Two Arm Binary Outcome Analysis Examples

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# Two Arm, Binary Outcome - Analysis Examples

This example demonstrates how to add new analysis functionality into East using an R function.

For all examples, we assume the trial design consist of control and an experimental treatments. There are 2 Interim Analysis, IA, and a Final Analysis, FA. At the IA, the analysis is performed and depending on the example may determine early efficacy or early futility depending on the design.

The examples include here are to provide different approaches for analyzing the data in the trial.

**East Workbook**: 2ArmBinaryOutcomeAnalysis.cywx

**R Studio Project File**: 2ArmBinaryOutcomeAnalysis.Rproj.

In the RCode directory of this example you will find the following R files:

1. TreatmentSelectionTemplate.R - This file provides a template that may be used as a starting point for developing new treatment selection functions in R.
2. 2ArmBinaryOutcomeAnalysisExample1.R - Contains a function named 2ArmBinaryOutcomeAnalysis to demonstrate the R code necessary for Example 1 as described below.
3. 2ArmBinaryOutcomeAnalysisExample2.R - Contains a function named AnalyzeUsingPropTest to demonstrate the R code necessary for Example 2 as described below.
4. 2ArmBinaryOutcomeAnalysisExample3.R - Contains a function named AnalyzeUsingPropLimitsOfCI to demonstrate the R code necessary for Example 3 as described below.
5. 2ArmBinaryOutcomeAnalysisExample4.R - Contains a function named AnalyzeUsingBayesAnalysisWithFutility to demonstrate the R code necessary for Example 4 as described below.
6. 2ArmBinaryOutcomeAnalysisExample4.R - Contains a function named AnalyzeUsingBayesAnalysisWithFutility to demonstrate the R code necessary for Example 4 as described below.

In addition, if you would like to experiment with these examples to and would like some code to help you get started we have provided fill-in-the-blank type code files in the FillInTheBlankRCode directory.

## Example 1 - Two-arm Arm Binary Analysis Using a User Defined Function

To replace the analysis, use the formula 28.2 in the East manual to compute the statistic. The purpose of this example is to demonstrate how would could modify the analysis and decision making in a simple approach. The test statistic is compared to the upper boundary computed and sent by East as an input. This example does NOT include a futility rule.

## Example 2 - Two-arm Arm Binary Analysis Using the prop.test function in R base.

This example utilizes the prop.test function in base R to perform the analysis. The p-value from prop.test is used to compute the Z statistic that is compared to the upper boundary computed and sent by East as an input. This example does NOT include a futility rule.

## Example 3 - Utilization of Confidence Interval Limits for Go/No GO Decision Making

In many phase II trials, teams like to utilize the upper and lower boundaries of a confidence interval (CI) for making Go and No Go type decision. In this type of trial, teams often set a Minimum Acceptable Value (MAV), which is the minimum treatment different that would warrant further development in a product and a Target Value (TV) which is the value that is highly desirable based on other consideration (TODO-Need more explanation here). In this simplified example, if it is likely that the treatment difference is above the MAV then a Go decision is made. If a Go decision is not made, then if is is unlikely that the treatment difference is above the TV a No Go decision is made.

In this example, the prop.test from base R is utilized to analyze the data and compute at 80% confidence interval. We assume the MAV = 0.1, TV=0.2, the team would like to make a Go decision if there is at least a 90% chance that difference is treatment than the MAV. If a Go decision is not make, then a No Go decision is made if there is less than a 10% chance the difference is greater than the TV. Using a frequentist CI an approximation to this design can be done by the logic described below.

At an Interim Analysis If the Lower Limit of the CI, denoted by LL, is greater than 10% then a Go decision is made. Specifically, if LL > 0.1 –> Go If a Go decision is not made, then if the Upper Limit of the CI, denoted by UL, is less than 0.2 a No Go decision is made. Specifically, if UL < 0.2 –> No Go Otherwise, continue to the next analysis

At the Final Analysis If the Lower Limit of the CI, denoted by LL, is greater than 10% then a Go decision is made. Specifically, if LL > 0.1 –> Go Otherwise, a No Go decision is made

Note, in this example the boundary information that is computed and sent from East is ignored in order to implement this decision approach.

## Example 4 - Bayesian Analysis

In this example, we utilize prior data on 50 patients and incorporate the data directly into the Bayesian model. In the prior data 10 patients had a response and 40 patients had a treatment failure. Denote the response rate for standard of care by and on Experimental by and we assume the following prior distributions:

Beta( 10, 40 ) which has a prior mean response rate of 20% and is equivalent to observing 50 prior patients with 10 responses.

Beta( 0.2, 0.8 ) which has a prior mean response rate of 20% and is equivalent to observing 1 prior patient.

The Beta distribution is conjugate for binary data. Assuming and patients have enrolled on S and E, respectively, the following data is observed at an interim analysis

| Treatment | Number of Responses | Number of Treatment Failures |
| --- | --- | --- |
| S |  |  |
| E |  |  |

Then posterior distributions are:

Beta( 10 + , 40 + )

Beta( 10 + , 40 + )

For analysis and decision make, the posterior distributions are used stop the trial for efficacy if it is very likely that the response rate on E is higher than on S and stop for futility if it is unlikely that the response rate on E is better than S. Specifically, compute the posterior probability that E has a higher response rate then S:

At the interim analysis:

If then make an early efficacy (Go) decision

If then make an early futility (No Go) decision.

and at the final analysis if make an efficacy decision, otherwise a futility decision is made.

This example demonstrates how the prior data and informative prior on can impact decision making. However, a full sensitivity analysis to the prior information and impact on Operating Charartherstics should be explored with approaches like this.