An Update from the FDA / Industry / Academia Safety Graphics Working Group: Adverse Event Sub Team

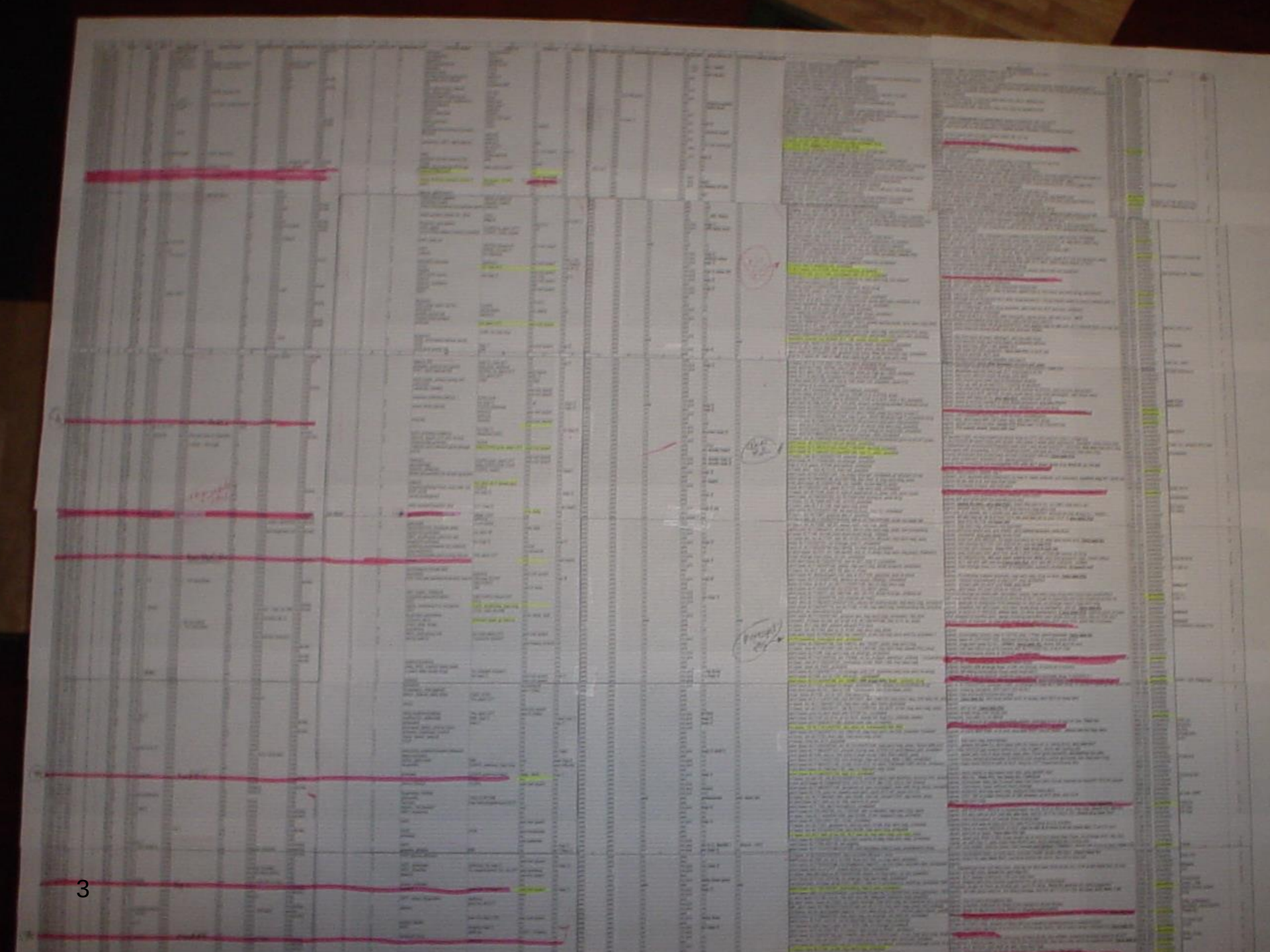
Qi Jiang and Liping Huang

on Behalf of the Adverse Event Sub Team

FDA/QSPI Summit, March 2012

The Disclaimer

The views expressed herein represent those of the presenters and do not necessarily represent the views or practices of the presenters' employers or any other party



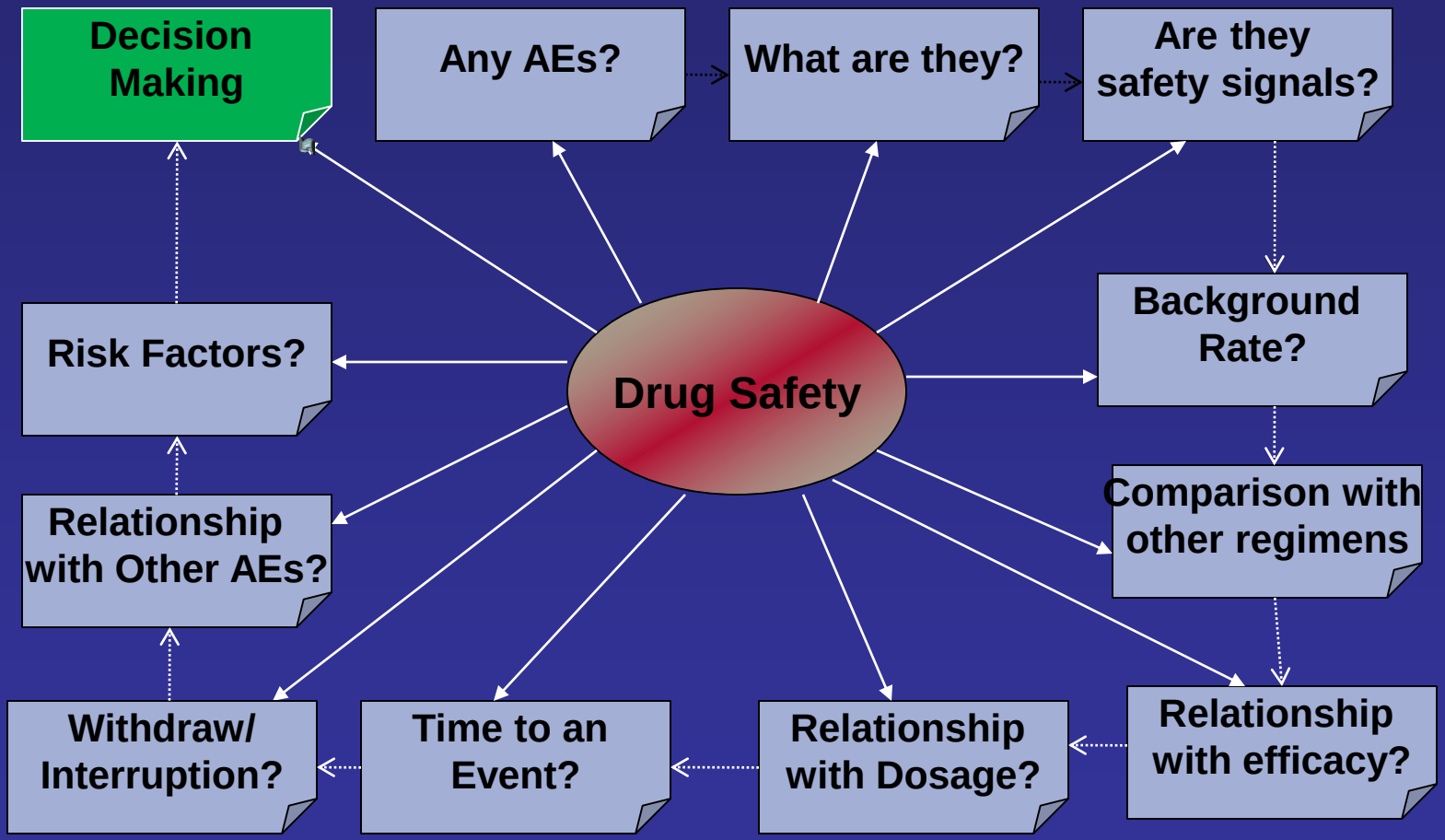
How to Achieve This?

By: David Walker

Motivations

- Information regarding adverse events in drug development is complex
- Communicating information effectively and efficiently is crucial in detecting safety signals and helping decision-making

Frequently Asked Questions Regarding Adverse Events



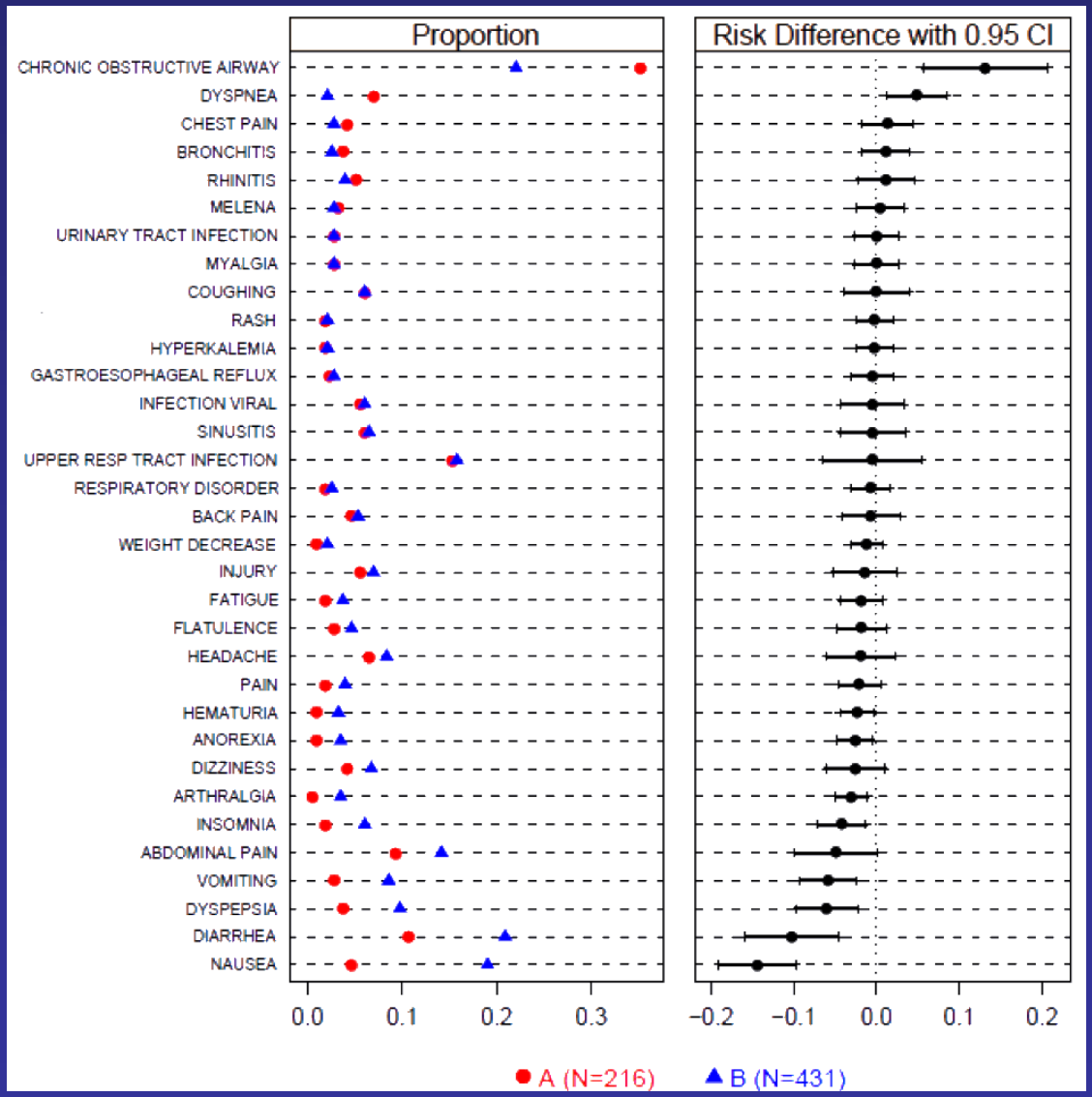
Categories of Graph

- Demographics and incidence of AEs
- AE occurrence over time across treatment groups
- Dosage and exposure
- Potential risk factors and their temporal relationship to AEs
- Withdrawal and interruption of treatment in relation to the occurrence of AEs
- Patient profile

Graphical Displays Addressing Key Clinical and Safety Issues

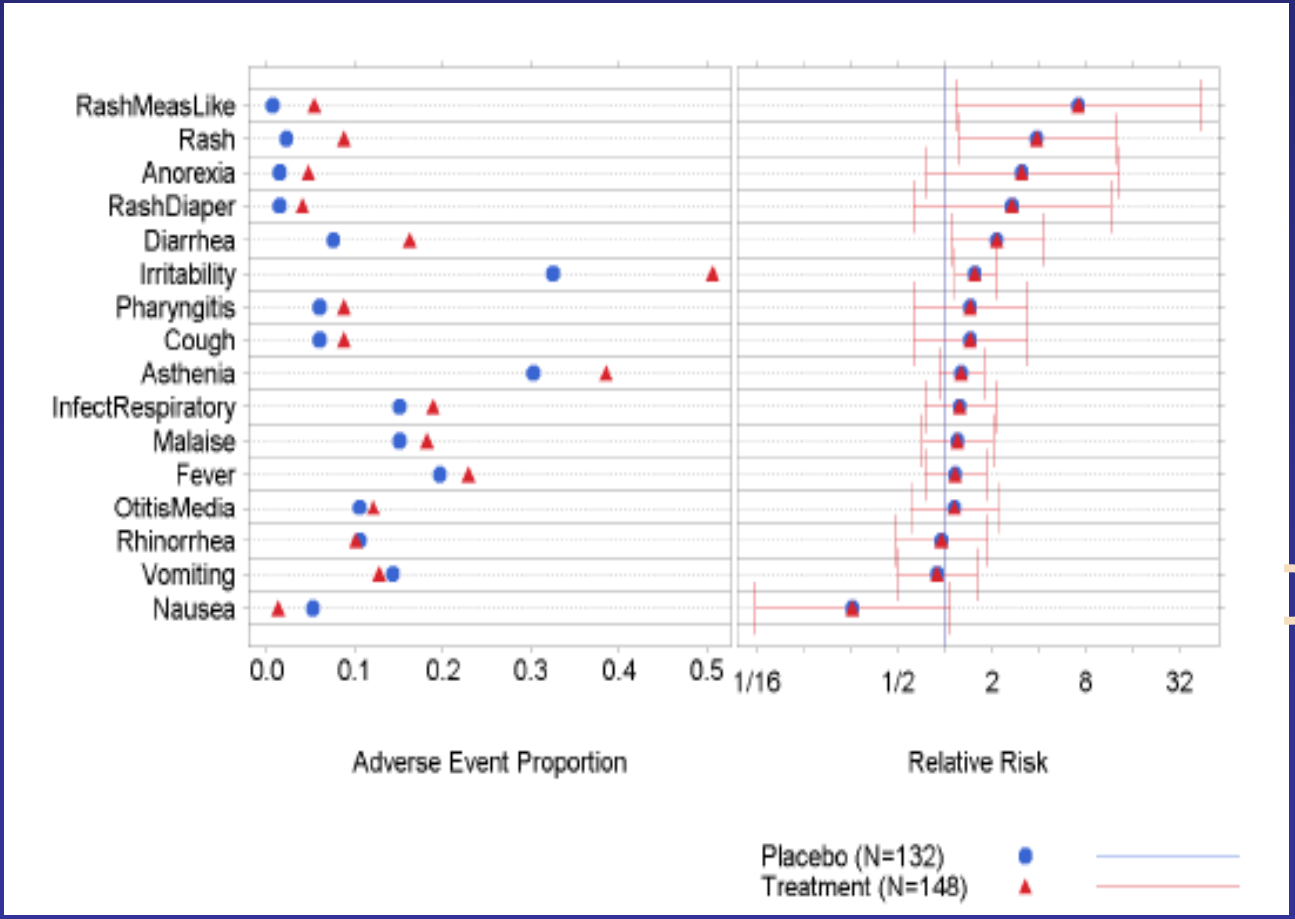
Most Frequent On-Therapy AE Sorted by Risk Difference

- Clinical Question: Which AEs are elevated in treatment vs. control?
- Type: Grouped Dotplot
- Contributed by: Frank E Harrell, Jr. modification of Amit et al 2008



Alternative Approach: Which AE Could Be A Safety Signal?

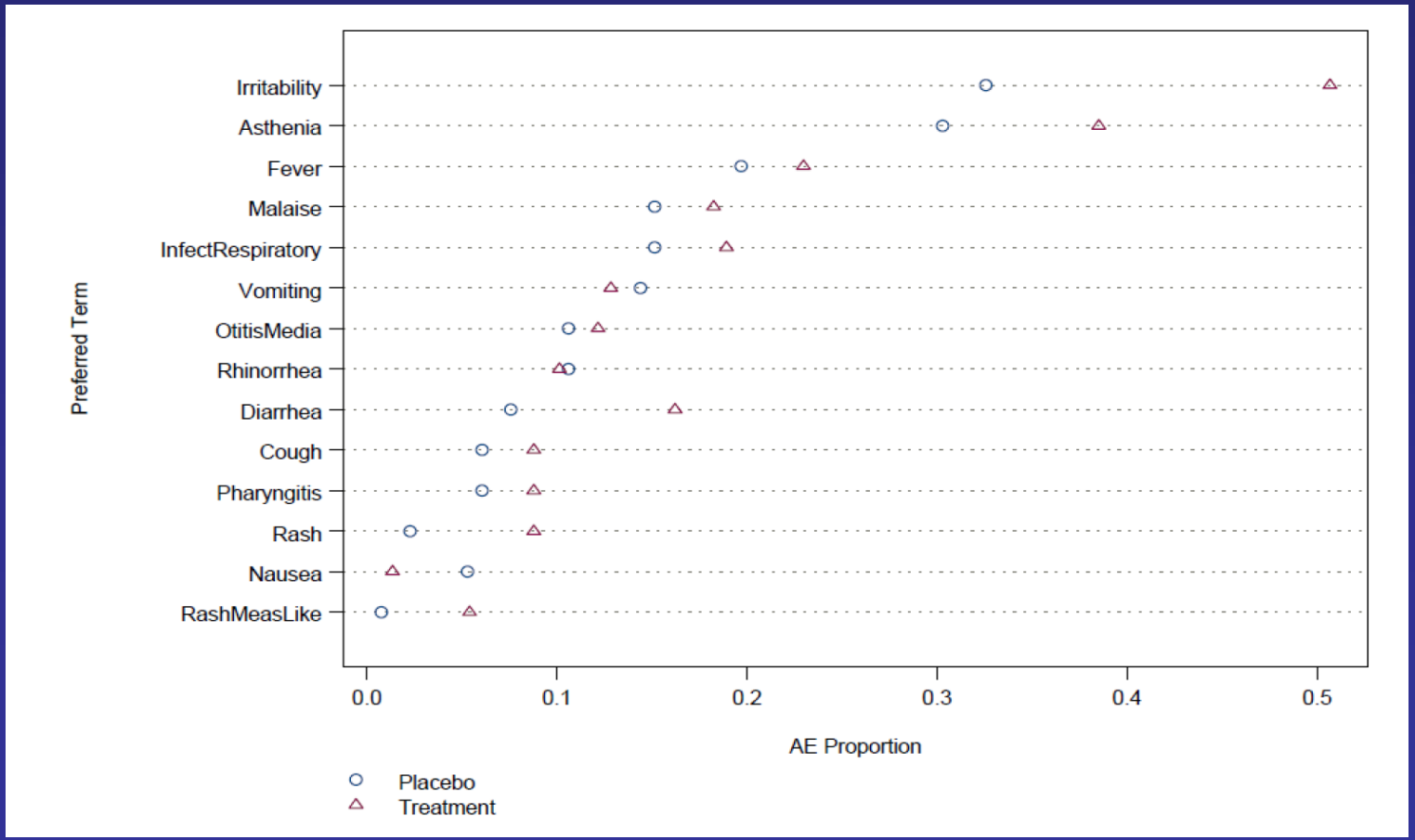
Dot Plot: Adverse Event Sorted by Relative Risk to address which AE could be caused by the drug



Source: Amit, Lane, Heiburger

Another Alternative: Which AEs Were Elevated?

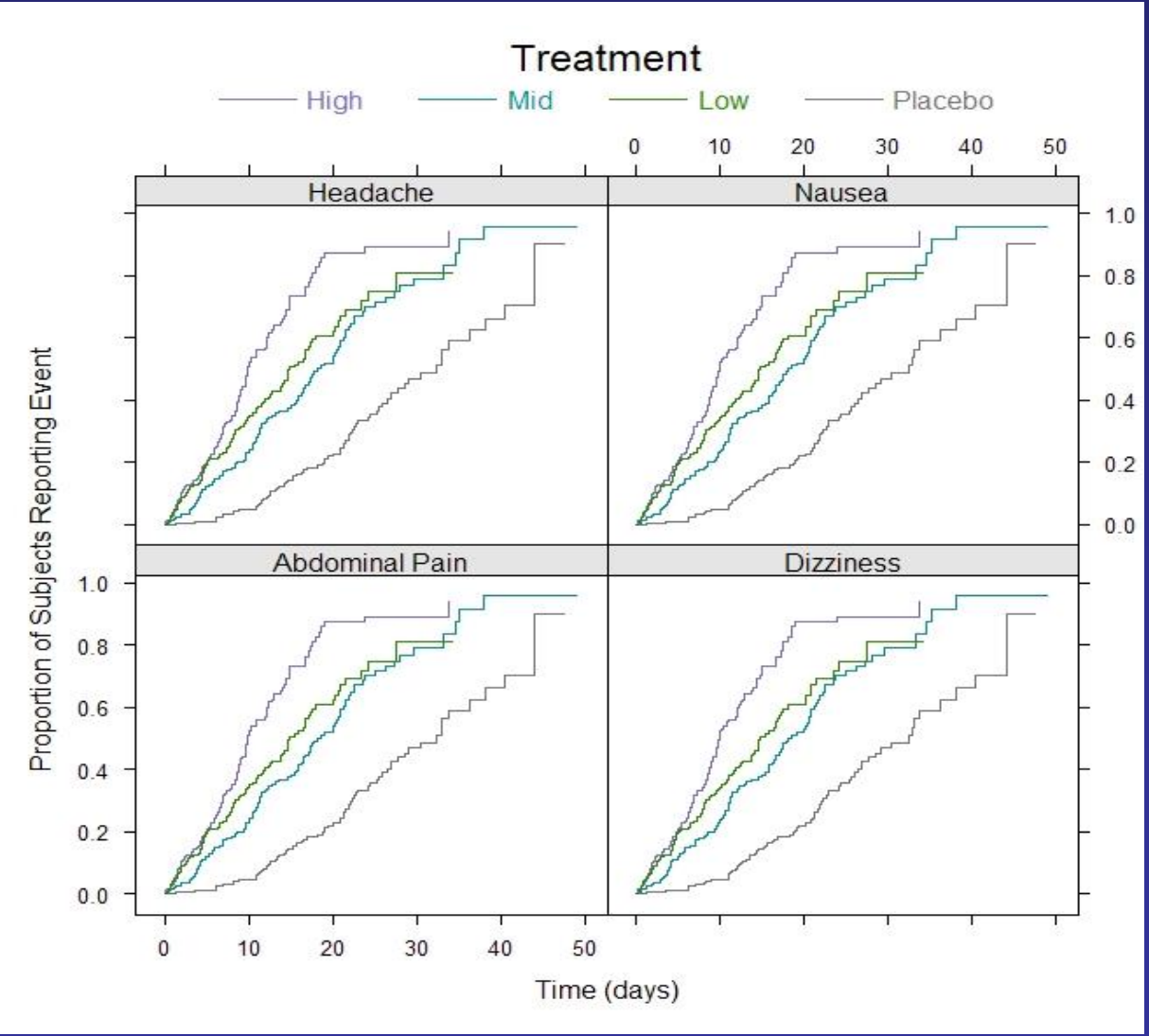
Dot Plot: Proportions of AE Occurrence Between Treatment and Placebo



Source: Michael O'Connell "Graphical Analysis and Reporting of Safety Data"

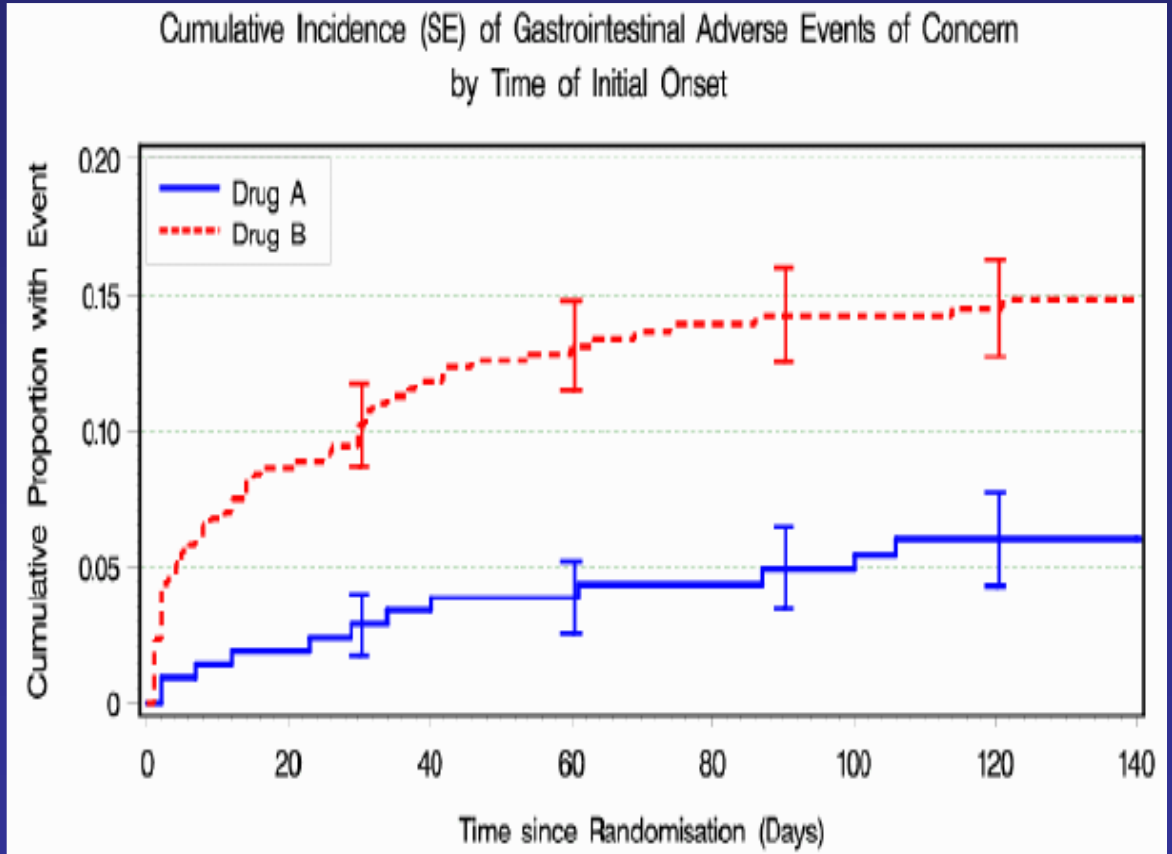
Adverse Event Occurrence Over Time

- Clinical Question:
  Is there a difference in the time to event across treatment groups?
- Type:
  Grouped Trellis Kaplan-Meier Plot
- Software: R
- Contributed by:
  Mat Soukup



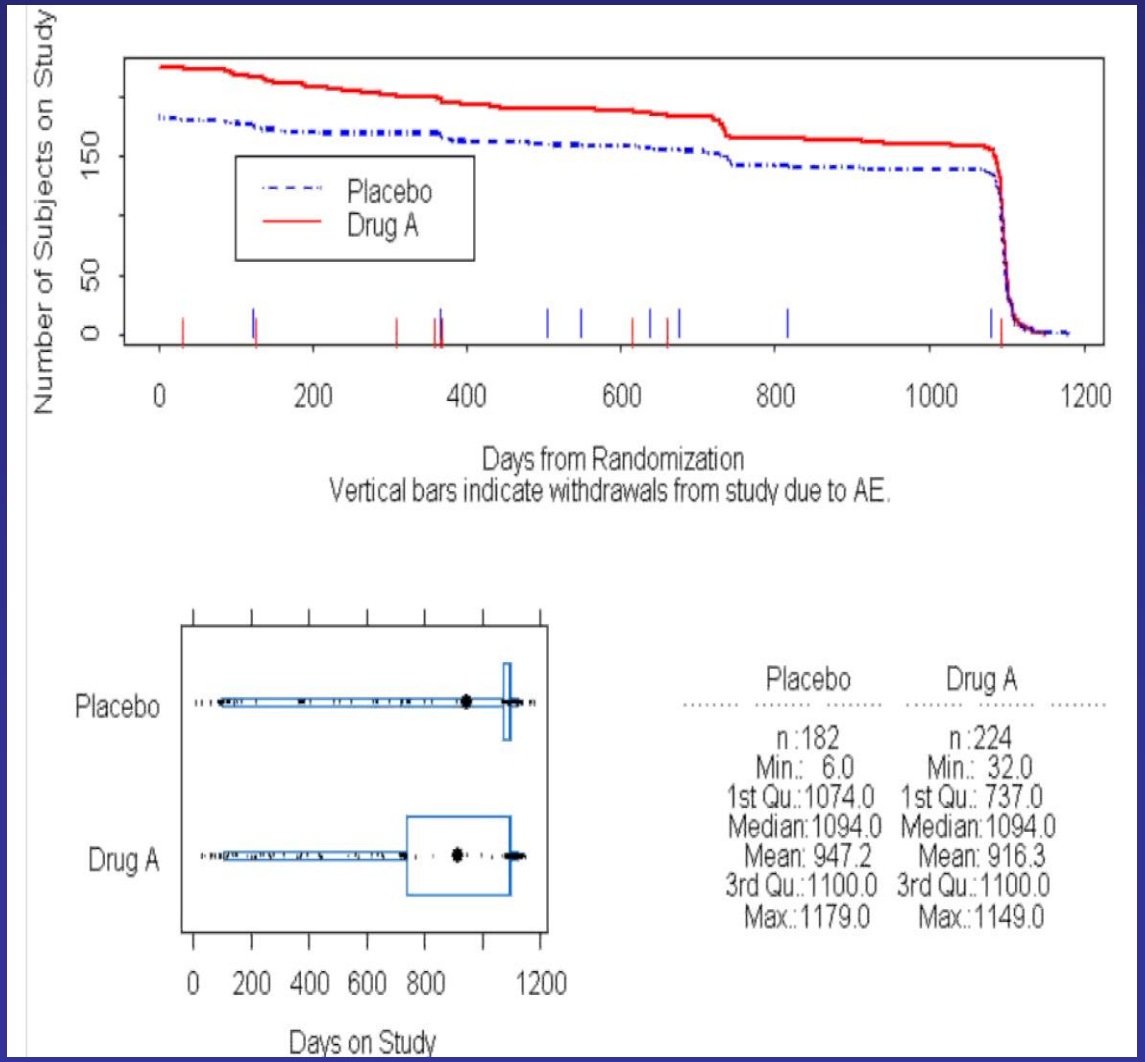
Cumulative Incidence of AE by Time of Initial Onset

- Clinical Question:
- Is there a difference in the time to event across treatment groups?
- Contributed by:
  Liping Huang



Summary of Safety Subjects Exposure to Treatment

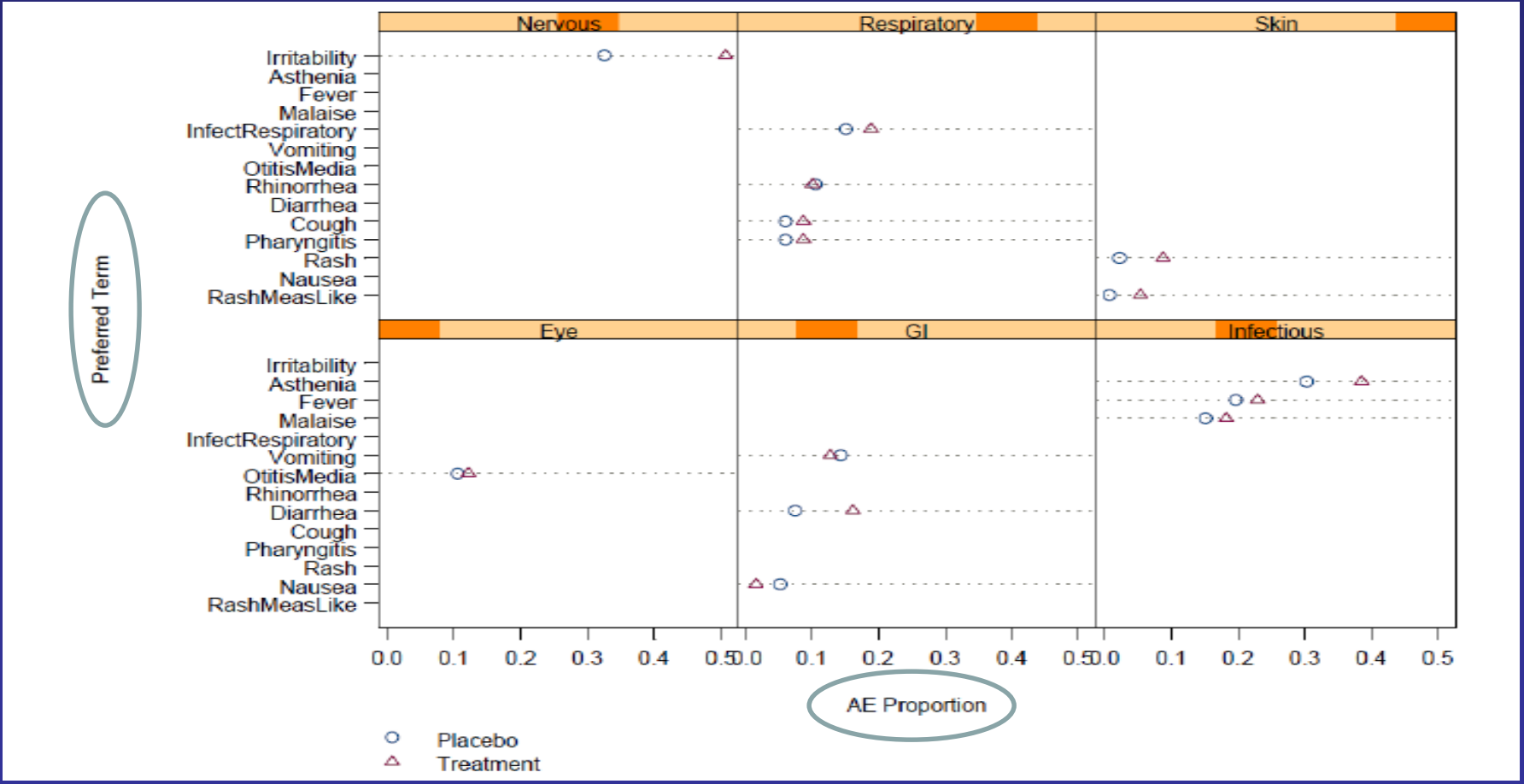
- Clinical Question:
- What is the safety profile of the drug? Are there any AEs associated with dropouts?
- Contributed by:
  Qi Jiang



A Few More Graphical Displays Addressing Key Clinical and Safety Issues

Which AEs Were Elevated in Treatment vs. Placebo?

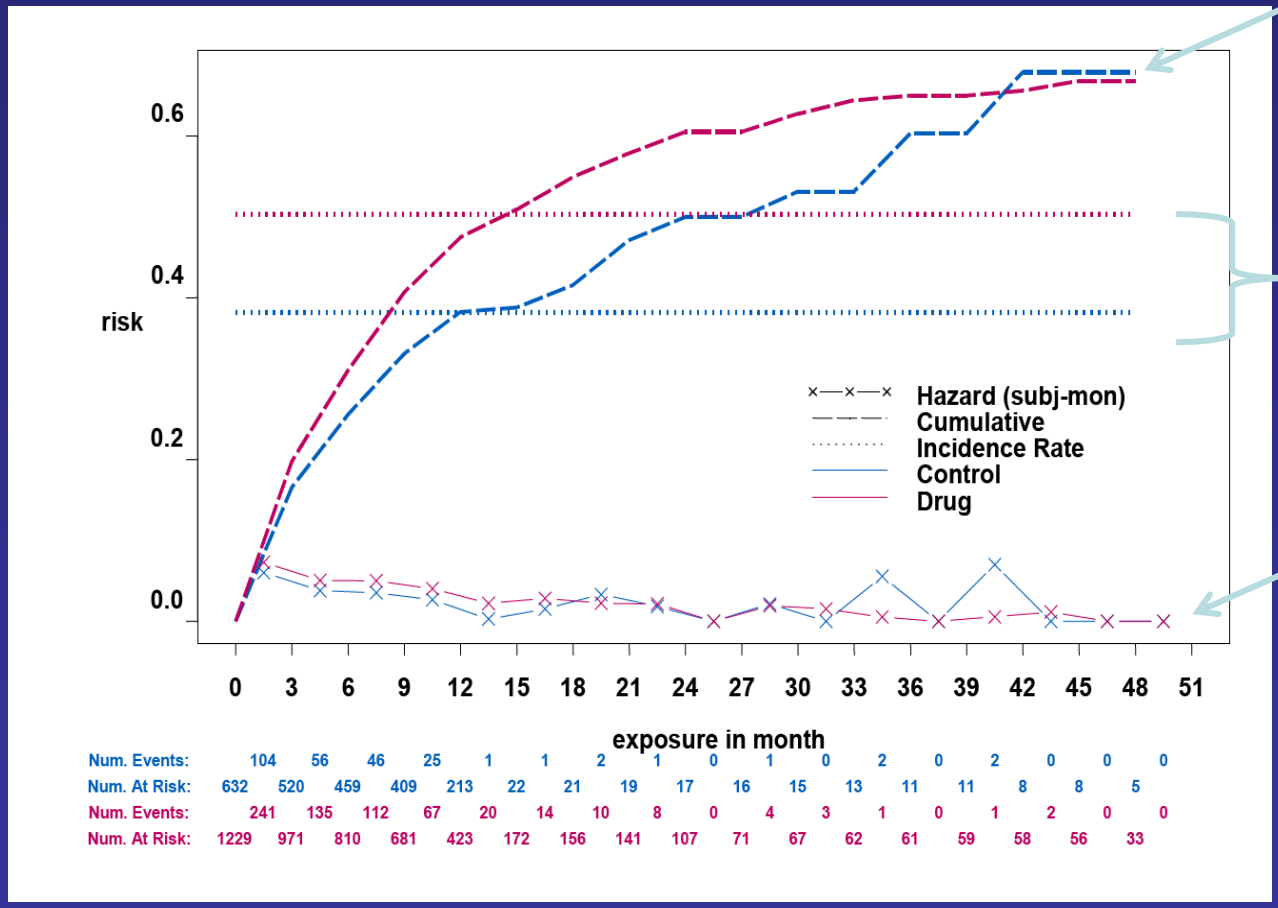
Grouped Trellis Dot Plot: AEs by Group of Special Interest



Source: Michael O'Connell "Graphical Analysis and Reporting of Safety Data"

Is There A Special Pattern of AE Onset?

Risk Over Time Plot for Adverse Event

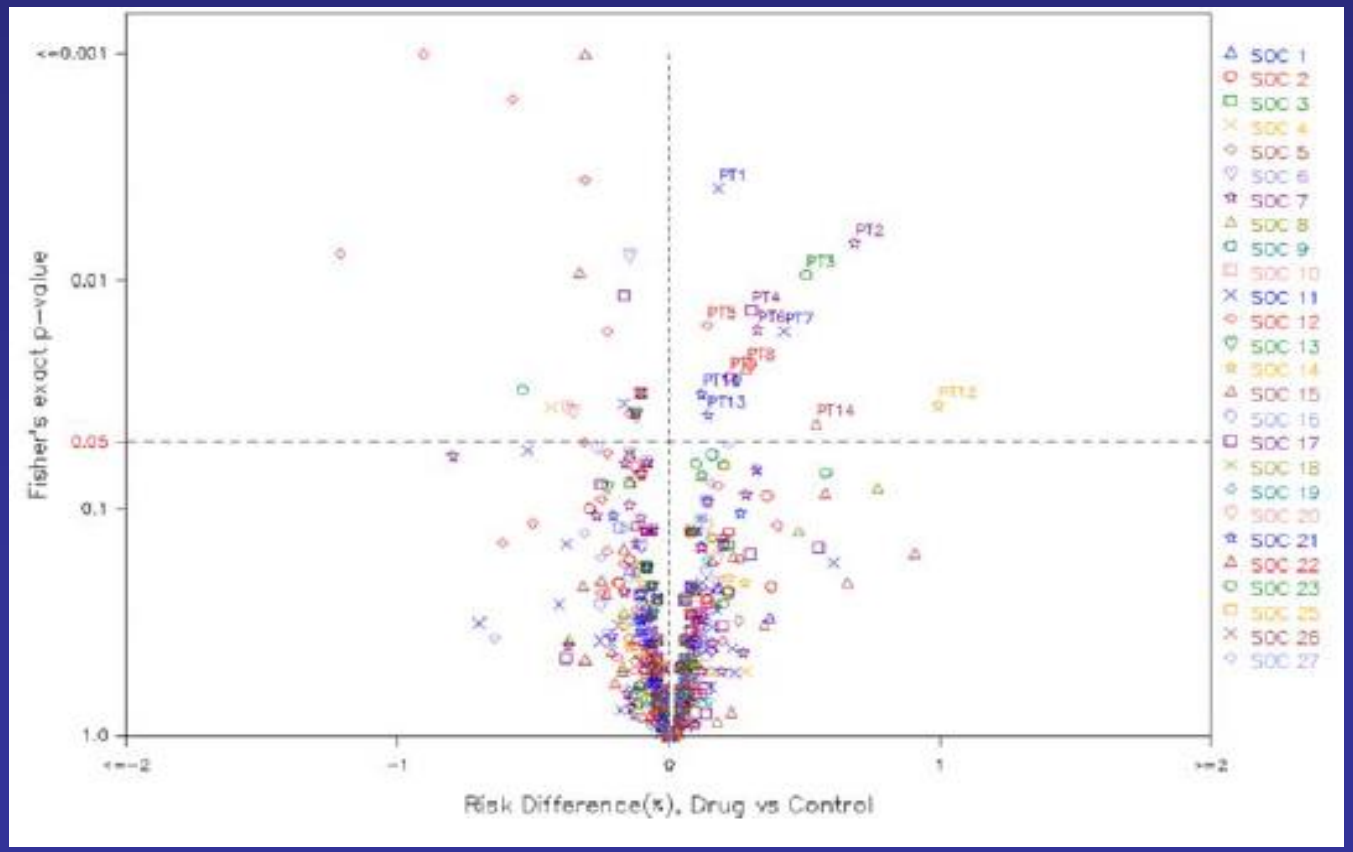


Source: Qi Jiang, Amgen

Which AE Could be A Safety Signal?

Volcano Plot:

Relationship Between Risk Difference and P-Value for AEs by SOC
Visualizations with different adjustments for multiplicity and shows impact of multiplicity adjustments



Source: Qi Jiang, Amgen

Conclusions

- Clear and informative graphs enhance the ability to understand the data
- Suitable graphical presentation for adverse events could increase the likelihood of detecting safety signals
- Graphs convey information more efficiently and better meet regulatory requirements for ongoing safety evaluation

Conclusions

Special Thanks

FDA / Industry / Academia Safety Graphics Working Group

Working Group Adverse Events Sub Team Members:

Liping Huang (co-lead) - CSL Behring
Qi Jiang (co-lead) - Amgen
Fabrice Bancken - Novartis
Andreas Brueckner - Bayer Healthcare
Larry Gould - Merck
Kenneth Koury - Merck
Mat Soukup - CDER

Former Sub Team Members:

Janelle Charles (co-lead) - CDER
Stephine Keeton (co-lead) - PPD
Suzanne Demko - CDER
Navdeep Boparai - Merck
Jeff Summers - CDER
Yaning Wang - CDER

In addition, Amgen Safety Biostat Graphical Team

Thank You!