

Optimizing PRO Data Analysis with Interactive Approach

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Business drivers

Patient-focused drug development

- FDA guidance on the use of PROs in support of medical product labeling claim
- Increased attention on patient experience on treatment tolerability

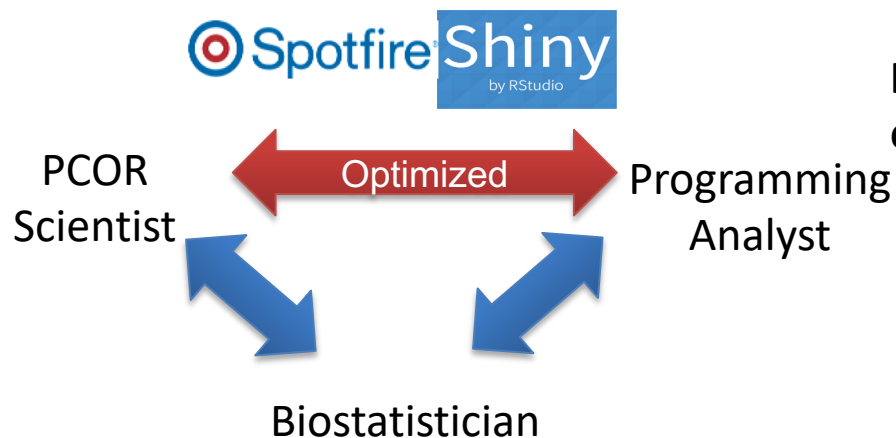
Imperative need for new way of working

- Resource prioritized for key endpoints (such as OS, PFS, ORR for oncology trials, and safety)
- PRO endpoints are secondary and exploratory; outputs often limited to standard CSR outputs
- Company striving for faster timelines between database lock to filing of treatment benefit evidence

Understand PRO data and analysis

- **PRO endpoints:** describing patient's experience while on treatment
 - Symptomatic adverse events and tolerability
 - Physical function
 - Disease-related symptoms
- **Complexity of PRO data by nature**
 - Instruments associated with different disease / indication
 - Various rating scales
 - Various scoring methods (eg. simple one-item score, composite of several multiple-item scores, or one single summary score)
 - Large volume with same analysis for different questions / items (i.e., parameters)

Piloting PRO Interactive Analyses



Early collaboration to optimize use of data visualization to supplement PRO outputs and strengthen data interpretation

Key learning from pilot experience:

- Positive feedback from PRO scientists
- Main challenge lies in analysis data standardization and readiness
- Require mindset shift in supporting use of interactive tools

Interactive Standardized Framework

Integrate PRO interactive analysis approach part of data analysis flow

Start early to discuss interactive approach as project-level programming and analysis strategy

Leverage interactive apps (Spotfire for patient-level access vs. Shiny for inferential statistics) to gain agility and control scope



Standardize VADs and interactive templates in Spotfire/Shiny for PRO data across oncology portfolio

Focus on commonly used analyses for decision-making to ensure consistency and quality



Training

To avoid scope creep

To show-case robustness of the output

To optimize use of data for analyses prioritization

PRO Interactive Analyses Proposal - details



Gain access to patient level data and additional analyses

- Demographic (patients with PRO data)
- For each PRO score:
 - Compliance by visit
 - Mean score and change from Baseline at each timepoint, PD and EoT
 - Summary of Clinically meaningful changes (improved/stable/deteriorated)
- For selected PRO scores:
 - Time to event and % responders



Gain access to additional inferential analyses and p values

- For each PRO score:
 - Time to event
 - Mixed model for change from baseline
- Easy cross check the results between different visualization

Interactive
Analysis Apps

Standardize
PRO data &
analysis

Established standard for EORTC QLQ C30

Additional scales: EQ5D, EORTC BR23, EORTC CR 29, SILC



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
Sphaggetti Plot and listings	Sphaggetti Plot of QS Score Listing: PRO Questionnaire Listing: Demog
Documentation:	PRO variable derivation spec Validation Tracking Version History

Online 179 of 200 rows 0 n

Provides overview with **table of contents** and **traceability** information such as source data location, data cutoff date, versions of software and application.

Primary Setup, Business Rules, and Bookmarks

The screenshot displays the application's primary setup and documentation interface. It is divided into three main sections:

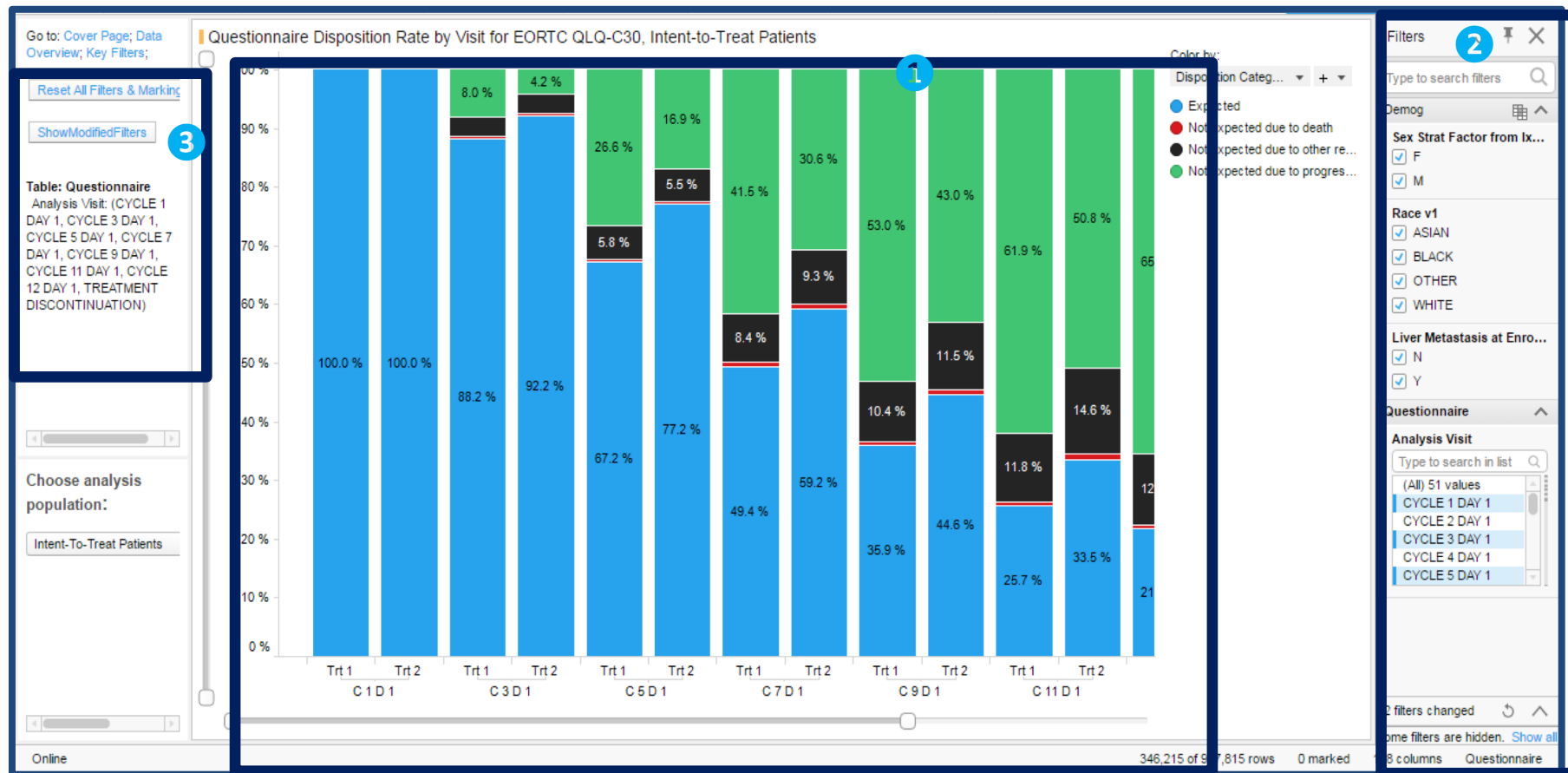
- Bookmarks (3):** A list of saved analysis results on the left. Each entry includes a title, a brief description, and a date. Examples include "Summary of Patients Who Improved, Worsened, or Remained Stable by Scale of the SILC from Baseline, PRO-Evaluable for SILC" and "EORTC Quality of Life Scores of EORTC QLQ-LC13 Compliance by Visit, PRO-Evaluable for EORTC QLQ-LC13".
- Configuration (1):** A central panel for setting analysis parameters. 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").
- Documentation (2):** A right-hand panel containing user guides. It includes sections for "For Webplayer users:" (explaining filters and buttons like "Reset All Filters and Markings" and "ShowModifiedFilters"), "Business Rules:" (defining terms like "intent-to-treat patients" and "PRO-Evaluable"), and "Compliance Rate:" and "Clinically Meaningful Changes" with detailed bullet points.

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 for EORTC QLQ-C30

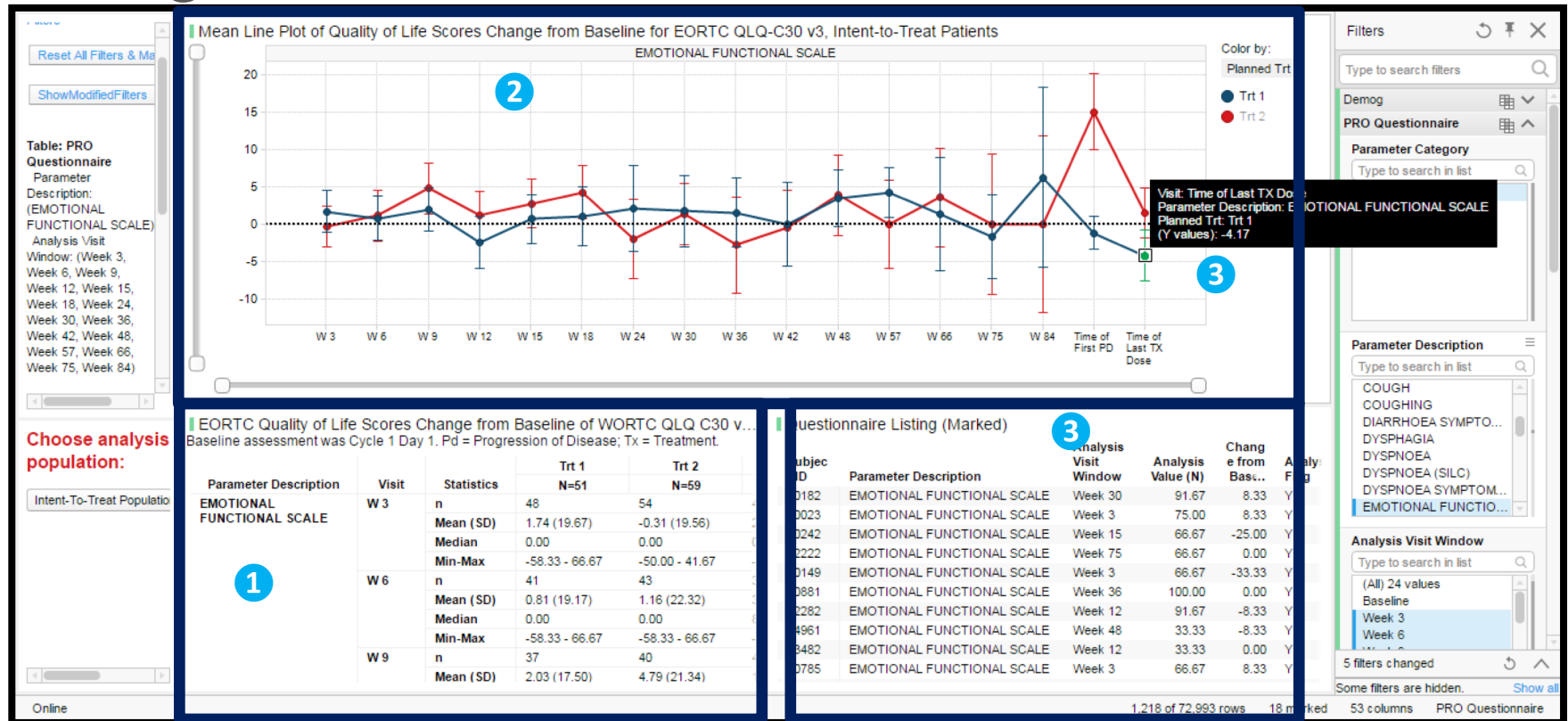


① **% Stacked bar chart** shows a good overview of patient disposition by treatment per scheduled assessment

② **Filter options** for sub-group analysis

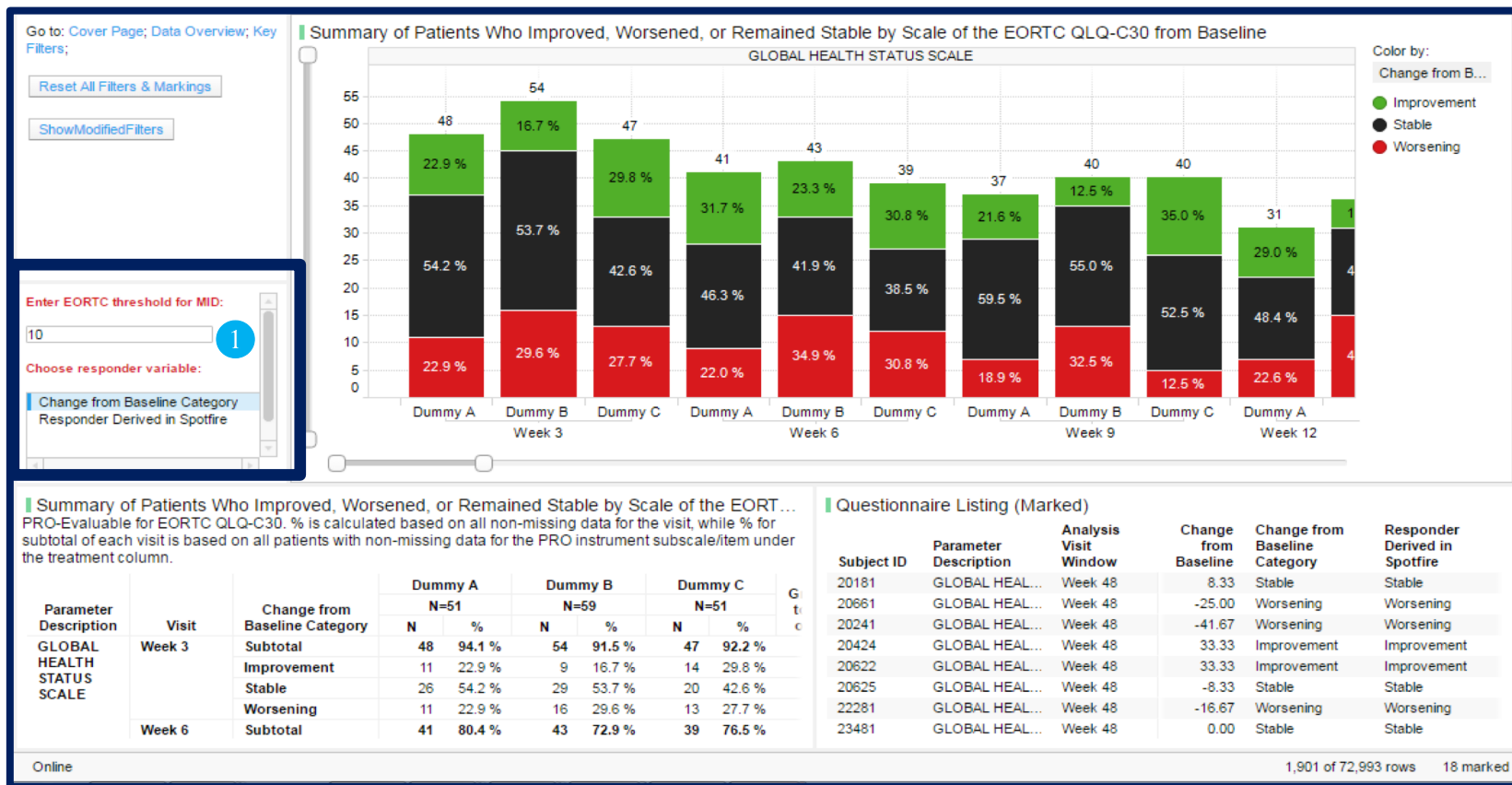
③ **Show Modified Filters command** reveals filters used for underlying data for accurate interpretation

Mean Line Plot of Quality of Life Scores Change from Baseline for EORTC QLQ-C30 v3



- 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 from Baseline



1 Dynamic calculation of PRO response to support sensitivity analysis

Time to Event Summary for Time to Confirmed Deterioration of 3-Symptom Composite

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

	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%

ASL.ITTWTFL remove

☒ Y

☐ N

Add Filter Variables

ASL

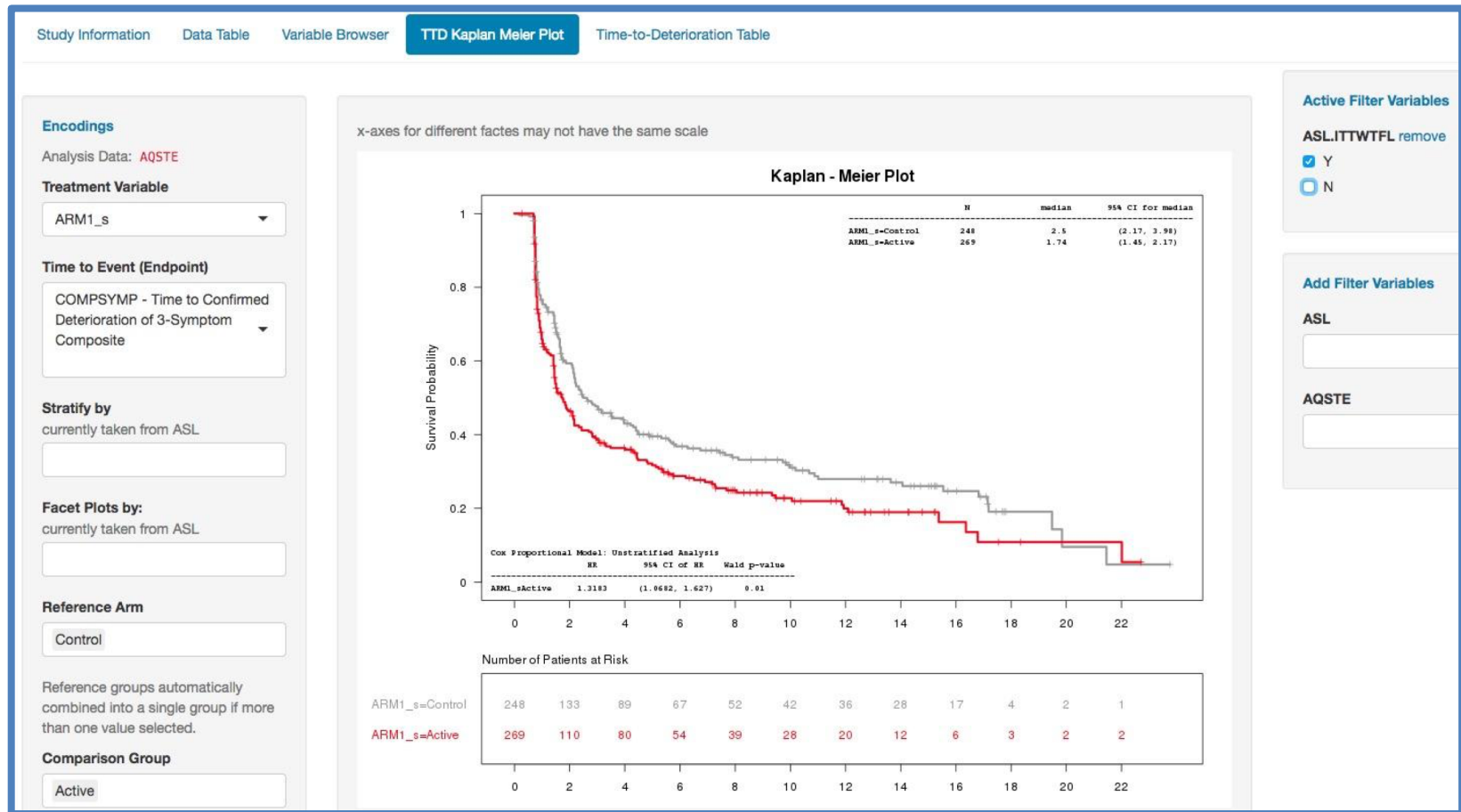
AQSTE

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

Kaplan-Meier Plot for Time to Confirmed Deterioration of 3-Symptom Composite



PRO Interactive Analyses vs. CSR reporting



100%



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

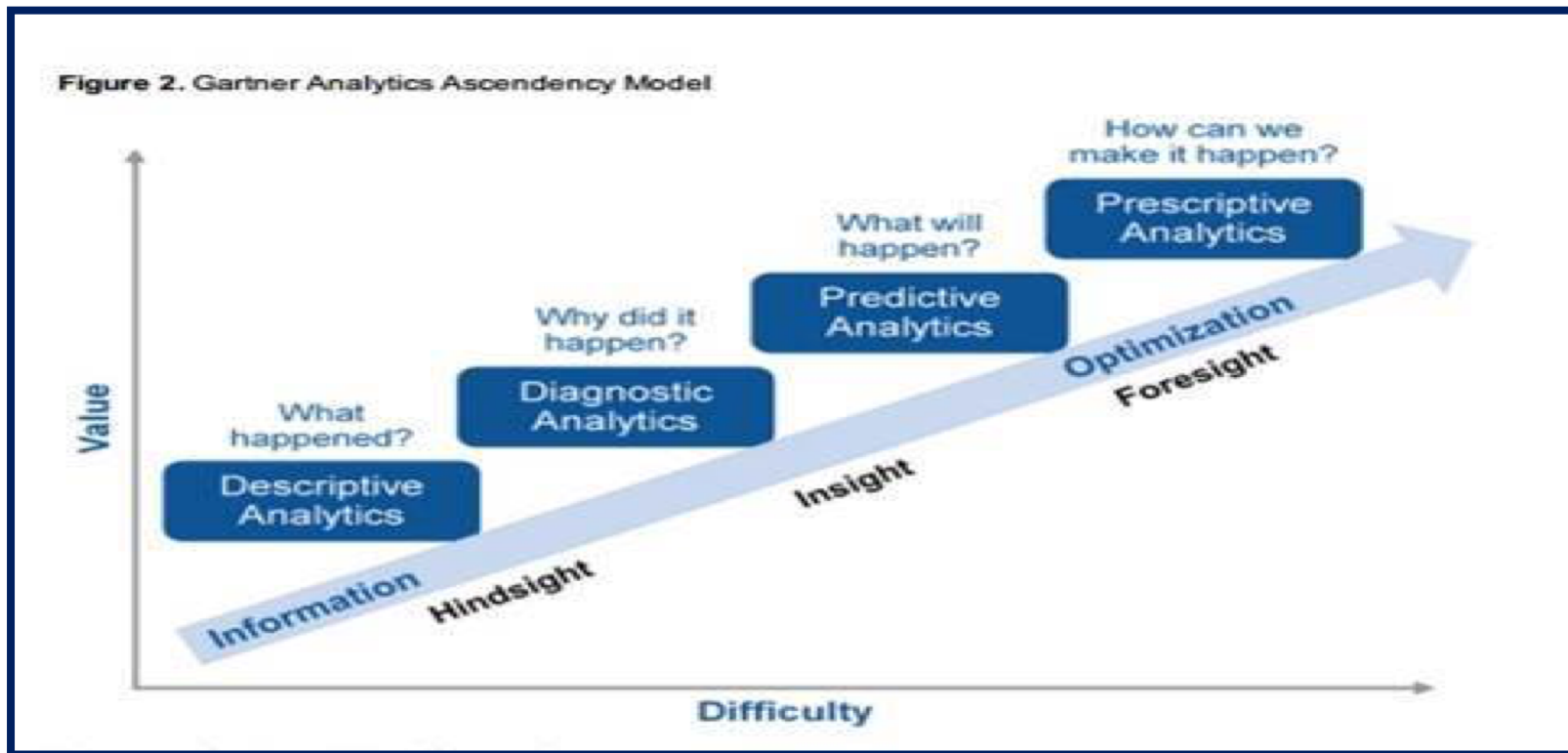


Initial learning curve and thus increase in resource needs, but ultimately, **minimized burden on Programming and PRO scientists**

Key Takeaway

- ❖ **PRO data standardization** is the foundation for standardized interactive framework
- ❖ **Active collaboration** strengthens our partnership and thus helps us develop a viable solution to meet business needs (eg. dynamic responder calculation to support sensitivity analysis per HA and HTA requests)
- ❖ The Mindset shift accompanying process improvement to **plan early and start early** is crucial to maximize the benefits of PRO interactive tools

Continue Analytics Journey



- ❖ Continue to explore a **more seamless approach** for analyzing COA/PRO to support the CSR, the access evidence dossier and some of the affiliates' (e.g., Germany)
- ❖ Explore **advanced analytics** to learn more about patients' treatment tolerability with real world data

Q&A

