# R-Shiny tool to pool Kaplan Meier curves from single-arm studies using a distribution-free approach

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R for Health Technology Assessment

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# Situation assessment and solution

## Existing methods

Existing methods often pool survival probabilities reported at the same time point, treating them as proportions and combining them using fixed-effect univariate or random-effect methods. However, these methods may have limitations, such as not accounting for correlations between survival probabilities at different times.

## Challenges

Make strong assumptions about the data, such as linearity or specific distributions, which may not always be supported, and the survival curves produced may not be non-increasing

## Solution

- It proposes a distribution-free method to derive a summary survival curve using a product-limit estimator combined with an extension of the DerSimonian and Laird methodology
- It does not require assumptions about the shape of the survival curve or the distribution of random effects

# Advantages

### Distribution-Free Approach

It does not require assumptions about the shape of the survival curve or the distribution of the random effects. This makes it more flexible and broadly applicable compared to parametric approaches.

### Incorporation of Between-Study Heterogeneity

By extending the DerSimonian and Laird methodology to multiple outcomes, the method accounts for heterogeneity between studies, providing a more accurate summary survival curve.

### Handling of Censored Data

Similar to the Kaplan-Meier estimator, the method appropriately handles right-censored data, ensuring that all available information is used without making strong assumptions about the underlying survival distributions.

### Output

Output from this method is a summary survival curve, which anyone can leverage for further analysis including the extrapolations of pooled Kaplan-Meier curve according to NICE TSD 14 and 21

# Disadvantages

**Approximation Issues**

The method uses transformations and approximations (e.g., arcsine transformation) that may not always be perfectly accurate, particularly in case of rare events reported in Kaplan-Meier curve

**Dependence on Published Data**

The accuracy of the summary survival curve relies on the quality and completeness of the published survival curves from the included studies. Missing or inaccurately reported data can affect the results.

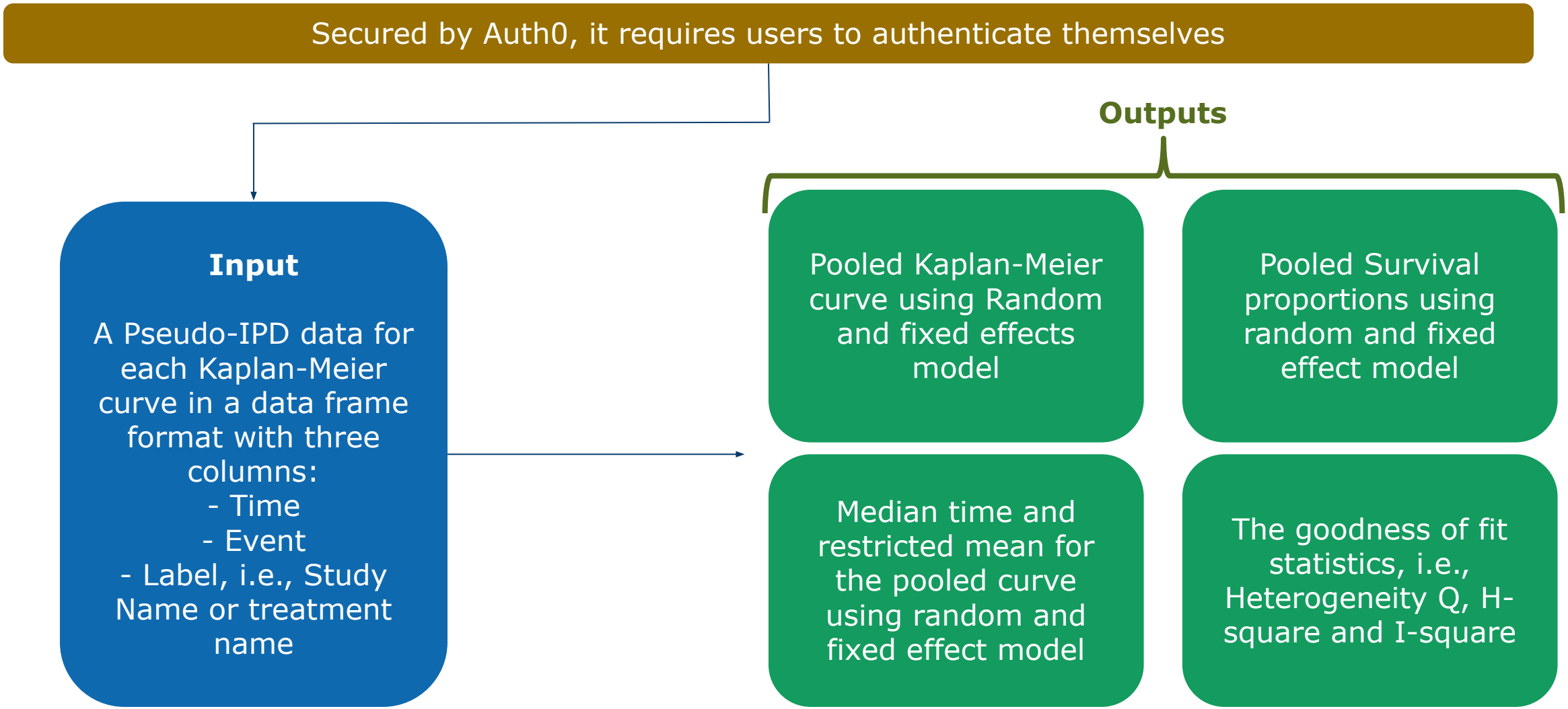
**Assumption of Independence**

While the method accounts for between-study heterogeneity, it assumes that the conditional survival probabilities within a study are independent. This may not always be the case, especially if there are underlying correlations not captured by the model

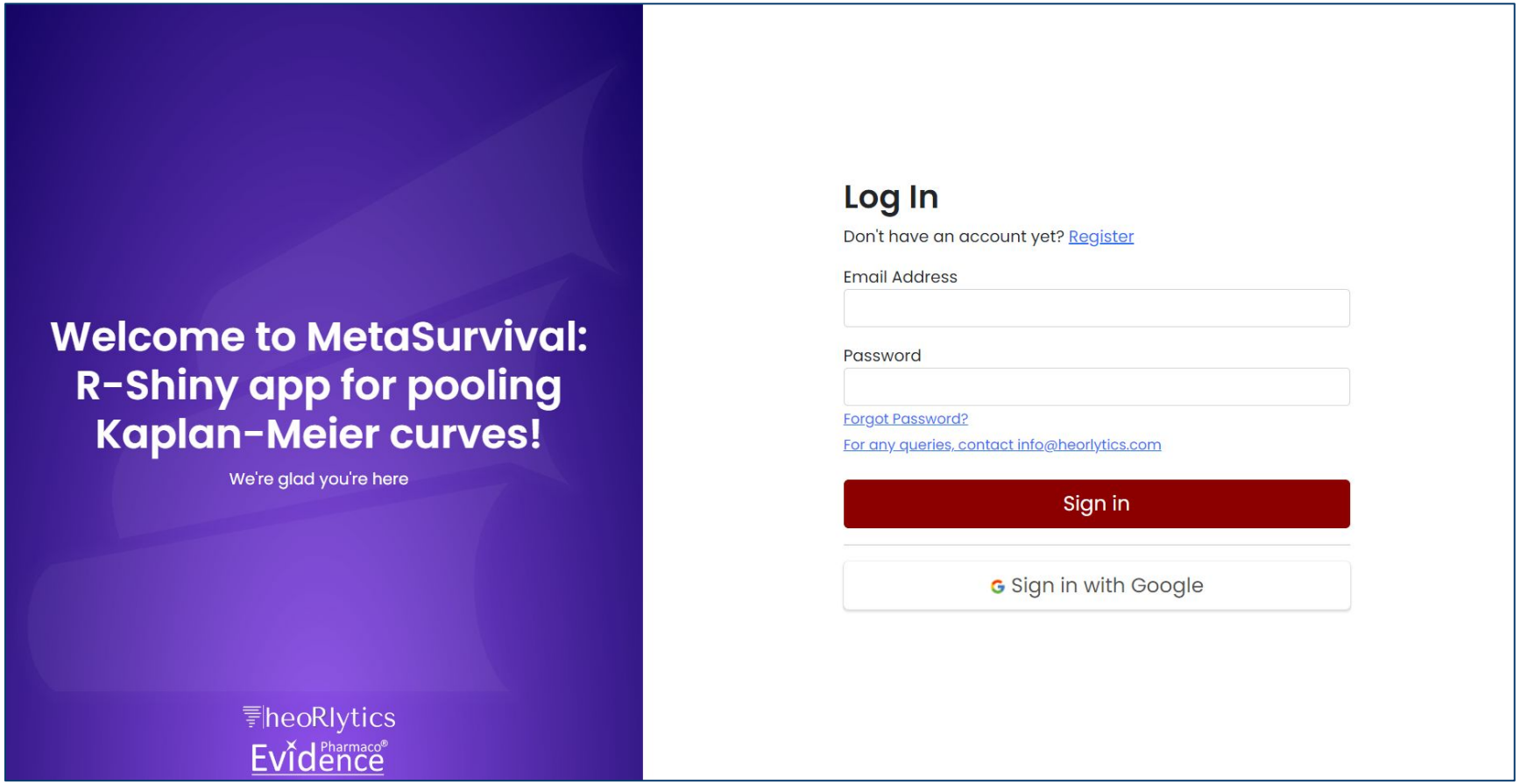
**Complexity of Implementation**

The method involves advanced statistical techniques and computations, which may be challenging for practitioners without specialized statistical training or software capabilities.

# Workflow



# Interface




Scan the QR to open the application

Go to https://metasurvival.survlytics.com/



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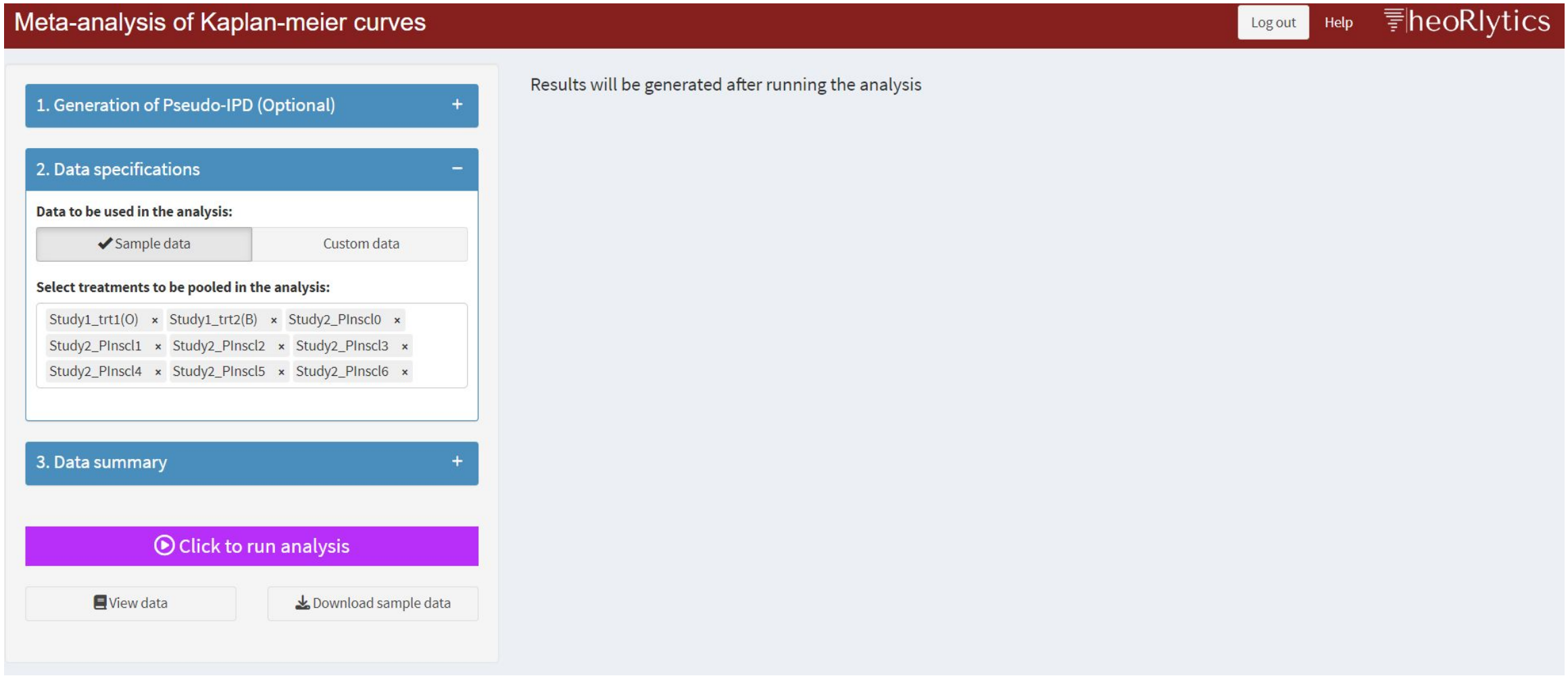
# After Authentication



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# After Running Analysis

Meta-analysis of Kaplan-meier curves

Log out | Help | TheoRIytics

1. Generation of Pseudo-IPD (Optional) +

2. Data specifications −

**Data to be used in the analysis:**

✔ Sample data | Custom data

**Select treatments to be pooled in the analysis:**

Study1_trt1(O) × Study1_trt2(B) × Study2_PInscl0 × Study2_PInscl1 × Study2_PInscl2 × Study2_PInscl3 × Study2_PInscl4 × Study2_PInscl5 × Study2_PInscl6 ×

3. Data summary +

Click to run analysis

View data | Download sample data

Median and restricted mean estimates

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| | Point estimate | Lower bound | Upper bound |
|---|---|---|---|
| Median fixed-effect model | 18.27 | 16.77 | 19.53 |
| Median random-effect model | 17.68 | 12.41 | 24.75 |
| Restricted mean fixed-effect model | 26.76 | 24.89 | 27.67 |
| Restricted mean random-effect model | 24.34 | 18.37 | 30.2 |

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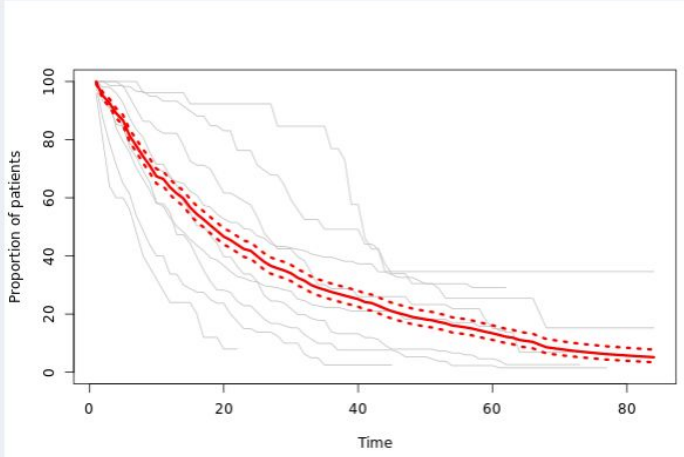
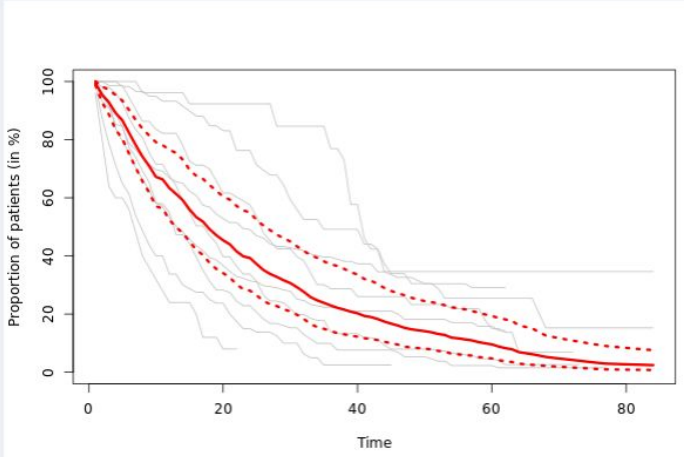
| | Heterogeneity-Q | H-squarred | I-squarred |
|---|---|---|---|
| Goodness of fit statistic | 661.13 | 1.16 | 13.48 |

Pooled Kaplan-meier plot (fixed-effect)




Pooled Kaplan-meier plot (random-effect)



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# THANK YOU!


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