

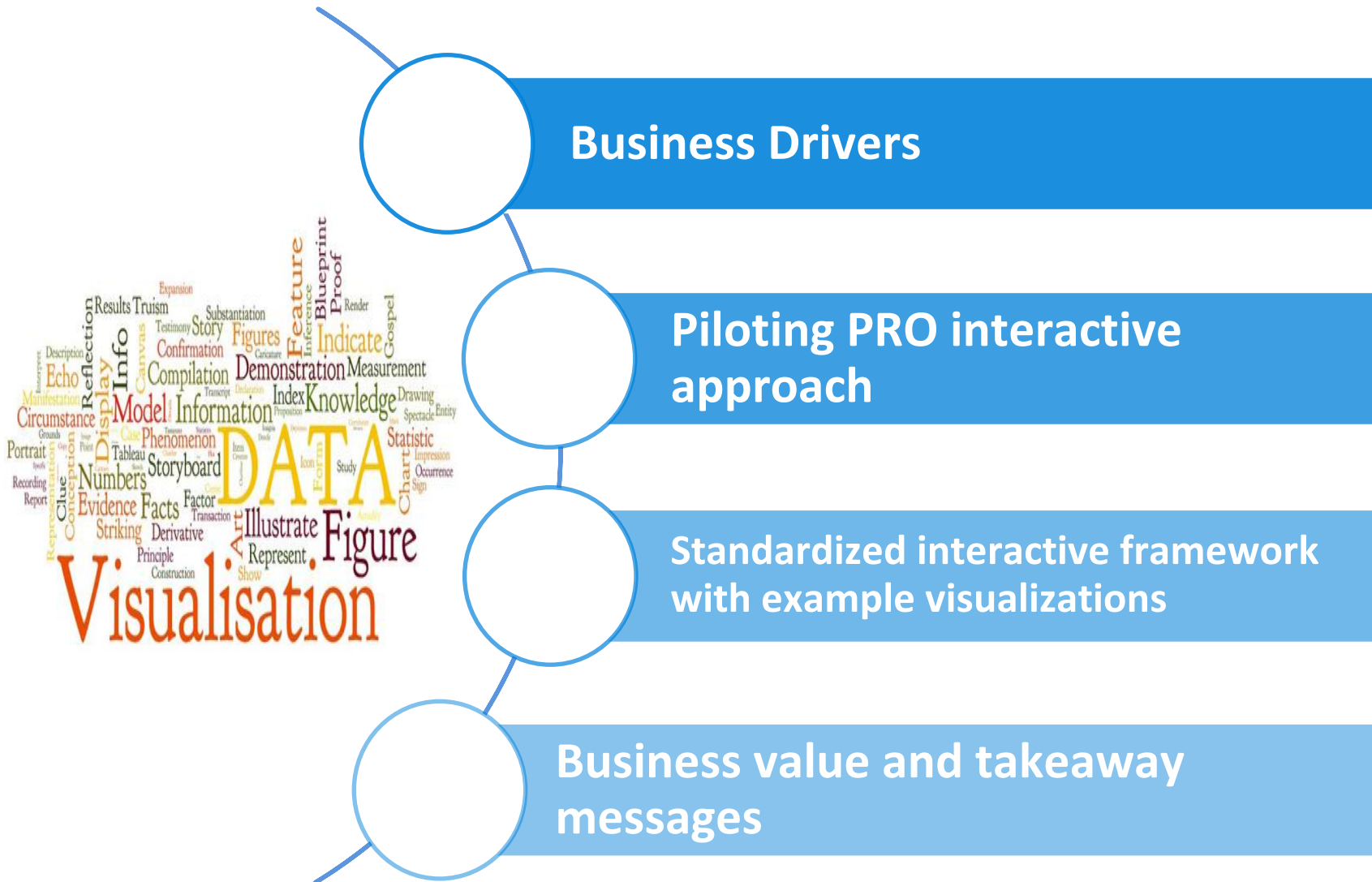
Optimizing PRO Data Analysis with Interactive Approach

PhUSE US Connect 2019

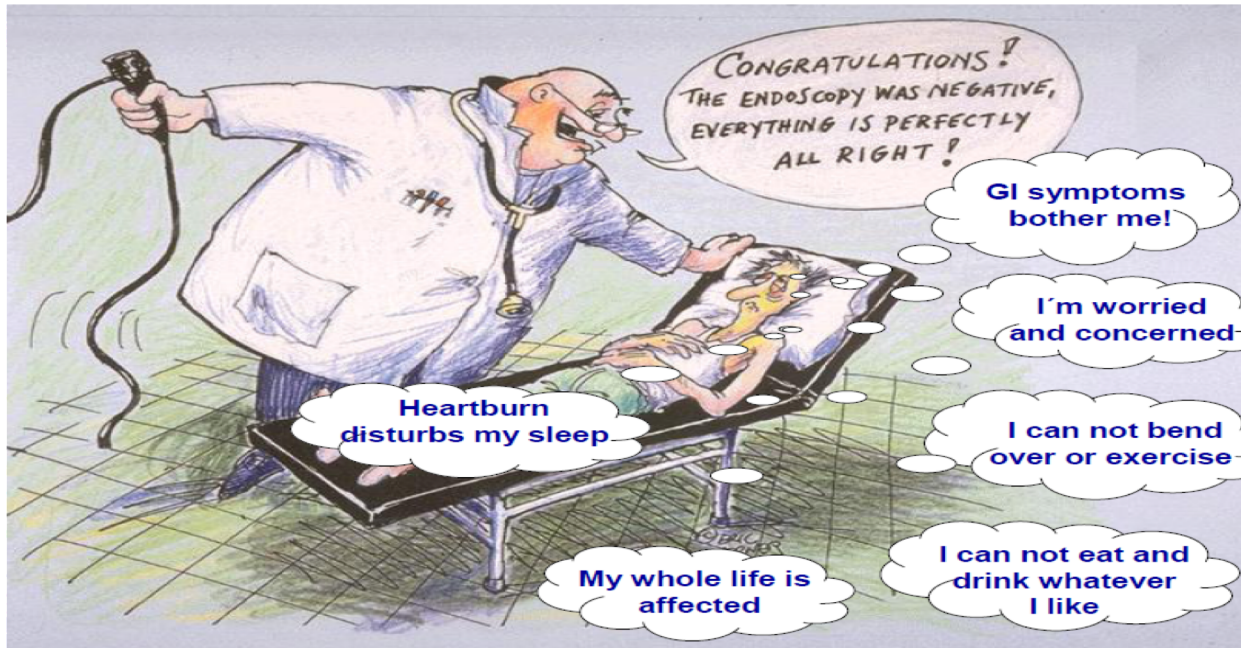
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Agenda



Patient Reported Outcomes



- Patient-reported outcomes provide information on symptoms, health related quality of life, for instance.
- This information often cannot be otherwise measured.

Collection of PRO Data



EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a <u>long</u> walk?	1	2	3	4
3. Do you have any trouble taking a <u>short</u> walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

- Generate **wealth** of information
 - Numerous individual scale scores
 - Standardized analytical approaches
 - Descriptive longitudinal analyses
 - Descriptive cross-sectional analyses
 - Inferential analyses

Business Drivers

Patient-focused drug development

- PRO data are **increasingly** used for decision making by Regulators, Payers, Clinicians and Patients
- PRO endpoints are secondary and exploratory to **complement** traditional endpoints

Acceleration of drug development

- **Resource constraints** → Prioritize output generation for key endpoints (OS, PFS, safety)
- **Faster** → Reduced timelines between database lock to filing of treatment benefit evidence

Imperative need to find new ways of delivering large volumes of outputs for increased efficiency and improved quality of the evidence interpretation

Interactive Analysis Apps for PRO Data



Scope

- User-friendly visualization interface
- Access to patient level data



Analyses per SAP specifications

- Patient disposition
- Completion compliance
- Longitudinal score changes
- Proportion of patients



- Interactive inferential analyses leveraging R suite
- Longitudinal analyses (e.g., mixed model)
- Time to event analyses
- Cross-sectional analyses



Interactive analyses

Opportunities to run the analyses for:

- Every scale scores generated by the PRO questionnaire
- Subgroups/Segmentation (demographics, clinicals, populations)
- Different analytical variables (e.g., MID)

PRO Interactive Tool: Cover Page

Protocol: GOnnnnn

Reporting Event: *Support PRO exploratory analysis*

Extraction Date: *07 Mar 2018*

Clinical Data Cutoff Date: *22 Jan 2018*

Data location: *\$PROD/xxxxx/libraries*

Study Status:

Created by: *XYZ*

Created date: *2/26/2018*

Version #: *v1.0*

Modified Date: *5/15/2018*

Spotfire Version: *7.7*

DISCLAIMER

This visualization package is developed to support internal data review and exploratory analysis to help inform PRO strategy. **Please work with**

Table of Contents

Analysis Type	Summary Tables/Plots
Instruction + Key Filters	Key Filters, Instructions and Bookmarks
Study Data Overview + demog	Study Data Overview Demog Summary
PRO Compliance	Compliance Rate for EORTC QLQ-C30 V3 Compliance Rate for EORTC QLQ-LC13 Compliance Rate for SILC Questionnaire Disposition Rate for EORTC QLQ-C30 V3
Summary Tables/Plot	Mean Plot of QS Score for EORTC QLQ-C30 v3 Mean Plot of QS Score Change from Baseline for EORTC QLQ-C30 v3 Mean Plot of QS Score for EORTC QLQ-LC13 Mean Plot of QS Score Change from Baseline for EORTC QLQ-LC13 Mean Plot of QS Score for SILC Mean Plot of QS Score Change from Baseline for SILC
Clinically Meaningful Changes	EORTC QLQ-C30 v3: Clinically Meaningful Changes EORTC QLQ-LC13: Clinically Meaningful Changes SILC: Clinically Meaningful Changes
Time to Deterioration	TTD Barchart
Spaghetti Plot and listings	Spaghetti Plot of QS Score Listing: PRO Questionnaire Listing: Demog
Documentation:	PRO variable derivation spec Validation Tracking Version History

Online 179 of 200 rows

- 1 Provides **traceability** information such as purpose of the deliverable, source data location, data cutoff date, versions of software and application.
- 2 Provide an overview with **table of contents** with dynamic link to the visualization page

Primary Setup, Business Rules, and Bookmarks

The screenshot displays a web application interface with three main sections highlighted by numbered callouts:

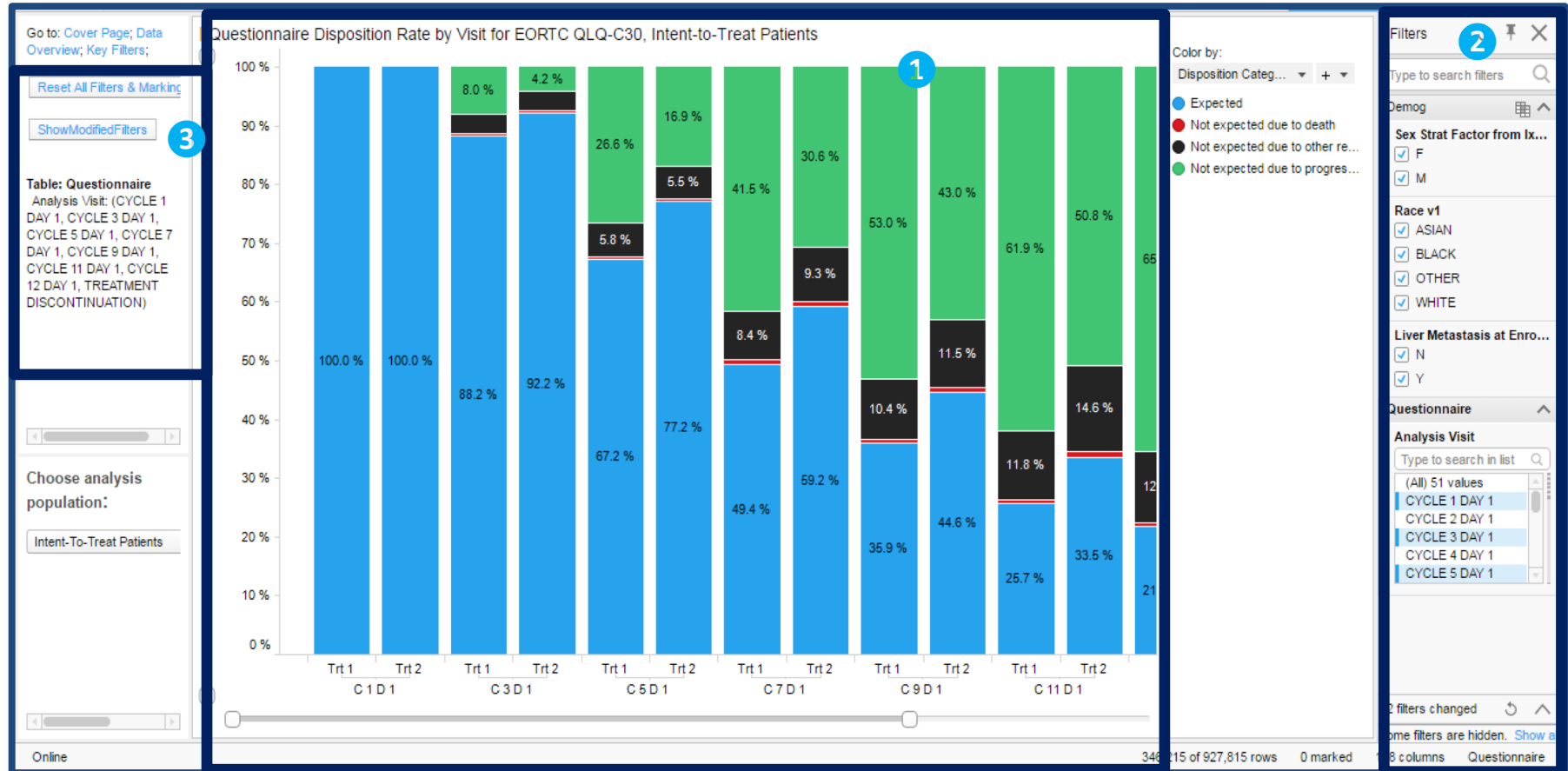
- 1. Configuration:** Located at the top right, it includes dropdown menus for "Choose grouping variable:" (set to "Description of Planned Arm v1") and "Choose analysis population:" (set to "Intent-to-Treat Patients").
- 2. Documentation:** A central panel containing instructions for webplayer users, such as "Filters: All filters are located on the right panel," and "Business Rules" which define terms like "Intent-to-treat patients" and "PRO-Evaluable" patients. It also lists specific rules for "Compliance Rate" and "Clinically Meaningful Changes".
- 3. Bookmarks:** A sidebar on the left titled "Bookmarks" with a "New bookmark name" input field. It lists several saved analysis results, each with a brief description and a date, such as "Summary of Patients Who Improved, Worsened, or Remained Stable by Scale of the SILC from Baseline, PRO-Evaluable for SILC" dated 4/8/2018.

1 Central configuration to offer flexibility in choosing analysis population (eg. Intent-to-treat patients, safety evaluable patients) and grouping variables (treatment, race) for summary results

2 Documentation helps users with instructions and understanding of business rules embedded in visualization results

3 Bookmarks link to saved analysis results

Questionnaire Disposition Rate

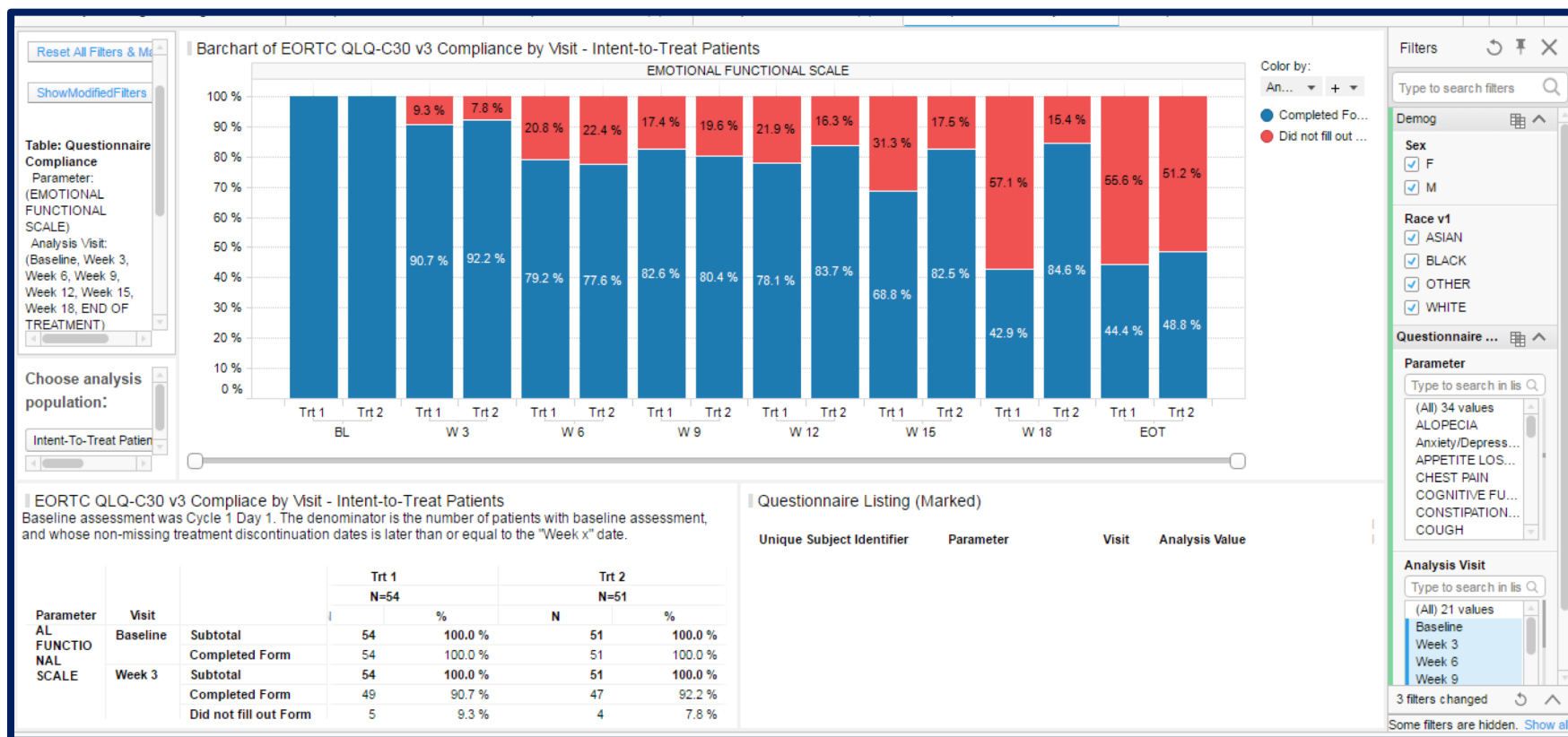


① % Stacked bar chart shows a good overview of patient disposition by treatment per scheduled assessment s

② Filter options for sub-group analysis

③ ShowModifiedFilters command reveals filters used for underlying data for accurate interpretation : while Reset Filters and Marking command brings it back to default

Questionnaire Completion Rate

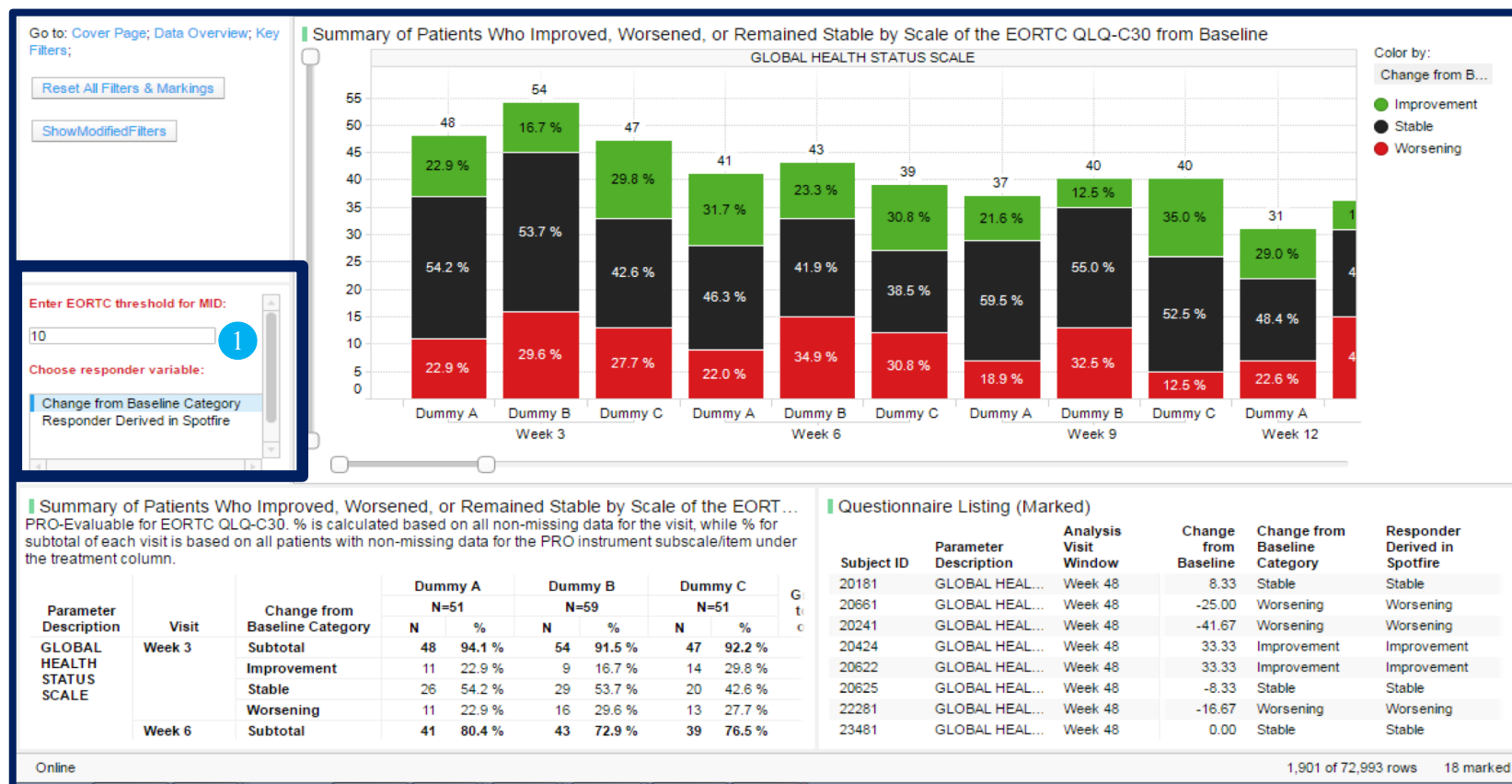


Mean Line Plot of Longitudinal Score Change



- 1 Summary table has the **same analysis results as CSR output**
- 2 Graphic display of Mean $\pm$ SE can help **easily identify data trend** and be used for publication /conference
- 3 Marking data points for **patient-level data review**

Proportion of Patients with Clinical Meaningful Change



1 Dynamic calculation of PRO response to support sensitivity analysis

Inferential: Time to Event

Analysis data: AQSTE

Select Endpoint

COMPSYMP - Time to Confirmed Deterioration of 3-Symptom Composite

ARM

ARM1_s

Reference Group

Control

Multiple reference groups are automatically combined into a single group.

Comparison Group

Active

☐ Combine all comparison groups?

Stratify by

from ASL

TCICLV2 STRATM1

Time Points

6 12

Show R Code

ASL.ITTWTFL remove

☒ Y

☐ N

Add Filter Variables

ASL

AQSTE

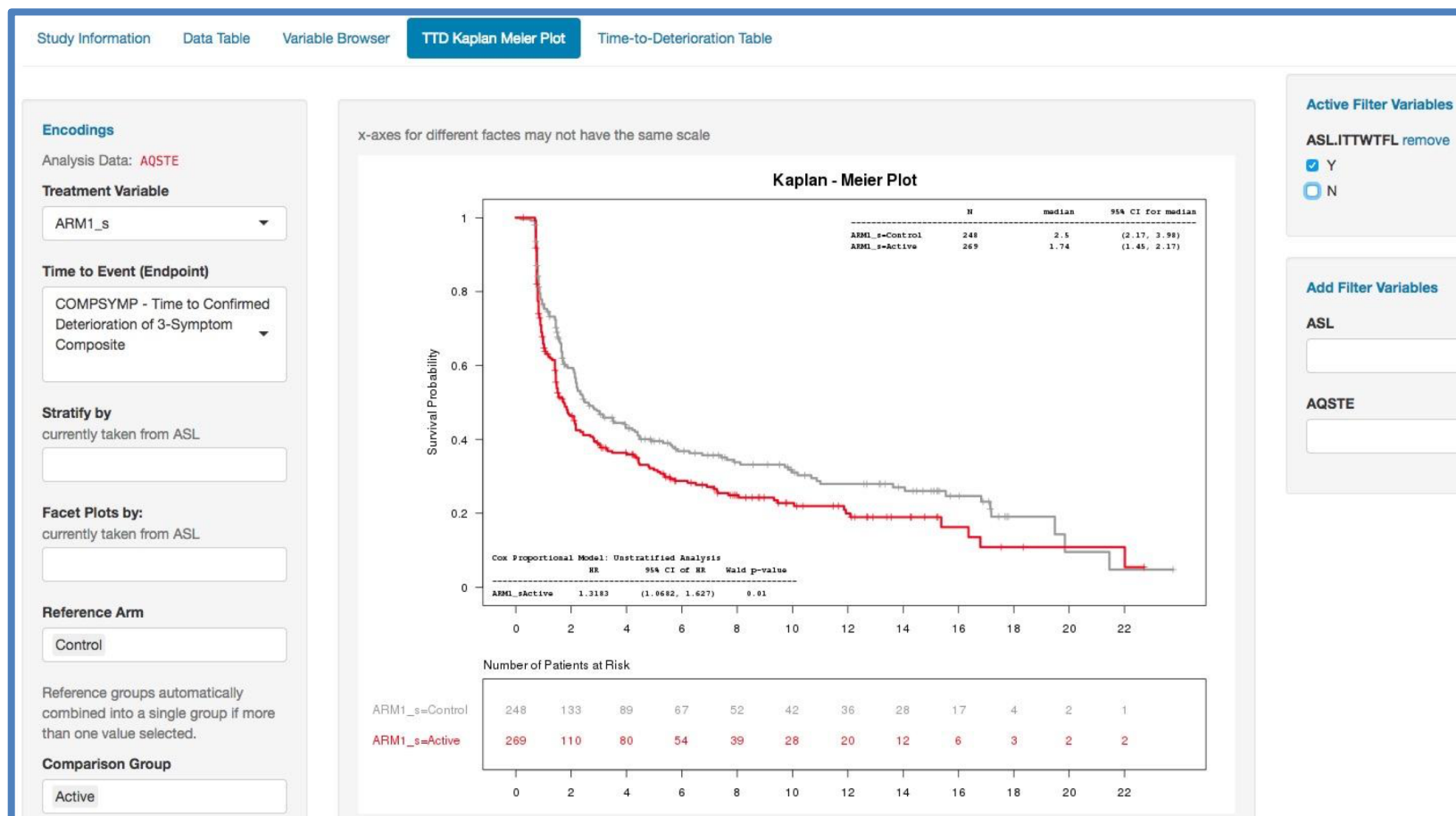
	Control (N=248)	Active (N=269)
Patients with event (%)	167 (67.34%)	195 (72.49%)
Earliest Contributing Event		
3-SYMPTOM COMPOSITE	167	195
Patients without event (%)	81 (32.66%)	74 (27.51%)
Time to Event (monthss)		
Median	2.5	1.74
95% CI	(2.2, 4)	(1.4, 2.2)
25% and 75%-ile	1.1, 15.5	0.8, 7.7
Unstratified Analysis		
p-value (log-rank)		0.0098
Hazard Ratio		1.3183
95% CI		(1.0682, 1.627)
Stratified Analysis		
p-value (log-rank)		0.0111
Hazard Ratio		1.3123
95% CI		(1.0633, 1.6195)
Time Point Analysis		
6 monthss		
Patients remaining at risk	67	54
Event Free Rate (%)	36.84%	28.78%

1 Customization & Modularity: tailor study specific analyses with modular approach and custom R code

2 Variable based filters

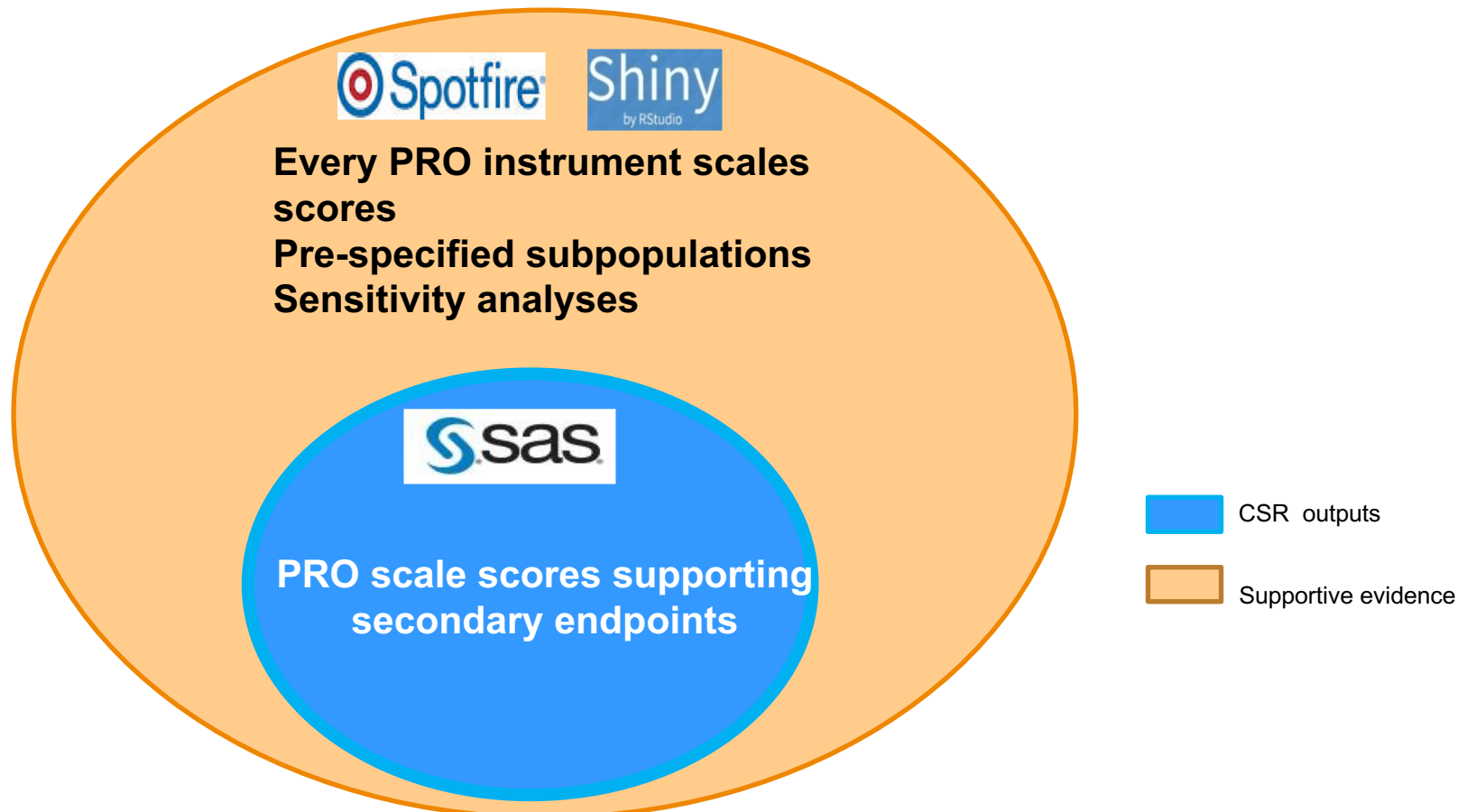
3 Reproducibility: R-code generation for displayed output

Inferential: Time to Event (cont'd)



Successful Pilot

- User friendly interface empowers PRO scientist to explore the data independently
- Comprehensive assessments of PRO data



Interactive Standardized Framework

EARLY Integration of interactive applications as part of the data analysis flow



Standardize:

PRO ADaM datasets
Interactive templates



Training

To avoid scope creep
To show-case robustness of the outputs

Business Value Highlights

Speed



Facilitate **timely and comprehensive interpretation** of PRO data

- Access to patient-level data
- Efficient identification of trends and outliers
- Enhanced data visualization capabilities for presentation / conference

Agility



Preliminary investigation of exploratory questions prior to requesting outputs

- Prioritization of analyses
- Limit post hoc analyses requests
- Inform development of evidence- and experience-based PRO endpoints for use in other programs (e.g., ph2 data inform ph3 endpoints)
- Support sensitivity analysis for HA and HTA

Efficiency



Initial learning curve and thus increase in resource needs, but ultimately, **minimized burden on Programming and PRO scientists**

Key Takeaway

- **Active collaboration** between PRO scientists and Programming analysts needed to frontload a comprehensive strategy to analyze PRO data
 - Format dataset
 - Format interactive application interface
- Use of interactive applications is a **fit for purpose solution** for efficient delivery of large volume data
 - Multidimensional scales
 - Standardized analytical approach
- User-friendly interface for data visualization enables **comprehensive** result review and interpretation
- Mindset shift needed to fully leverage the application:
 - **Plan smart**
 - **Start early**

Q&A

Genentech



***Doing now what patients need
next***