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CVARS - Transforming Drug Safety Analytics for Enhanced and Comprehensive E2E Review, Analysis, Signal Detection, Reporting, and Regulatory Submissions with the Aid of AI

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Disclaimer

- The discussions and conclusions in this presentation have not been formally disseminated by the US Food and Drug Administration and should not be construed to represent any Agency determination or policy.

Outline

- Introduction & Overview
- Key Considerations & Examples
- Question-Based Approach to Safety Review
- CVARS Approach & Current Capabilities
- CVARS Ongoing/Planned Enhancements
- E2E Safety Review & Signal Detection
- Acknowledgments & Q&A

Introduction and Overview

- Drug safety analysis is complex → data curation, interpretation, reporting challenges
- Collaboration is essential → regulators, sponsors, investigators, safety boards
- Limitations of traditional outputs → static tables = slow review, harder to interpret
- Visual analytics (Forest, Volcano, OCMQs) → faster insights, clearer communication
- Expanding capabilities → AI, GenAI, Bayesian methods, Agent AI

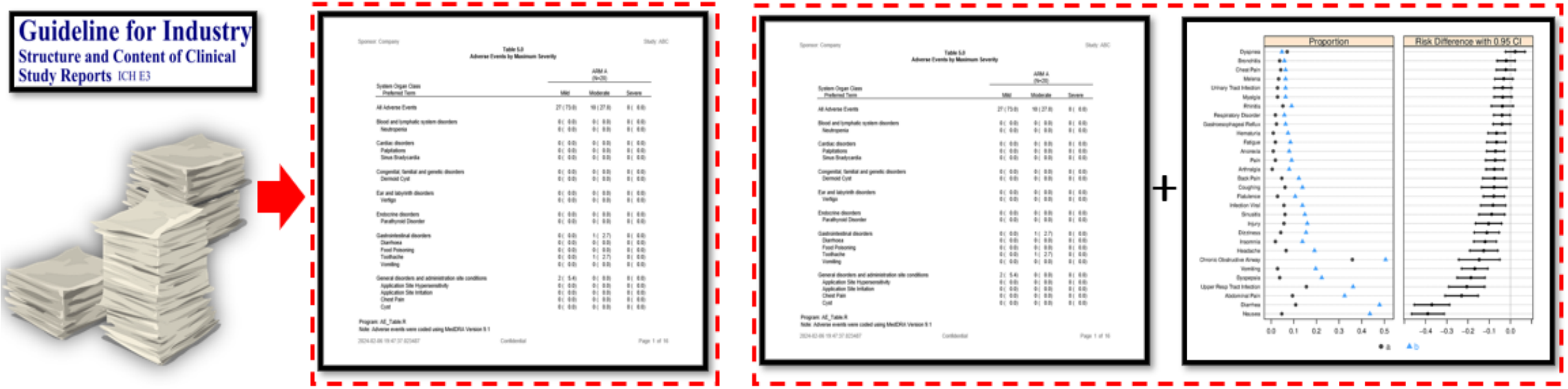
Key Considerations

- Shift focus → from static tables to interactive graphical outputs
- Reduce volume → avoid generating hundreds of PDF tables; prioritize key visuals
- Best practices → adopt structured safety review & signal detection frameworks
- Stakeholder alignment → design outputs for regulators, clinicians, and data monitors
- Regulatory compliance → align with evolving standards (OCMQs, benefit–risk guidance)
- Balanced approach → visuals should enhance, not replace, medical discernment

Example: Shift Focus

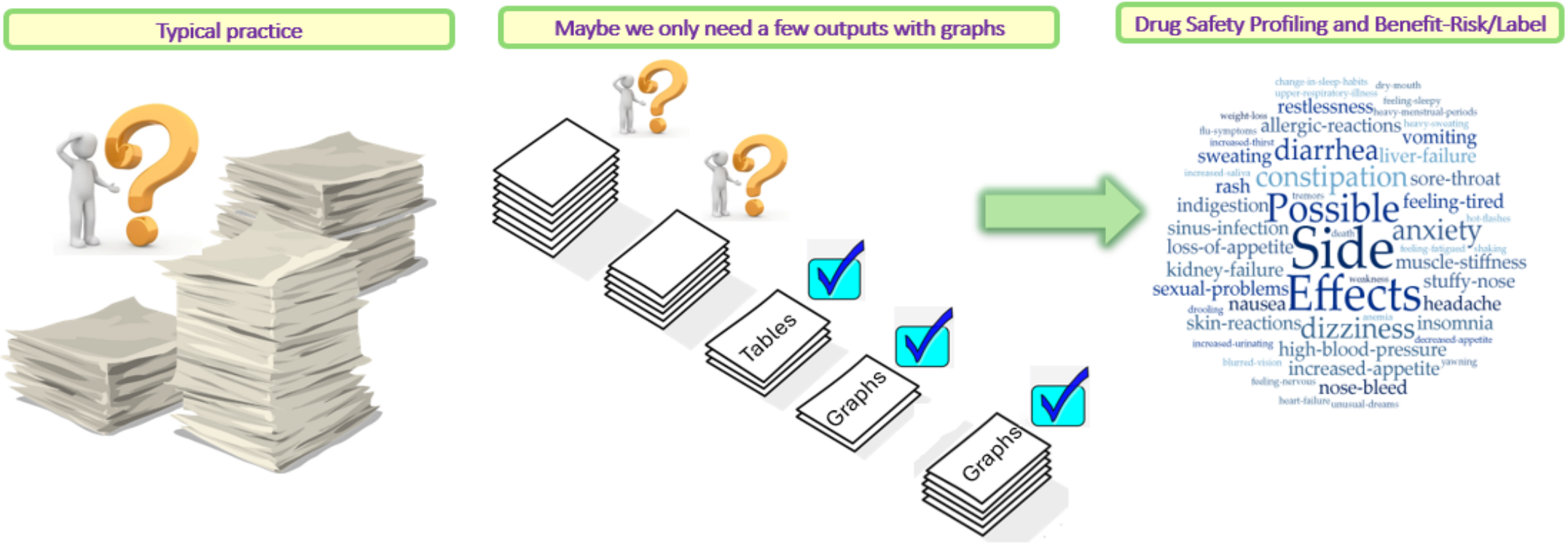
- *Data display is critical to data analysis. Graphs allow us to explore data to see overall patterns and to see detailed behavior; no other approach can compete in revealing the structure of data so thoroughly* - **Cleveland**

Tabular Outputs only versus Tabular Plus Graphical Outputs



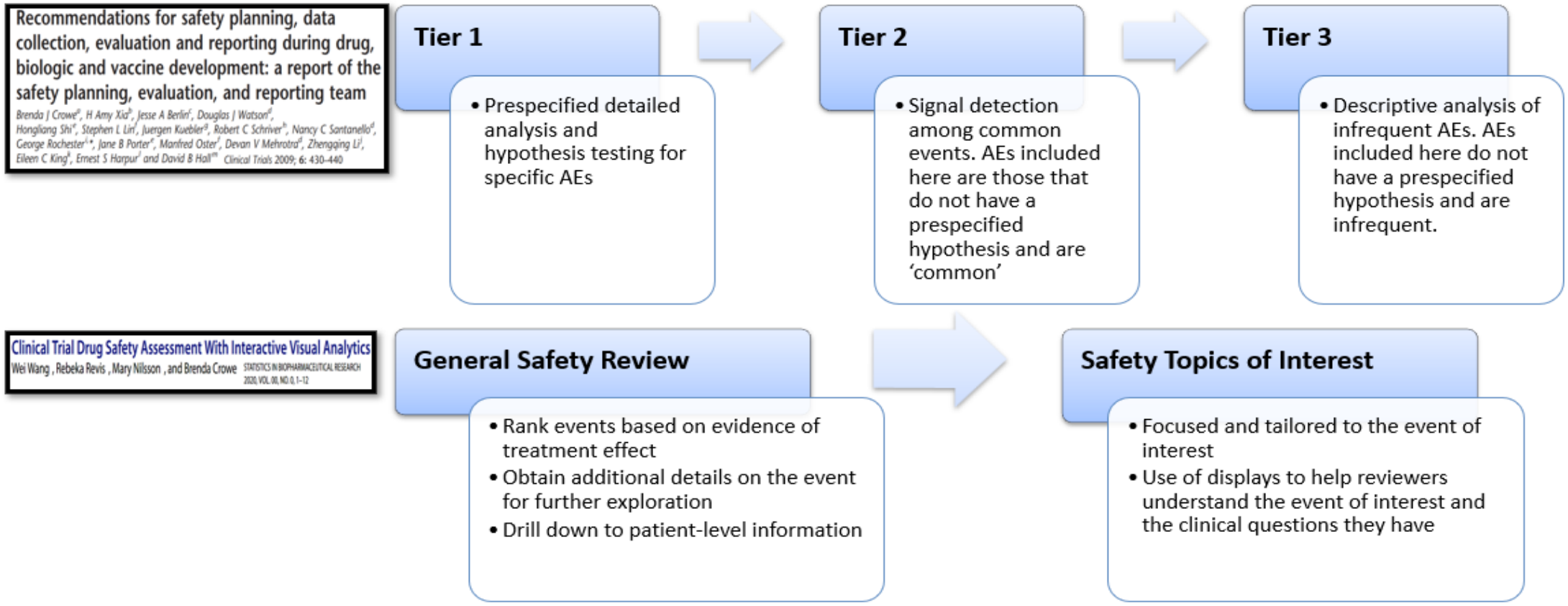
Example: Reduce Volume

- Do we really need hundreds of tables in PDFs?



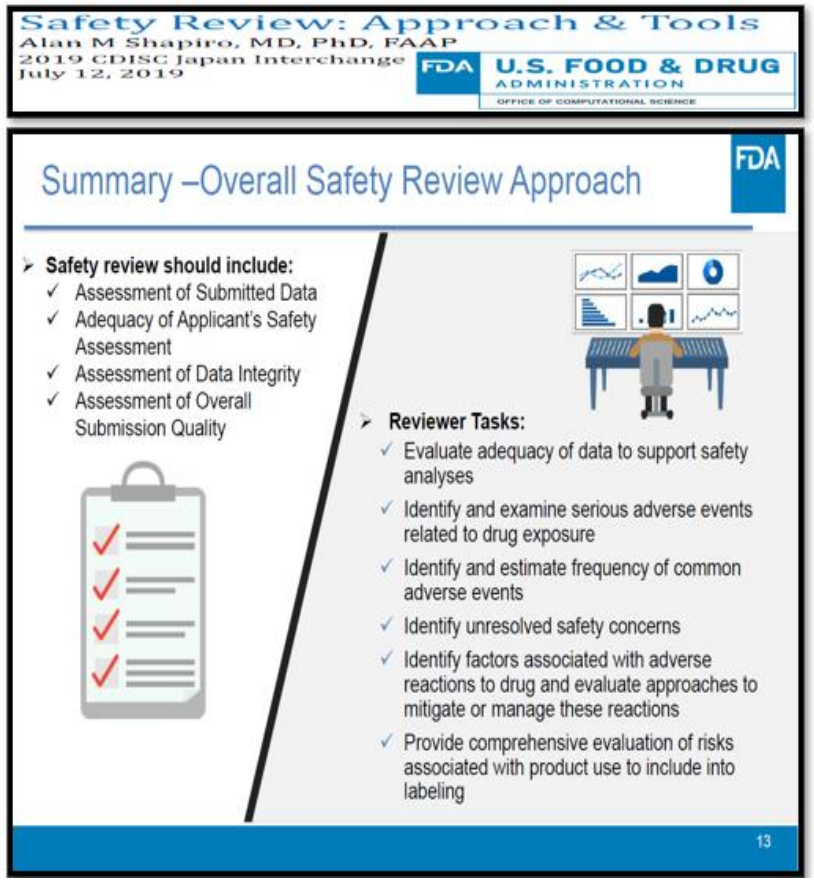
Example: Best Practices in Safety Review

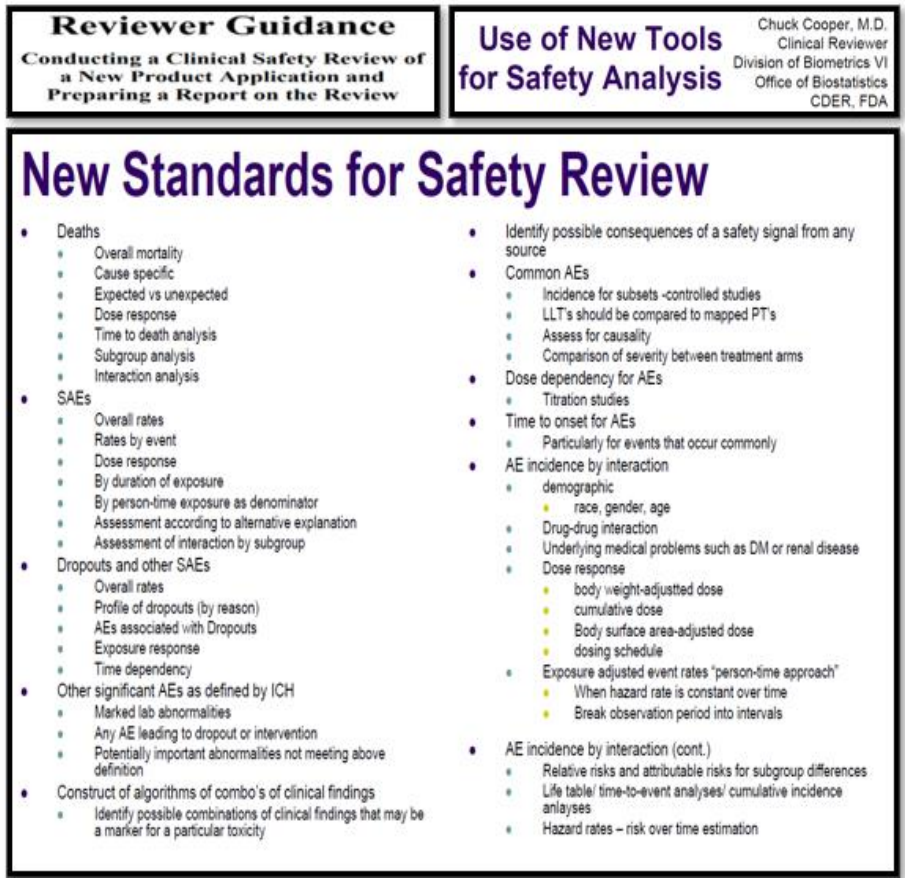
- Ensuring best practices by applying structured safety review and signal detection approaches.



Example: Stakeholder Alignment

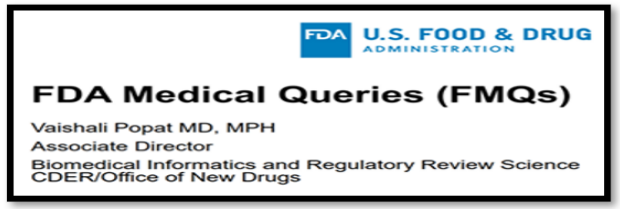
- Regulatory practices and emerging regulatory practice

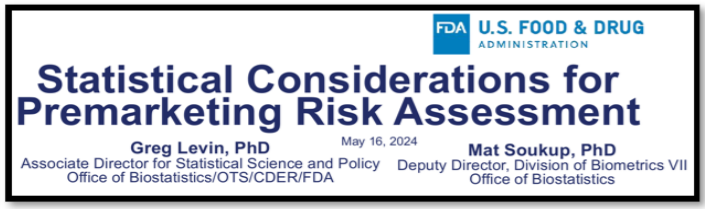


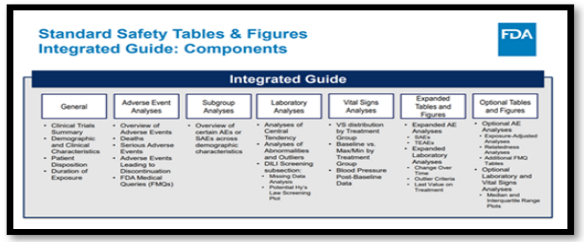


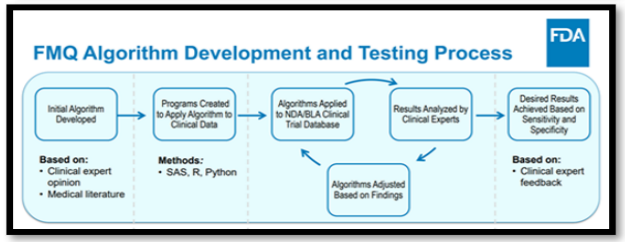
Example: Regulatory Compliance & Balance

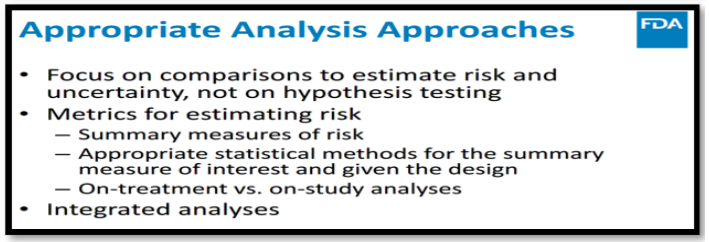
- Regulatory alignment: Evolving practices encourage the use of visuals alongside traditional tables.
- Graphical outputs: Can complement or replace tabular outputs when validated and reproducible.
- Quantitative methods: Bayesian and frequentist approaches to strengthen safety assessments.
- Balanced approach: Ensure outputs remain fit-for-purpose and support structured benefit–risk review.

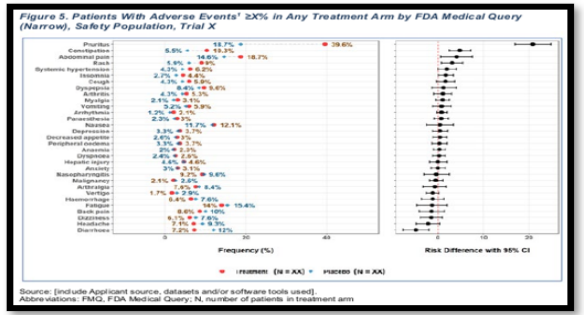


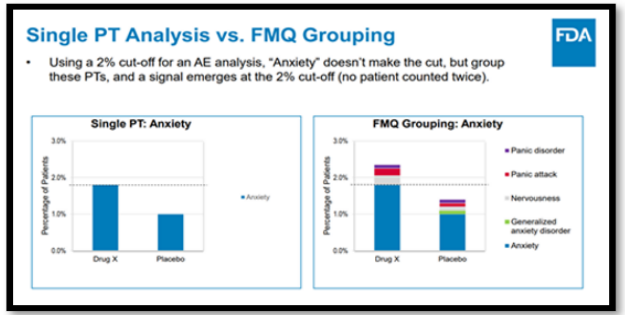


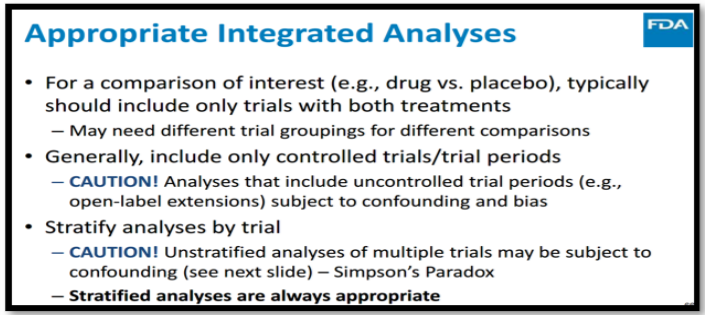






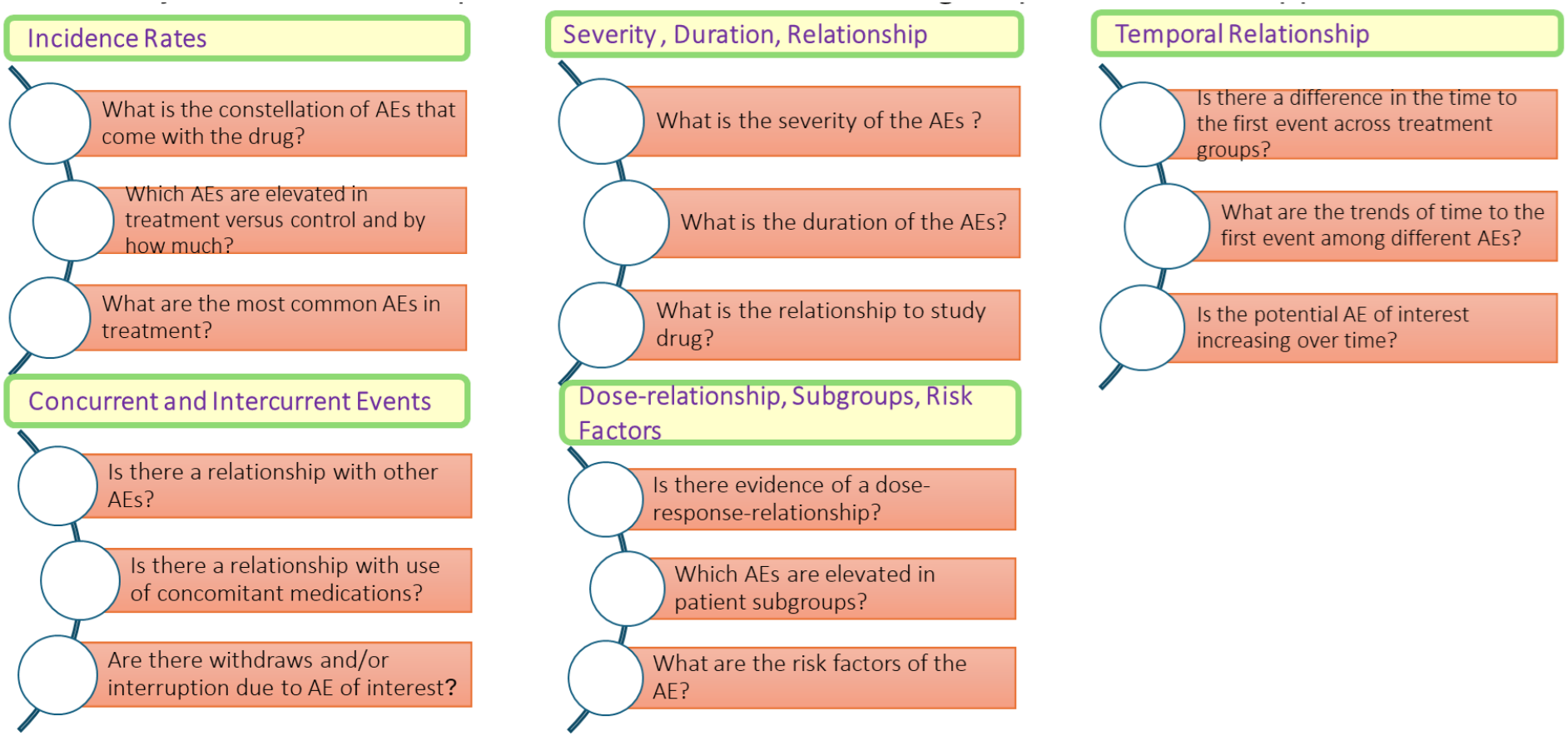






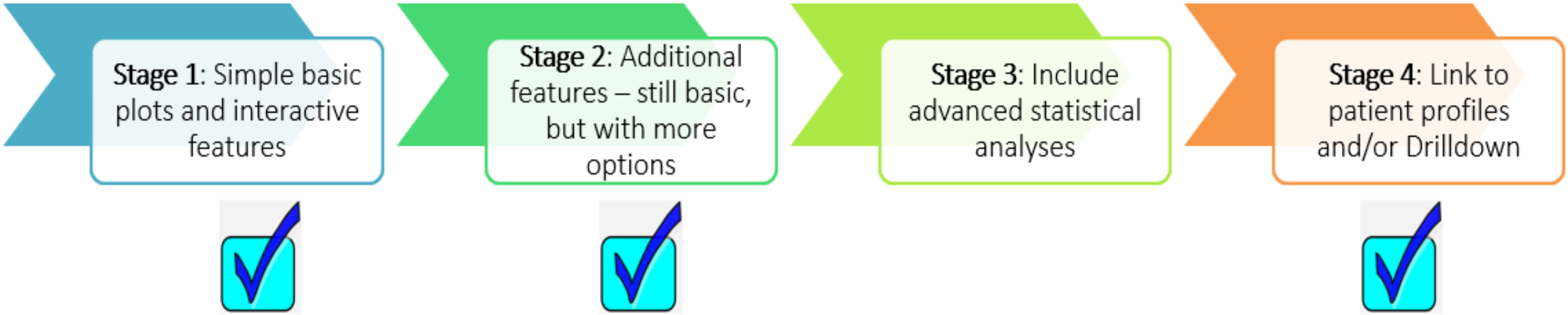
Question-Based Approach to Safety Review

- For example, adverse events



CVARS Staged Development Approach

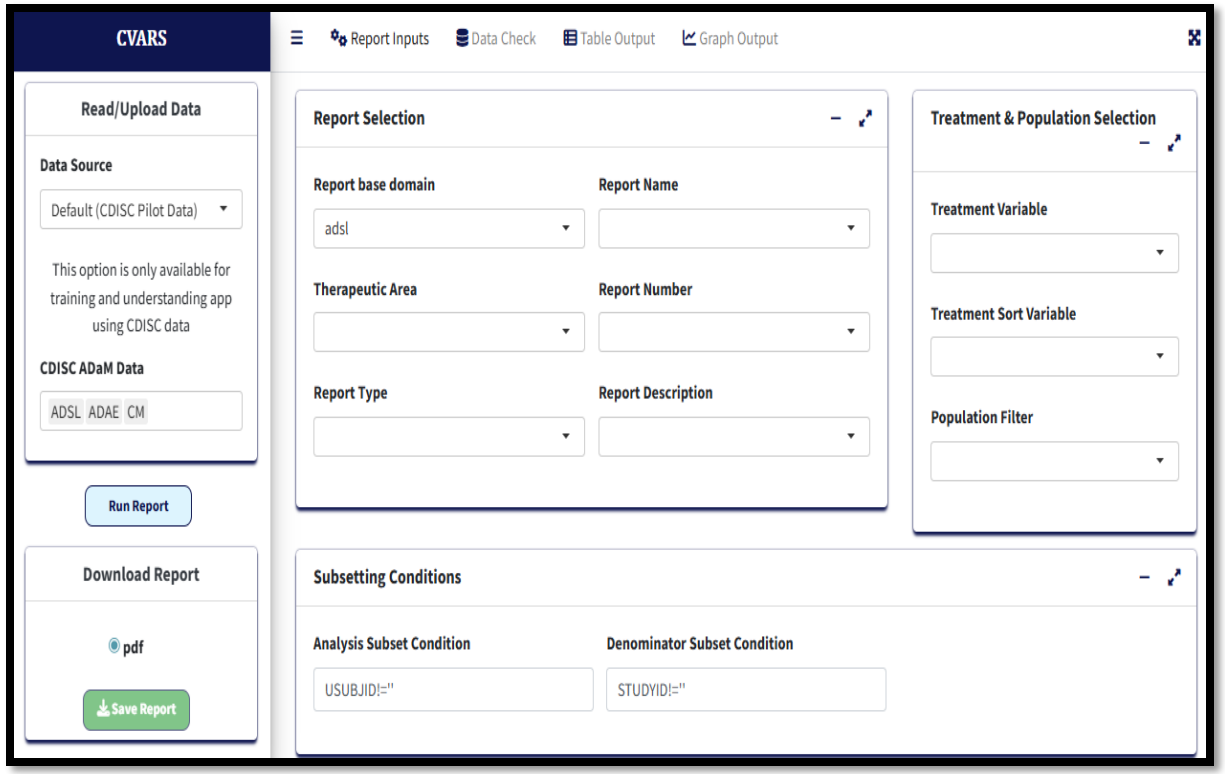
- Planned, stepwise development to ensure regulatory readiness
- Consider functionality, output modality, reproducibility, and stakeholder needs at each stage

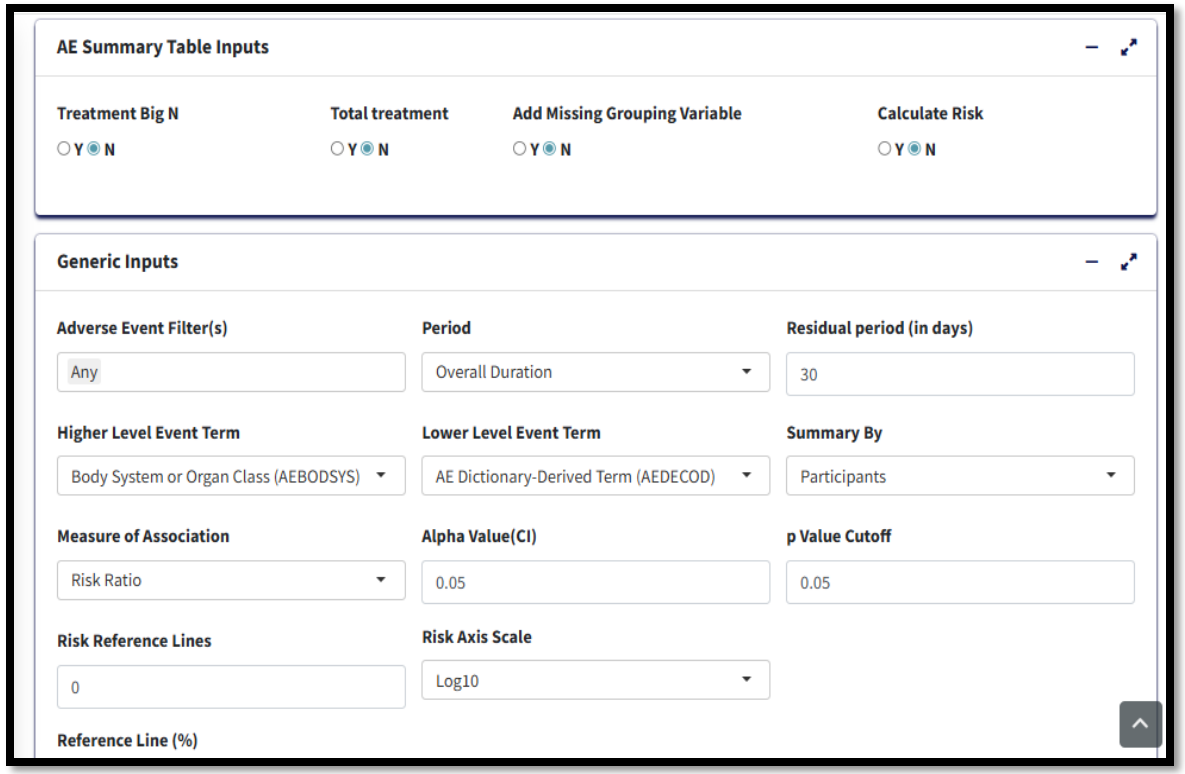


Stage 1: Core plots and basic interactive features
Stage 2: Expanded functionality and visualization options
Stage 3: Integration of advanced statistical analyses (e.g., Bayesian, clustering, subgroup)
Stage 4: Link to patient profiles and drill-down exploration

CVARS Current

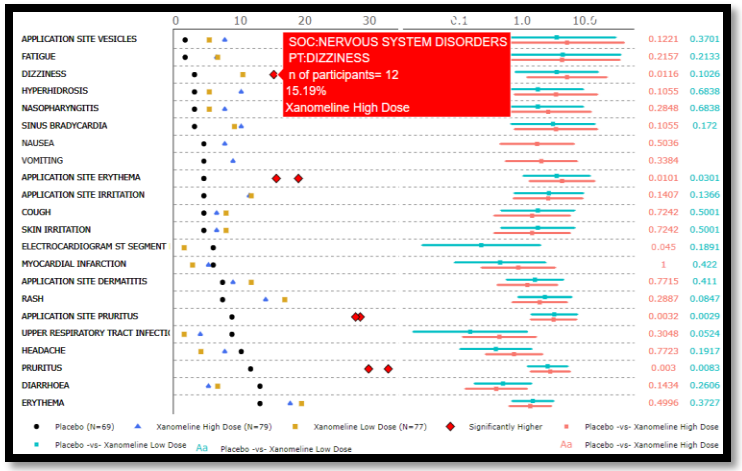
- Current version provides an intuitive interface for data input and configuration
- Supports upload, report generation, and customizable filters
- Output available in tabular/graphical formats, exportable to HTML, PDF, DOCX, PPTX

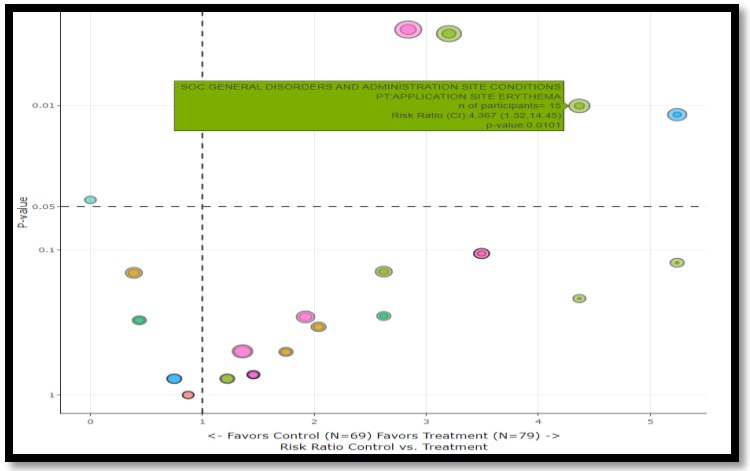




CVARS Current

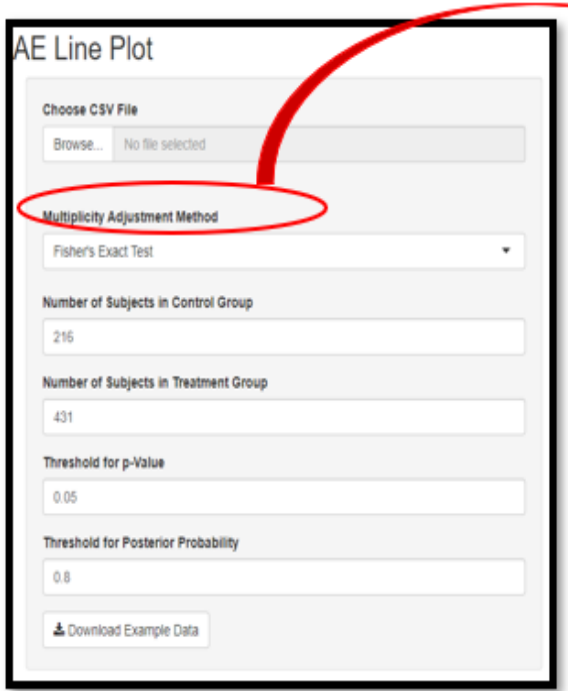
- Current version – forest plots, volcano plots, FMQs(*OCMQs), tabular output, patient profiles, listings

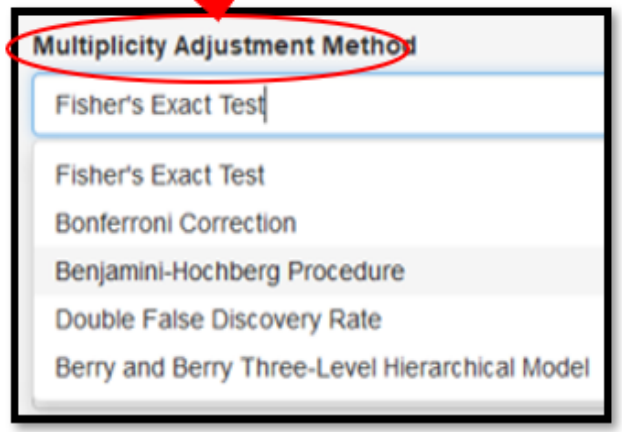


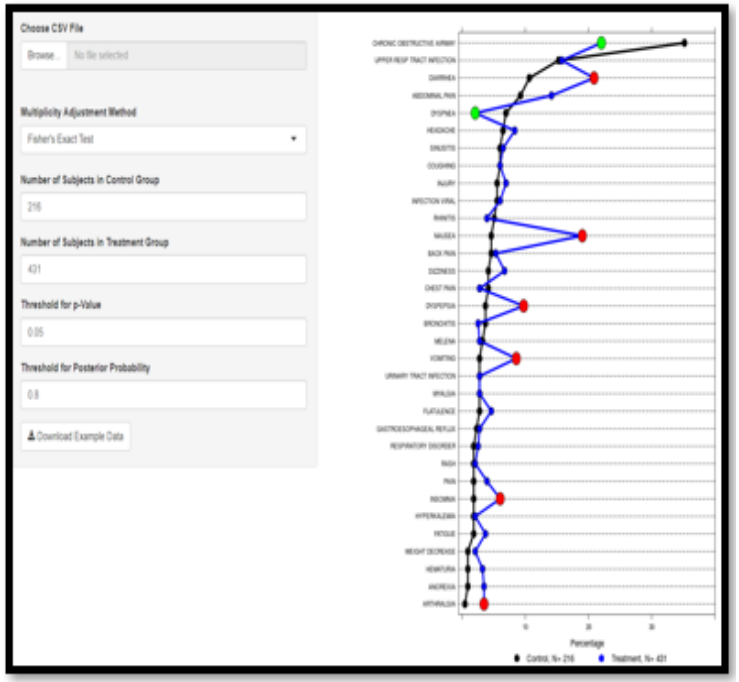


CVARS Ongoing/Planned Enhancements

- Advanced analytics: Bayesian methods for signal detection, Clustering & subgroup exploration, Dose–response and time-to-event modeling

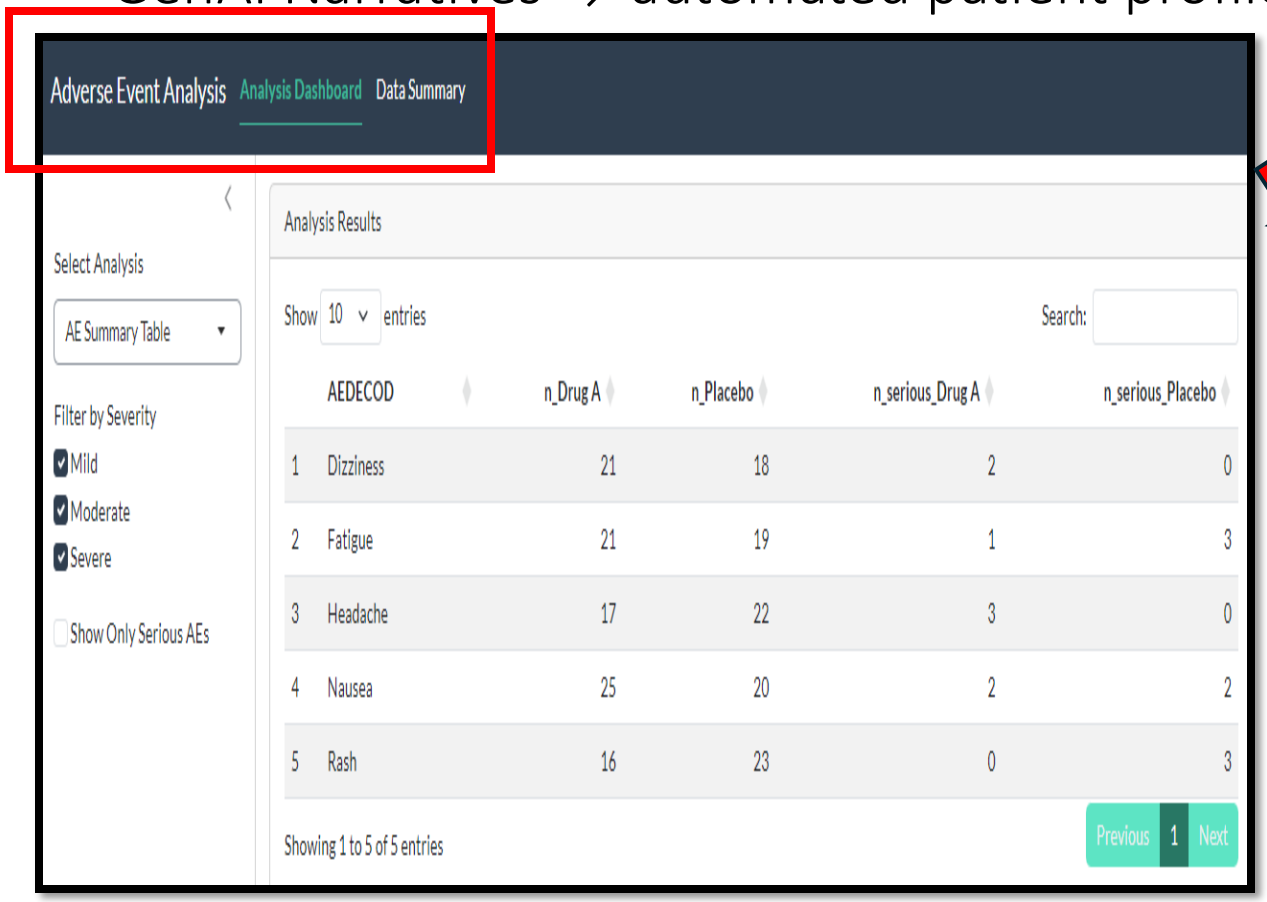


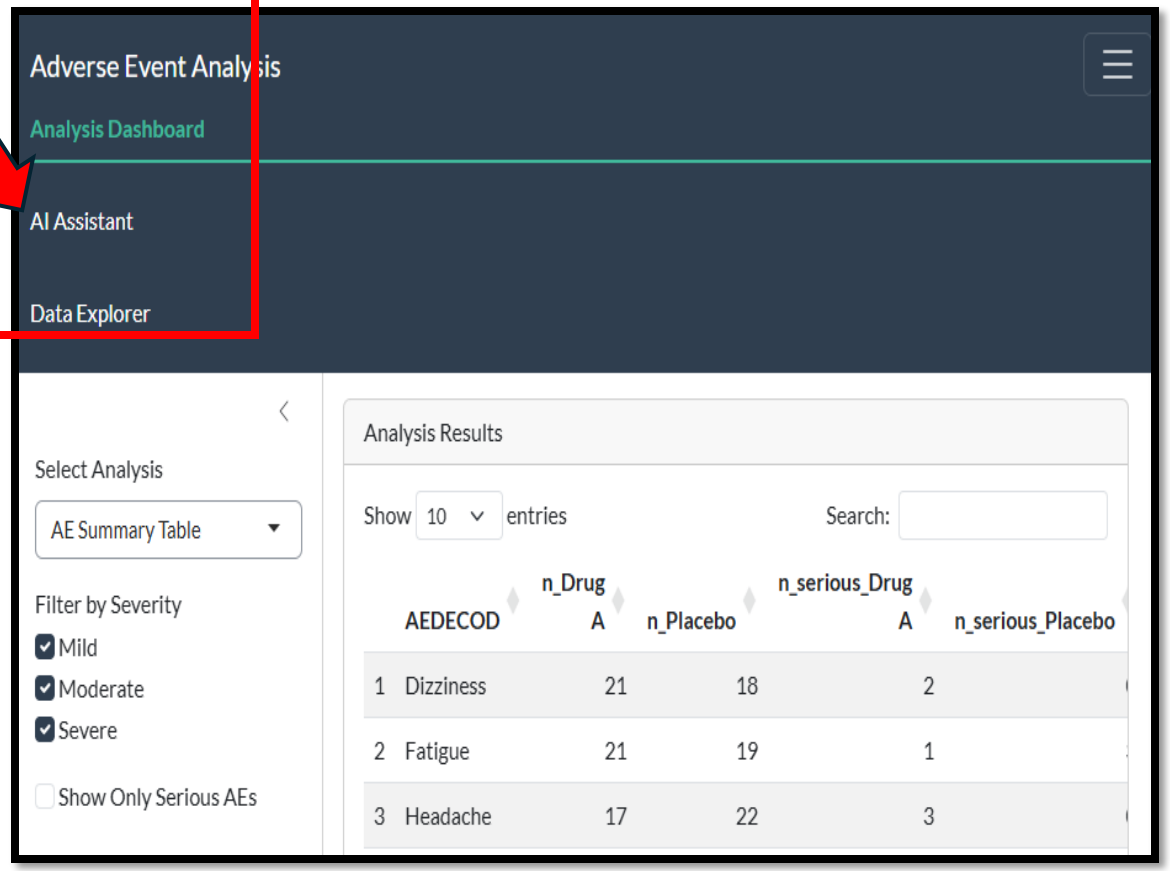




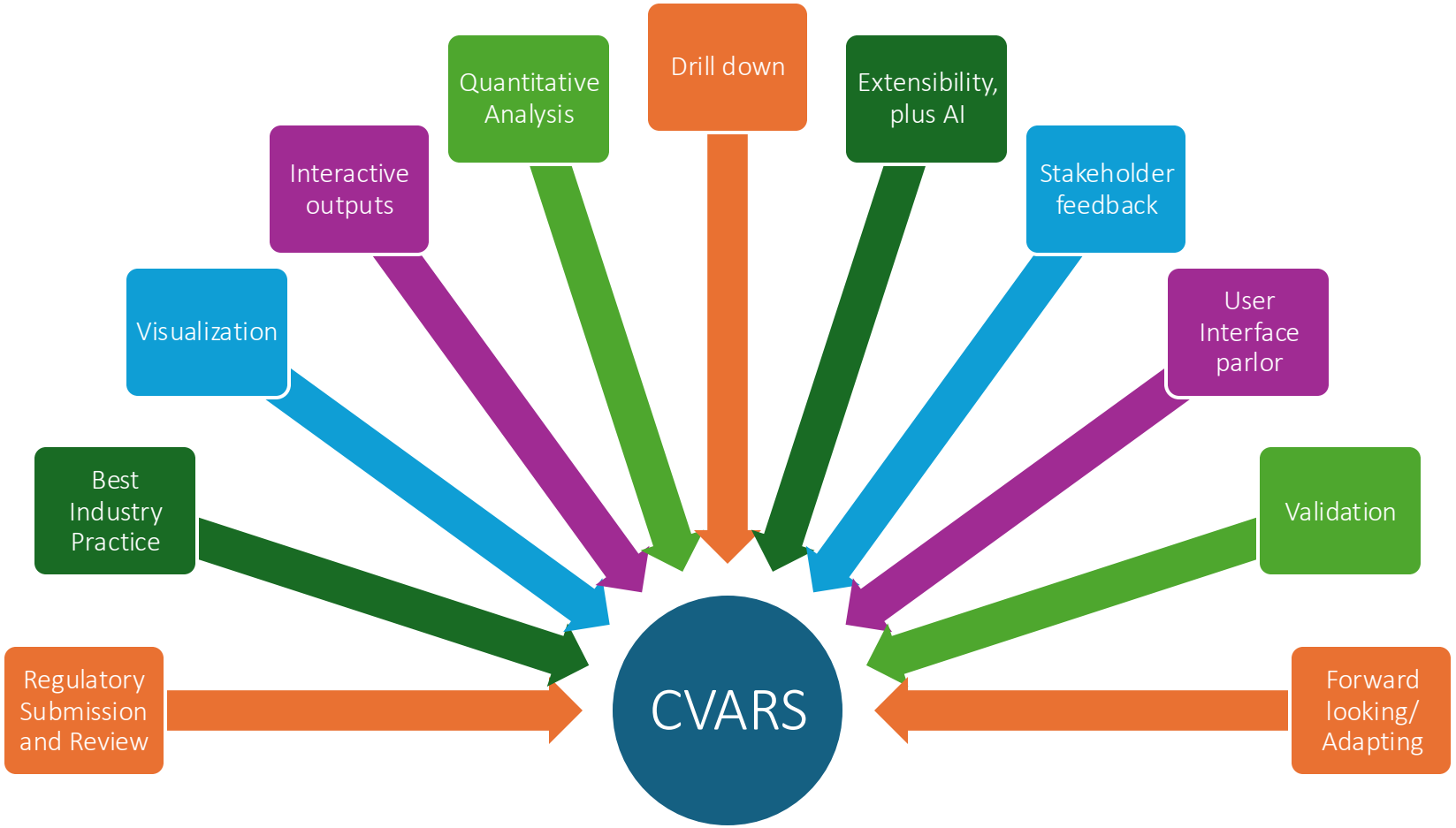
CVARS Ongoing/Planned Enhancements

- AI Assistant → query interface for rapid review ("Which AEs are elevated in old patients?")
- Data Explorer → drill-down by population, treatment arm, or severity
- GenAI Narratives → automated patient profiles and benefit–risk summaries





CVARS Ongoing/Planned Enhancements



E2E Safety Review and Signal Detection

- Data Ingestion & Preparation
  - LLMs for data pipelines, Automated lineage, consistency checks, and audit trails
- Core Safety Analytics
  - Expanded visual analytics, Interactive Outputs, reproducible, submission-ready
- Signal Detection & Advanced Methods
  - Bayesian signal detection, Clustering & subgroup exploration, Dose–response and time-to-event modeling
- AI/GenAI-Enabled Interpretation
  - GenAI support → narrative interpretation, AI assistant → reviewer Q&A
- Regulatory Alignment & Continuous Improvement
  - Adaptation to OCMQs & benefit–risk frameworks
  - Continuous stakeholder input from regulators & clinicians

Executive Summary

- CVARS modernizes drug-safety analytics by coupling standardized tables, interactive, question-led visualizations.
- Expanded capabilities include additional core safety plots, OCMQs, and patient-profile views, supported by robust multi-format export.
- The roadmap adds Bayesian signal detection, advanced subgrouping, dose–response and time-to-event modeling, and AI/GenAI features for reviewer Q&A and narrative generation.
- Across all releases, CVARS prioritizes regulatory alignment, reproducibility, and stakeholder usability to accelerate insight while preserving clinical judgment.

Result: Faster reviews, Clearer signals, and Stronger, Submission-ready outputs.

Acknowledgments & Q&A

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