# Even Projection Tool in R-Shiny

Yingsi Yang, Hua Dong, Xiaomin Lu, and Wei Deng

# Overview

- Event projection tool
  - Challenge
  - Event projection model
- Tool interface
  - Input dataset
  - Projection parameters
  - Projection plot
  - Options for plot
  - Extract information from projection
- Recommendation when using the tool

# Event Projection Tool

- Challenge
- Event projection model

# Challenge

- Event projection is critical for study planning and executing in event-driven studies
- Impact factors for event projection
  - Accrual
  - Actual distribution of the outcome in the population studied
  - Follow-up/drop-out
- Questions to be answered
  - When can we reach required number of events?
  - How reliable is this projection?
  - …
- Our event projection tool
  - Provide an estimate of the event accumulation hence the analysis timing
  - Estimate based on observed enrollment, event accumulation, and follow-up

# Event Projection Model

- Model for event
  - Exponential (current trend)
- Model for drop-out
  - Time to drop-out
    - Exponential (current trend)
  - Drop-out proportion
    - Binomial (current trend)
- Model for enrollment
  - Uniform (piecewise)

# Tool Interface

1. Input dataset
2. Projection parameters
3. Projection plot
4. Options for plot
5. Extract information from projection

# Tool Interface http://rshiny.gilead.com/dev/event_projection/

Event Projection

Developed by Yingsi Yang, Hua Dong, Xiaomin Lu, and Wei Deng

Quick Guide

1. Input dataset

**Event Dataset (.csv or .sas7bdat)**

Choose File | pfs_example.csv

Upload complete

(Event dataset examples: example.csv , example.sas7bdat )

6. Quick Guide

Event Projection | Data Preview

Projected Date

2017-06-23 | Get Event

5. Extract information from projection

Projected Number of Events

Get Date

Coefficient for dropout rate = 1

**Projection Parameters**

| Current Date | Max. Projection Days | Number of simulation |
|---|---|---|
| 2014-03-03 | 1300 | 20 |

| Total Events Needed | Total Enrollment Needed |
|---|---|
| 185 | 255 |

Automatically choose coefficient for dropout rate

2. Projection parameters

**Median Survival (Months) Under H1 and H0:**

| Treatment Group | Control Group |
|---|---|
| 5 | 3 |

**Enrollment Assumption:**

(Note: Enrollment assumption should be provided from the beginning of enrollment. In the projection, observed enrollment will be used for observed period.)

Number of Enrollment Periods (max. 3)

1

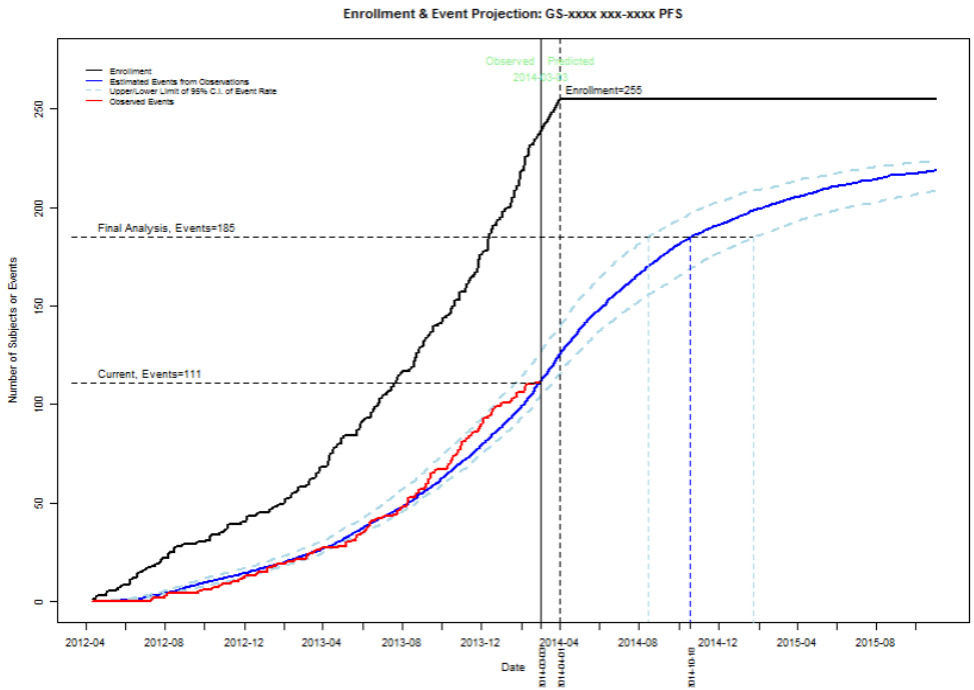
Enrollment Rate (Subject/Month)

17

Go!

Click the button to generate the projection.

3. Projection Plot




**Plot Parameters**

Show event curve under H1

Number of Events for Interim Analysis (Enter 0 if no interim analysis)

0

4. Options for plot

Main Title

GS-xxxx xxx-xxxx PFS

Update Plot

Reset Plot Parameters to update projection plot.

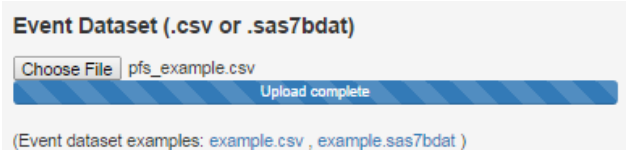
Download Plot

# Input Dataset

- File type: csv or SAS dataset (.sas7bdat)
  - example input files available for download from webpage
- Required columns in file
  - rgmndtn (date format): randomization/enrollment date
  - edate (date format): event/censor date
  - status: survival status
  - reason: indicator for censoring type
    - Data cut-off: reason = “data cut-off”
- Date format
  - .csv: yyyy-mm-dd
  - .sas7bdat: yymmdd10.
- Upload dataset in the App
  - Upload dataset on left panel
  - Check dataset uploaded from “Data Preview” tab

| RGMNDTN | reason | status | edate |
|---|---|---|---|
| 2012-04-17 | | 1 | 2012-08-03 |
| 2012-05-02 | | 1 | 2013-01-04 |
| 2012-05-03 | | 1 | 2012-07-09 |
| 2012-05-21 | | 1 | 2012-07-11 |
| 2012-05-25 | | 1 | 2013-03-04 |
| 2012-06-05 | | 1 | 2012-07-30 |
| 2012-06-08 | | 1 | 2013-03-08 |
| 2012-06-18 | gap before death | 0 | 2012-11-29 |
| 2012-06-21 | discontinued with... | 0 | 2013-04-17 |

| RGMNDTN | reason | status | edate |
|---|---|---|---|
| 2013-01-08 | data cut-off | 0 | 2014-03-03 |

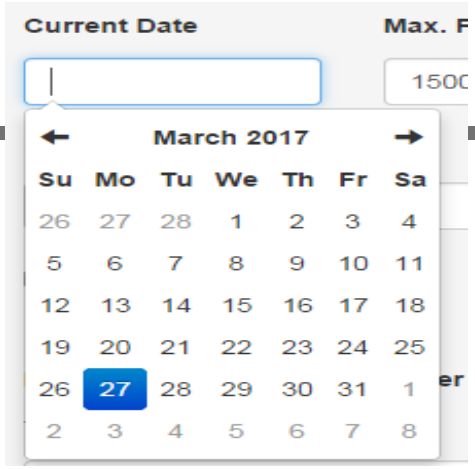



Event Projection | Data Preview

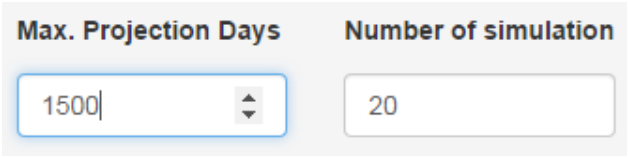
| | rgmndtn | reason | status | edate | tenroll | tevent | dcut |
|---|---|---|---|---|---|---|---|
| 1 | 2012-04-17 | | 1.00 | 2012-08-03 | 9.00 | 109.00 | 0.00 |
| 2 | 2012-05-02 | | 1.00 | 2013-01-04 | 24.00 | 248.00 | 0.00 |
| 3 | 2012-05-03 | | 1.00 | 2012-07-09 | 25.00 | 68.00 | 0.00 |
| 4 | 2012-05-21 | | 1.00 | 2012-07-11 | 43.00 | 52.00 | 0.00 |
| 5 | 2012-05-25 | | 1.00 | 2013-03-04 | 47.00 | 284.00 | 0.00 |
| 6 | 2012-06-05 | | 1.00 | 2012-07-30 | 58.00 | 56.00 | 0.00 |
| 7 | 2012-06-08 | | 1.00 | 2013-03-08 | 61.00 | 274.00 | 0.00 |
| 8 | 2012-06-18 | gap before death | 0.00 | 2012-11-29 | 71.00 | 165.00 | 0.00 |
| 9 | 2012-06-21 | discontinued without pfs | 0.00 | 2013-04-17 | 74.00 | 301.00 | 0.00 |

# Projection Parameters

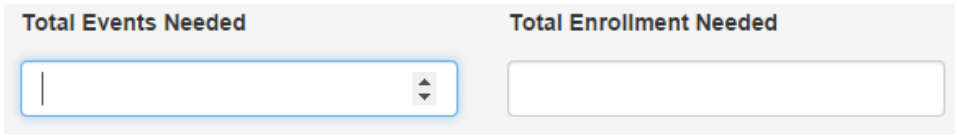
- Current date (for projection)



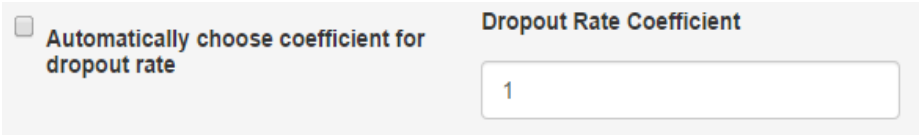

- Maximum days for projection
  - Maximum value on the x-axis of the projection plot (days from first randomization date)
- Number of simulation
  - Default is 20 simulations




- Total events/enrollment needed

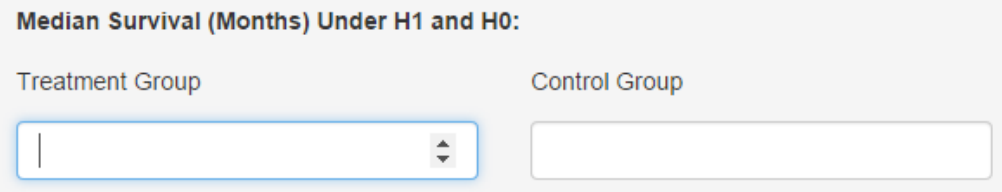



- Coefficient for drop-out proportion
  - Proportion of the current drop-out rate to be applied in the projection for the future observation
  - Automatically chosen by the app or manually input. **Coefficient is chosen such that the projected (blue) curve is close enough to the observed (red) curve.**

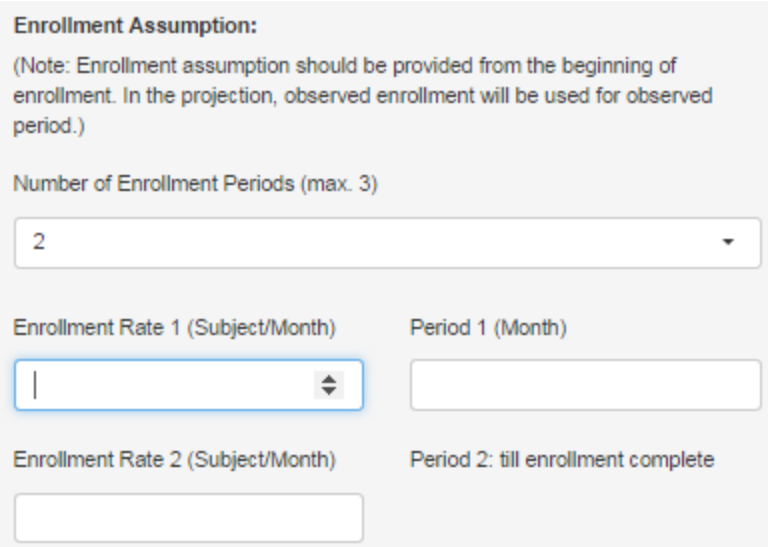


# Projection Parameters (cont.)

- Assumption under $H_0$ and $H_1$

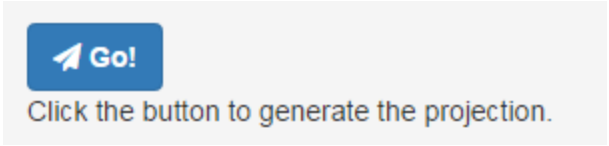



- Enrollment specification
  - Total number of enrollment periods (up to 3)
  - Enrollment duration/rate in each episode
  - Note
    - Enrollment parameters should be provided from the beginning of the enrollment period.
    - Observed enrollment will be used for the observed period.
    - Enrollment in the predicted part will be simulated with the provided parameters.

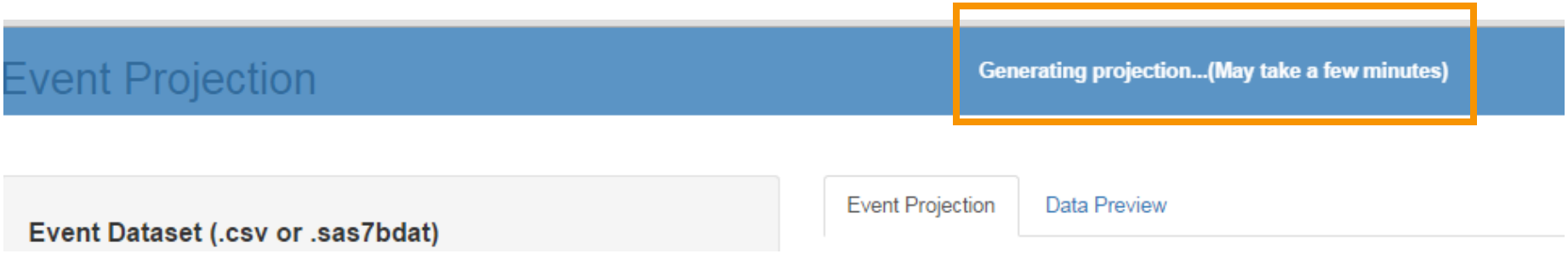


# Projection Parameters (cont.)

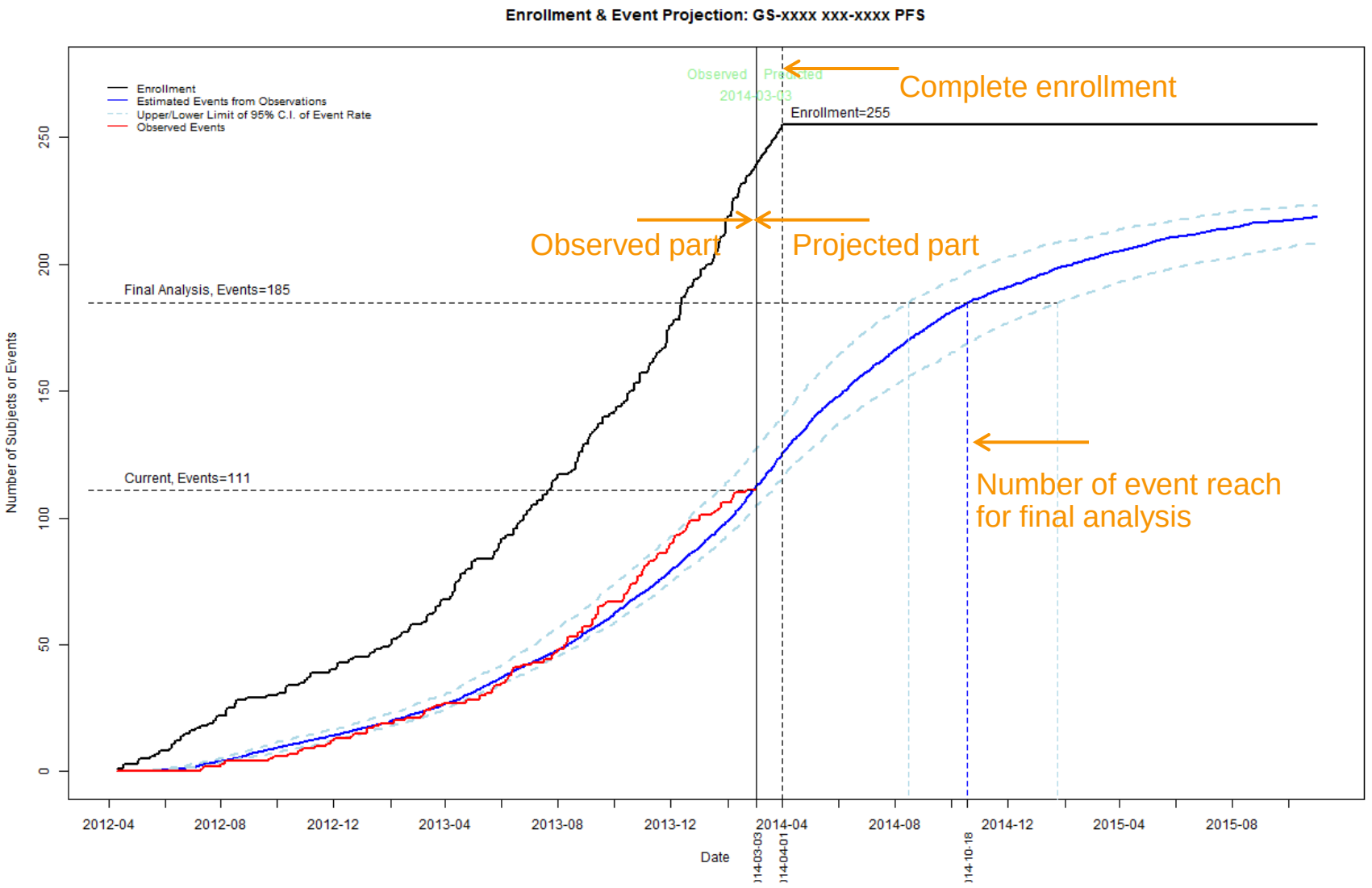
- Generate event projection
  - After all the projection parameters are set up, hit “Go!”




  - Generating the projection may take time (depending on scale of the study, number of simulations, whether the coefficient for dropout rate is specified, etc.). Please be patient when “Generating projection” is shown on the upper banner.



# Projection Plot



# Options for Plot

- Add a reference line for all subjects follow the assumption in $H_1$

  ☑ Show event curve under H1

- Add the projection for interim analysis (one interim for a projection)

  Number of Events for Interim Analysis (Enter 0 if no interim analysis)

  100

- Update plot title

  Main Title

  GS-xxxx xxx-xxxx PFS

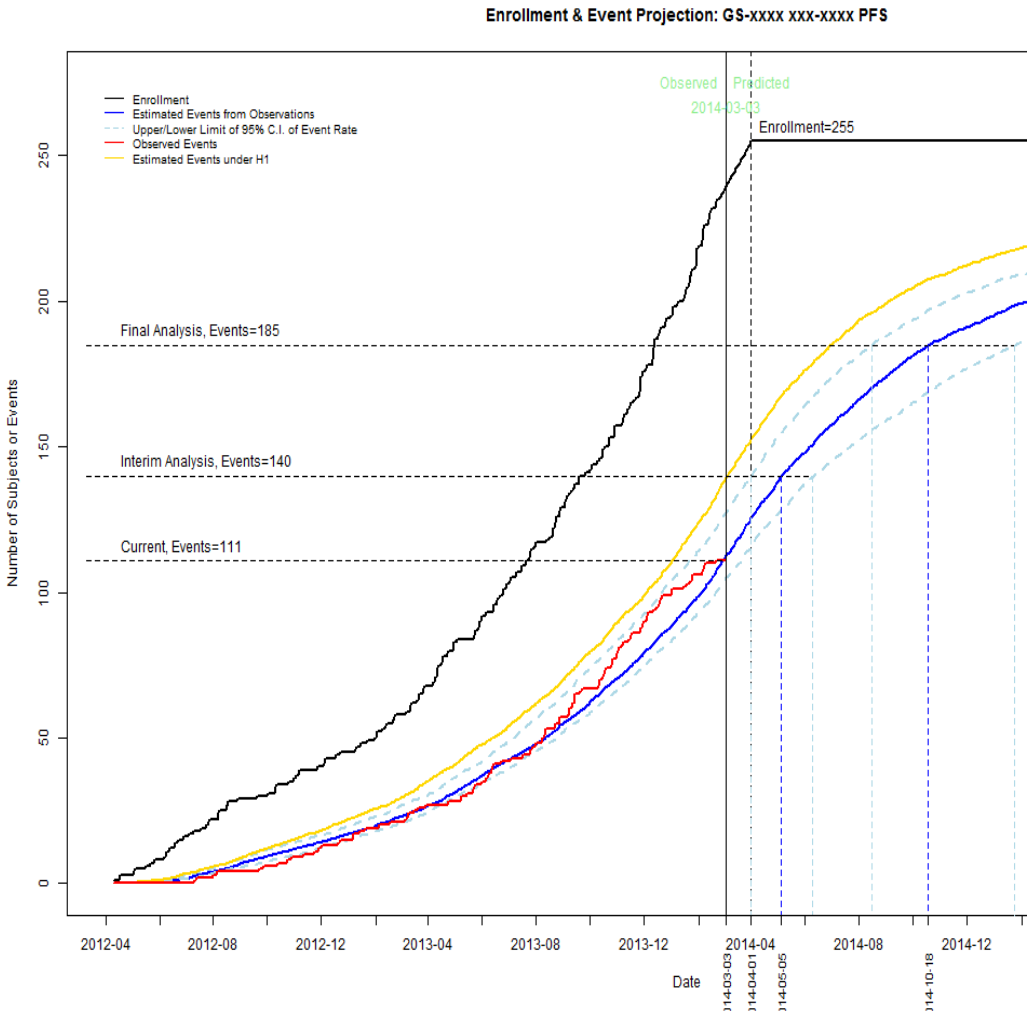
- Hit “Update Plot” after all options are set up

  Update Plot

  Reset Plot Parameters to update projection plot.

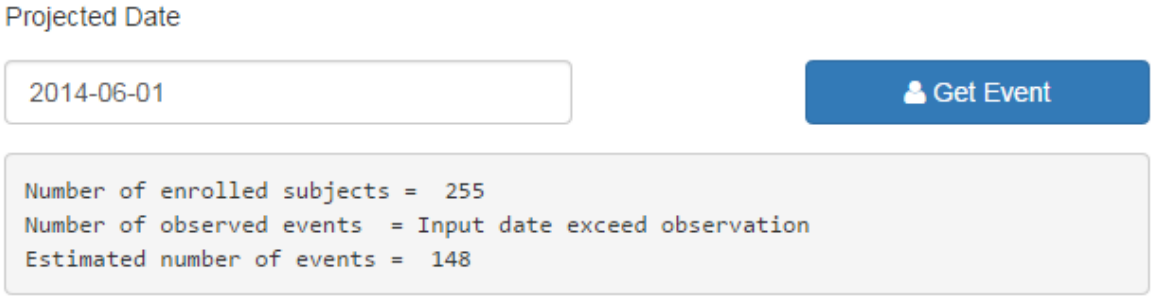
- Download plot as PDF file

  Download Plot

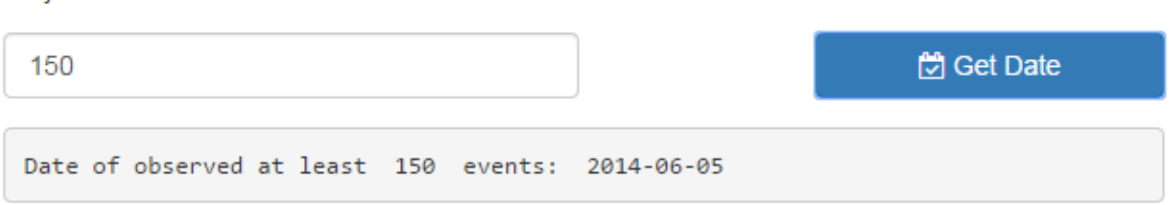


# Extract Information from Projection

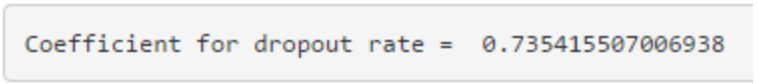
- Estimated enrollment and number of events at a given date




- Estimated date for a given number of events




- Coefficient for dropout rate used in the projection
  - If automatically choose, display the coefficient from the optimization
  - If manually input, display the specified coefficient



# Recommendation When Using the Tool

# Recommendation

- Implement the tool to support study conduct
  - Perform the projection only when sufficient information is observed from the study (e.g., half of the required events have been observed)
  - Communicate to the study team with a projected date range instead of a specific date

- Use the tool to generate projection
  - Use “Data Preview” tab to check whether the event dataset is uploaded successfully
  - Get the coefficient of drop out by choosing the optimization first, then adjust it manually if necessary
  - Number of simulations is set to 20 by default – it should be sufficient to generate a smooth curve for projection. It can be changed by manual input. Please also note that the more simulations, the longer time to generate the projection

# Still Have Questions?

Send email to:

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Link to the App:
http://rshiny.gilead.com/dev/event_projection/