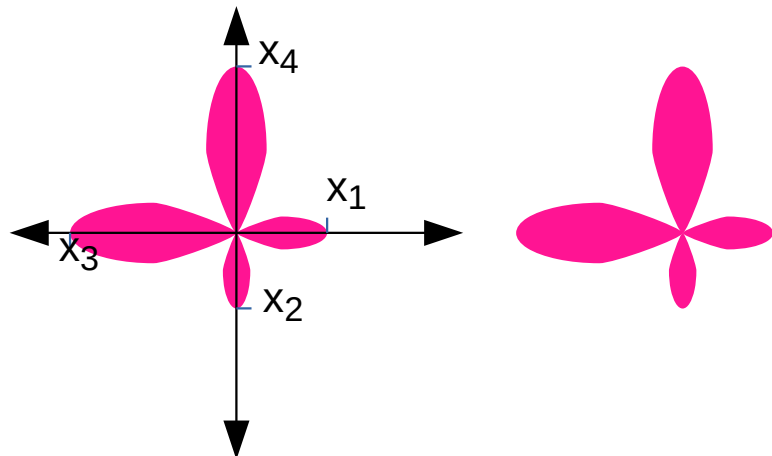
◆ **Star glyph:** (or stardiates)

- Axes share the same origin
- The glyph is a closed polygon
- Axes are usually not shown



◆ **Flower glyph:** (or Nightingale's Rose plot)

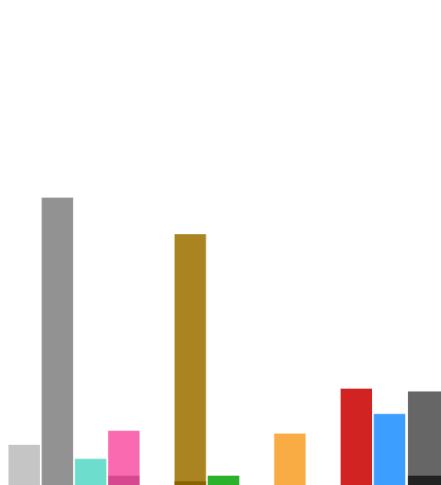
- Axes share the same origin
- One petal per dimension
- Petal length is proportional to the value
- Axes are usually not shown



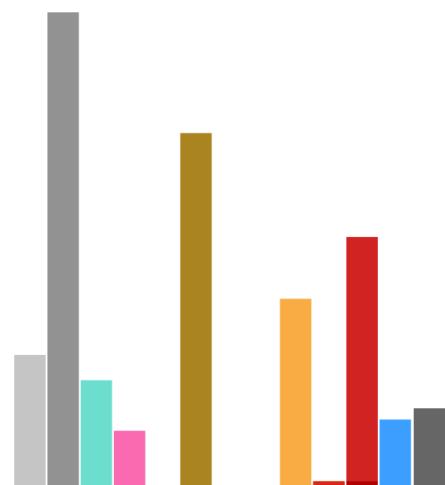
# Visual analytics #1: Vertical stacked bar chart

- ◆ 13 bars: one per category
- ◆ 2 stacks: one for serious events and the other for non-serious
- Darker colors for serious events

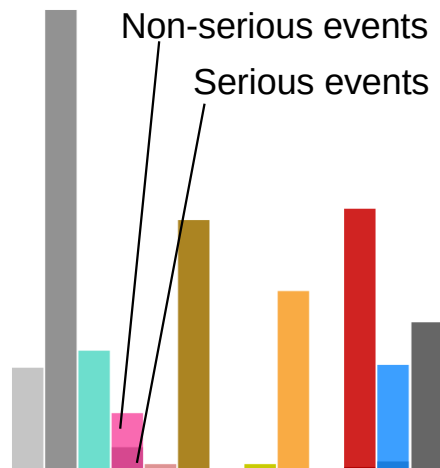
## Example on trial NCT00333866:



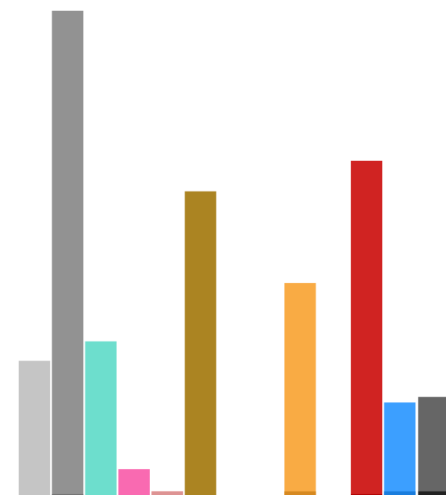
**#1:** placebo oral (in 2 daily intakes)  
for chronic pain, fibromyalgia  
All: 96.7% Serious: 3.8%



**#2:** pregabalin oral (300 mg in 2  
daily intakes)  
for chronic pain, fibromyalgia  
All: 165.7% Serious: 1.0%



**#3:** pregabalin oral (450 mg in 2  
daily intakes)  
for chronic pain, fibromyalgia  
All: 163.7% Serious: 4.4%



**#4:** pregabalin oral (600 mg in 2  
daily intakes)  
for chronic pain, fibromyalgia  
All: 180.1% Serious: 2.6%

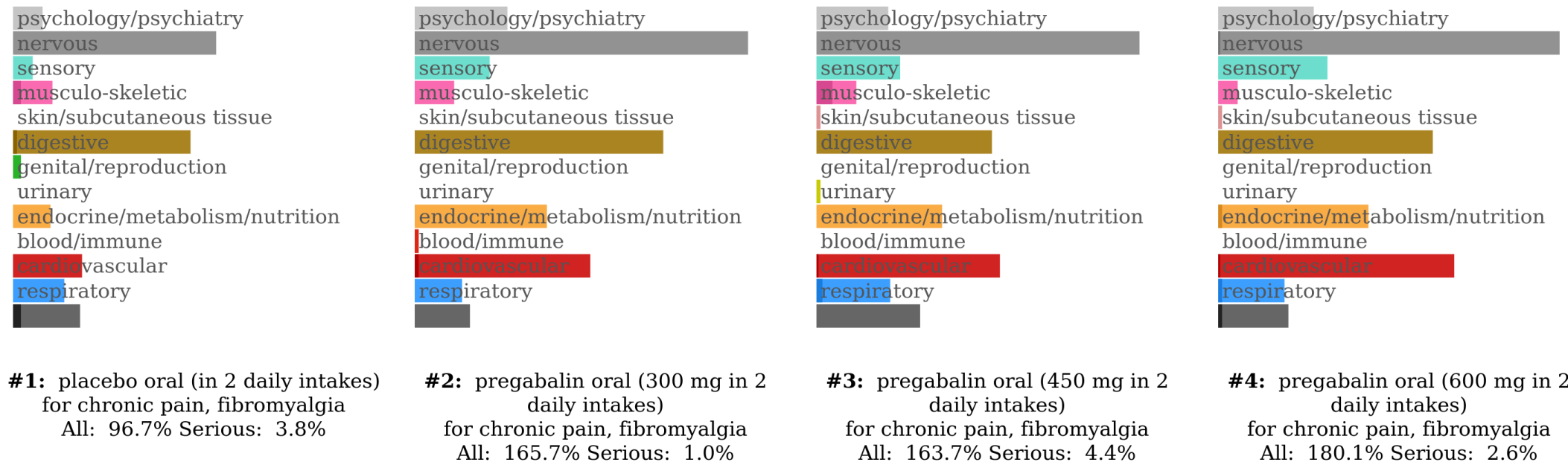
# Visual analytics #2:

## Horizontal stacked bar chart

◆ Similar to the vertical bar chart

● We added short labels, indicating the event categories

### Example on trial NCT00333866:



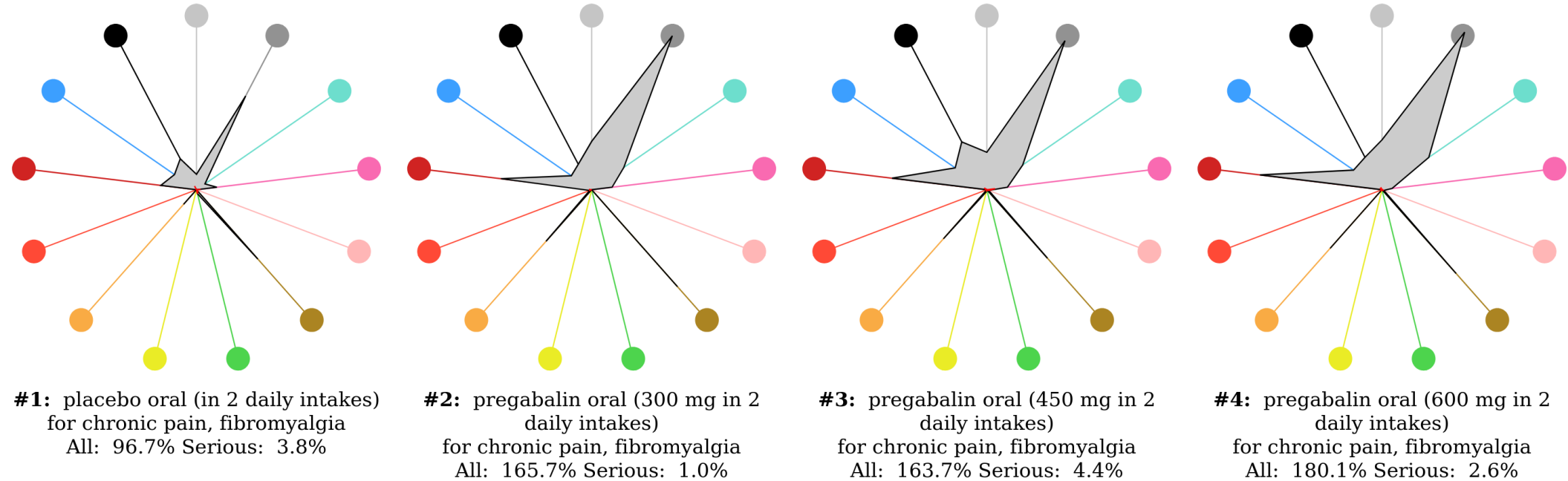
# Visual analytics #3: Star glyph

◆ 13 dimensions, one per event category

◆ 2 superposed glyphs:

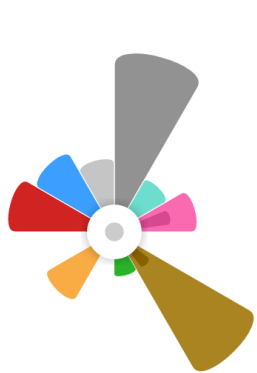
● One for serious events (in red)

● One for all events (serious and non-serious, in gray)

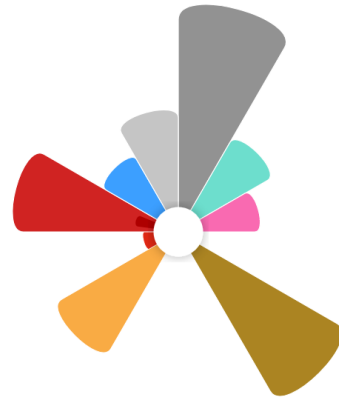


# Visual analytics #4: Flower glyph

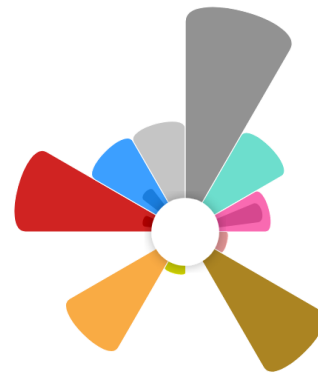
- ◆ 12 petals for the 12 specific event categories  
+ 1 central region for unclassified events
- ◆ Petal area is proportional to event rate (not petal length)
  - Human eye is more sensitive to area than to length
  - Event rates are usually non linear (many small values)



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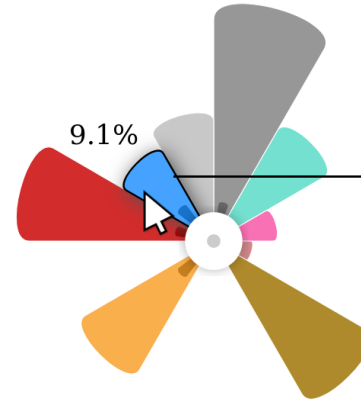


**#4:** pregabalin oral (600 mg in 2  
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for chronic pain, fibromyalgia  
All: 180.1% Serious: 2.6%

# Interactivity

## Details-on-demand

- ◆ Popup bubbles on bars / axes / petals



### Respiratory system: 9.14%

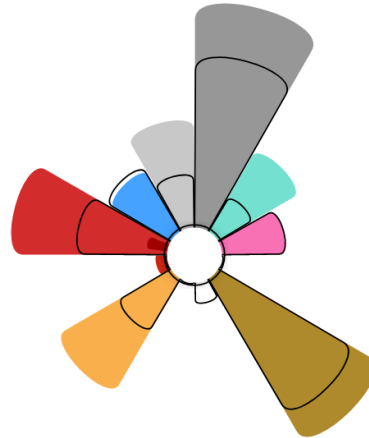
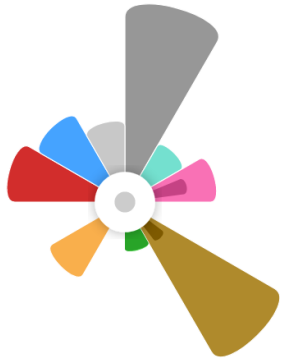
Influenza: 5.38%

Nasopharyngitis: 3.23%

Pneumonia: 0.54%

### Incl. serious events: 0.54%

Pneumonia: 0.54%



## Detailed comparison

- ◆ The user can select one patient group and its outline is shown on top of other patient groups

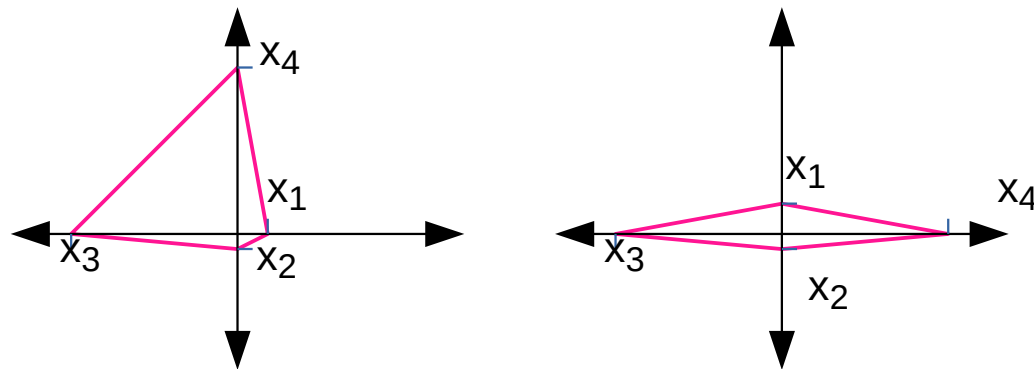
# User opinion

- 8 users in the field of medical informatics
- Online study
- Each participant ranked the four visual analytics
  - ◆ Visual analytics ranked first gets 3 points, second 2 points, third 1 point
- Results:
  - ◆ Mean score (higher is better):
    - Flower glyph: 2.0
    - Horizontal stacked bar chart: 1.375
    - Vertical stacked bar chart: 1.25
    - Star glyph: 1.25

# User opinion

## ➤ Analysis of participants comments:

- ◆ Participants preferring star glyph thought that it is area proportional (while it is not)
  - Star glyph area depends on axes ordering — star glyph seems misleading here!

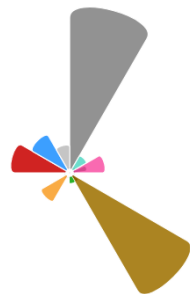


- ◆ Participants preferring horizontal bar chart appreciated the labels
- ◆ Participants preferring flower glyph appreciated its visual attractiveness, the area-proportionality and the fact that it emphasizes small values

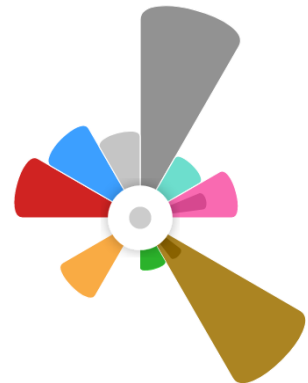
# Discussion

Horizontal stacked bar chart	Vertical stacked bar chart	Flower glyph	Star glyph
+ Well-known diagram + Area-proportional + Can include textual labels	+ Well-known diagram + Area-proportional	+ Area-proportional + Favor small values + Visually attractive + Offer the possibility to put unclassified ADE in the center region + Direction can be used as hint for organs ( <i>e.g.</i> brain at the top) – Not well-known	– Not well-known – Overall shape depends on axis ordering – Values surrounded by zero values are almost invisible – Serious ADE are difficult to read – Misleading: the surface is wrongly perceived as proportional to the ADE rate

Length-proportional flower glyph



VS



Area-proportional flower glyph

# Conclusion

## ➤ **Two visual analytics seems interesting for our application:**

- ◆ Horizontal bar chart, due to its ability to display labels
- ◆ Flower glyph, due to its ability to favor small values
  - In the long term, learning the 13 categories and their colors is easy  
=> Flower glyph seems preferable

## ➤ **Area-proportional flower glyph may be better than length-proportional one**

# Perspectives

Use of the proposed visual analytics in a platform for analyzing adverse drug events observed during clinical trials

- ◆ Aggregates similar trials
- ◆ Application to pain treatment

[JB Lamy, Arxiv 2020]



# References

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