

Revolutionizing Cancer Trials with Adaptive Designs and Bayesian Analysis

A Bayesian Adaptive Approach for Relapsed/Refractory Acute Myeloid Leukemia (AML)

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Agenda

- ✓ Introduction
- ✓ Bayesian Adaptive Designs
- ✓ Case Study:
 - Study Design & Methodology
 - Statistical Methods
 - Key Results
 - Conclusion
- ✓ Regulatory Considerations
- ✓ Conclusion & Future Directions

Introduction

Challenges in AML trials

**High patient
variability &
genetic
heterogeneity**

**Limited
Subjects
recruitment**

**Long approval
timelines**

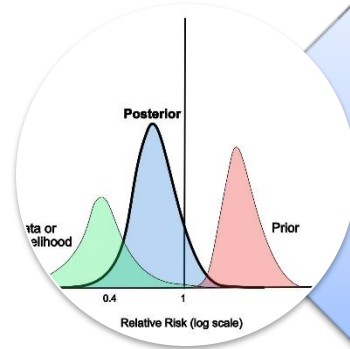
**Large sample
size
requirements**

Introduction

The Need for Adaptive Trials



Cancer Trials Designs



Bayesian Adaptive Designs



Platform/Umbrella/Basket Trial Designs

Introduction

Bayesian Adaptive Designs

What is Bayesian Adaptive Design?

- Prior knowledge
- Allows Real-time modifications
- More flexible & efficient



**Early Stopping for
Inefficacy**



**Sample Size
Adjustments**



**Patient
Reallocation**

Introduction

Bayesian Adaptive Designs

How This Differs from Conventional Approaches?

Feature	Frequentist Methods	Bayesian Predictive Model
Inference Type	Point estimates & confidence intervals	Full posterior distribution of treatment success
Flexibility	Fixed sample size	Allow real-time updates as new data arrives
Decision Criteria	Hypothesis testing (p-value, HR)	Predictive probability of success (e.g., $P(\theta > 0.85)$)

Case Study

Key Question
Should the trial continue based on Bayesian adaptive criteria?



Case Study

Step 1: Study Design



Study Population

100 patients RCT with
relapsed/refractory AML

44 control

56 experimental



Primary Endpoints

- Overall Survival (OS)
- Progression-Free Survival (PFS).



Censoring Criteria

Patients lost to follow-up
or
event-free at last
recorded visit

Case Study

Step 2: Study Data

Data: *Simulated data – using SAS program

Key Subjects Characteristics:

- Age (years): Control: 57.19 (± 9.96), Experimental: 56.94 (± 8.87):
- Prior Treatment (%): Control: 80.7%, Experimental: 70.5%:
- Disease Severity (%): Control: Moderate (45.5%), Severe (54.5%). Experimental: Moderate (42.0%), Severe (58.0%).
- Baseline WBC Count ($10^9/L$): Control: 50.30 (± 28.88), Experimental: 47.83 (± 29.53).
- Baseline HB (g/dL): Control: 12.18 (± 3.53), Experimental: 11.95 (± 3.51).

Censoring Rates: Control group (11.36%) vs. Experimental group (25.00%).

*Access: The dataset supporting SAS program this analysis is accessible mentioned in paper

Case Study

Step 3: Statistical Methods



Kaplan-Meier Survival Analysis

Estimates survival probabilities for OS & PFS.



Bayesian Cox Proportional Hazards

Uses MCMC sampling for hazard ratio estimation.



Bayesian Predictive Probability

Predicts trial continuation based on accumulating data.

Case Study

Step 4: SAS Code

PROC PHREG: Bayesian Cox PH model was used to estimate hazard ratios (HR) for the experimental treatment for OS/PFS. The following SAS code was used

```
/* Bayesian Cox Proportional Hazards Model for PFS/OS */  
PROC PHREG DATA=aml_adtte;  
    CLASS TRT01A;  
    MODEL AVAL * CNSR(1) = TRT01A;  
    WHERE PARAMCD = "&varname";  
    BAYES SEED=12345 NBI=1000 NMC=10000 THIN=10 OUTPOST=Bayesian_Cox;  
RUN;
```

Case Study

Step 4: SAS Code

PROC MCMC: Bayesian predictive probability was used to determine whether the trial should continue, expand, or stop early. The following SAS code was used

```
TITLE "Bayesian Predictive Probability for OS/PFS";  
  
PROC MCMC DATA=aml_adtte NBI=1000 NMC=10000 THIN=10 SEED=12345 OUTPOST=Bayes_Predictive_&paramcd;  
  WHERE PARAMCD = "&paramcd";  
  PARMS theta;  
  PRIOR theta ~ BETA(1,1);  
  MODEL AVAL ~ NORMAL(theta, VAR=100);  
  
RUN;
```

Case Study

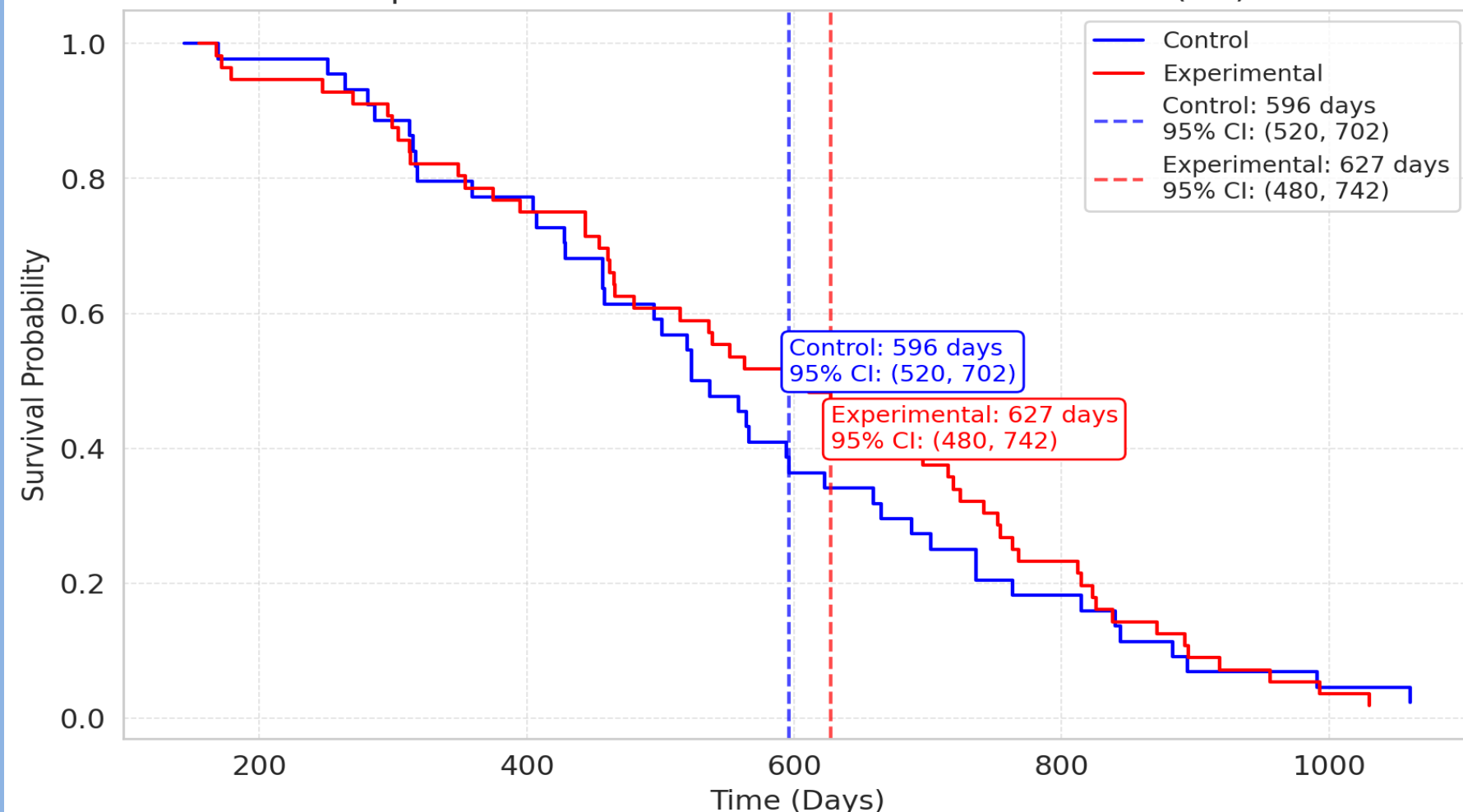
Step 5: Key Results (KM)

Kaplan-Meier Analysis

OS: **627** days (Exp) vs. **596** days (Control);

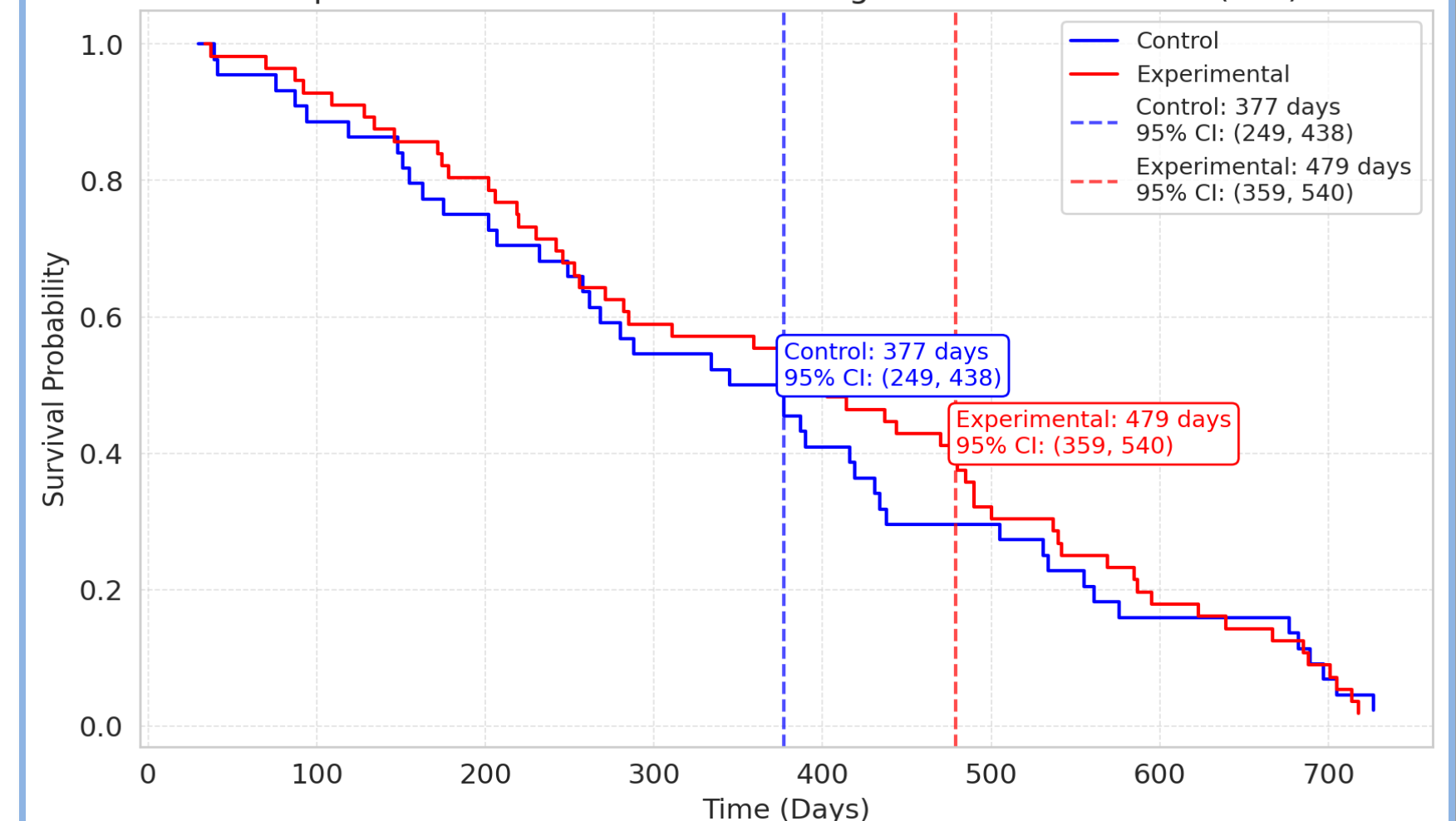
PFS: **479** days (Exp) vs. **377** days (Control).

Kaplan-Meier Survival Curve for Overall Survival (OS)



KAPLAN-MEIER SURVIVAL CURVE FOR OS

Kaplan-Meier Survival Curve for Progression-Free Survival (PFS)



KAPLAN-MEIER SURVIVAL CURVE FOR PFS

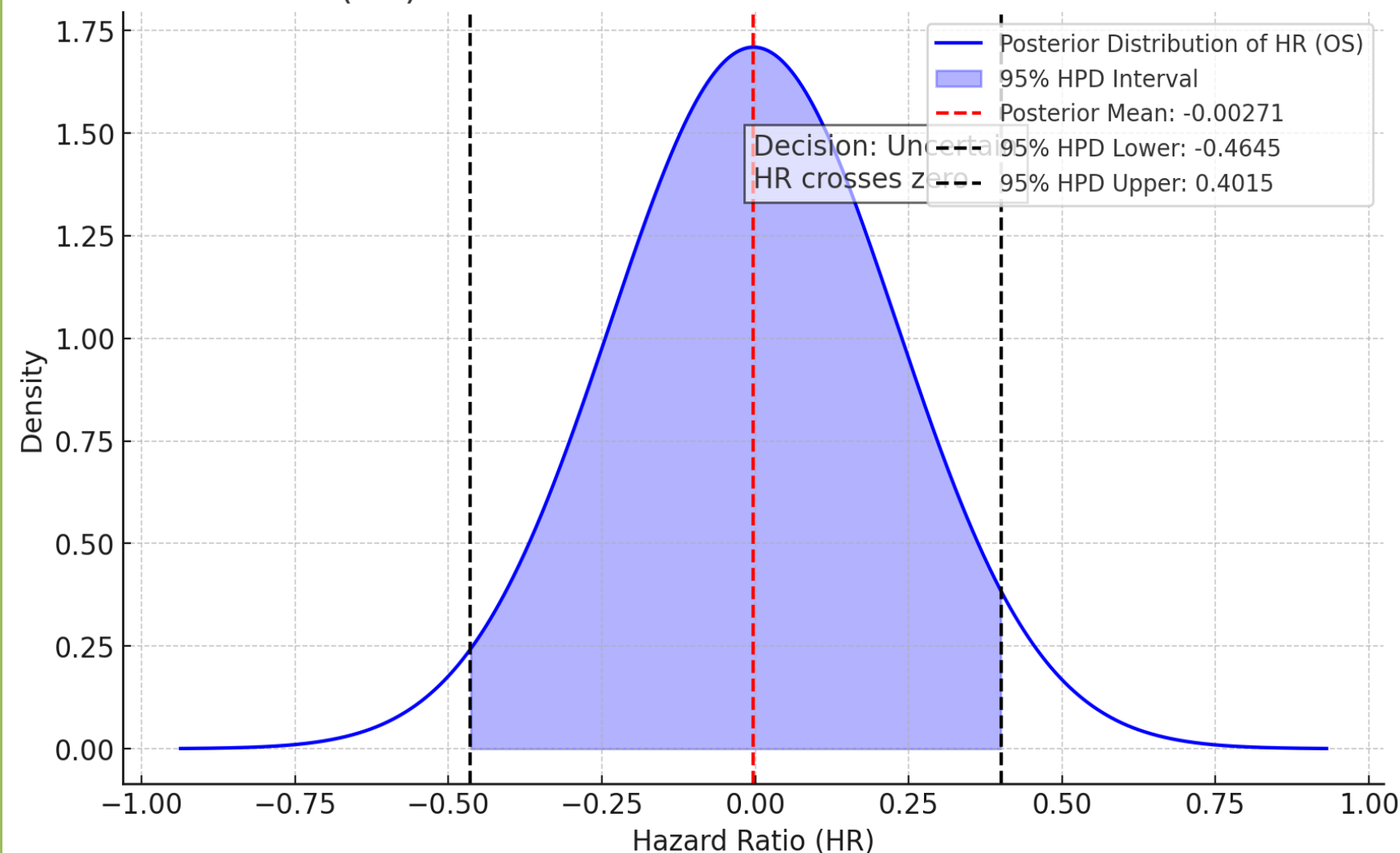
Case Study

Step 5: Key Results (Bayesian Cox PH)

Bayesian Cox PH Model (OS)

HR: **-0.00271 (95% HPD: -0.4645, 0.4015)** – No strong treatment effect

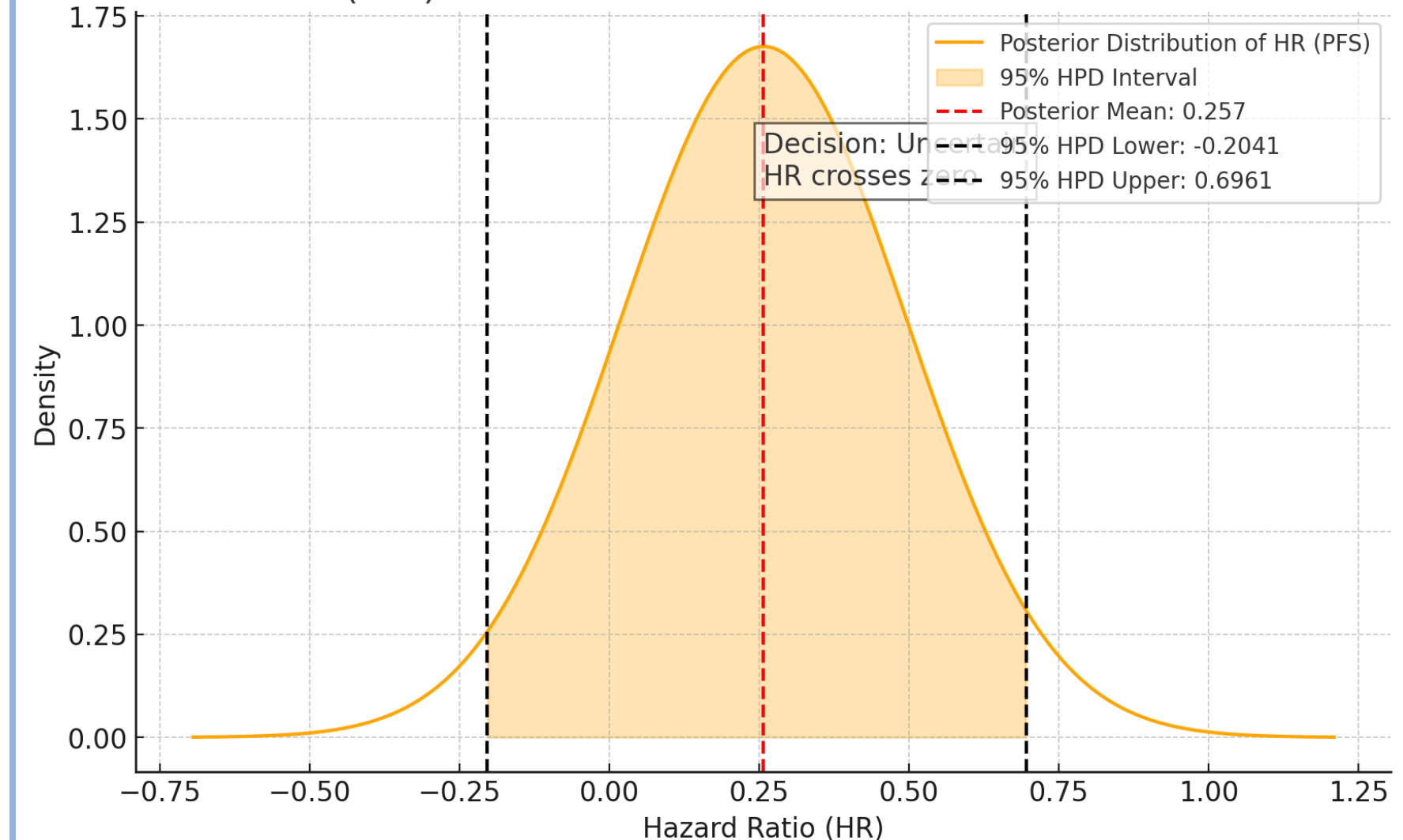
HR (OS) Posterior Distribution with 95% HPD Interval



Bayesian Cox PH Model (PFS)

HR: **0.257 (95% HPD: -0.2041, 0.6961)** – Possible clinical benefit.

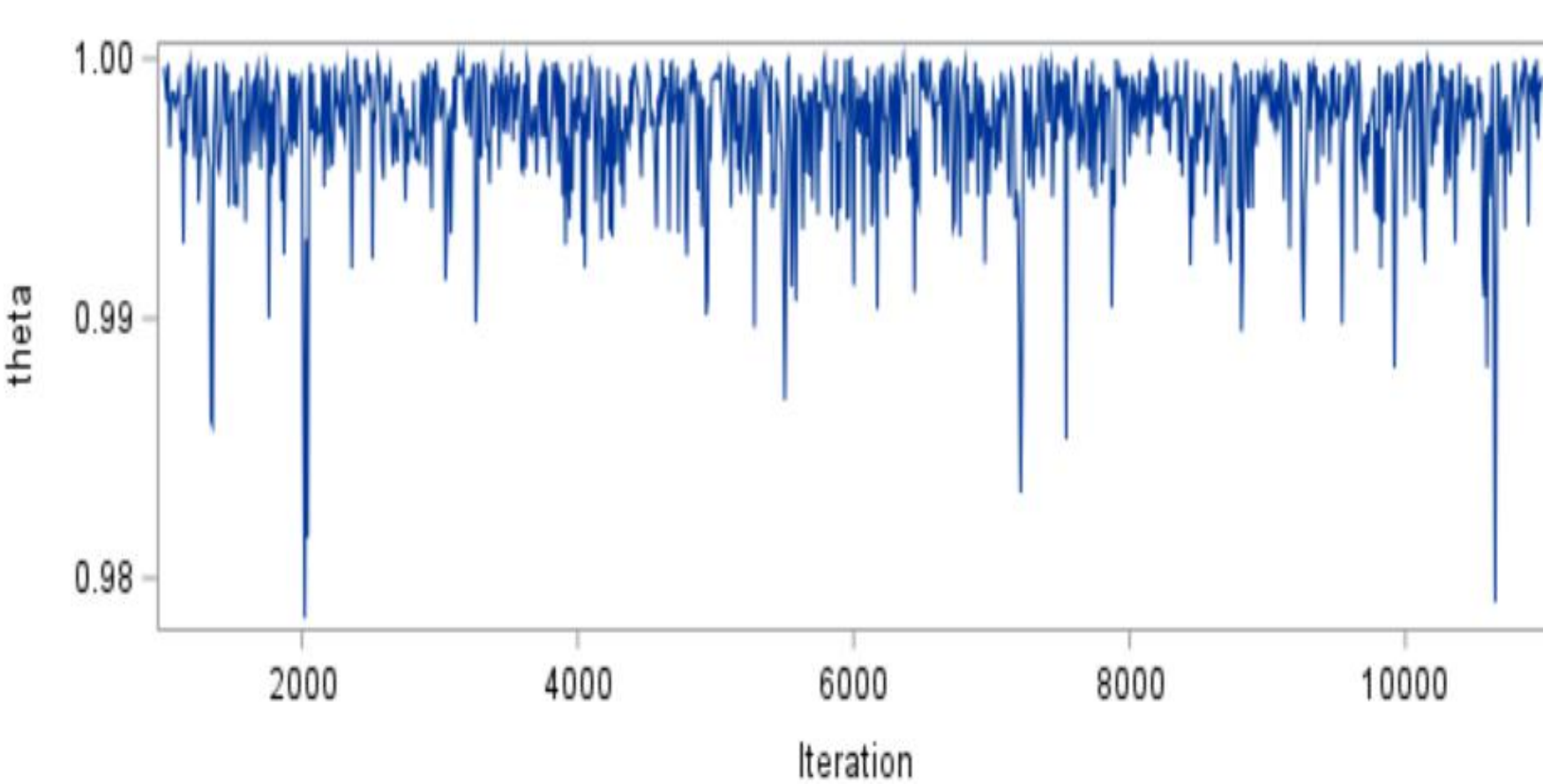
HR (PFS) Posterior Distribution with 95% HPD Interval



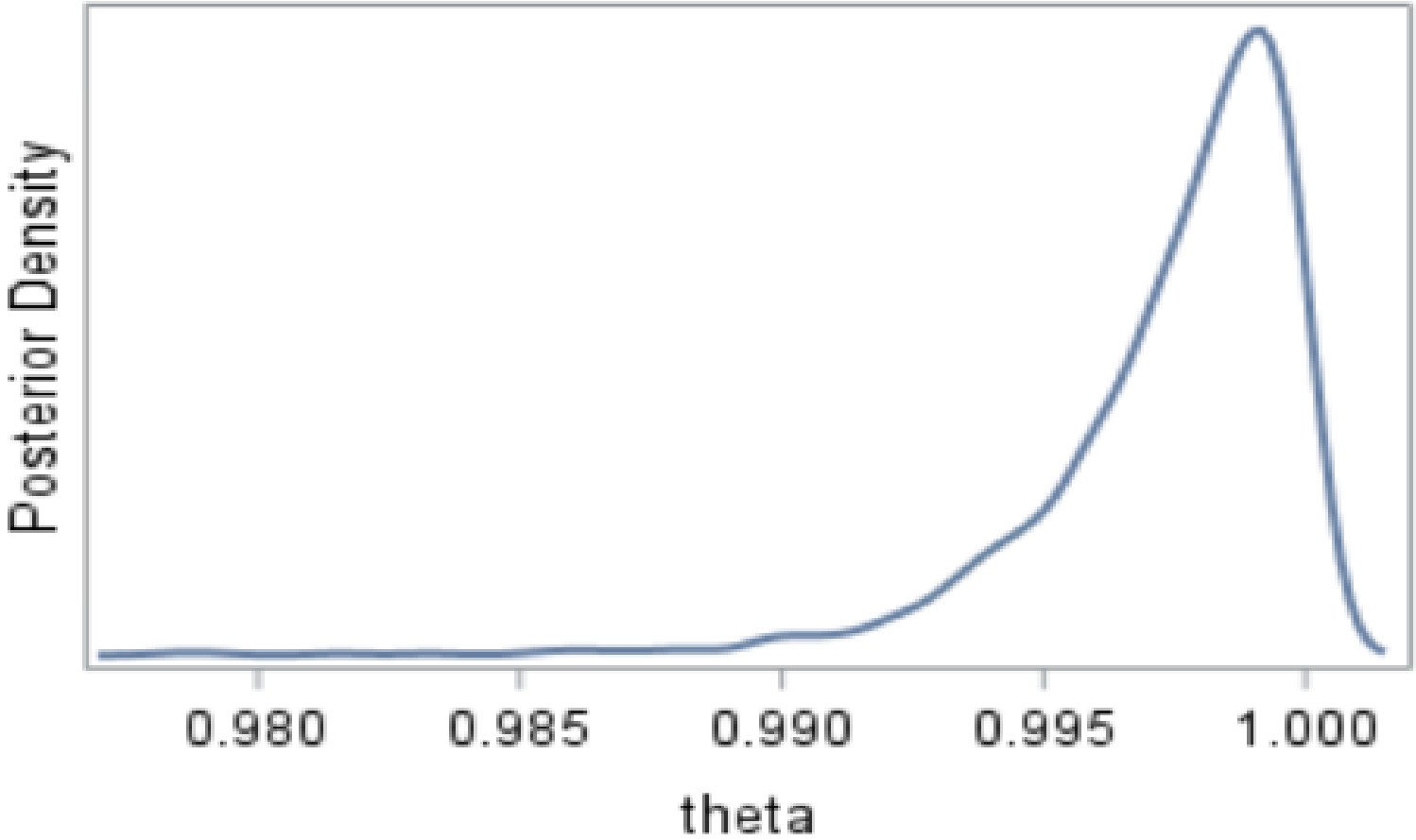
Case Study

Step 5: Key Results PFS (Θ)

Posterior Summaries and Intervals					
Parameter	N	Mean	Standard Deviation	95% HPD Interval	
theta	1000	0.9974	0.00253	0.9929	1.0000



TRACE PLOT (ITERATION VS. THETA) for PFS

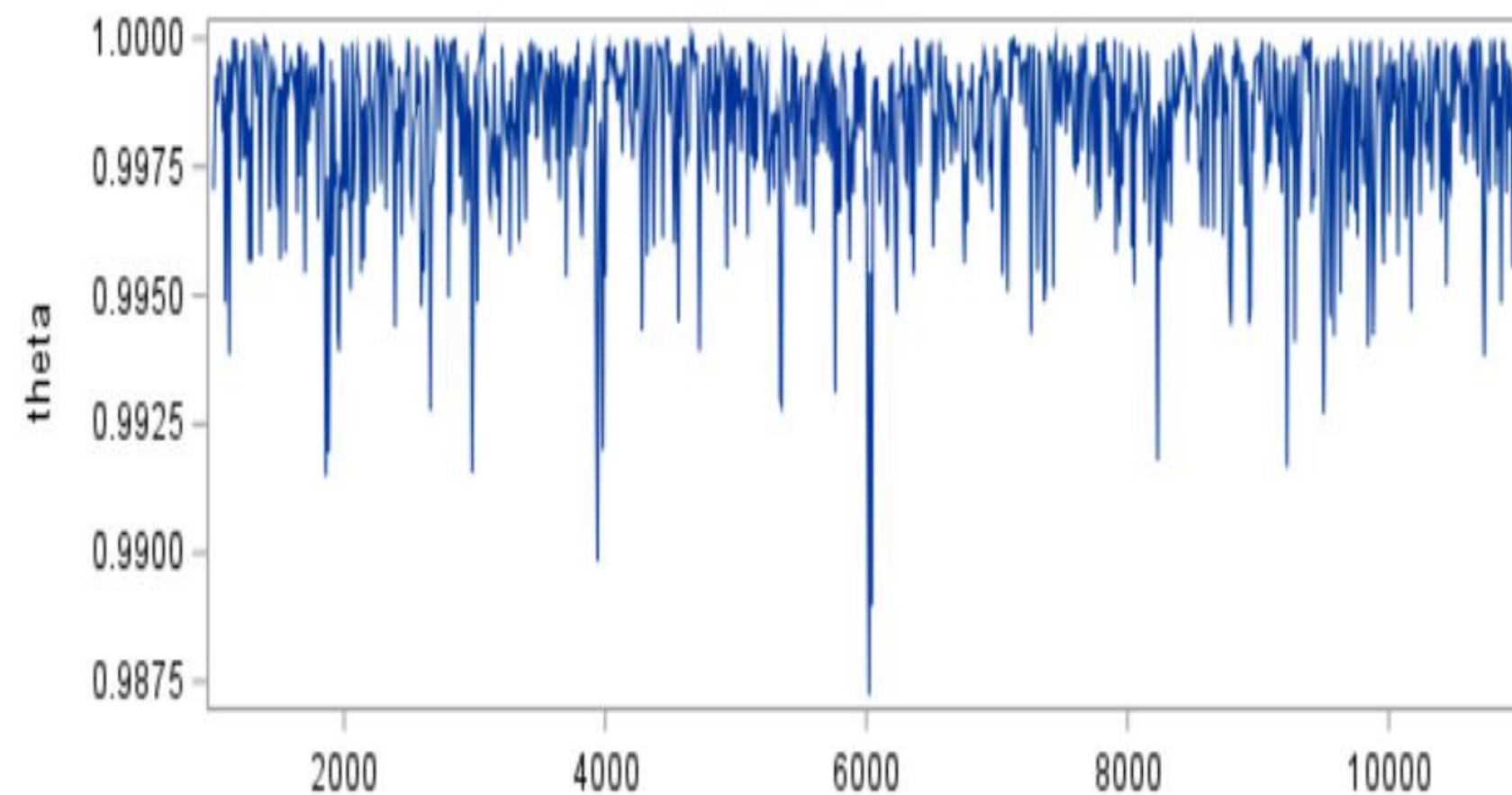


POSTERIOR DENSITY PLOT FOR PFS

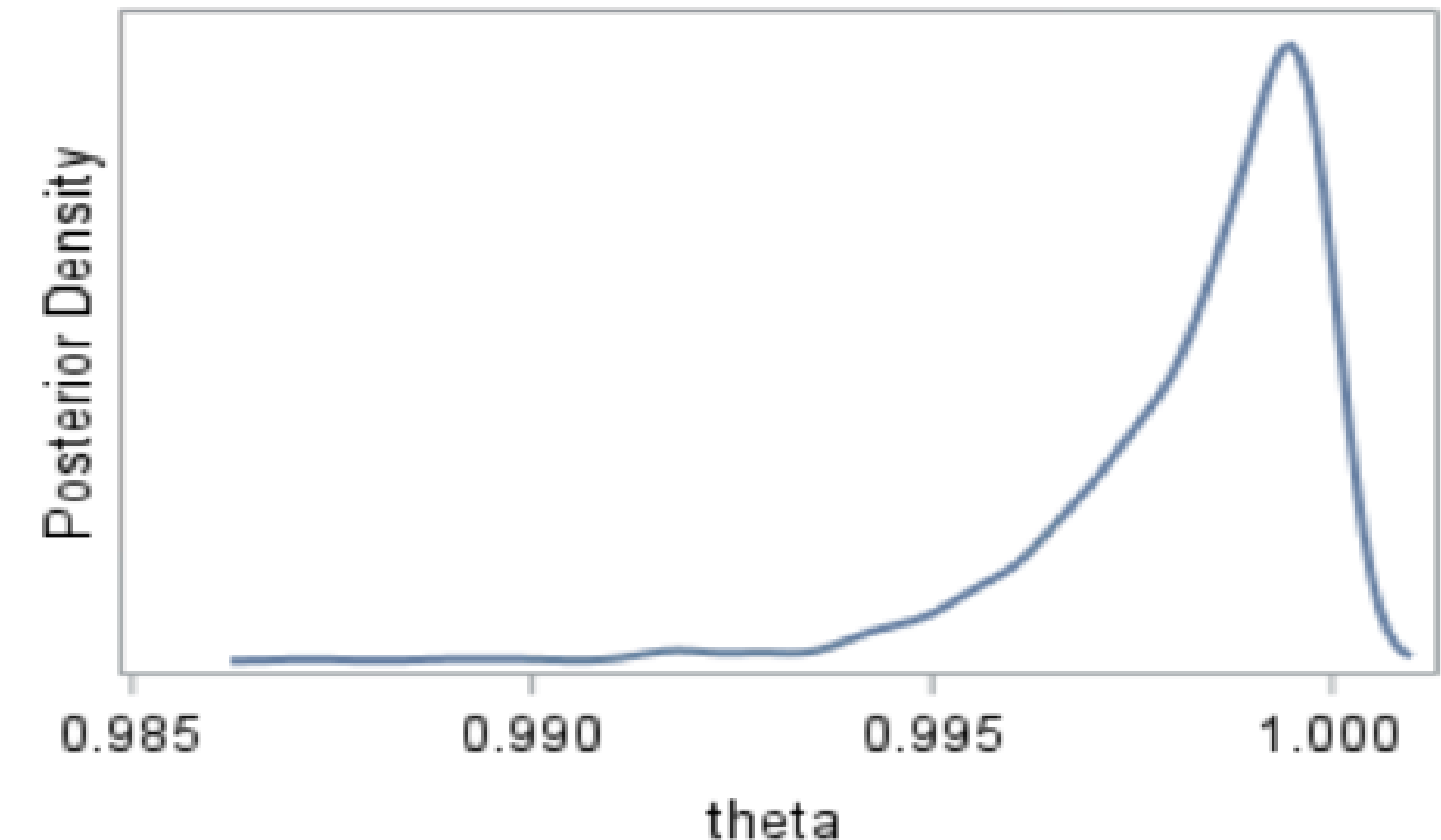
Case Study

Step 5: Key Results OS (Θ)

Posterior Summaries and Intervals					
Parameter	N	Mean	Standard Deviation	95% HPD Interval	
theta	1000	0.9984	0.00160	0.9954	1.0000



TRACE PLOT (ITERATION VS. THETA) for OS



POSTERIOR DENSITY PLOT FOR OS

Case Study

Step 6: Conclusion

Kaplan-Meier Interpretation OS and PFS trends favor experimental but lack statistical significance.

Bayesian Cox PH Interpretation (OS) HR: -0.00271 (95% HPD: -0.4645, 0.4015) – No strong treatment effect.

Bayesian Cox PH Interpretation (PFS) HR: 0.257 (95% HPD: -0.2041, 0.6961) – Possible clinical benefit

Bayesian Predictive Probability Histogram confirms ~99% probability supports for Both PFS and OS continued investigation.

Decision Rules & Regulatory Compliance

Insights on Trial Continuation

Bayesian Predictive Probability

Decision Thresholds

Continue if $\theta > 85\%$,
expand if $50\% \leq \theta \leq 85\%$,
stop if $\theta < 50\%$.

Ethical & Regulatory Compliance

Aligns with FDA adaptive trial guidelines

LIMITATIONS & FUTURE WORK

Challenges & Next Steps



Sample Size

Larger datasets needed for stronger statistical power.



Biomarker Integration

FLT3, NPM1 mutations could refine patient selection.



Machine Learning Potential

AI-driven Bayesian models may enhance trial accuracy.

**Without data,
you're just
another person
with an opinion.**

– W. EDWARDS DEMING

Thank you!

– W. EDWARDS DEMING