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## Research Article Performance of Bayesian Using Conjugate Prior Estimator for Weibull Right Censored Survival Data

<sup>1</sup>Sri Astuti Thamrin, <sup>2</sup>Masli Nurcahya Zoraida, <sup>1</sup>Andi Kresna Jaya and <sup>3</sup>Ansariadi

<sup>1</sup>Statistics Study Program, Faculty of Mathematics and Natural Science, Hasanuddin University, Makassar, South Sulawesi, Indonesia <sup>2</sup>Pharmacy Study Program, Makassar Islamic University, Makassar, South Sulawesi, Indonesia <sup>3</sup>Department of Epidemiology, Faculty of Health, Hasanuddin University, Makassar, South Sulawesi, Indonesia

### Abstract

**Background and Objective:** The Weibull distribution is widely used to model and to analyze data on the survival time. Bayesian estimation approach has received much attention as it has been in contention with other estimation methods. In this study, it was examined the performance of the Bayesian estimator using conjugate prior information for estimating the parameters of Weibull distribution with censored survival data for dengue fever (DF). **Materials and Methods:** Through the simulated Weibull distributed survival dataset, the performance of conjugate estimator for estimating the Weibull distribution parameters can be checked before applying it to the DF survival dataset in Makassar, Indonesia. Statistical analysis of the simulation data and collected DF data were analyzed through summary tables and Markov Chain Monte Carlo method via Gibbs sampling algorithm. It was performed using R version 3.3.3 and Win BUGS. **Results:** Based on the simulation study, the mean of posterior means of all Weibull distribution parameter estimates are still reasonably accurate. After fitting the Weibull models to the DF survival time's dataset using the conjugate prior distribution, the age factor substantially described DF patients' survival times and had a positive effect on the estimated survival time. **Conclusion:** To choose sample size and censoring level, the estimates generated by the conjugate prior do not only depend on the data but also on the parameters of the prior distribution. The amount of uncensored data must be more than one in order to obtain an estimate of greater than zero. The results of estimated parameters of Weibull model using conjugate prior either with simulated survival data or the DF data is good.

Key words: Conjugate prior, dengue fever, gibbs sampling, right censored, survival time, Weibull distribution

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Corresponding Author: Sri Astuti Thamrin, Statistics Study Program, Faculty of Mathematics and Natural Science, Hasanuddin University, Makassar, South Sulawesi, Indonesia Tel: +6285298934579

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**Competing Interest:** The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

#### INTRODUCTION

In conducting survival analysis, survival data is required. Survival data is observational data from the beginning of the study until the end of the time specified or until the occurrence of an event. Survival data can be uncensored observation and censored observation. Uncensored observations are recorded from the beginning of observation to a certain events such as failure or death. Furthermore, censored observation is an observation in which the survival time of an individual is not known for certain<sup>1</sup>.

Survival data obtained from life test observations can be complete data, type I censored data, type II censored data and type III censored data. Survival data are categorised as complete data if all objects in observation are tested until they are dead. The survival data is categorized as type I if the survival data is generated after the observation runs for a specified time. The survival data is categorized as type II if the observation is terminated after a certain number of deaths or failures have occurred. Meanwhile the survival data is categorized by type III if the individual or test unit enters into the research at different times during the study period<sup>2</sup>.

The most popular distributions used in dealing with survival problems are Weibull<sup>1,3</sup>, Gamma distribution, Log-normal, Logistics<sup>3</sup> and Exponential (special case of Weibull)<sup>1,3,4</sup>. Weibull distribution has two parameters, namely the shape parameter, which describes the distribution form and the scale parameter represents the distribution of data. These parameters should be known in order to further explore the properties and characteristics of Weibull distribution. To find out whether the distribution of life time data assumed to have described the actual data, the analysis of the life time data is required. One way to analyze the survival time function is to estimate the value of the distribution parameters.

Parameter estimation is a procedure to estimate the parameters of a model that best fit on an existing observation data. Parameter estimation can be used in two approaches, classical (frequentist) and Bayesian<sup>5</sup>. In the classical approach, the procedure is developed only by looking at the performance of all possible random samples at this time. Random sample information obtained previously or experiments in the past are ignored. Meanwhile, the Bayesian approach views parameters as variables that describe initial knowledge about parameters before observations are made and represented in a distribution, called prior distribution<sup>5</sup>. In the Bayesian approach the information from the prior data and information of the parameters are combined. By merging the two information, it is obtained parameters sought. The

posterior distribution expresses a person's degree of confidence about a parameter after the sample is observed<sup>5</sup>.

There have been many developments on the estimation of parameter of Weibull distribution in the field of survival analysis using Bayesian approach. Ahmed et al.<sup>6</sup> and Alabadee et al.<sup>7</sup> compared the Bayesian and maximum likelihood estimation for Weibull distribution using non-survival data. In the area of survival analysis, Ahmed et al.8 proposed Bayesian survival estimator for Weibull distribution with censored data. Ahmed and Ibrahim9 also proposed Bayesian approach with Jeffrey prior in estimating of Weibull parameter using censored data. Meanwhile, extension of Jeffreys's prior estimator for Weibull distribution either based on censored data using Lindley's approximation or based on type-I and II censored data have been developed by Ahmed and Ibrahim<sup>9</sup> and Ahmed<sup>10</sup>, respectively. Thamrin *et al.*<sup>11</sup> used Bayesian Weibull survival model in prediction of patients' survival with lymphoma disease based on the gene expression. Therefore, in this paper, it was developed Bayesian approach via Markov Chain Monte Carlo and Gibbs sampling algorithm with conjugate prior in estimating of Weibull distribution parameters using right censored survival data. This method applied to a simulated Weibull distributed survival dataset and the dengue fever dataset in Makassar, Indonesia.

#### **MATERIALS AND METHODS**

**Data collection:** In this study, dengue fever (DF) data were collected from 38 Community Health Centers (PUSKESMAS) in the Makassar City, Indonesia. Only quantitative methodology was used for this research. The dataset comprises survival time's measurements, sex and age. A total of 2740 DF cases and 360 patients with positive DF, which the ones admitted to hospital, were collected from period May, 2010-June, 2014 in the Makassar City. It was assumed that each DF patient in the dataset that is not linked with a death must have been alive at the end of June, 2014.

The number of days they hospitalized until they recovered or were allowed to go home was treated as the response in these models, while the remaining survivors were treated as 'censored' or in other words, alive at the end of the study period. There were 276 (76.7%) censored patients and 84 (23.3%) uncensored patients. The predictor variables used in this study were sex and age with survival times as the dependent variable. Patients with missing values were excluded from all analyses involving that element. Data were analyzed through summary tables and Bayesian survival analysis using R software and WinBUGS.

**Weibull distribution:** Weibull distribution was often used in modeling survival analysis which have positive area of probability density function with continuous random variables. Weibull distribution has two parameters, namely, shape parameter ( $\tau$ ) describes the shape of the distribution of the Weibull and scale parameter ( $\lambda$ ) describes the distribution of the data on the Weibull distribution. If  $\tau = 1$ , the Weibull distribution becomes exponential distribution, while if  $\tau > 1$  then the curve is like a bell and resemble normal curve but rather oblique.

Let the probability density function for Weibull distribution as follows:

$$f_{x|\theta,\tau}\left(x\left|\theta,\tau\right)=\frac{\tau}{\theta}x^{\tau-1}exp\left(-\frac{x^{\tau}}{\theta}\right)\quad x\geq0,\ \theta\geq0,\ \tau\geq0 \tag{1}$$

The mean ( $\mu$ ) and variance ( $\sigma^2$ ) of a random variable x which has a Weibull distribution can be seen in Eq. 2 and 3, respectively:

$$\mu = \lambda^{-\frac{1}{\tau}} \Gamma\left(\frac{1}{\tau} + 1\right)$$
(2)

$$\sigma^{2} = \lambda^{\frac{2}{\tau}} \Gamma\left(\frac{2}{\tau} + 1\right) - \mu^{2}$$
(3)

**Gamma and inverse gamma distributions:** A random variable x is said to be distributed Gamma if it has a probability density function as follows:

$$f_{x}(x) = \frac{x^{\alpha - 1} \exp\left(-\frac{x}{\beta}\right)}{\Gamma(\alpha)\beta^{\alpha}} \qquad 0 < x < \infty, \, \alpha > 0, \, \beta > 0$$
(4)

with  $\alpha$  and  $\beta$  is the parameters of Gamma distribution<sup>12</sup>.

The transformation of Gamma distribution in Eq. 4 results the inverse Gamma distribution. Given a random variable x~Gamma ( $\alpha$ ,  $\beta$ ) and the variable Y where,  $Y = \frac{1}{x}$ , then the distribution of the random variable  $Y = \frac{1}{x}$  will be the inverse Gamma ( $\alpha$ ,  $\beta$ ). A random variable Y was said to be the inverse Gamma distribution with the probability density function<sup>9</sup> as follows:

$$f_{Y}(y) = \frac{\left(\frac{1}{y}\right)^{\alpha+1}}{\Gamma(\alpha)\beta^{\alpha}} \left(e^{-\frac{1}{y\beta}}\right) \qquad 0 < y < \infty, \alpha > 0, \beta > 0$$
(5)

**Likelihood functions for right censored data:** On the right-censored data, the time an occurrence was not observed

(x>X), so the probability density function can not represent what are the probability for an occurrence. Therefore the probability of an occurrence for right censored data P(x>X) is known as a survival function (S<sub>x</sub>(X)). The likelihood function is a joint probability function of n variabel random X<sub>1</sub>, X<sub>2</sub>, ... X<sub>n</sub> and can be represented as f(t<sub>1</sub>, t<sub>2</sub>, ..., t<sub>n</sub>;  $\theta$ ). If t<sub>1</sub>, t<sub>2</sub>, ..., t<sub>n</sub> are specified, then the likelihood function is a function of parameter  $\theta$  and denoted by L( $\theta$ ). If X<sub>1</sub>, X<sub>2</sub>, ... X<sub>n</sub> represent a random sample of f(t;  $\theta$ ), then the likelihood function becomes:

$$L(\theta) = f(t_1; \theta) f(t_2; \theta) \dots f(t_n; \theta) = \prod_{i=1}^n f(t_i; \theta)$$
(6)

If the probability function and the survival function of the Weibull distributions were written as:

$$f(t,\lambda,\tau) = \frac{\tau}{\lambda} t^{\tau-1} \exp\left[-\frac{t}{\lambda}\right]^{\tau}$$
(7)

and:

$$S(t;\theta,p) = \exp\left[-\frac{x}{\theta}\right]^{\tau}$$
(8)

then its likelihood function as follows:

$$L(\theta|t_1, t_2, ..., t_n) = \prod_{i=1}^n \frac{\tau}{\lambda} t^{\tau-i} \exp\left[-\frac{t}{\lambda}\right]^{\tau}$$
(9)

If the survival data of an individual experiencing the right sensor for n observation is  $X = x_1, x_2, ..., x_n$  where  $x_i$  and  $\delta_i$  are random variables, for the observation time  $x_i$  and the indicator function of  $\delta_i$ . Therefore, the likelihood function in Eq. 9 for the right censored data can be obtained by substituting in Eq. 7 and 8 into Eq. 6 as follows:

$$\begin{split} L(\mathbf{X};\lambda,\tau,\delta) &= \prod_{i=1}^{n} \left[ \left[ f(t_{i};\lambda,\tau)^{\delta_{i}} \left[ \mathbf{S}(t_{i};\lambda,\tau) \right]^{1:\delta_{i}} \right] \\ &= \prod_{i=1}^{n} \left[ \left[ \frac{\tau}{\lambda} t_{i}^{\tau-1} exp\left(-\frac{t_{i}}{\lambda}\right)^{\tau} \right]^{\delta_{i}} \left[ exp\left(-\frac{t_{i}}{\lambda}\right)^{\tau} \right]^{1:\delta_{i}} \right] \end{split}$$
(10)

**Bayesian approach:** The Bayesian statistical idea in survival analysis was to combine initial knowledge with the present set of observations to make statistical inference. Prior information can be obtained from observational data, from the same observations as before or from knowledge techniques<sup>13</sup>. By combining prior information, posterior distributions for

parameters can be obtained and conclusions about the model and its parameters function can be made<sup>11</sup>.

Let  $\theta$  be an unknown quantity and  $p(\theta)$  denote the prior distribution of  $\theta$ . Furthermore, y is the observed data, the probability of the event being assumed depend on  $\theta$ . This dependence is expressed by  $p(y|\theta)$ , the conditional probability of y for each value of probability  $\theta$ , the function of  $\theta$  is known as likelihood<sup>13</sup>. The probability for different values, taking into account y is denoted by  $p(\theta|y)$ . Generally Bayes's theorem is written:

$$p(\theta|y) = \frac{p(y|\theta)p(\theta)}{p(y)}$$
(11)

where, p (y) is  $\int p(\theta|y)d\theta$  and considered as a normalizing factor  $\int p(y|\theta)d\theta = 1$  to ensure that  $p(\theta|y) \propto p(y|\theta)p(\theta)$  which says that the posterior distribution in Eq. 11 is equal to the yield of likelihood and prior<sup>11,13</sup>.

It can be seen that the functional form of f(x) in Eq. 1 associated with  $\theta$  is  $\frac{1}{\theta} \exp\left(-\frac{x}{\theta}\right)^{t}$ . This is the functional form of the density function of the inverse Gamma in Eq. 5. Therefore, the conjugate prior is probably the inverse Gamma. The density function of inverse Gamma distribution in Eq. 5 can also be represented as follows:

$$fx(x) = \frac{1}{\Gamma(\alpha)\beta^{\alpha}} \left(\frac{1}{x}\right)^{\alpha+1} exp\left(-\frac{1}{x\beta}\right) \qquad x \ge 0, \, \alpha \ge 0, \, \beta \ge 0 \qquad (12)$$

with the priors as follows:

$$f_{\theta}(\theta) = \frac{1}{\Gamma(\alpha)\beta^{\alpha}} \left(\frac{1}{\theta}\right)^{\alpha+1} \exp\left(-\frac{1}{\theta\beta}\right) \qquad \theta \ge 0, \ \alpha > 0, \ \beta > 0$$

$$f_{\alpha}(\alpha) = \frac{1}{\Gamma(\alpha)\beta^{\alpha}} \left(\frac{1}{\theta}\right)^{\alpha+1} \exp\left(-\frac{1}{\theta\beta}\right) \qquad \theta \ge 0, \, \alpha > 0, \, \beta > 0$$

$$f_{\beta}(\beta) = \frac{1}{\Gamma(\alpha)\beta^{\alpha}} \left(\frac{1}{\theta}\right)^{\alpha+1} \exp\left(-\frac{1}{\theta\beta}\right) \qquad \theta \ge 0, \, \alpha > 0, \, \beta > 0$$

Then, the posterior distributions for right censored data with the Weibull distribution in Eq. 1, the likelihood function in Eq. 10 and the conjugate prior in Eq. 12 can be written as:

$$f(\theta|x) = \frac{f(\theta).f(x|\theta)}{\int_0^1 f(\theta)f(x|\theta)d\theta}$$
(13)

$$f(\theta, \alpha, \beta \mid x) = \frac{\frac{1}{\Gamma(\alpha)\beta^{\alpha}} \left(\frac{1}{\theta}\right)^{\alpha + 1 + \sum_{i=1}^{n} \delta_{i}} \left(p \sum_{i=1}^{n} x^{p-1}\right)^{\sum_{i=1}^{n} \delta_{i}} exp\left[-\frac{\left(1 + \beta \sum_{i=1}^{n} x^{p}\right)}{\theta\beta}\right]}{\left(p \sum_{i=1}^{n} x^{p-1}\right)^{\sum_{i=1}^{n} \delta_{i}}}$$
$$= \frac{1}{\Gamma(\alpha)\beta^{\alpha}} \left(\frac{1}{\theta}\right)^{\alpha + 1 + \sum_{i=1}^{n} \delta_{i}} exp\left[-\frac{\left(1 + \beta \sum_{i=1}^{n} x^{p}\right)}{\theta\beta}\right]$$
(14)

Since the integration of the joint posterior density is not easy to perform, the joint posterior density of ( $\alpha$ ,  $\theta$ ,  $\beta$ ) in Eq. 13 and 14 are an analytically intractable. Hence, inferences are based on MCMC simulation methods via Metropolis-Hastings algorithms or slice sampling to simulate samples of  $\alpha$ ,  $\theta$  and  $\beta$ . The Win BUGS system can be used as the implementation of MCMC computations<sup>14</sup>.

#### RESULTS

**Simulation study:** It was simulated a Weibull model with covariates. The sample size of n = 300 was used for the experiment with 82% censoring level. The simulation algorithm was described as follows:

- For each of the Weibull distributions, fixed the value of each parameter shape and scale to W(2,10)
- Generate the random variable u<sub>i</sub>~U(0,1)
- Generate the survival time t<sub>i</sub>, for i = 1,2,...,n. The value of random variable u<sub>i</sub>~U(0,1) can be used to generate the survival time t<sub>i</sub> as t<sub>i</sub> =  $\tau^{\lambda}\sqrt{-In(u_i)}$
- Generated the censored time  $T_i$  from the value of random variable  $T_i \sim U(0,1)$  with the assumption that the data are the right censored and  $\gamma_i$  is the censored indicator:

$$\gamma_{i} = \begin{cases} 0 & \text{if } t_{i} > T_{i} \text{ censored} \\ 1 & \text{uncensored} \end{cases}$$

- Generate the covariates  $X_i = (X_{age i}, X_{sex i})$  for i = 1, 2, ..., n.  $X_{age i} \sim U(5; 50), X_{sex i} \sim binomial(1; 0, 5)$
- Combine the survival time t<sub>i</sub>, the censored indicator γ<sub>i</sub> and the covariates X<sub>i</sub>
- Repeat step 1-6, 100 times

Based on the simulated data, there is 82% of censored and 12% of uncensored. Meanwhile, the variable age lies at intervals of 5 years up to 50 years and the sex is at 50% was

Parameters	True value	Posterior mean		
		Mean	Standard deviation	95% credible interval (CI)
Shape	2	2.5670	0.282	(2.021, 3.251)
Scale	10	10.0740	3.193	(4.734, 16.88)
Age	-	-0.0037	0,0105	(-0.009, 0.036)
Sex	-	-0.0696	0.3591	(-0.700, 0,511)

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Table 1: Posterior estimates of parameters for Weibull model for simulated data with 100 times replication



Fig. 1: Plots of parameter shape ( $\tau$ ) and scale ( $\lambda$ ), (a) History iteration plots and (b) Posterior distribution

male and 50% were female, respectively. Before determining the estimated parameters in the model, the convergence of the estimation results need to be checked first. In this simulation study, we ran the MCMC algorithm with 100,000 iterations, discarding 10,000 as burn-in. Summary statistics of the posterior distributions of the models based on 100 times replications were given in Table 1. The checking was conducted by showing the convergence plots of the each estimated parameter. This plot is a plot of the values that is obtained at each iteration. The results of the estimation process using Markov Chain Monte Carlo (MCMC) indicated that the estimated process has reached the convergence conditions. It was based on the diagnostic plot of MCMC i.e., posterior density, autocorrelation and history plot. Overall, Table 1 showed the mean of posterior means of all parameter estimates are still reasonably accurate for up to 82% censoring.

**Application to dengue fever data:** It was analyzed a DF dataset which was collected from 38 Community Health Centers (PUSKESMAS) in the Makassar City to illustrated

conjugate estimator of Weibull distribution based on right censored data for fitting Weibull model. Before fitting the Weibull model to the DF dataset, it checked the assumption whether the DF patients' survival time is followed by Weibull distribution. It can be conducted by plotting log [-log S(t)] versus log t. The survival time fulfilled the Weibull distribution, was indicated by a straight line plot. The Weibull model was suitable for DF dataset. It was indicated by a straight line plot of the DF patients' survival time. Based on this, therefore, it was employed the Weibull model to the DF dataset.

The Weibull models were fitted to the DF dataset using the prior distributions. As in the simulation study, the MCMC algorithm with 100,000 iterations was ran, discarding 10,000 as burn-in before checking the convergence of the estimation results. Figure 1 and 2 presented posterior distribution and iteration history plots of the MCMC output of the significant parameters. In these figures, x and y indicate iteration and mean of posterior for history plot, respectively. From Fig. 1 and 2, all the posterior distribution of parameters perform a normal distribution and their history iteration shows such fastly mixing MCMC processes.



Fig. 2: Plots of parameter age (Beta 1) and sex (Beta 2), (a) History iteration plots and (b) Posterior distribution

Table 2: Estimated posterior mean of the parameters of the Weibull model, the 95% credible intervals (CI), for DF dataset in 43 PUSKESMAS in Makassar, 2010-2014

Parameters	Mean	Standard deviation	95% credible interval (CI)
shape (τ)	3.163	0.1583	(2.863, 3.483)
scale (λ)	9.151	3.0670	(4.181, 16.04)
Age	0.010	0.0040	(0.0021, 0.0185)
Sex	-0.2378	0.1319	(-0.4967, 0.0218)

The posterior estimate for parameters of the Weibull model are given in Table 2. The age substantially described DF patients' survival times and had a positive effect on the estimated survival time. This can be observed from its CI values for each parameter. The parameters that is contains zero in its credible interval does not affect the survival time of individuals.

#### DISCUSSION

In this study, it was developed a Weibull model to account for model uncertainty in the estimation of survival using conjugate prior. The method developed will be applied in a simulated Weibull distributed survival dataset and the analysis of DF datasets in Makassar, Indonesia, with covariates given by age and sex. There has been a substantial literature on constructing Bayesian Weibull models with censored data. For example, Ahmed *et al.*<sup>8</sup> Guure *et al.*<sup>15</sup>, Erto and Giorgio<sup>16</sup>, Alabadee *et al.*<sup>7</sup>, Ahmed<sup>10</sup> and Gupta and Singh<sup>17</sup>. Overall, the results of the simulations showed that by using the conjugate prior, the mean of posterior means of all Weibull distribution parameter estimates were still reasonably accurate. In this result, it was supported by the work of Alabadee *et al.*<sup>7</sup> and Gupta and Singh<sup>17</sup>, who indicated that Bayesian was the good estimator with the small value of mean square error. However, the study of Ahmed<sup>10</sup> indicated that under the same circumstances with a Jeffry prior information, Bayes using Jeffrey prior gives better result than Bayes using extension of Jeffrey prior. In contrast, it was shown that the estimated parameters of Weibull model obtained from using conjugate prior either with simulated survival data or the DF data were good. For choosing sample size and censoring level, the estimate generated by the conjugate prior not only depend on the data but also on the parameters of the prior distribution. Apart from bias and precision criteria used for estimating the two parameters of Weibull distribution, the Bayesian inference coupled with MCMC enable us to estimate the parameters of Weibull survival models for dealing with such right censored survival data situations and maintain identifiability. These was a significant advantage of the proposed Bayesian inference. Furthermore, the flexibility of Bayesian approach, ease of extension to more complicated scenarios such as the application of Jeffry prior to the estimation of the parameter contained the prior information which was obtained from the conjugate prior<sup>10</sup> and an importance sampling procedure to obtain the Bayes estimates and to also construct the Bayesian credible interval<sup>18</sup>.

#### CONCLUSION

Conjugate prior is a method of determining prior on Bayesian method with the presence of a relation between prior and posterior distribution. Estimated parameters in the Weibull distribution for the right censored survival data using conjugate prior are derived from their prior data and distribution information. It can be concluded that the estimates generated by the conjugate prior depend on the data, the parameters of the prior distribution and the amount of uncensored data having to be more than one in order to obtain an estimate of greater than zero. Overall, the result of the estimator using conjugate prior for fitting Weibull model for DF dataset indicated that the factor of age substantially described DF patients' survival times and had a positive effect on the estimated survival time.

#### SIGNIFICANCE STATEMENT

In this study, it was discovered that the conjugate estimator of Weibull distribution using right censored survival data that can be beneficial for measuring the performance of Bayesian estimator for estimating the parameters of Weibull distribution with censored data for dengue fever (DF) survival time. This study will help the researchers to uncover the critical area of using conjugate prior in estimating parameter of Weibull distribution to determine the factors influenced the DF patients' survival time that many researchers were not able to explore. Thus, a new theory on Bayesian estimator using conjugate prior with right censored survival data and possible other priors, may be arrived at.

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