

Bayesian Methods in Survival Analysis: Enhancing Insights in Clinical Research

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ABSTRACT

Survival analysis has long been a cornerstone in understanding time-to-event data. However, traditional survival analysis often relies on frequentist statistics, which can be limited in handling complex scenarios and incorporating prior knowledge. Hence, it is a prudent decision to integrate Bayesian methods, a transformative approach that offers a fresh perspective to survival analysis.

This paper peers into the application of Bayesian methods in survival analysis, presenting a nuanced perspective that enhances insights in clinical research. Bayesian approaches provide a robust framework for handling complex survival data, incorporating prior knowledge, and facilitating more informed decision-making. This paper demonstrates how Bayesian approaches increase the understanding of survival outcomes, contributing significantly to the advancement of clinical research. Attendees will gain insights into the advantages of Bayesian techniques, contributing to a more comprehensive and detailed interpretation of survival data, and ultimately enhancing the quality of conclusions drawn from clinical research studies.

INTRODUCTION

There are two primary branches of statistics, each advocating for its unique advantages. The first, dominant, and most widely used approach is the frequentist approach, centered around null hypothesis significance testing, notably utilizing P-values and confidence intervals. The alternative is the Bayesian approach, guided by Bayes' theorem. The main difference between these methodologies lies in their conceptualization of uncertainty and probability: while the frequentist approach assigns probabilities solely to observed data rather than hypotheses, the Bayesian approach assigns probabilities directly to hypotheses. Moreover, Bayesian models integrate prior knowledge into analyses, adjusting the probabilities of hypotheses as additional data is acquired.

FREQUENTIST VS BAYESIAN STATISTICS

Two schools of statistics, two different approaches, and a bunch of different thoughts. The discussion regarding Bayesian and frequentist statistics is continuously fueled by passionate debates and differing viewpoints. Let's investigate the details of both methods by examining some examples and try to assess the strong and weak sides of each of them.

BASICS OF FREQUENTIST STATISTICS

Frequentist statistics view probability as the long-term frequency of an event occurring.

For instance, in the scenario of rolling a fair, six-sided die hundreds of times, there might be instances where you roll a "2" multiple times consecutively. However, across numerous rolls, you can expect to obtain a "2" approximately once in every six rolls. Frequentists would employ this reasoning to conclude that you have a one-in-six chance of rolling a "2" on the next attempt.

Using a frequentist approach to A/B testing, the process starts with the assumption of no difference between the two variations (null hypothesis). The aim is to determine if the results provide substantial evidence to reject the initial assumption (alternative hypothesis).

You will often encounter mentions of p-values in discussions about frequentist statistics. The p-value quantifies the strength of evidence against the null hypothesis. If the p-value falls below a specific significance level, typically 0.05 or lower, you would reject the null hypothesis, indicating a significant difference in performance between the variations.

Imagine you're testing the efficacy of a new medication (Treatment A) by comparing it against a placebo (Treatment B) to determine if the drug has a significant effect beyond the placebo effect. Your null hypothesis is that there is no difference in the effectiveness of new medication compared to placebo.

During the clinical trial, data is collected for both Treatment A and Treatment B, and p-values are calculated to assess the significance of the difference in treatment effects between the two groups. If the p-value is less than or equal to 0.05 (the significance level), you would conclude that your results are statistically significant. This means the evidence is strong enough to reject the null hypothesis in favor of the alternative hypothesis. Advantages and disadvantages of frequentist statistics are summarized in Table 1.

Advantages	Disadvantages
Each type of data has a specific test	Operates within rigid frameworks
No prior knowledge of the data is required	Provides only binary ("Yes" or "No") answers and point estimates
Widely accepted in medical and research practices	Results can vary based on the number of experiments conducted
Interpretation is straightforward	Experimental design must be predetermined
Computationally simple to perform	The p-value primarily assesses the null hypothesis and doesn't directly inform about the alternative hypothesis

Table 1. Advantages and Disadvantages of Frequentist Statistics

BASICS OF BAYESIAN STATISTICS

Bayes' Theorem, named after 18th-century British mathematician Thomas Bayes, is a mathematical formula for determining conditional probability. Conditional probability evaluates the probability of an event happening based on the occurrence of a previous event under similar circumstances. This theorem offers a mechanism to adjust or update existing predictions or theories by incorporating new evidence or information.

Bayes' theorem depends on the integration of prior probability distributions to produce posterior probabilities.

In Bayesian statistical inference, prior probability refers to the likelihood of an event happening before gathering new data. Essentially, it reflects the most reasoned evaluation of the probability of a specific outcome based on existing knowledge prior to conducting an experiment.

The posterior probability represents the adjusted likelihood of an event occurring following the incorporation of new information. It is computed by updating the prior probability using Bayes' theorem. Statistically, the posterior probability denotes the probability of event A transpiring given the occurrence of event B.

For instance, if a disease is correlated with age, Bayes' theorem enables a more precise estimation of the probability of an individual having the disease by considering their age, compared to estimating the probability without knowledge of their age.

Advantages of Bayesian statistics:

- Calculates the probability distribution of the hypotheses.
- Bayesian inference offers a systematic approach to integrating prior knowledge with new data, grounded in a robust decision-making framework. It allows for the incorporation of historical information regarding a parameter to establish a prior distribution for subsequent analyses. As new observations emerge, the previous posterior distribution serves as the basis for updated inferences. All conclusions logically stem from Bayes' theorem.
- It provides inferences that are data-conditioned and precise, without depending on asymptotic approximation. The process of small sample inference mirrors that of a large sample, ensuring consistency in methodology regardless of sample size.
- It adheres to the likelihood principle, meaning that if two different sampling designs yield proportional likelihood functions, the resulting inferences should be identical irrespective of the design choice. Classical inference, on the other hand, does not universally adhere to the likelihood principle.
- All information is contained within the data itself, rather than relying on unobserved frequencies.

Disadvantages of Bayesian statistics:

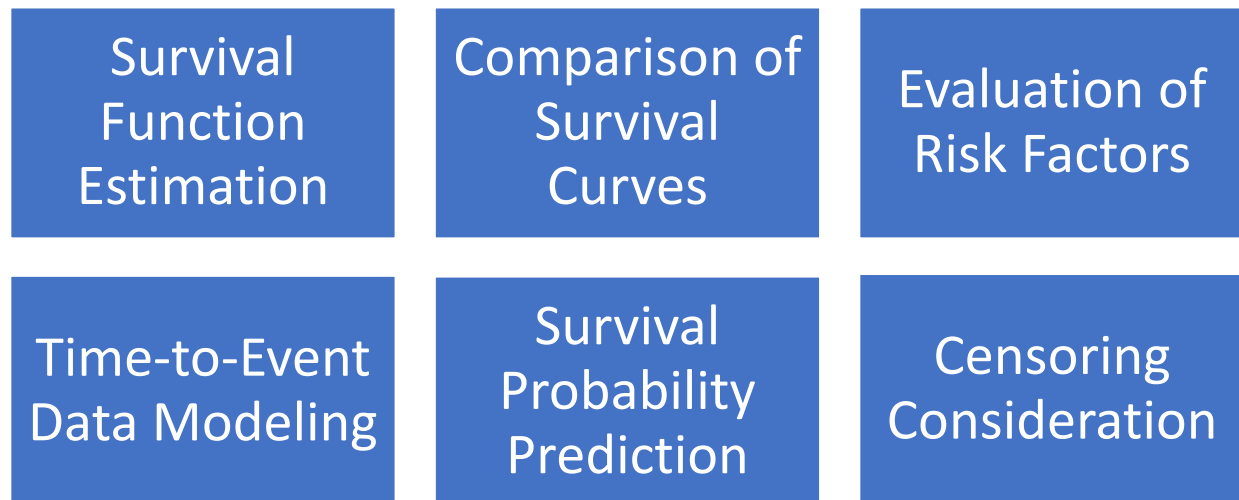
- Establishing the prior probabilities of hypotheses can involve varying subjective values, potentially appearing arbitrary. Bayesian inference does not prescribe a method for selecting a prior, leaving this

decision open-ended. Consequently, there is no universally correct approach to choosing a prior.

- It may generate posterior distributions strongly influenced by the priors. Practically, it can pose challenges in persuading subject matter experts who disagree with the validity of the selected prior.
- It often involves a significant computational cost, particularly in models with a large number of parameters. Additionally, simulations may yield slightly different outcomes unless the same random seed is utilized.

SURVIVAL ANALYSIS

Survival analysis is a statistical method used in clinical trials to analyze the time until a particular event of interest occurs. This event could be anything from the onset of a disease, the occurrence of a complication, or death. It's commonly used in medical research, especially in situations where the outcome of interest involves the timing of events. In a clinical trial, survival analysis helps researchers understand how long it takes for certain events to happen, and it allows them to compare different treatments or interventions in terms of their effects on the time to event outcome. It takes into account censoring, which occurs when participants are lost to follow-up or when the event of interest hasn't occurred by the end of the study period. Main goals of the survival analysis are shown in the Display 1.



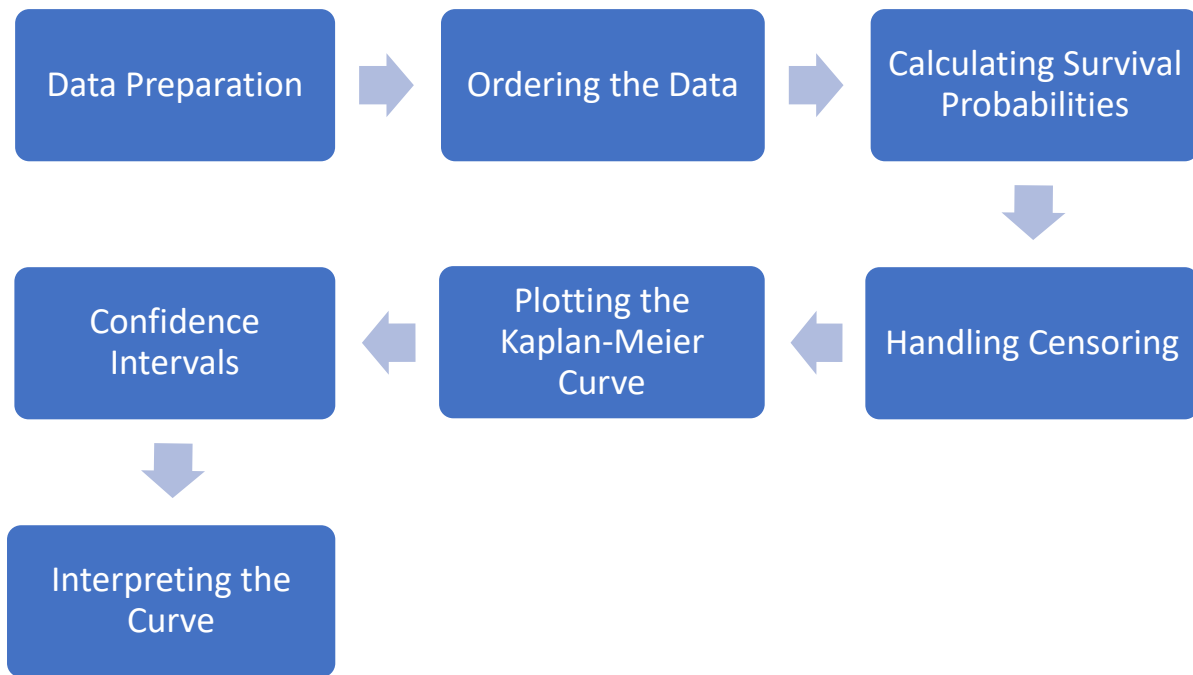
Display 1. Primary Goals of Survival Analysis

The Kaplan-Meier estimator is widely utilized in survival analysis to estimate the survival function, representing the probability of survival past specific time points, using observed data. Moreover, the Cox proportional hazards model is frequently applied to evaluate the impact of diverse factors (e.g., treatment groups, patient characteristics) on the hazard rate, which denotes the rate of experiencing the event of interest over time, while accounting for other covariates.

KAPLAN-MEIER APPROACH

The Kaplan-Meier approach, also known as the Kaplan-Meier estimator or product-limit estimator, is a non-parametric method used in survival analysis to estimate the survival function from time-to-event data. It's commonly employed when analyzing data where the event of interest is whether or not an event occurs (such as death, relapse, or failure) within a specified time frame.

An outline of the Kaplan-Meier approach implementation presented in Display 2.



Display 2. Implementation of Kaplan-Meier Approach

Below is an example of a basic PROC LIFETEST call for Kaplan-Meier (KM) analysis in SAS®:

```
/* KM approach */
ods output ProductLimitEstimates = ple Quartiles = quartiles;
proc lifetest data=tte plots=survival;
    time survtime*event(0);
run;
ods output close;
```

This PROC LIFETEST call performs Kaplan-Meier analysis on the provided data set TTE, estimating the survival function and producing a plot of the Kaplan-Meier curve. The TIME statement specifies the time-to-event data, with SURVTIME representing the time variable indicating the time until the event occurs, and EVENT(0) representing the censoring variable where 0 indicates censoring. The estimates of the survival function and quartiles are stored in the output data sets PLE and QUARTILES, respectively, for further analysis or reporting.

The Kaplan-Meier approach is widely used in clinical trials and observational studies for its simplicity and robustness in estimating survival probabilities, particularly when the underlying survival distribution is unknown or non-parametric assumptions are violated. However, it's important to note that the Kaplan-Meier estimator does not allow for the inclusion of covariates or the assessment of their effects on survival, which can be addressed using more advanced methods like the Cox proportional hazards model.

COX PROPORTIONAL HAZARDS REGRESSION ANALYSIS

The Cox proportional hazards model, also known as Cox regression or simply Cox model, is a widely used statistical method for analyzing survival data in medical research and other fields. It's a semi-parametric model that allows researchers to assess the effect of multiple covariates (independent variables) on the hazard rate (the rate of experiencing the event of interest) over time while assuming the hazard ratios remain proportional.

Below is an outline of how the Cox proportional hazards model works:

1. Data Preparation: Gather a data set consisting of time-to-event data, including the times at which events occur (or censoring times) and the values of covariates for each subject.

2. Model Assumption: The Cox model assumes that the hazard function for any individual is a product of two components: a baseline hazard function that varies with time but not with covariates, and an exponential function of the covariates. Mathematically, the hazard function $H(t)$ for an individual at time t is expressed as:

$$H(t|X) = H_0(t) \times \exp(b_1X_1 + b_2X_2 + b_3X_3 + \dots + b_kX_k)$$

where:

- $H(t|X)$ is the hazard function at time t given the values of covariates X .
- $H_0(t)$ is the baseline hazard function, which describes the hazard rate over time in the absence of covariate effects.
- b_1, b_2, b_3, b_k are the coefficients associated with the covariates X_1, X_2, X_3, X_k , representing the logarithm of the hazard ratios (HRs) associated with each covariate.

3. Parameter Estimation: Estimate the coefficients (b_1, b_2, b_3, b_k) in the model using maximum likelihood estimation (MLE). The Cox model does not require specifying the baseline hazard function, so it estimates the hazard ratios without making assumptions about the underlying hazard distribution.

4. Interpreting Hazard Ratios: Interpret the estimated hazard ratios to understand the relative effects of the covariates on the hazard rate. A hazard ratio greater than 1 indicates an increased hazard (risk), while a hazard ratio less than 1 indicates a decreased hazard.

5. Model Checking: Assess the validity of the proportional hazards assumption using diagnostic techniques such as Schoenfeld residuals or graphical methods. If the assumption is violated, appropriate adjustments or stratification may be necessary.

6. Inference and Prediction: Conduct statistical inference on the estimated coefficients to determine their significance and make predictions about the hazard rate for new individuals based on their covariate values. Below is an example of a basic PROC PHREG call for Cox proportional hazards model analysis in SAS:

```
/* Cox model */
proc phreg data=tte;
  model survtime*event(0) = age sex;
run;
```

As you can see, it is quite similar to the Kaplan-Meier approach. The main distinction is the inclusion of age and sex in the model as covariates.

The Cox proportional hazards model is flexible and widely used due to its ability to handle time-varying covariates, accommodate censoring, and provide interpretable results in terms of hazard ratios. It's a powerful tool for analyzing survival data in both clinical trials and observational studies.

BAYESIAN METHODS IN SURVIVAL ANALYSIS

Bayesian methods in survival analysis provide a flexible framework for analyzing time-to-event data while incorporating uncertainty in model parameters and predictions. Unlike traditional frequentist approaches, which rely on p-values and confidence intervals, Bayesian methods provide estimates of parameters as probability distributions, allowing for more intuitive interpretation and incorporation of prior knowledge.

Here's an overview of how Bayesian methods are applied in survival analysis:

- **Bayesian Inference:** Bayesian inference begins with specifying a prior distribution for the parameters of interest, reflecting existing knowledge or beliefs about their values before observing the data. This prior distribution is then updated based on observed data using Bayes' theorem to obtain the posterior

distribution, which represents our updated knowledge about the parameters after observing the data.

- **Prior Specification:** The choice of prior distribution is crucial in Bayesian analysis. Priors can be informative, reflecting strong prior beliefs about parameter values, or uninformative, allowing the data to drive the inference. Subject matter expertise and previous research findings often inform the choice of priors.
- **Model Specification:** Bayesian survival analysis typically involves specifying a likelihood function, which describes the probability of observing the data given the parameters of the model. Common likelihood functions used in survival analysis include the exponential, Weibull, and log-logistic distributions. The likelihood function is combined with the prior distribution to obtain the posterior distribution using Bayes' theorem.
- **Markov Chain Monte Carlo (MCMC):** In practice, Bayesian inference often relies on computational techniques such as Markov Chain Monte Carlo (MCMC) methods to draw samples from the posterior distribution. MCMC algorithms, such as Gibbs sampling and Metropolis-Hastings, iteratively sample from the posterior distribution, allowing for estimation of parameter values and uncertainty.
- **Posterior Inference:** Once samples from the posterior distribution have been obtained, posterior inference involves summarizing the posterior distribution to draw conclusions about the parameters of interest. This may include estimating posterior means, medians, confidence intervals, and other summaries of interest.
- **Model Checking and Sensitivity Analysis:** Bayesian methods allow for model checking and sensitivity analysis to assess the adequacy of the chosen model and the impact of prior assumptions on the results. Diagnostic tools, such as posterior predictive checks and sensitivity analyses, can help identify model misspecification and assess the robustness of conclusions.

Overall, Bayesian methods offer a powerful and flexible approach to survival analysis, allowing for incorporation of prior knowledge, uncertainty quantification, and complex modeling while providing interpretable results. However, Bayesian analysis requires careful consideration of prior specification, computational resources for MCMC sampling, and thoughtful interpretation of results.

If we intend to incorporate Bayesian analysis, we simply need to introduce the BAYES statement.

```
/* Bayesian survival analysis using PROC PHREG */
ods graphics on;
proc phreg data=tte;
  model survtime*event(0) = age sex;
  bayes seed=1 diagnostic=all plots=all outpost=post;
run;
```

Naturally, there are several additional options available within the BAYES statement. However, to perform a Bayesian analysis using SAS in procedures such as GENMOD, PHREG, LIFEREG, or COUNTREG, you simply need to include the BAYES statement. It's important to note that certain other options or sub-options may not be compatible with the BAYES statement.

Let's look closer into the above piece of code. This code snippet utilizes PROC PHREG in SAS to conduct a Bayesian analysis of a Cox proportional hazards model. It fits the model to survival data from the data set TTE considering variables such as age and sex as covariates. It generates diagnostic information and plots while storing posterior samples of model parameters in an output data set named POST.

CASE STUDY

Random dummy data were generated for the purposes of analysis. Let's consider an Oncology study where we are evaluating time to relapse along with corresponding estimates of interest. The structure of the time-to-event analysis data set from our case study is presented in the Table 2.

SUBJID	TRTN	TRT	AGE	HIST	CIGAR	STRATA	PARAM	AVAL	CNSR
1	1	Treatment	56	yes	5	Severe	Time to Relapse	125	1
2	2	Placebo	65	no	10	Moderate	Time to Relapse	95	0
3	1	Treatment	72	yes	15	Severe	Time to Relapse	134	1
4	2	Placebo	69	no	20	Moderate	Time to Relapse	140	1
5	1	Treatment	66	yes	15	Severe	Time to Relapse	100	0
6	2	Placebo	71	no	10	Moderate	Time to Relapse	111	0

Table 2. Input data set structure

The HIST variable provides information about prior related diseases. A value of "1" in the CNSR variable indicates that the event occurred, while "0" signifies that the event did not occur and was therefore censored. Additionally, the STRATA variable contains information about disease severity. The remaining variables are self-explanatory.

First, let's calculate the simple Hazard ratios using the standard approach. A Cox regression model stratified by randomization factor (disease severity) will be used to estimate the hazard ratio (HR) of time to relapse, along with the associated Wald 95% CI. The PHREG procedure in SAS with option TIES=EXACT will be used to fit the Cox proportional hazards model.

```

/* Cox proportional hazards regression analysis */
ods output ParameterEstimates=hr;
proc phreg data = tte;
  class trt(ref = 'Treatment') hist(ref = 'no');
  model aval*cnsr(1) = trt age hist/ risklimits ties=exact;
  strata stratan;
run;

```

This code models the time-to-event data using covariates such as treatment, age, and history of related diseases, with stratification by the disease severity. The parameter estimates are then outputted to the data set HR for further analysis and reporting. Results of the above procedure can be found in Display 3.

Analysis of Maximum Likelihood Estimates										
Parameter		DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits		Label
TRT	Placebo	1	1.12995	0.44262	6.5170	0.0107	3.096	1.300	7.370	TRT Placebo
AGE		1	-0.06523	0.01710	14.5535	0.0001	0.937	0.906	0.969	
HIST	yes	1	-0.53191	0.35988	2.1846	0.1394	0.587	0.290	1.189	HIST yes

Display 3. Results of Cox proportional hazards regression analysis

Before moving directly to the Bayesian analysis let's step aside and briefly discuss the importance of informative and noninformative priors.

In Bayesian analysis, priors represent our initial beliefs or knowledge about the parameters of interest before observing the data. Informative priors encode specific information or beliefs about the parameters, often based on previous studies, expert opinion, or theoretical considerations. They provide strong constraints on the parameter values and can significantly influence the posterior distribution.

On the other hand, noninformative priors express minimal prior information about the parameters, allowing the data to largely determine the posterior distribution. They are preferred when there is limited prior knowledge or when we want to let the data speak for itself without imposing strong prior beliefs. The impact of the Bayesian analysis on the results using noninformative priors would be minimal. In other words, unless

informative priors are provided, the results are similar to those of frequentist approaches.

That being said, let's explore a basic example of Bayesian analysis with a noninformative prior.

```
/* Bayesian survival analysis with noninformative prior */
ods output ParameterEstimates=hr_bayes_noninf;
proc phreg data = tte;
  class trt(ref = 'Treatment') hist(ref = 'no');
  model aval*cnsr(1) = trt age hist/ ties=exact;
  strata stratan;
  bayes seed = 1 outpost = post;
run;
```

The BAYES statement initiates Bayesian estimation within PROC PHREG. Since no additional options are specified, a noninformative prior is assumed. Please note that the RISKLIMITS option is ignored for a Bayesian analysis. PROC PHREG first fits the Cox model by maximizing the partial likelihood. The maximum likelihood estimate (MLE) of the parameters and their 95% confidence interval are shown in Display 4.

Maximum Likelihood Estimates					
Parameter	DF	Estimate	Standard Error	95% Confidence Limits	
TRTPLACEBO	1	1.1300	0.4426	0.2624	1.9975
AGE	1	-0.0652	0.0171	-0.0987	-0.0317
HISTYES	1	-0.5319	0.3599	-1.2373	0.1734

Display 4. Classical parameter estimates

Since no prior is specified for the regression coefficient, the default uniform prior is used. Summary statistics of the posterior samples are displayed in Display 5. Note that the mean and standard deviation of the posterior samples are comparable to the MLE and its standard error, respectively, because of the use of the uniform prior.

Posterior Summaries and Intervals					
Parameter	N	Mean	Standard Deviation	95% HPD Interval	
TRTPLACEBO	10000	1.1945	0.4561	0.3240	2.0870
AGE	10000	-0.0668	0.0172	-0.1024	-0.0343
HISTYES	10000	-0.5275	0.3665	-1.2648	0.1651

Display 5. Posterior summaries and intervals

Now it is time to dig deeper and investigate another example which represents the use of an informative prior. To illustrate, let's consider a hypothetical recent clinical trial that demonstrated a 30% higher likelihood of disease acquisition among subjects who smoke an additional 10 cigarettes per day on average. This indicates that increasing cigarette consumption by 10 per day changes the hazard from no effect to a significant threefold increase. This opinion could be converted to an informative prior. Mathematically, we could present it like this:

$$1 < e^{10x} < 3$$

And after transformations, we will receive the next equation:

$$0 < x < 0.109$$

Now you can find a normal distribution that best approximates this belief by placing the majority of the prior distribution mass within this range. Assuming this interval is $\mu \pm 2\sigma$ where μ and σ are the mean and standard deviation of the normal prior, respectively, the hyperparameters μ and σ are computed as follows:

$$\mu = \frac{0 + 0.109}{2} = 0.0545$$

$$\sigma = \frac{0.109 - 0}{4} = 0.02725$$

Note that a normal prior distribution with a mean of 0.0545 and standard deviation of 0.02725 indicates that you believe, before looking at the data, that an increase of 10 cigarettes per day will probably change the hazard rate from 1 to 3-fold.

Assume the prior distributions are independent for all the parameters. For the coefficient of cigarettes, you use a normal prior distribution with mean 0.0545 and variance 0.00074, which is obtained by raising standard deviation to the second degree. For other parameters, you resort to using a normal prior distribution with mean 0 and variance 1E6, which is fairly noninformative. Means and variances of these independent normal distributions are saved in the data set *Prior* as follows:

```
/* Means and variances of the prior distributions */
data prior;
  input _type_ $ cigar age histyes trttreatment;
  datalines;
  mean 0.00545 0 0 0
  var 0.00074 1e6 1e6 1e6
run;

/* Bayesian survival analysis with informative prior */
ods graphics on;
ods output ParameterEstimates=hr_bayes_inf;
proc phreg data=tte;
  class trt(ref = 'Treatment') hist(ref = 'no');
  model aval*cnsr(1) = cigar age hist trt/ ties=exact;
  strata stratan;
  bayes seed=1 coeffprior=normal(input=Prior) statistics=(summary
interval)
      diagnostics=(autocorr ess) plots=trace;
  hazardratio 'Hazard Ratio Statement 1' trt;
  hazardratio 'Hazard Ratio Statement 2' age / unit=10;
  hazardratio 'Hazard Ratio Statement 3' hist;
run;
```

In the following BAYES statement, COEFFPRIOR=NORMAL(INPUT=PRIOR) specifies the normal prior distribution for the regression coefficients whose details are contained in the data set *Prior*. Posterior summaries (means, standard errors, and quantiles) are requested by the STATISTICS= option. Autocorrelations and effective sample sizes are requested by the DIAGNOSTICS= option as convergence diagnostics along with the trace plots (PLOTS= option) for visual analysis. For comparisons of hazards, three HAZARDRATIO statements are specified.

PROC PHREG computes the maximum likelihood estimates of regression parameters (Display 6). These estimates are used as the starting values for the simulation of posterior samples.

Maximum Likelihood Estimates					
Parameter	DF	Estimate	Standard Error	95% Confidence Limits	
CIGAR	1	0.0162	0.0276	-0.0380	0.0703
AGE	1	-0.0652	0.0170	-0.0986	-0.0318
HISTYES	1	-0.5383	0.3633	-1.2503	0.1737
TRTPLACEBO	1	1.1538	0.4451	0.2815	2.0262

Display 6. Parameter estimates

Display 7 shows the independent normal prior for the analysis.

Independent Normal Prior for Regression Coefficients		
Parameter	Mean	Precision
CIGAR	0.00545	1351.351
AGE	0	1E-6
HISTYES	0	1E-6
TRTPLACEBO	0	1E-6

Display 7. Independent normal prior

Summary statistics of the posterior samples are shown in Display 8. These results are quite comparable to the classical results based on maximizing the likelihood as shown in Display 6, since the prior distribution for the regression coefficients is relatively flat.

Posterior Summaries						
Parameter	N	Mean	Standard Deviation	Percentiles		
				25%	50%	75%
CIGAR	10000	0.0109	0.0195	-0.00239	0.0108	0.0240
AGE	10000	-0.0666	0.0171	-0.0778	-0.0660	-0.0550
HISTYES	10000	-0.5397	0.3669	-0.7870	-0.5469	-0.2947
TRTPLACEBO	10000	1.2257	0.4578	0.9078	1.1962	1.5170

Display 8. Posterior summaries from the Bayesian analysis

Finally in Display 9 we could see comparisons of three hazards.

Hazard Ratio Statement 1: Hazard Ratios for TRT									
Description	N	Mean	Standard Deviation	Quantiles			95% Equal-Tail Interval		95% HPD Interval
				25%	50%	75%			
TRT Placebo vs Treatment	10000	3.8045	2.0145	2.4789	3.3075	4.5585	1.4863	8.9063	1.1315 7.6791

Hazard Ratio Statement 2: Hazard Ratios for AGE									
Description	N	Mean	Standard Deviation	Quantiles			95% Equal-Tail Interval		95% HPD Interval
				25%	50%	75%			
AGE Unit=10	10000	0.5214	0.0889	0.4595	0.5170	0.5769	0.3618	0.7124	0.3488 0.6944

Hazard Ratio Statement 3: Hazard Ratios for HIST									
Description	N	Mean	Standard Deviation	Quantiles			95% Equal-Tail Interval		95% HPD Interval
				25%	50%	75%			
HIST no vs yes	10000	1.8342	0.6904	1.3427	1.7278	2.1967	0.8208	3.4841	0.6873 3.1972

Display 9. Customized hazard ratios

From the obtained results, it appears that employing Bayesian analysis with an informative prior yields higher hazard ratio values. This suggests that by integrating findings from another independent clinical trial, we have refined our understanding and obtained more accurate estimates.

CONCLUSION

In this paper, we have discussed the main principles and applications of Bayesian statistics in general, and specifically, we have detailed its implementation in survival analysis.

In conclusion, Bayesian methods offer a powerful and flexible approach to survival analysis that holds great promise for enhancing insights in clinical research. The ability to integrate prior knowledge with observed data enables researchers to make more informed decisions and extract deeper insights into complex survival patterns.

Moving forward, it's essential for researchers to actively promote and integrate Bayesian methods to unlock their full potential and advance the field of survival analysis.

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