Update on the ASA/PHUSE/FDA Collaboration/Initiative on Interactive Safety Graphs for Regulatory Submissions

Melvin Munsaka, PhD, AbbVie

Neetu Sangari, PhD, Pfizer

Disclaimer

- Opinions expressed in this presentation are the authors' own and do not represent in any way opinions of their respective employers

Drug Safety Review

Interactive Tools for Drug Safety Data Review - Update
A Collaboration of

ASA   FDA   phuse

Recap: Overview

Some background

- Initiative put together to promote collaboration between ASA, FDA, and PHUSE

- ASA participation - Biopharmaceutical Section and SSPA – put aside some bureaucratic considerations

- PHUSE - participation is via Data Visualization and Open-Source Technology in Clinical Research

- Current team consists of participants from ASA, PHUSE, FDA, and Industry

Deliverables

- Spirited discussion of deliverable and where and how to deliver

- Focused on development of a tool for generating forest plots for adverse events

- Full R package - tool, guide, training, open source, submissions

- Reviewed PHUSE volcano pilot submission initiative as a point of reference

- Discussed different considerations and requirements for the tool

Recap: Project Scope

- Development of R-shiny application(s) to enable the generation of identified plots for direct inclusion in submission packages for regulatory agencies

- Initial scope is to develop tools to generate forest plots for inclusion in submission to FDA

Strategy/Some Considerations

- Start small - what are the minimal requirements/options:
  - Not expecting statistical expertise to user interface
  - Enough intuitive self-explanatory details/manual; Demos; Training materials; Self-contained instructions – explanations

- Consider end user perspectives/parlor and experience (who are the end users?)
  - Medical Reviewers in industry and regulatory agencies
  - May also include statistical reviewers/so part of submission package

- Challenges for developers?

- Where/how to share/deliver the tool?

- Need to keep track of recommendations

Tier 1

- Prespecified detailed analysis and hypothesis testing for specific AEs

General Safety Review

Tier 2

- Signal detection among common events. AEs included here are those that do not have a prespecified hypothesis and are 'common'

Tier 3

- Descriptive analysis of infrequent AEs. AEs included here do not have a prespecified hypothesis and are infrequent.

Working Groups

phuse.global

Recap: Strategy/Some Considerations

- Staged development

  o Opted for a staged development approach in terms of functionality focusing on AEs and forest plot

Stage 1: Simple basic plots and interactive features	**Stage 2**: Additional features – still basic, but with more options	**Stage 3**: Include advanced statistical analyses	**Stage 4**: Link to patient profiles and/or Drilldown

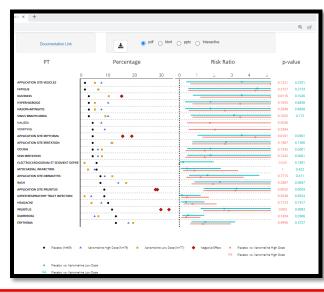 o Team agreed to incorporate volcano plot

Development Stages

Stage 1

- Of note, this stage is:
  - Visual alternative to static pdf tables
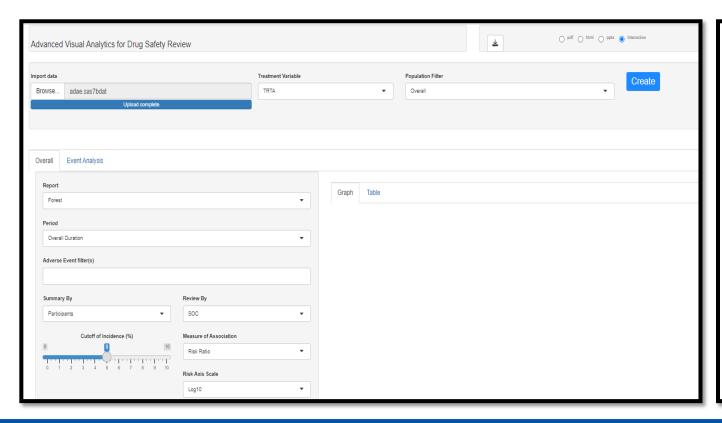 - Limited functionality with regards to a comprehensive/full safety review

PDF

HTML

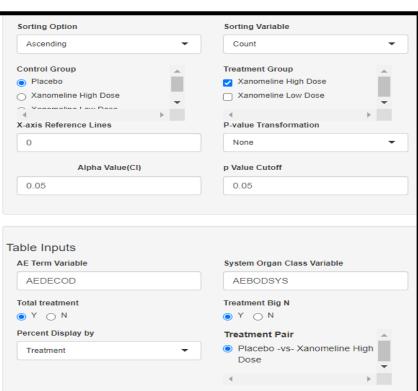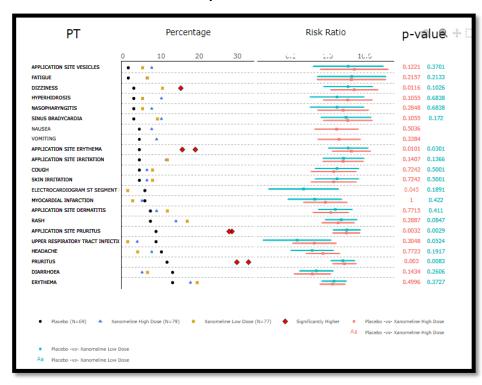# Current Prototype – Forest Plot

Source:

- https://github.com/phuse-org/aesummaries
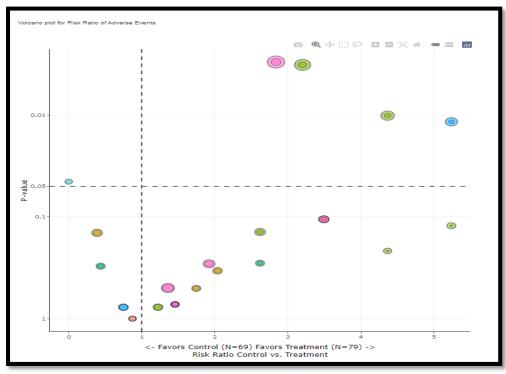- https://phuse-org.shinyapps.io/aesummaries/
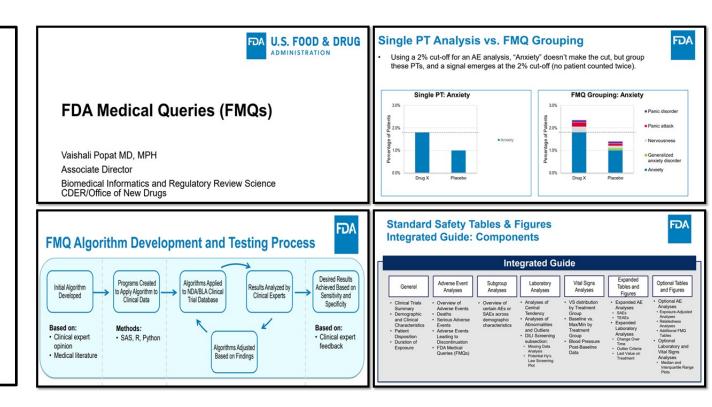
Current Prototype

Forest plot

Forest2023-03-26 (1).html

Volcano plot

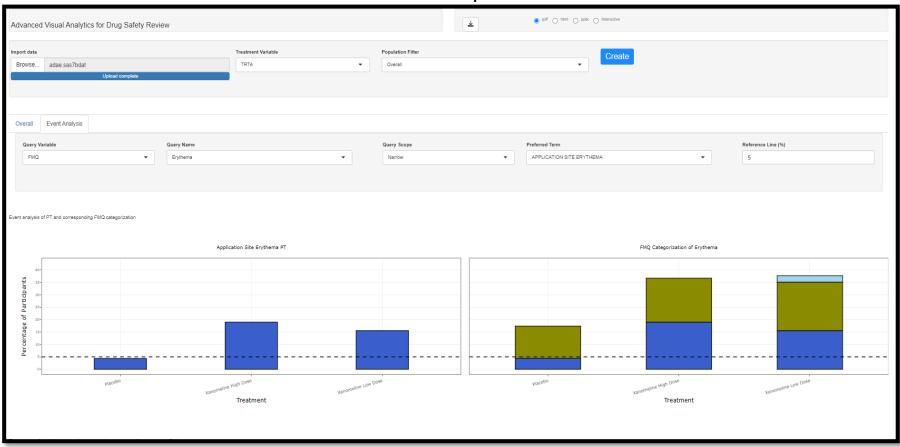Volcano2023-03-26 (1).html

Current Prototype

- **Other considerations**
  - Duke-Margolis FDA Workshop input – FMQs
  - R Markdown template for submission

Current Prototype

Volcano plot

Next Steps

- Complete ascertain of all Stage 1 requirements/additional input
- Take into consideration discussions from Duke-Margolis/FDA Workshop
- Complete Stage 1 tool validation
- Complete guidance documentation for Stage 1
- Continue with the remaining stages

Acknowledgments

- Vipin Arora, Eli Lilly
- Bryant Chen, FDA
- Maya Gans, Atorus
- Jiang Jessica Hu, FDA
- Harivardhan Jampala, Chiltern
- Mary Nilsson, Eli Lilly

- Paula Riley, PHUSE
- Mike Stackhouse, Atorus/PHUSE
- Hanming Tu, Frontage Lab/PHUSE
- Lauren White, PHUSE
- Jeremy Wildfire, Gilead

Working Groups

phuse

phuse.global

The premier community
for people working in the
biometrics area

@phusetwitta
/phusebook
/phusetube
/company/phuse