Predicting Patient Recruitment in Multicenter Clinical Trials

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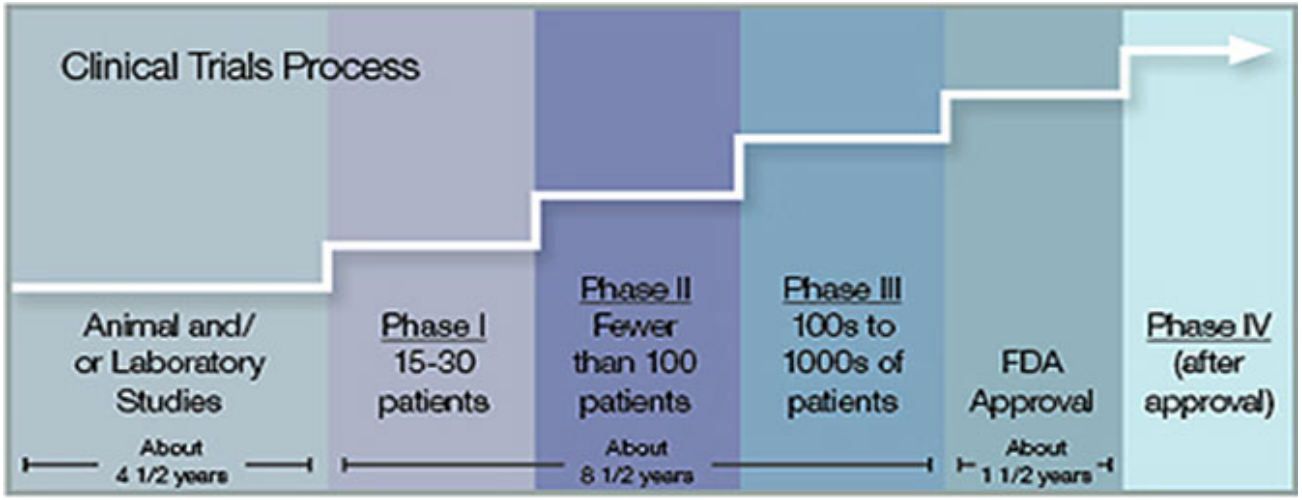
Overview

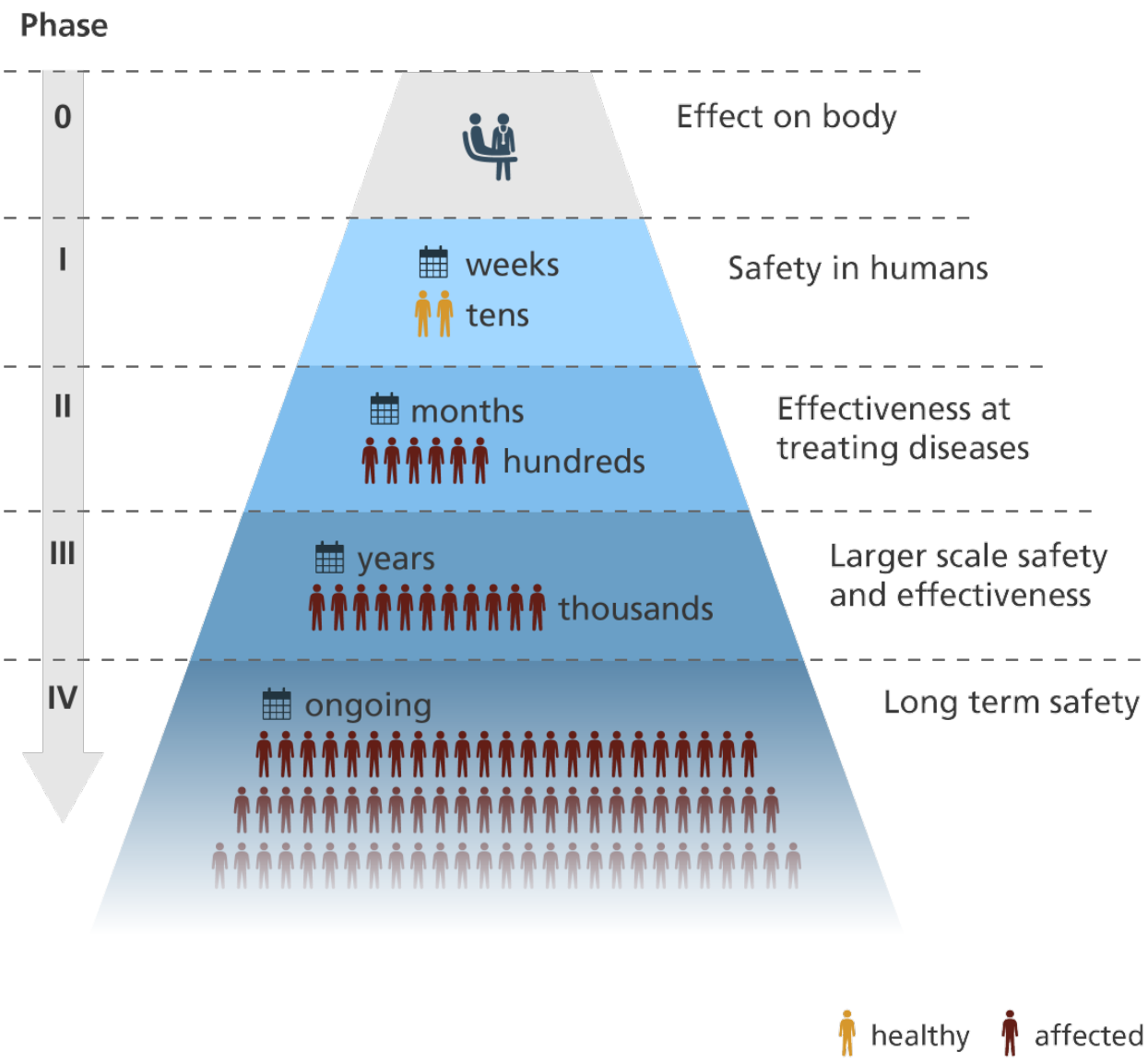
- Background & Introduction
- Methodology
- Demo in JMP Clinical

Background: Clinical Trials

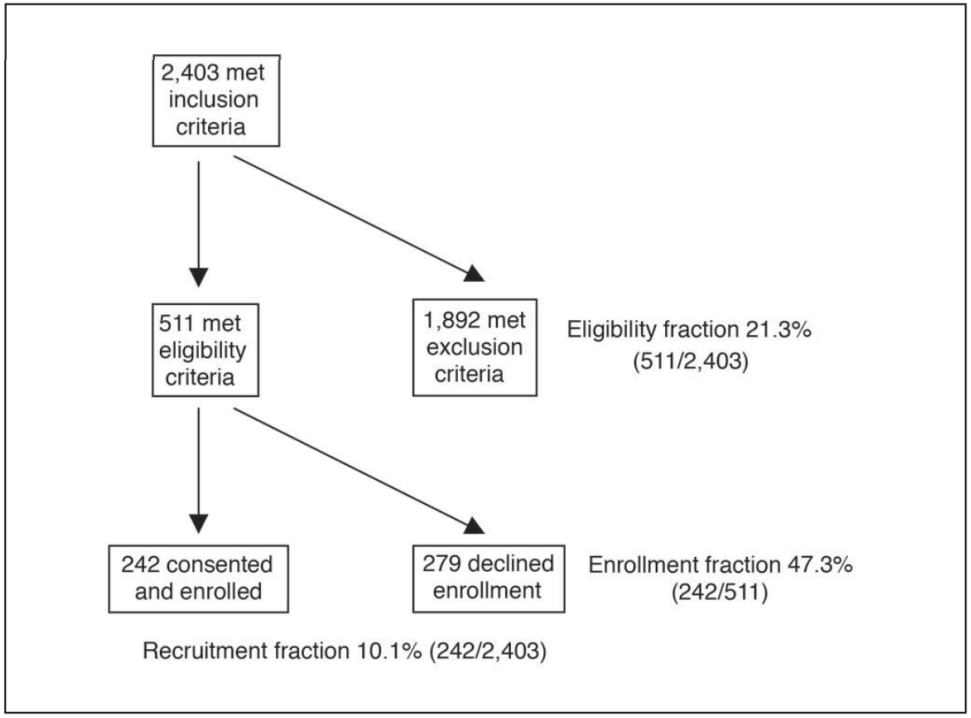


- Research studies that test whether a new drug, device, or therapy works and is safe for people
- Have protocols (or action plans)
- Result in three main consequences: Improvement, No Benefit, Harm
- One of the final stages of a long and careful research process

Background: Clinical Trials

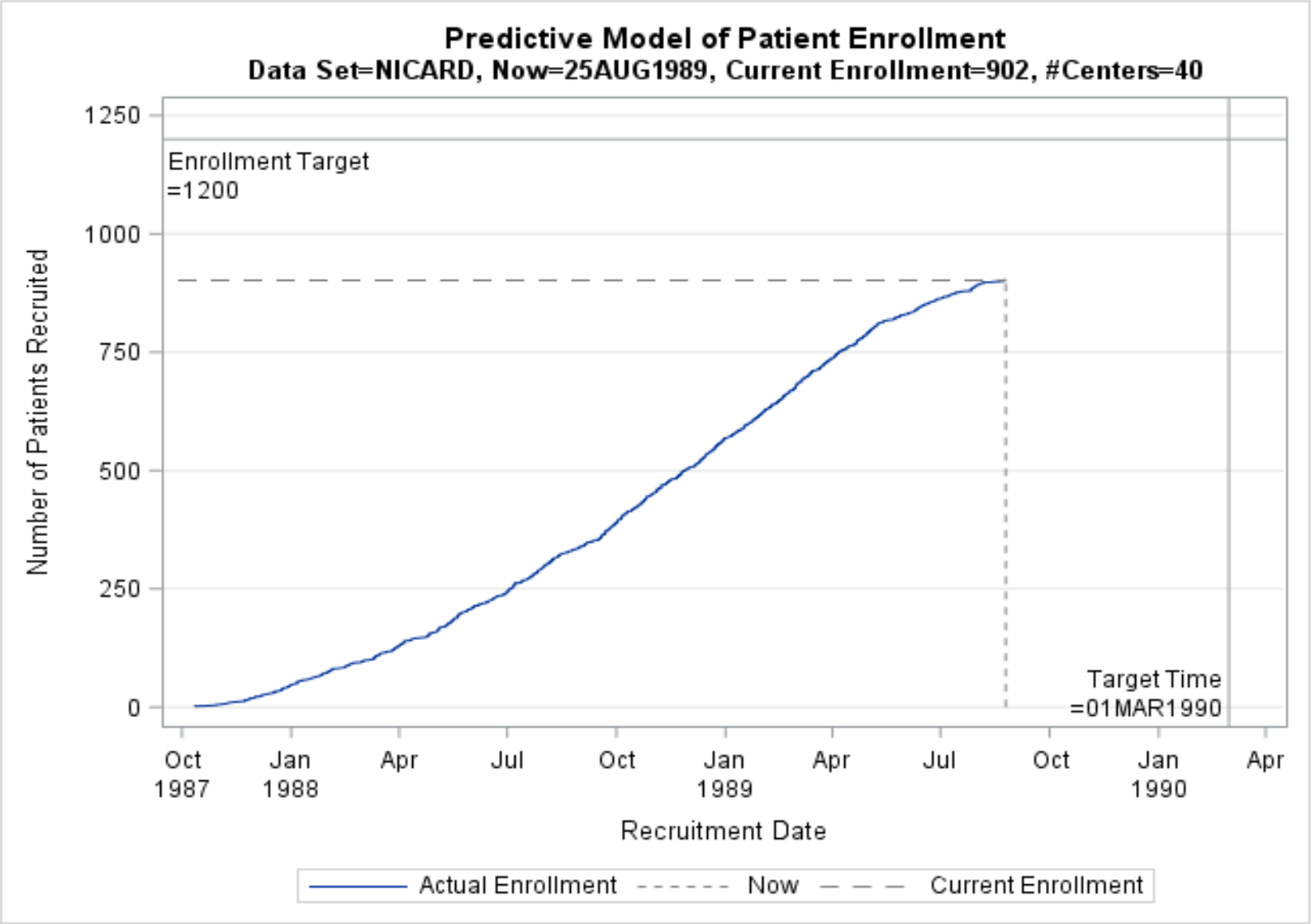


Background: Patient Recruitment



According to the National Institutes of Health (NIH), more than 80% of clinical trials in the US fail to meet their patient recruitment timelines, which can cause additional costs, shortage in resources, and significant delay in trials.

Background: Patient Recruitment



The Model: Assumptions

Poisson-Gamma Distribution, Anisimov and Fedorov (2007)

- The arrival of patients at each center follows an independent Poisson process with parameter λ_i
- λ_i is
  - the recruitment rate at center i
  - unknown
  - non-constant across centers but constant within center
  - sampled from a Gamma distribution (α, β), conjugate prior

The Model: Estimation and Prediction

Given data of current enrollment (k_i, τ_i):

- Parameter Estimation: maximum likelihood $\hat{\alpha}, \hat{\beta}$

$$K \sim NegBin(p, r)$$

- Prediction of Remaining Recruitment Time
  - If # center > 20, Bayesian Simulation

$$\tilde{T}_1 = \frac{\text{Gamma}(K_2, 1)}{\sum_i \text{Gamma}(\alpha + k_i, \beta + \tau_i)}$$

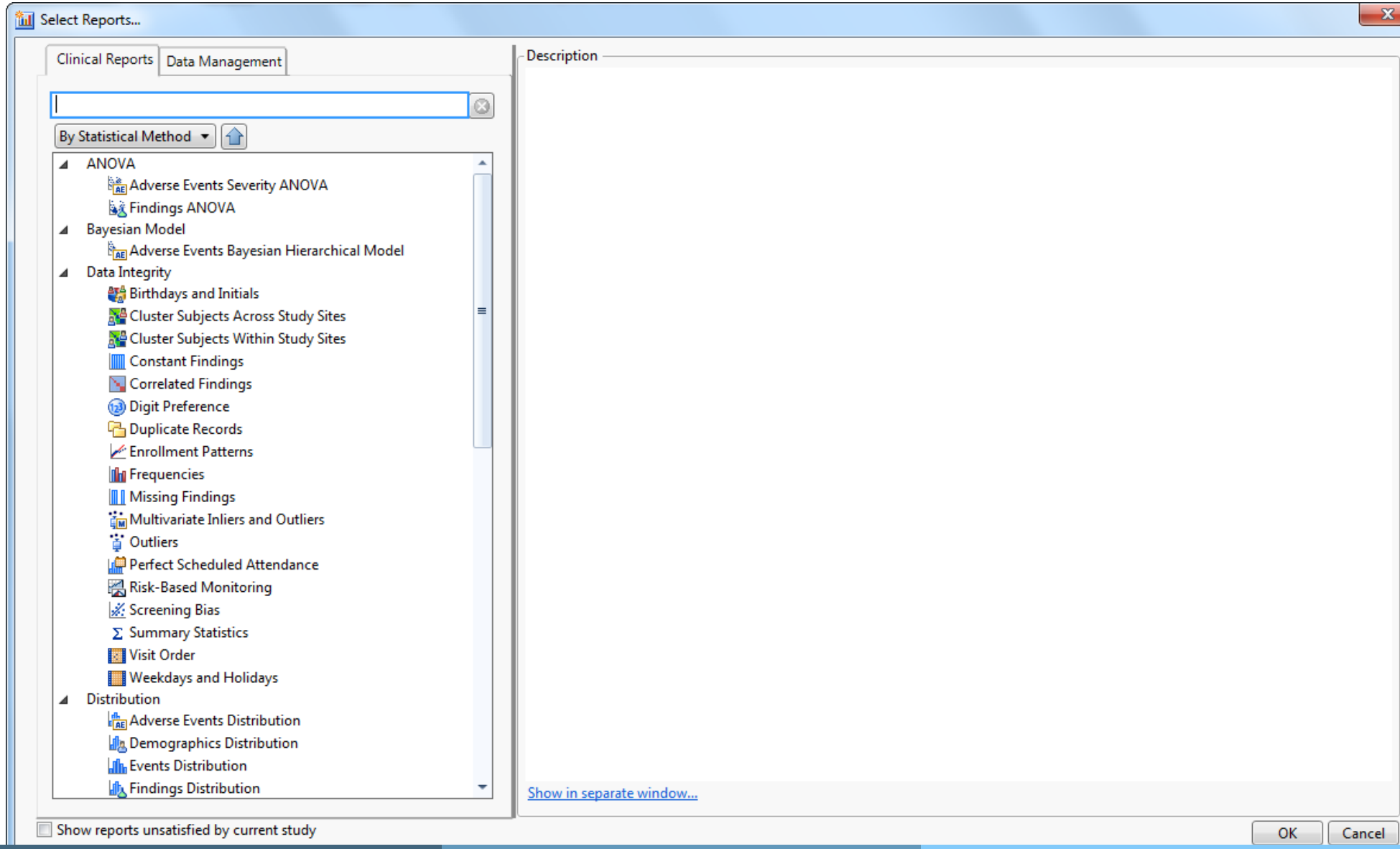
  - If # center ≤ 20, MLE

$$\tilde{T}_2 = \frac{\text{Gamma}(K_2, 1)}{\sum_i \frac{k_i}{\tau_i}}$$

- Adaptive Adjustment, if necessary

$$\tilde{T}(M) = d + \frac{\text{Gamma}(K_3, 1)}{\tilde{\Lambda}_1 + \text{Gamma}(\alpha M, 1) m/\alpha}$$

JMP Clinical



The dialog

Patient Recruitment

Options

General

* Target Enrollment
1000 ?

* Target Date
01Feb1993 Clear Calendar ?

☑ Use the Last Randomization Date as Current Dat ?

Current Date
Clear Calendar ?

☐ Truncate Early Recruitment Data ?

Truncation Date
Clear Calendar ?

☑ Use site active date from the Risk Data Set, if availabl ?

Options

Number of Simulations
10000 ?

Seed Number
123 ?

Amount of Increment in the Remaining Enrollment (How Often to Simulate)
10 ?

Number of Days Delayed at New Centers
30 ?

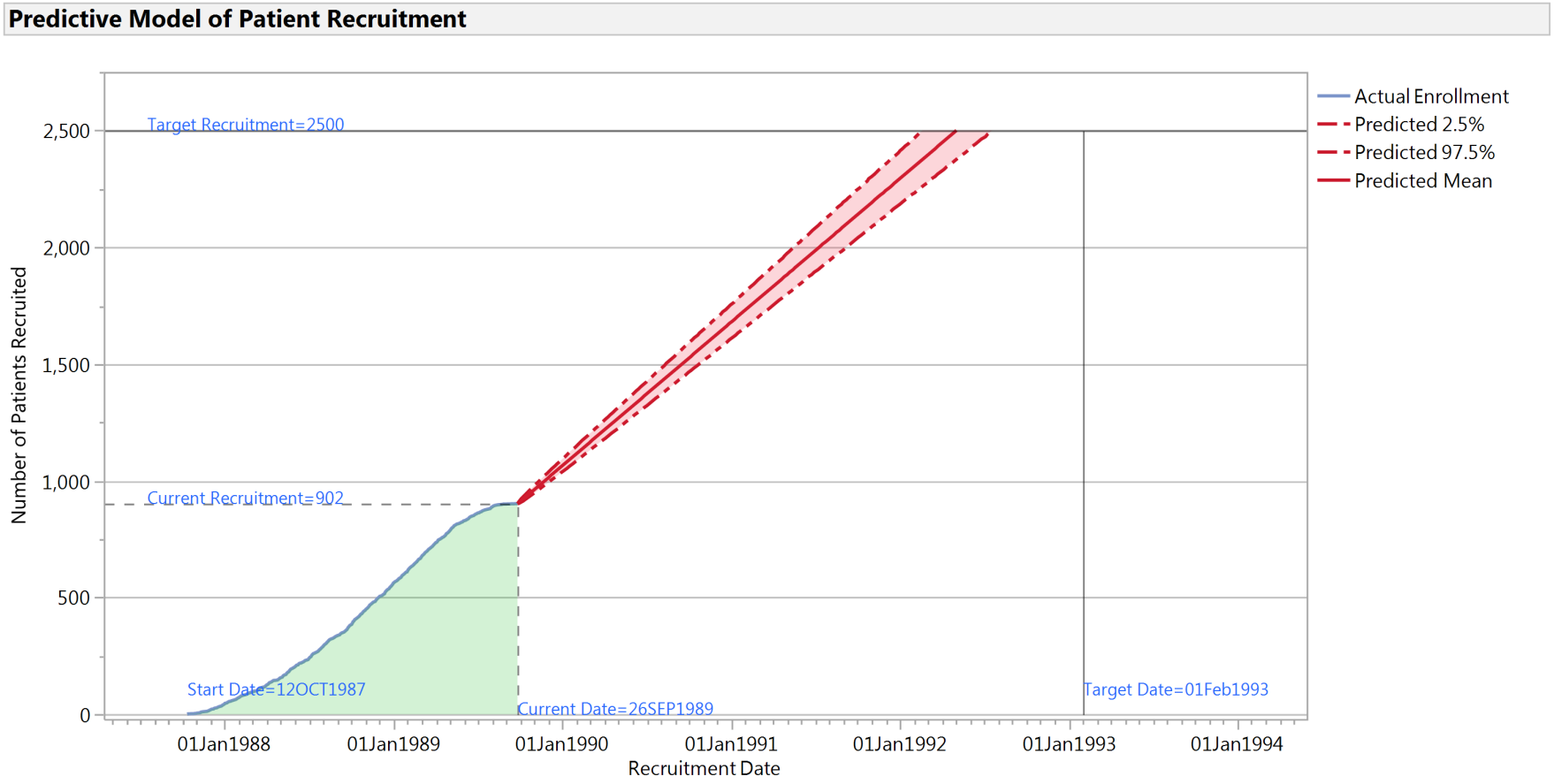
Maximum Probability of Meeting the Target Date to Initiate Adaptive Adjustment
0.85 ?

Minimum Probability of Meeting the Target Date to Stop Adding New Centers
0.85 ?

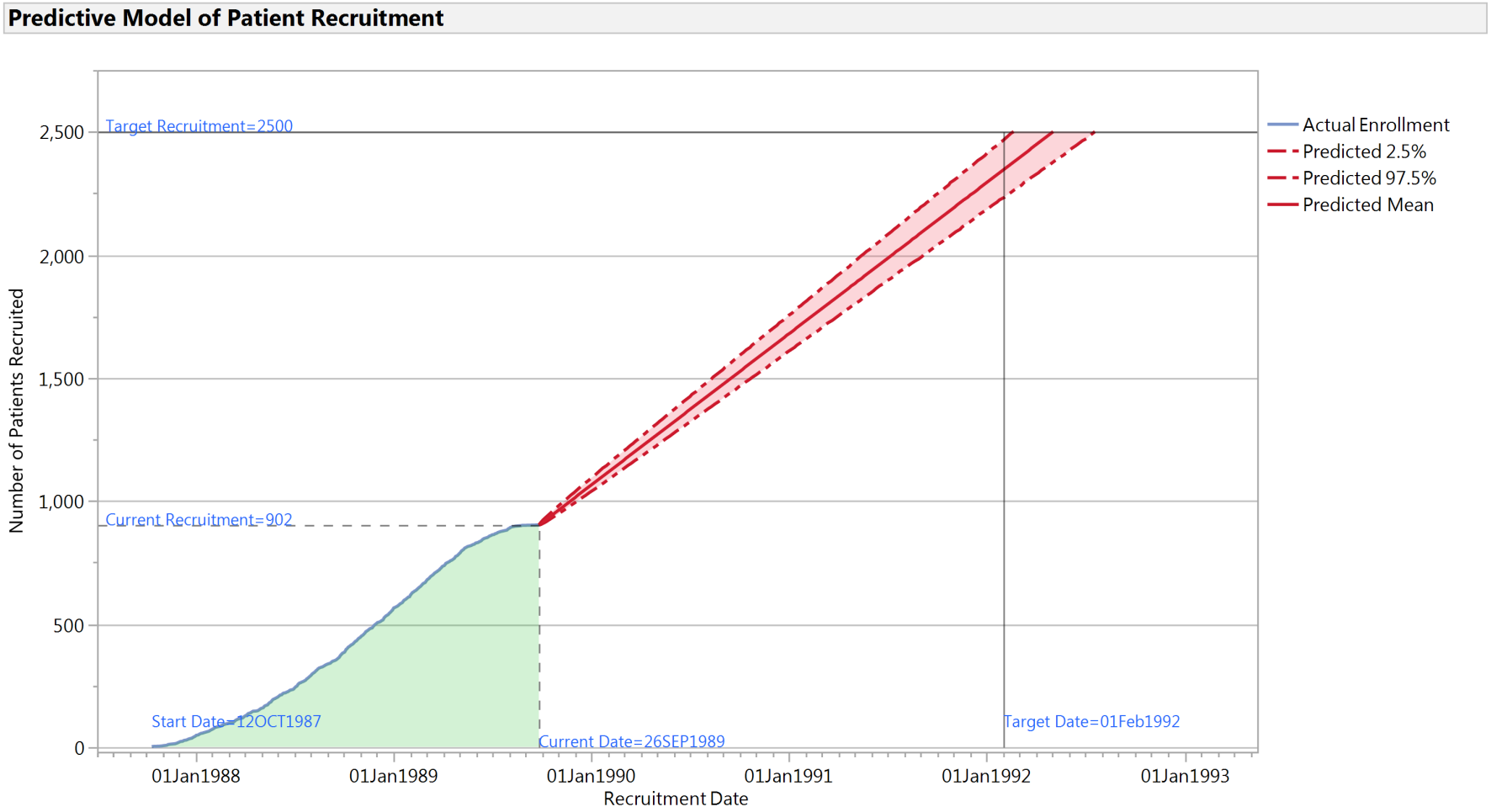
Initial Number of Additional Centers
1 ?

* Required Parameter

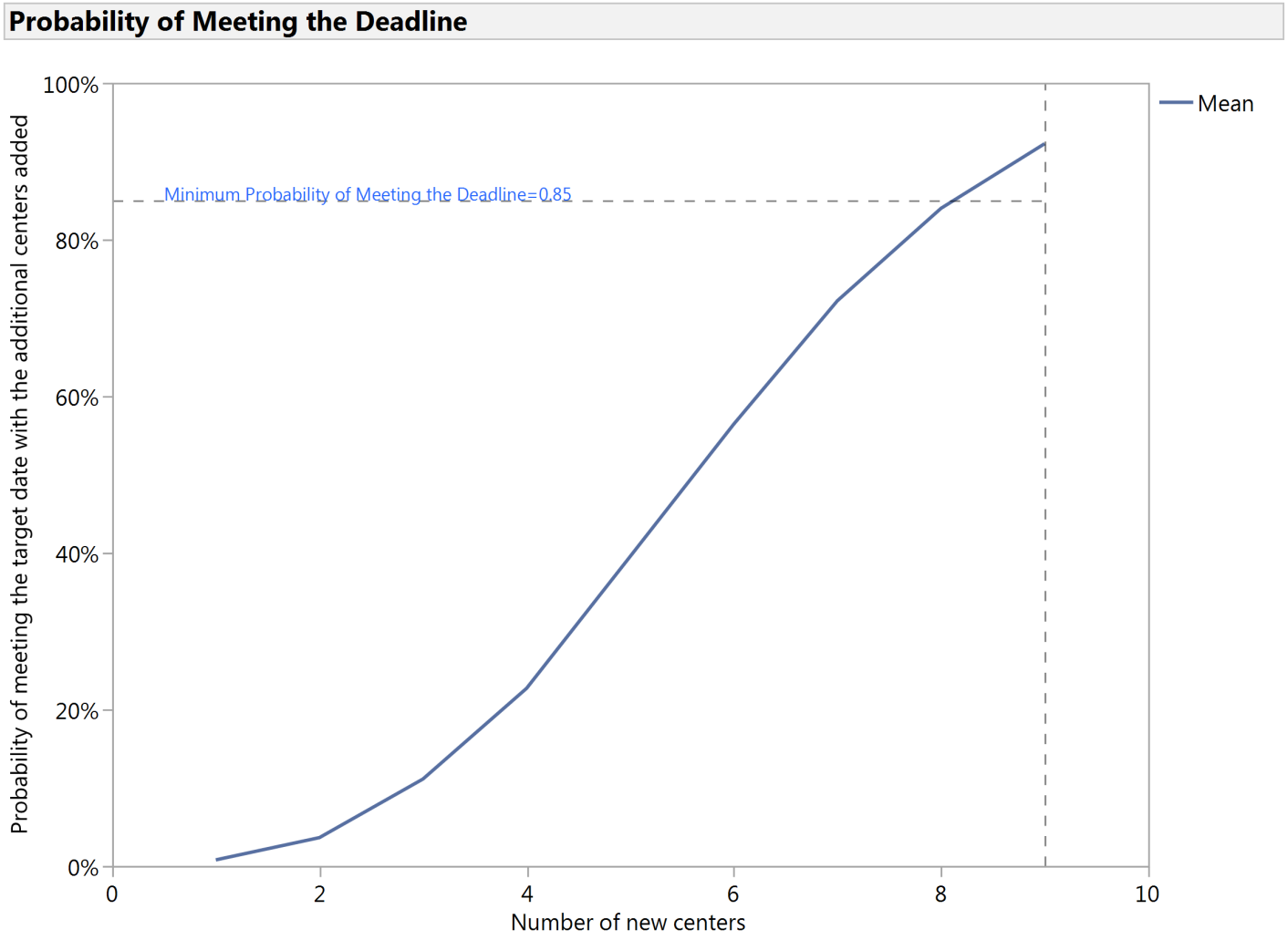
When we meet the deadline



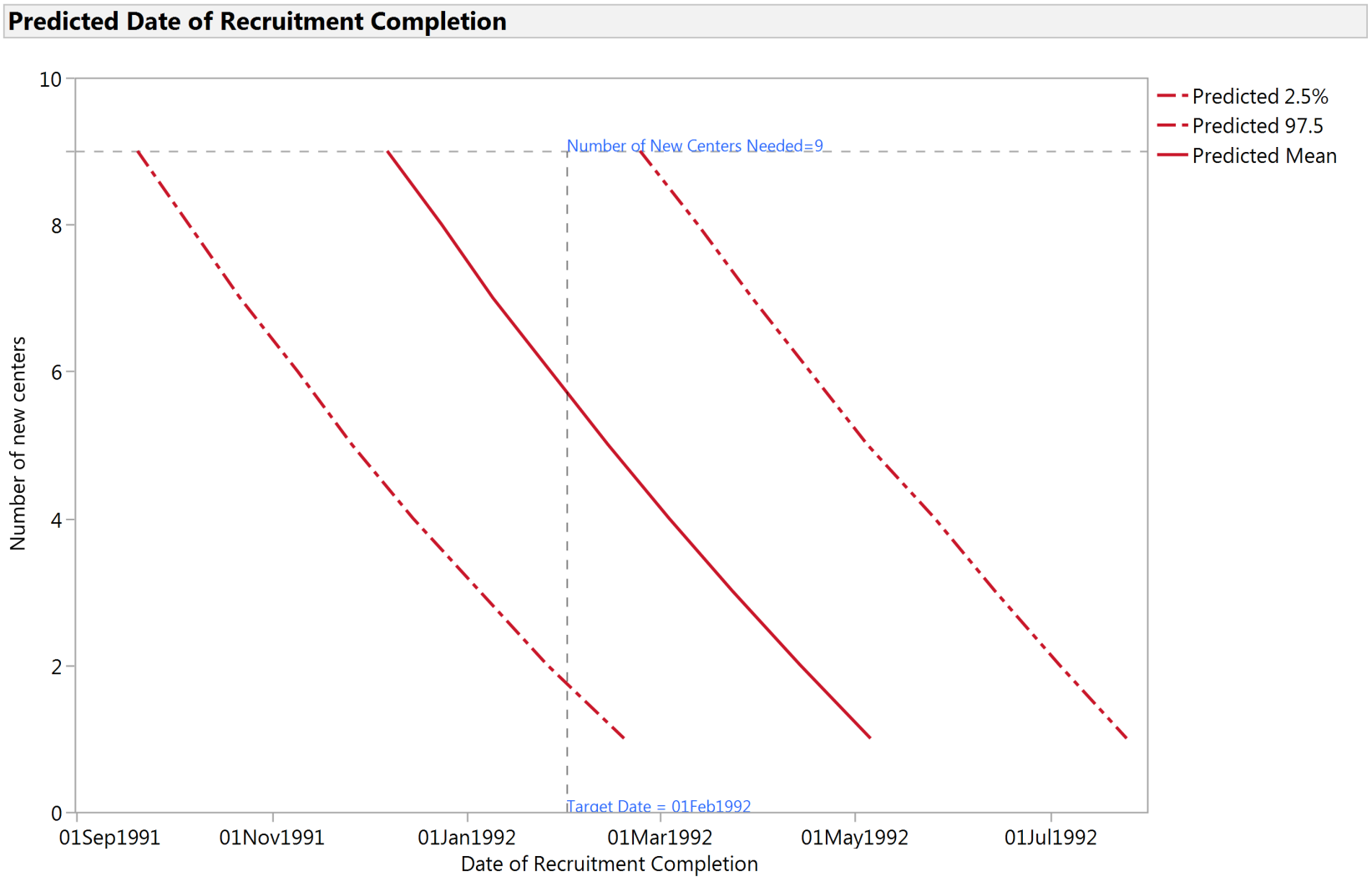
When we miss the deadline



Adaptive adjustment



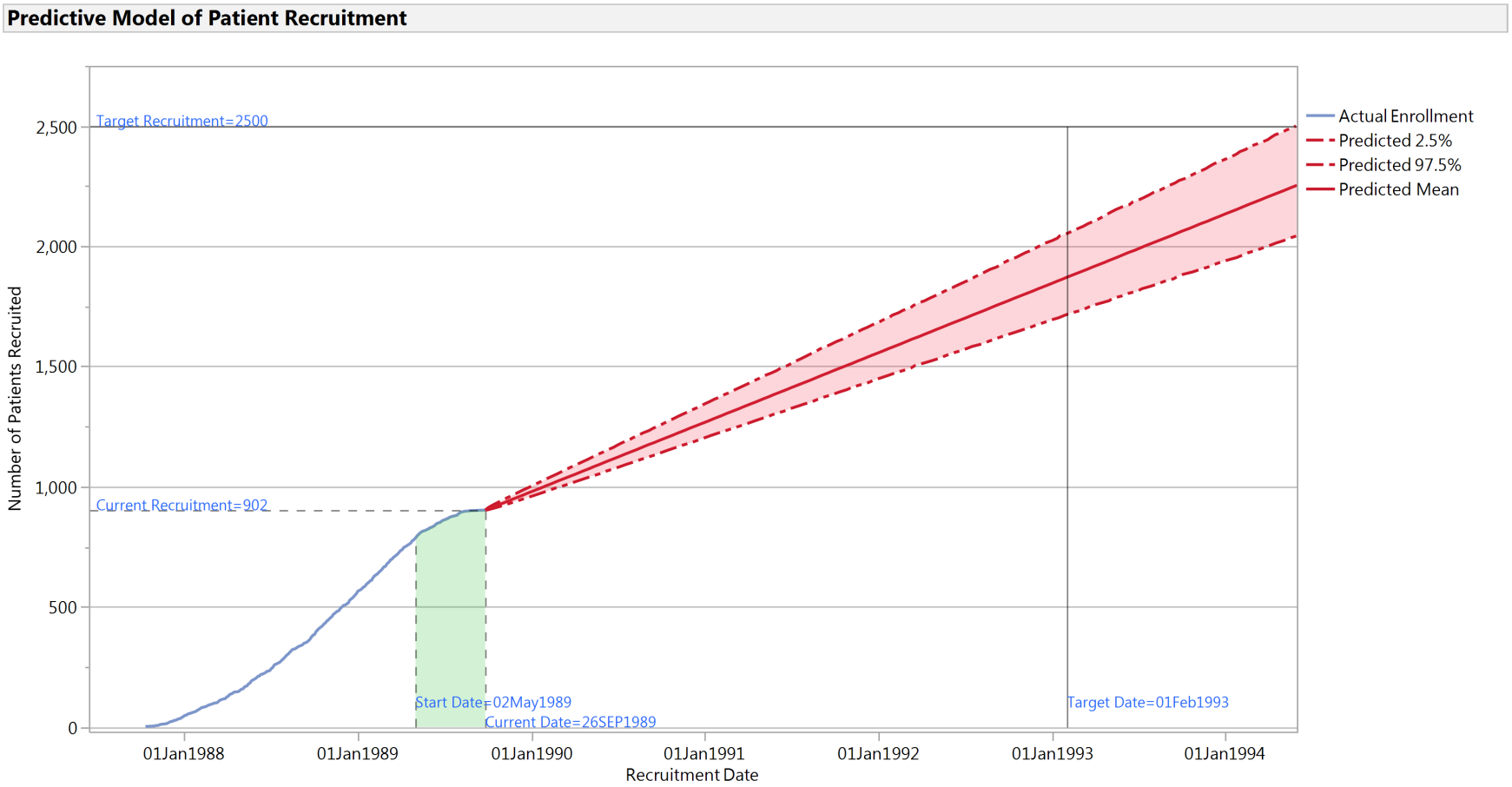
Adaptive adjustment



Adaptive Adjustment

Number of new centers	Probability of meeting target date with the additional centers added	Average predicted date of enrollment completion	2.5th percentile of predicted date of enrollment completion	97.5th percentile of predicted date of enrollment completion	Target date
1	0.77%	06May1992	19Feb1992	25Jul1992	01Feb1992
2	3.61%	14Apr1992	26Jan1992	04Jul1992	01Feb1992
3	11.10%	24Mar1992	05Jan1992	14Jun1992	01Feb1992
⋮	⋮	⋮	⋮	⋮	⋮
7	72.17%	09Jan1992	22Oct1991	30Mar1992	01Feb1992
8	83.97%	24Dec1991	06Oct1991	13Mar1992	01Feb1992
9	92.22%	07Dec1991	20Sep1991	24Feb1992	01Feb1992

Truncate the data



Thank you for your attention

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