



Presentation# AD13

Connecting Open-Source and Enterprise Software

Enhancing Phase III Clinical Trial Design Through
R Integration in **East Horizon™**

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Disclaimer

The slides and views expressed in this presentation are those of speakers and are not representative of Cytel's views or opinions.



Outline

Open-Source and Enterprise Software

East Horizon™ for Design of Clinical Trials

Motivation : Open-Source Integration in East Horizon™

R Integration in East Horizon™ – Workflow Demo

Conclusions

Open-Source and Enterprise Software



Highly Customized and Novel Analysis

Open-Source Community Support

Popularity with Statisticians



Structure : Performance, Scalability, Security

Vendor Accountability & Support

Usability for Cross-Functional Team

Open-Source and Enterprise Software



East Horizon™ Explore: for Design of Clinical Trials

DESIGNS

Provide Study Alternatives Through Designs

Strategic, **controllable aspects** of the trial e.g. *sample sizes, type I errors, choice of test statistics.*

SCENARIOS

Manage Real-world Uncertainty With Scenarios

Uncontrollable trial dynamics e.g. effect sizes, enrollment and dropout rates and their *likelihoods*

SIMULATION

Simulate The Full Model Space

All models formed by **Scenarios × Designs** inputs are executed using simulation-based Engine.

OPTIMIZATION

Find Optimal Design using Tradeoff Advisor (ToA)

Heatmap, table with clever **filters**

Score based on operating characteristics and relative weights

Robustness of design across scenarios

East Horizon™ Explore: for Design of Clinical Trials

For illustration, we consider a Phase III oncology trial to compare the efficacy of an investigational treatment against control using Overall Survival (OS) as the primary endpoint.

Trial Type	Two-Arm Confirmatory
Hypothesis	Superiority
Type I error	$\leq 2.5\%$
Sample Size	≤ 250 patients
Study Duration	≤ 60 Months
Target Power	$\geq 80\%$

Response	Control Hazard Rate = 0.08, HR : 0.55 – 0.65
Dropouts	Control = 5% , Treatment = 3%, by 10 Months
Enrolments	20-30 patients per month

Goal: Select few candidate designs abiding to the requirements and operational/ regulatory constraints [across possible scenarios.](#)

East Horizon™ Explore: for Design of Clinical Trials

DESIGNS

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Strategic, **controllable aspects** of the trial e.g. *sample sizes, type I errors, choice of test statistics.*

The screenshot displays the 'Base Input Set' configuration page in the East Horizon Explore software. The interface is divided into a left sidebar and a main content area.

Left Sidebar:

- Design (2)
- Response (1)
- Enrollment (1)
- Cost & Revenue Optional
- Weights
- Assurance Priors
- Simulation Setup
- 162 Models (i)
- Save
- Save & Simulate

Main Content Area:

Design (Fixed Sample Design | Group Sequential +)

Fixed Sample Design ... (9 Designs)

Arms: 2

Statistical Design: Fixed Sample

General

Hypothesis: Superiority

Number of Events: 180,200,220

Sample Size: 230,240,250

1-Sided Type 1 Error: 0.025

Critical Point: -1.959964

Test Statistic: Logrank

Randomization Method: Completely Randomized Design

Allocation Ratio: 1

Clear Changes

East Horizon™ Explore: for Design of Clinical Trials

SCENARIOS

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Response Response Card 1 +

Response Card 1 ... Preferred **3** Response Scenarios

Endpoint 1 Dropout Rate

Distribution: Exponential Pieces: 1 Input Method: Hazard Rate

Control: 0.08 Treatment: Computed Hazard Ratio: 0.55,0.6,0.65

Enrollment Card 1 ... Preferred **2** Enrollment Scenarios

Accrual

Type: Global Input Method: Enrollment Rate Distribution: Uniform

Period	Starting at Time	Average Subjects Enrolled (per Month)
1	0	20,30

+ Add Period

East Horizon™ Explore: for Design of Clinical Trials

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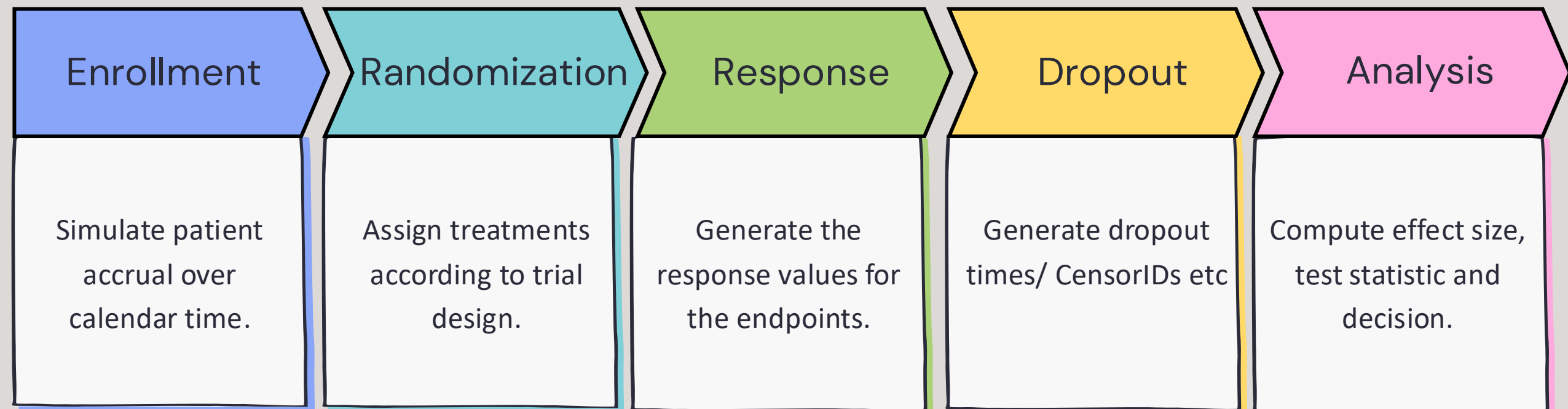
Simulation Setup

Number of Simulations Run: 10000

Random Number Seed: Fixed

Fixed Seed: 100

Generate Data File for All Simulated Models



East Horizon™ Explore: for Design of Clinical Trials

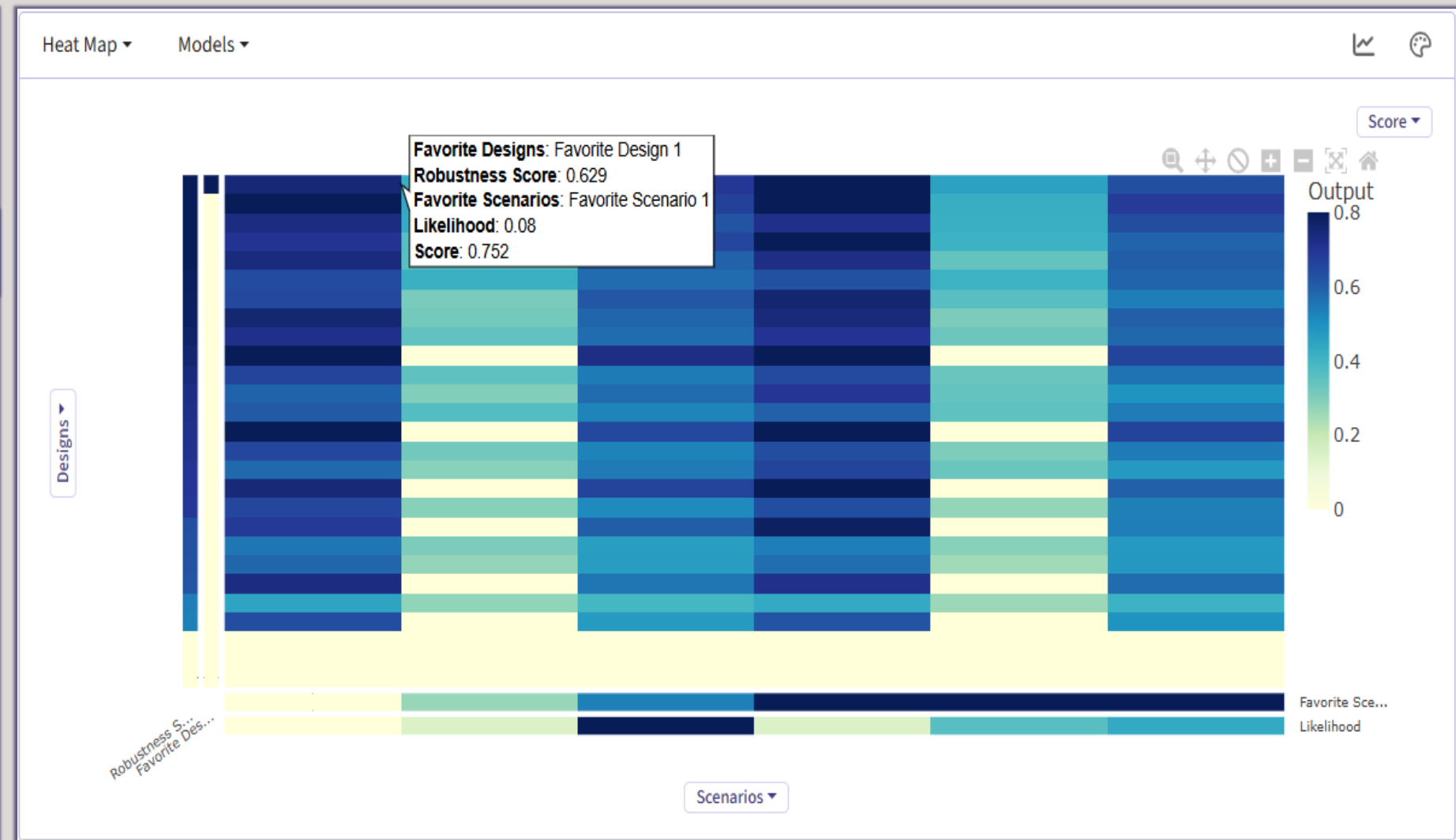
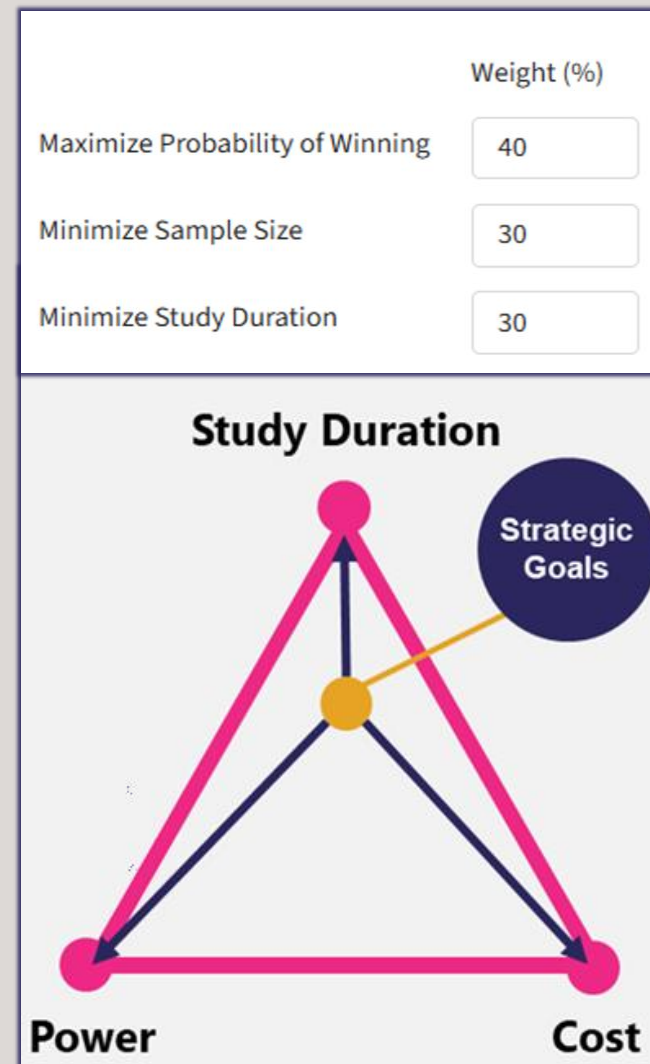
OPTIMIZATION

Find Optimal Design using Tradeoff Advisor (ToA)

Heatmap, table with clever filters

Score based on operating characteristics and relative weights

Robustness of design across scenarios



Best Across All Scenarios	Wt. Power [Power]	Avg. SS Min - Max	Avg Study Duration Min - Max
GSD, Events : 200, SS : 230	91.46% [83.36% - 98.46%]	218.97 - 229.13 patients	33.14 - 38.19 months

Motivation: Open-Source Integration in East Horizon™

Expected Response

Scenario 1: Proportional Hazard

Control Hazard Rate = 0.08
Hazard Ratio : 0.6

Scenario 2: NPH : Delayed Effect-1

Control Hazard Rate = 0.08

<i>Starting at time</i>	0	6	9
<i>Hazard Ratio</i>	1	0.7	0.5

Scenario 3: NPH : Delayed Effect-2

Control Hazard Rate = 0.08

<i>Starting at time</i>	0	3	9
<i>Hazard Ratio</i>	1	0.7	0.5

Motivation: Open-Source Integration in East Horizon™

Choice of Analysis:

Modestly Weighted Log Rank (MWLR) test statistic (Magirr, 2021)

- Delayed Effect → Higher Power
- Proportion Hazard → Reasonable Power
- Better Type I Error Control than Harrington-Fleming Family

✘ Not available with East Horizon™.



Write a **R function** to compute MWLR test Statistic and let **East Horizon™** handle the remaining simulation flow.

Test Statistic

User Specified - R

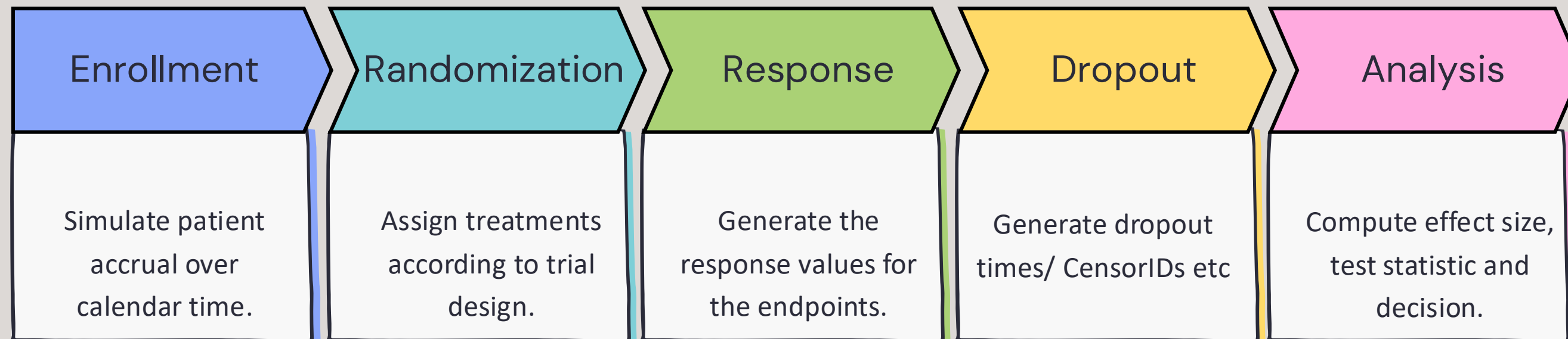
Logrank

Harrington Fleming

Max Combo

User Specified - R

R Integration in East Horizon™ – Workflow Demo



R Integration for :

Custom, sophisticated methods

Computing additional summaries.

Harnessing power of Tradeoff Advisor (ToA)

R Integration in East Horizon™ – Workflow Demo

Select File

Manual writing and uploading the R function.

The screenshot displays two windows from the East Horizon™ interface. The top window, titled "User Specified - R - Time to Event - Analysis", shows a "Getting Started" section with two options: "Select File" (with subtext "Select or upload an R file in the File Manager.") and "R Code Assistant" (with subtext "Use our AI code assistant to help generate your R script."). The bottom window, titled "R Code Assistant - Time to Event - Analysis", features a heading "Can I help you with your R code?" and a prompt: "You can enter your own prompt below to generate R code that can be used in your input set. There is a limit of 25 prompts per session." Below this is a text input field containing a detailed prompt about the Modestly Weighted Log Rank test statistic. At the bottom of the window are "Back" and "Cancel" buttons.

R Code Assistant

Code generation in the prescribed format

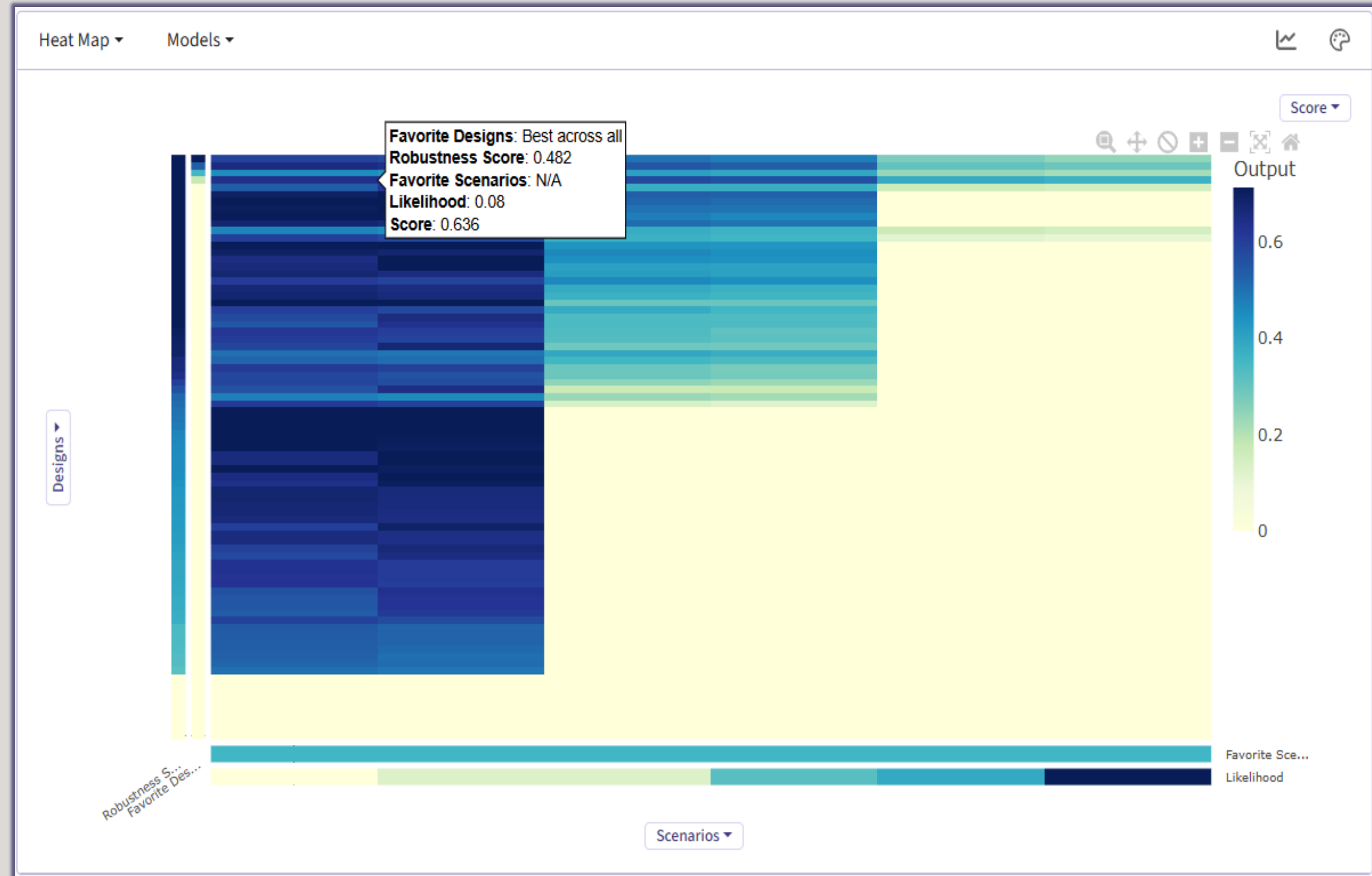
R Integration in East Horizon™ – Workflow Demo

Test Statistics

Log-Rank
MWLR (Delay= 9, MaxWt= 5)
MWLR (Delay=1 2, MaxWt= 5)

Simulations

of Designs : 81 (27 × 3)
of Scenarios : 6 (3 × 2)
of Models : 486 (27 × 6)



R Integration in East Horizon™ – Workflow Demo

Candidate Designs : Best Across All Scenarios

<i>Original Weights</i>	<i>Wt. Power [Power]</i>	<i>Avg. SS Min – Max</i>	<i>Avg Study Duration Min – Max</i>
Fixed Sample , MWLR (delay=12, MaxWt =5), Events : 200, SS : 230	87.94% [83.30% -93.84%]	230 patients	45.38– 49.09 months
<i>Maximum Power</i>	<i>Wt. Power [Power]</i>	<i>Avg. SS Min – Max</i>	<i>Avg Study Duration Min – Max</i>
Fixed Sample , MWLR(delay=12, MaxWt =5), Events : 220, SS : 250	90.36% [86.32% -95.12%]	250 patients	48.56 – 52.81 months
<i>Minimum Study Duration</i>	<i>Wt. Power [Power]</i>	<i>Avg. SS Min – Max</i>	<i>Avg Study Duration Min – Max</i>
Fixed Sample , MWLR(delay=12, MaxWt =5), Events : 200, SS : 240	85.97% [80.12% -93.91%]	240 patients	37.69– 41.23 months

Note: Best Minimum Sample Size Design was found to be same as best Original Weights Design.

Conclusions

- **Open-Source + Enterprise Software : best of both worlds**
 - Structure & Validation
 - Flexibility & Community Support
- **Development of complementary tools: More accessible integration**
 - AI-powered assistance
 - Dedicated documentation/repository
- **East Horizon™ demonstrates this by Providing R – Integration points to Simulation components.**

Thank you! Any questions?

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