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FLEXIBLE PARAMETRIC MODELING OF MALARIA SURVIVAL: APPLICATION TO BURKINA FASO

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ABSTRACT

Objectives: Severe malaria remains a major cause of childhood mortality in sub-Saharan Africa. Identifying prognostic factors associated with death among hospitalized children is therefore an important public health priority. This study aimed to identify the parametric model that best describes hospital survival among children with severe malaria and to determine the clinical factors associated with death.

Methods: We analyzed a cohort of 444 children aged 1–59 months who were hospitalized for confirmed malaria at Dori Regional Hospital, Burkina Faso. Five parametric survival models were fitted and compared: Exponential, Weibull, three-parameter Weibull, Beta-Weibull, and modified Beta-Weibull models. Model performance was assessed using the Akaike information criterion (AIC) and Bayesian information criterion (BIC). A simulation study was conducted to assess estimator stability. Clinical factors associated with death were investigated using the selected model under an accelerated failure time (AFT) formulation.

Results: The three-parameter Weibull model provided the best fit (AIC = 595.11; BIC = 607.40). Its shape parameter was k=0.912, indicating a decreasing hazard. The estimated threshold parameter was approximately one day. The Beta-Weibull and modified Beta-Weibull models showed identifiability problems. In the multivariable analysis, respiratory distress (TR = 0.209; p<0.001) and shock (TR = 0.147; p<0.001) were the factors most strongly associated with shorter survival times. These findings correspond to reductions of 79% and 85% in survival time, respectively.

Conclusions: Flexible parametric modeling, particularly the three-parameter Weibull model, provided a suitable framework for characterizing hospital mortality among children with severe malaria. Respiratory distress and shock were major warning signs and may warrant early intensive management.

1. Introduction

Malaria remains one of the leading causes of childhood morbidity and mortality in sub-Saharan Africa. According to the World Health Organization World Malaria Report, approximately 610,000

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deaths and 282 million malaria cases were reported in 2024. The African Region accounted for nearly 95% of malaria deaths, most of which occurred among children under five years of age WHO (2025). Burkina Faso is among the countries most affected by malaria worldwide. Despite a decline in the national burden between 2024 and 2025, malaria remains the leading cause of consultation and hospitalization in the country's health facilities Severe Malaria Observatory (2026). The Sahel region, where Dori Regional Hospital is located, is particularly affected. This burden is compounded by geographic and security-related barriers to healthcare.

Statistical analysis of outcomes among children hospitalized with severe malaria is important for identifying clinical priorities. Common approaches include logistic regression, which treats death as a binary outcome at hospital discharge, and the Cox model, which accounts for time to event without specifying the baseline hazard function. Both approaches have been applied to the pediatric cohort from Dori Regional Hospital. Parametric survival models provide an alternative approach. They specify the distribution of survival time and describe the hazard function over the hospital stay. When appropriately fitted, these models may improve interpretation and estimation.

This study proposes a flexible parametric analysis of hospital survival among children treated for severe malaria. Several distributions of time to death are compared. The primary objective is to identify the parametric model that best describes the observed mortality dynamics in this cohort. The candidate models include the Exponential, two-parameter Weibull, three-parameter Weibull, Beta-Weibull, and modified Beta-Weibull models.

The specific objectives were to:

- assess the stability and robustness of the maximum likelihood estimators through a simulation study before fitting the models to the hospital data;
- fit and compare the candidate parametric distributions using the Akaike information criterion (AIC) and Bayesian information criterion (BIC), with Kaplan–Meier estimation as a non-parametric reference;
- characterize the shape of the instantaneous hazard during hospitalization, including its potential non-monotonic behavior;
- identify clinical factors associated with death under the selected parametric model and compare these findings with previously reported prognostic factors in the same cohort using semi-parametric and logistic approaches.

1 Literature review

1.1 Previous studies on the Dori pediatric cohort

The cohort comprised 444 children aged 1–59 months who were hospitalized for confirmed malaria at Dori Regional Hospital between August and September 2022. This cohort has already been investigated in two separate studies. The first study, published in BMC Infectious Diseases, used a Cox proportional hazards model. The case-fatality rate was 14.4% ($n = 64$), with a median time to death of five days. Respiratory distress, shock, hypoglycemia, impaired consciousness, acute gastroenteritis, and hyperparasitemia were the main prognostic factors associated with death. Adjusted hazard ratios ranged from 2.1 to 4.1 Dango et al. (2025a). A second analysis of the same cohort was reported as a preprint. It used univariable and multivariable logistic regression. The results identified a similar, but not identical, set of significant determinants. These included severe anemia, absence of blood transfusion, and ambulance transfer Dango et al. (2025b).These studies therefore covered two complementary approaches: a semi-parametric time-to-event model and a binary regression model. Neither study explicitly specified a parametric distribution for survival time. The precise shape of the hospital hazard function therefore remains unclear. A formal comparison of alternative distributional assumptions using information criteria has also not been reported for this cohort.

1.2 Parametric survival modeling and childhood mortality

Recent studies on childhood mortality in sub-Saharan Africa illustrate the potential value of parametric approaches. Fenta et al. compared a semi-parametric Cox model with shared-frailty parametric models using Demographic and Health Survey data from 33 sub-Saharan African countries. The parametric models included the Exponential, Weibull, Gompertz, log-normal, and log-logistic distributions. Four frailty distributions were also considered. The Exponential model with log-normal frailty provided the best fit according to the Akaike and Bayesian information criteria. It also outperformed the Cox model Fenta et al. (2025). Fenta et al. also discussed flexible parametric models, including the Royston–Lambert framework. These models directly represent the log-transformed cumulative hazard using spline functions. They provide an extension of standard parametric survival distributions Fenta et al. (2025). From a related methodological perspective, Okonek, Wilson, and Wakefield developed a survey-weighted parametric approach for reconstructing complete survival curves among children under five years of age. Their approach was designed for complex survey data from low- and middle-income countries. They argued that parametric models can be useful when data are limited and stronger modeling assumptions are required Okonek et al. (2025).

1.3 Survival modeling in pediatric malaria

Outside Burkina Faso, several studies have applied survival methods to childhood malaria. However, few have compared multiple parametric distributions. Jumi and Mohmmed analyzed hospital records from 6,410 children admitted with malaria to Al Sabah Children's Hospital in Juba, South Sudan. Hospital survival was analyzed using a Cox proportional hazards model. Age, body weight, treatment received, and comorbidities were significantly associated with the risk of death Jumi and Mohmmed (2025).This study illustrates the predominant use of semi-parametric methods in research on pediatric malaria survival. This pattern is also observed in African settings with epidemiological characteristics comparable to those of the Burkinabe Sahel.

1.4 Study rationale and positioning

The reviewed studies show a common pattern. Hospital survival among children with severe malaria is mainly analyzed using Cox regression or logistic regression. Cox regression accounts for time to event but leaves the baseline hazard unspecified. Logistic regression does not model the time dimension of the event. Few studies have compared several parametric survival distributions. The study by Fenta et al., for example, focused on overall childhood mortality using large demographic surveys rather than on a hospital-based cohort of children with severe malaria. The methodological gap is particularly relevant for the Dori cohort. Two previous studies have already analyzed these data. However,

neither study explicitly modeled the distribution of time to death using parametric survival models. The present study addresses this gap by applying a flexible parametric framework to the same cohort. Several candidate distributions are fitted and compared using information criteria. This approach provides an explicit assessment of the shape of the hospital hazard function and extends the analyses previously conducted on these data.

2 Methods

2.1 Study design and data source

This study used a hospital-based cohort of 444 children aged 1–59 months who were treated for confirmed malaria in the pediatric units of Dori Regional Hospital, Burkina Faso. The database included clinical covariates recorded at admission, including neurological, respiratory, hemodynamic, and biological signs. It also included discharge status and length of hospital stay.

The time variable T was defined as the length of hospital stay, measured in days. The event indicator δ was derived from discharge status. Thus,

$$\delta = \begin{cases} 1, & \text{if the child died during hospitalization,} \\ 0, & \text{if the child was discharged alive.} \end{cases}$$

A child discharged alive was treated as a right-censored observation. The survival data were therefore represented by the pair (T, δ).

2.2 Parametric survival models

Five parametric distributions were fitted and compared: the Exponential, Weibull, three-parameter Weibull (Weibull 3P), Beta-Weibull (BW), and modified Beta-Weibull (BWM) models.

The parameterization was harmonized across the models where appropriate. For the Weibull-based distributions, λ denotes the scale parameter and k denotes the shape parameter. The BW and BWM models introduce the additional shape parameters a and b from the Beta distribution used to transform the baseline Weibull distribution. The BWM model includes an additional parameter c, which generalizes the standard Beta transformation Famoye et al. (2005); Khan (2015).

The three-parameter Weibull model introduces a location parameter $\tau \geq 0$. This parameter shifts the origin of the distribution and allows for a minimum delay before the event can occur.

Let

$$G(t) = 1 - \exp\left[-\left(\frac{t}{\lambda}\right)^{k}\right]$$

denote the cumulative distribution function (CDF) of the baseline Weibull distribution, and let $g(t)$ denote its density. The BW model is obtained by applying a Beta(a, b) transformation to $G(t)$Famoye et al. (2005). The BWM model extends this construction through a modified Beta transformation involving the additional parameter cKhan (2015). The BW model is recovered as the special case $c = 1$ of the BWM model.

The complete parameterizations of the five distributions are given in Table 1. For the BW and BWM models, the probability density and cumulative distribution functions involve the regularized incomplete Beta function,

$$I_z(a, b) = \frac{1}{B(a, b)} \int_0^z u^{a-1} (1-u)^{b-1} \, du,$$

where

$B(a, b) = \frac{\Gamma(a)\Gamma(b)}{\Gamma(a+b)}$is the Beta function.

Table 1: Parameterization of the five survival distributions.

Model	Parameters	Mean	Variance	PDF $f(t)$	CDF $F(t)$
Exponential	$\lambda > 0$	$\frac{1}{\lambda}$	$\frac{1}{\lambda^2}$	$\lambda e^{-\lambda t}$	$1 - e^{-\lambda t}$
Weibull	$\lambda > 0, k > 0$	$\lambda\Gamma\left(1+\frac{1}{k}\right)$	$\lambda^2\left[\Gamma\left(1+\frac{2}{k}\right) - \Gamma\left(1+\frac{1}{k}\right)^2\right]$	$\frac{k}{\lambda}\left(\frac{t}{\lambda}\right)^{k-1} e^{-(t/\lambda)^k}$	$1 - e^{-(t/\lambda)^k}$
Weibull 3P	$\lambda > 0, k > 0, \tau \geq 0$	$\tau + \lambda\Gamma\left(1+\frac{1}{k}\right)$	$\lambda^2\left[\Gamma\left(1+\frac{2}{k}\right) - \Gamma\left(1+\frac{1}{k}\right)^2\right]$	$\frac{k}{\lambda}\left(\frac{t-\tau}{\lambda}\right)^{k-1} e^{-\left(\frac{t-\tau}{\lambda}\right)^k}, t > \tau$	$1 - e^{-\left(\frac{t-\tau}{\lambda}\right)^k}, t > \tau$
BW	$\lambda, k, a, b > 0$	Cordeiro et al. (2011)	Cordeiro et al. (2011)	$\frac{k}{\lambda B(a,b)}\left(\frac{t}{\lambda}\right)^{k-1} e^{-b(t/\lambda)^k}\left[1 - e^{-(t/\lambda)^k}\right]^{a-1}$	$I_{G(t)}(a,b)$
BWM	$\lambda, k, a, b, c > 0$	Khan (2015)	Khan (2015)	$\frac{cak}{\lambda B(a,b)}\left(\frac{t}{\lambda}\right)^{k-1} e^{-b(t/\lambda)^k}\left[1 - e^{-(t/\lambda)^k}\right]^{a-1}$ $\times \left[1 - (1-c)G(t)\right]^{-(a+b)}$	$I_{z(t)}(a,b)$

Sources: Klein and Moeschberger (2003); Kalbfleisch and Prentice (2002); Famoye et al. (2005); Cordeiro et al. (2011); Khan (2015).

Note: The event time is denoted by $T > 0$. For the Weibull-based models,

$$G(t) = 1 - \exp\left[-\left(\frac{t}{\lambda}\right)^k\right],$$

and, for the BWM model,

$$z(t) = \frac{cG(t)}{1 + (c-1)G(t)}.$$

Explicit mean and variance of the BW model. The mean of the BW distribution is

$$\mu_{BW} = \lambda\Gamma(a)\,\Gamma\left(1+\frac{1}{k}\right)\sum_{j=0}^{\infty}\frac{(-1)^j}{\Gamma(a-j)\,j!\,(b+j)^{1+1/k}\,B(a,b)}.$$

Its variance is

$$\mathrm{Var}(T) = \lambda^2\Gamma(a)\,\Gamma\left(1+\frac{2}{k}\right)\sum_{j=0}^{\infty}\frac{(-1)^j}{\Gamma(a-j)\,j!\,(b+j)^{1+2/k}\,B(a,b)} - \mu_{BW}^2.$$

Explicit mean and variance of the BWM model. The mean of the BWM distribution is

$$\mu_{BWM} = \lambda\int_0^1 \frac{z^{a-1}(1-z)^{b-1}}{B(a,b)}\left(\ln\frac{c-(c-1)z}{c(1-z)}\right)^{1/k} dz.$$

Its variance is

$$\mathrm{Var}(T) = \lambda^2\int_0^1 \frac{z^{a-1}(1-z)^{b-1}}{B(a,b)}\left(\ln\frac{c-(c-1)z}{c(1-z)}\right)^{2/k} dz - \mu_{BWM}^2.$$

Table 1 summarizes the five candidate models. The Exponential model assumes a constant hazard during hospitalization. The Weibull model allows the hazard to increase or decrease according to the value of k. The three-parameter Weibull model adds a time threshold before the event can occur. The BW and BWM models provide greater flexibility. Their Beta-based transformations can accommodate non-monotone hazard functions, including unimodal and bathtub-shaped patterns Famoye et al. (2005); Khan (2015). The corresponding hazard and survival functions are given in Table 2.

Table 2: Hazard and survival functions of the five candidate models.

Model	Hazard function $h(t)$	Survival function $S(t)$
Exponential	$h(t) = \lambda$	$S(t) = e^{-\lambda t}$
Weibull	$h(t) = \frac{k}{\lambda}\left(\frac{t}{\lambda}\right)^{k-1}$	$S(t) = e^{-(t/\lambda)^k}$
Weibull 3P	$h(t) = \frac{k}{\lambda}\left(\frac{t-\tau}{\lambda}\right)^{k-1},\ t > \tau$	$S(t) = e^{-\left(\frac{t-\tau}{\lambda}\right)^k},\ t > \tau$
BW	$h(t) = \frac{f(t)}{S(t)} = \frac{\frac{k}{\lambda B(a,b)}\left(\frac{t}{\lambda}\right)^{k-1} e^{-b(t/\lambda)^k}\left[1-e^{-(t/\lambda)^k}\right]^{a-1}}{1-I_{G(t)}(a,b)}$	$S(t) = 1 - I_{G(t)}(a,b)$
BWM	$h(t) = \frac{f(t)}{S(t)}$	$S(t) = 1 - I_{z(t)}(a,b)$

Sources: Klein and Moeschberger (2003); Kalbfleisch and Prentice (2002); Famoye et al. (2005); Khan (2015).

Note: $I_z(a,b)$ denotes the regularized incomplete Beta function. Moreover,

$$G(t) = 1 - e^{-(t/\lambda)^k}, \qquad z(t) = \frac{cG(t)}{1+(c-1)G(t)}.$$

Table 2 summarizes the hazard and survival functions of the five candidate models. For the Exponential, Weibull, and three-parameter Weibull models, both functions have explicit forms. For the BW and BWM models, the hazard is expressed as the ratio of the density to the survival function. The survival function is defined through the regularized incomplete Beta function.

2.3 Modeling framework

The analysis involved two complementary stages. First, a non-parametric analysis based on the Kaplan–Meier estimator was used to estimate the survival function without imposing a distributional assumption. This estimate served as a graphical reference for assessing the fit of the parametric models.Second, the five parametric distributions described above were fitted to the survival object (T, δ). Here, T denotes the length of hospital stay and δ indicates whether death occurred during hospitalization. Before fitting the models to the observed data, a simulation study was conducted for each distribution. Samples were generated from plausible parameter values. The parameters were then re-estimated by maximum likelihood over a large number of replications. Bias, root mean square error (RMSE), and estimator stability were assessed before applying the models to the hospital data.

2.4 Parameter estimation and model selection

The parameters of each model were estimated by maximum likelihood. For a right-censored sample, the log-likelihood function is

$$\ell(\theta) = \sum_{i=1}^{n}\{\delta_i \log f(t_i;\theta) + (1-\delta_i)\log S(t_i;\theta)\},$$

where θ denotes the parameter vector of the selected model, t_i is the observed time for patient i, and δ_i is the corresponding event indicator.

The five models were compared using the Akaike information criterion (AIC),

$$\text{AIC} = -2\hat{\ell} + 2p,$$

Akaike (1974) and the Bayesian information criterion (BIC),

$$\text{BIC} = -2\hat{\ell} + p\log(n),$$

Schwarz (1978), where $\hat{\ell}$ is the maximized log-likelihood, p is the number of model parameters, and n is the sample size.

Lower AIC and BIC values indicate better model fit after accounting for model complexity. The preferred model was selected based on the overall agreement between these two criteria.

2.5 Implementation

All analyses were performed in R. The survival object and Kaplan–Meier estimator were obtained using the *survival* package. The Exponential and Weibull models were fitted using the *flexsurv* package. The three-parameter Weibull, Beta-Weibull, and modified Beta-Weibull models are not directly available in standard survival-analysis packages. These models were therefore implemented using direct numerical maximization of the log-likelihood with the *maxLik* package.A logarithmic reparameterization was used for strictly positive parameters. This transformation ensured positive parameter values during optimization and improved numerical stability.

2.6 Analytical strategy

The analysis followed five main steps.First, descriptive statistics were used to summarize the distribution of hospital stay and the clinical covariates according to vital status at discharge. Second, the overall survival function was estimated using the Kaplan–Meier method. Third, a simulation study was conducted to assess the stability of the maximum likelihood estimators for each of the five candidate distributions. Fourth, the five parametric models were fitted to the hospital data and compared using AIC and BIC.Finally, the selected model was used to examine the estimated hazard function and identify clinical covariates associated with death. These findings were compared with prognostic factors previously identified in the same cohort using semi-parametric and logistic regression approaches.

3 Results

3.1 Descriptive characteristics of the cohort

The study included 444 children hospitalized for severe malaria. The median age was 27 months. It was 25.5 months among survivors and 34.0 months among children who died. Girls accounted for 44.8% of the cohort. The hospital case-fatality rate was 14.4% ($n = 64$). The median length of hospital stay was 3 days among children who died and 6 days among survivors.

The most frequent clinical findings were severe anemia (48.0%), impaired consciousness (34.2%), and convulsions (31.3%). Table 3 summarizes the main characteristics of the cohort by vital status.

Table 3: *Descriptive characteristics of the cohort by vital status.*

Characteristic	Survivors ($n = 380$)	Deaths ($n = 64$)	Total ($n = 444$)
Median age (months)	25.5	34.0	27.0
Female sex (%)	45.0	43.8	44.8
Hospital stay, mean ± SD	6.69 ± 3.17	4.11 ± 4.23	6.32 ± 3.46
Hospital stay, median (days)	6	3	6
Respiratory distress (%)	19.2	64.1	25.7
Coma stage (%)	28.7	67.2	34.2
Hypoglycemia (%)	11.8	48.4	17.1
Severe anemia (%)	49.2	40.6	48.0
Convulsions (%)	29.7	40.6	31.3

3.2 Non-parametric survival analysis

Figure 1 shows the Kaplan–Meier estimate of overall hospital survival.

The estimated survival probability was 89.6% at 3 days (95% CI: 86.8–92.5%), 85.0% at 7 days (95% CI: 81.4–88.8%), and 77.5% at 14 days (95% CI: 68.4–87.9%).

The median survival time was estimated at 24 days, with wide confidence intervals because few patients remained under observation at later times.

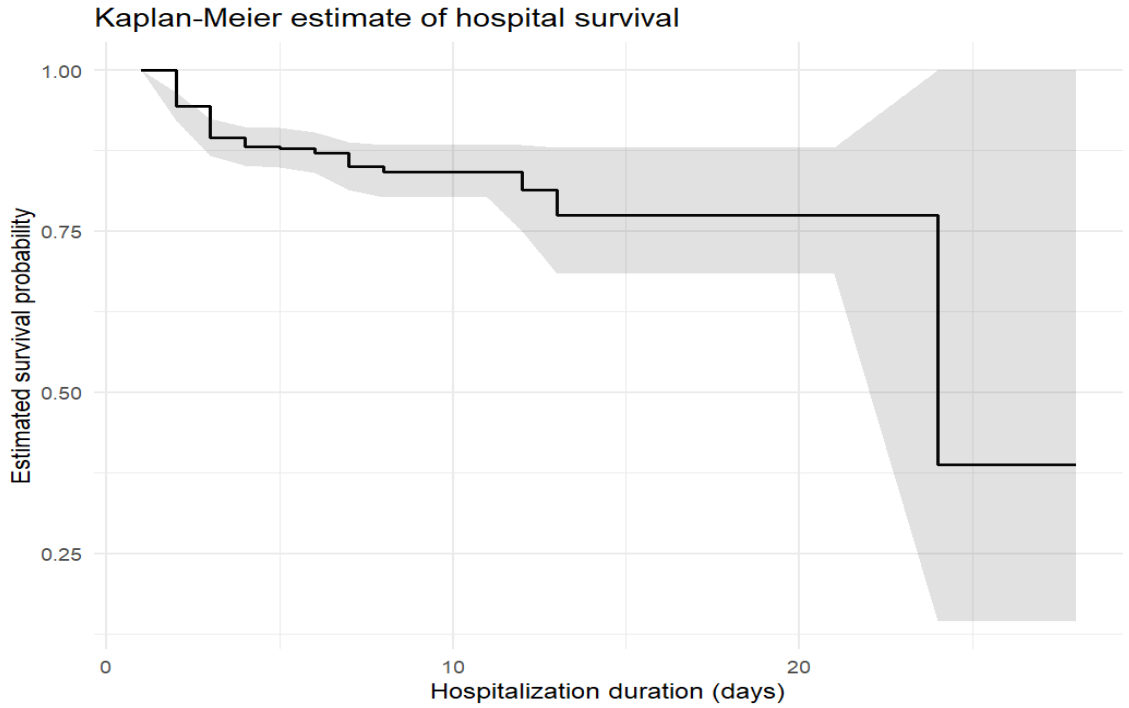

Figure 1: *Kaplan–Meier estimate of hospital survival.*

3.3 Simulation study: estimator stability

The simulation study considered three sample sizes ($n = 100,300$, and 500) and 500 replications for each of the five models.For the Beta-Weibull (BW) and modified Beta-Weibull (BWM) models, the shape parameters were constrained to plausible ranges to improve numerical stability.Table 4 reports the bias and root mean square error (RMSE) for the parameter estimates under each model.

Table 4: *Simulation results: bias and RMSE of parameter estimates.*

Model	Parameter	Bias (n=100)	Bias (n=300)	Bias (n=500)	RMSE (n=100)	RMSE (n=300)	RMSE (n=500)
Exponential	λ	0.0044	0.0008	-0.0002	0.0444	0.0253	0.0199
Weibull	λ	0.1228	0.0208	0.0208	0.4306	0.1876	0.1562
	k	0.1038	0.0769	0.0201	1.4405	0.8225	0.5767
Weibull 3P	λ	0.2133	0.0615	0.0509	1.2320	0.6379	0.4563
	k	0.0602	0.0161	0.0043	0.3256	0.1467	0.1077
	τ	-0.0145	-0.0057	-0.0031	0.1318	0.0306	0.0172
BW	λ	-0.2956	0.9149	1.9268	3.5209	4.1066	4.7410
	k	1.0222	0.3809	0.2852	2.3989	1.4634	1.0379
	a	7.7877	4.0338	1.5971	13.7424	9.2937	5.3285
	b	1.0129	2.1807	2.4778	4.3009	4.8942	5.1976
BWM	λ	0.0113	0.2271	0.5227	3.5966	3.4428	8.2726
	k	2.1887	1.6112	1.2271	2.9352	2.3775	1.9670
	a	1.1709	1.1208	0.9232	4.9222	5.1050	4.4437
	b	1.5471	3.1591	3.0024	6.2307	8.7272	8.5096

Model	Parameter	Bias (n=100)	Bias (n=300)	Bias (n=500)	RMSE (n=100)	RMSE (n=300)	RMSE (n=500)
	c	14.8474	10.9635	9.3252	20.3443	16.4220	14.4066

The Exponential, Weibull, and three-parameter Weibull models showed high convergence rates, reaching 100% in almost all settings. Their biases generally decreased as the sample size increased. This pattern supports the stability of the corresponding estimators. For the Exponential model, the bias of λ decreased from 0.0044 at $n = 100$ to -0.0002 at $n = 500$. The corresponding RMSE decreased from 0.0444 to 0.0199. The three-parameter Weibull model showed a similar pattern. The bias of λ decreased from 0.2133 to 0.0509. The bias of k decreased from 0.0602 to 0.0043, while the bias of τ decreased from -0.0145 to -0.0031. The RMSE of λ decreased from 1.2320 to 0.4563. For the BW and BWM models, bounds on the shape parameters a, b, and c improved numerical stability. However, substantial bias remained. For the BW model, the bias of a decreased from 7.79 at $n = 100$ to 1.60 at $n = 500$. Its RMSE decreased from 13.74 to 5.33. The bias of the BW shape parameter k also decreased, from 1.02 to 0.29. For the BWM model, the bias of c decreased from 14.85 at $n = 100$ to 9.33 at $n = 500$. The parameter remained unstable despite the imposed constraints. This finding suggests an identifiability problem within the BWM parameterization.

3.4 Comparison of parametric models

Five parametric survival models were fitted to the observed data. Table 5 reports the log-likelihood, number of parameters, AIC, and BIC for each model.

Table 5: *Comparison of the parametric survival models.*

Model	Log-likelihood	No. of parameters	AIC	BIC
Weibull 3P	**-294.56**	**3**	**595.11**	**607.40**
Beta-Weibull (BW)	-299.57	4	607.14	623.52
Modified Beta-Weibull (BWM)	-299.57	5	609.14	629.62
Weibull	-304.74	2	613.49	621.68
Exponential	-305.94	1	613.88	617.97

The three-parameter Weibull model provided the best overall fit. It had the lowest AIC (595.11) and BIC (607.40). The BW model ranked second according to AIC (607.14). The BWM model had an AIC of 609.14 and the same log-likelihood as the BW model. This result suggests that the additional parameter c did not improve the likelihood.The Exponential model had the highest AIC (613.88), followed closely by the Weibull model (AIC = 613.49).

Figure 2 compares the survival curves obtained from the five parametric models with the empirical Kaplan–Meier estimate.

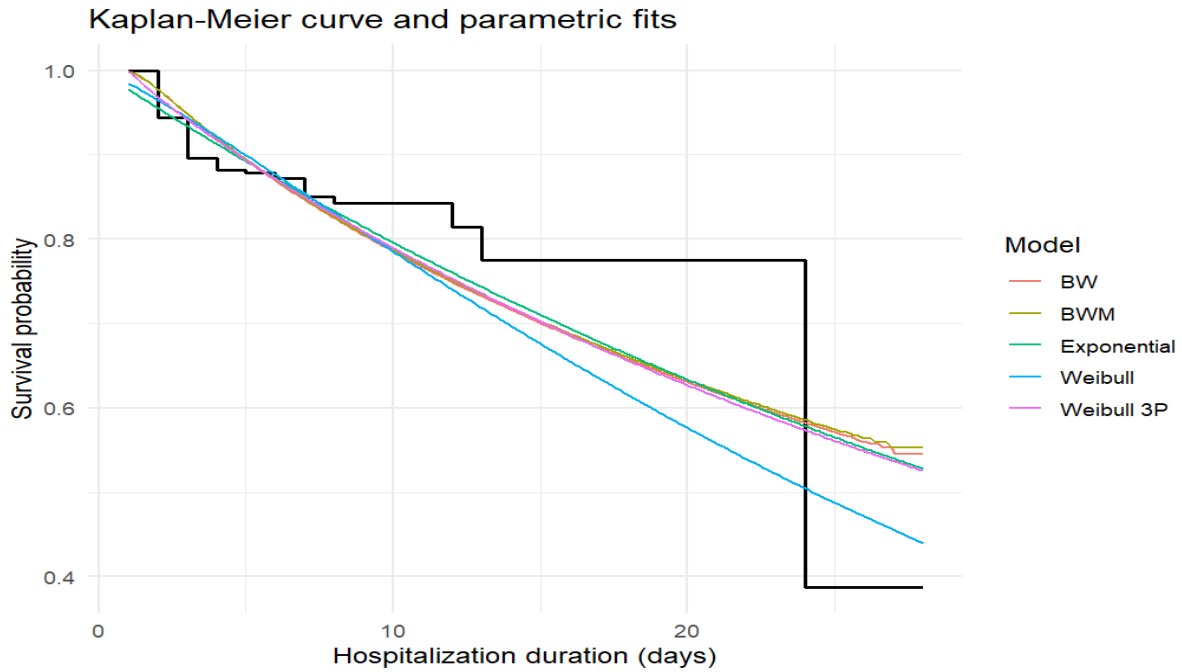

Figure 2: *Kaplan–Meier and parametric survival curves.*

3.5 Parameter estimates for the selected model

Table 6 reports the parameter estimates obtained for the five candidate models.

Table 6: *Parameter estimates for the five survival models.*

Model	λ	k	τ	a	b	c
Exponential	0.0228	–	–	–	–	–
Weibull	33.0365	1.1877	–	–	–	–
Weibull 3P	**43.7972**	**0.9120**	**0.9989**	–	–	–
BW	0.2440	0.7632	–	29.642	0.0185	–
BWM	0.2439	0.7613	–	29.642	0.0185	1.0000

The BW and BWM models were fitted with parameter constraints to improve numerical stability. Their estimates of a and b were close to the specified boundaries ($a = 29.642$ and $b = 0.0185$). This pattern indicates persistent identifiability difficulties.For the BWM model, c was estimated at 1.0000. Thus, the fitted BWM model effectively reduces to the BW model.

Figure 3 displays the estimated hazard functions for the five candidate models.

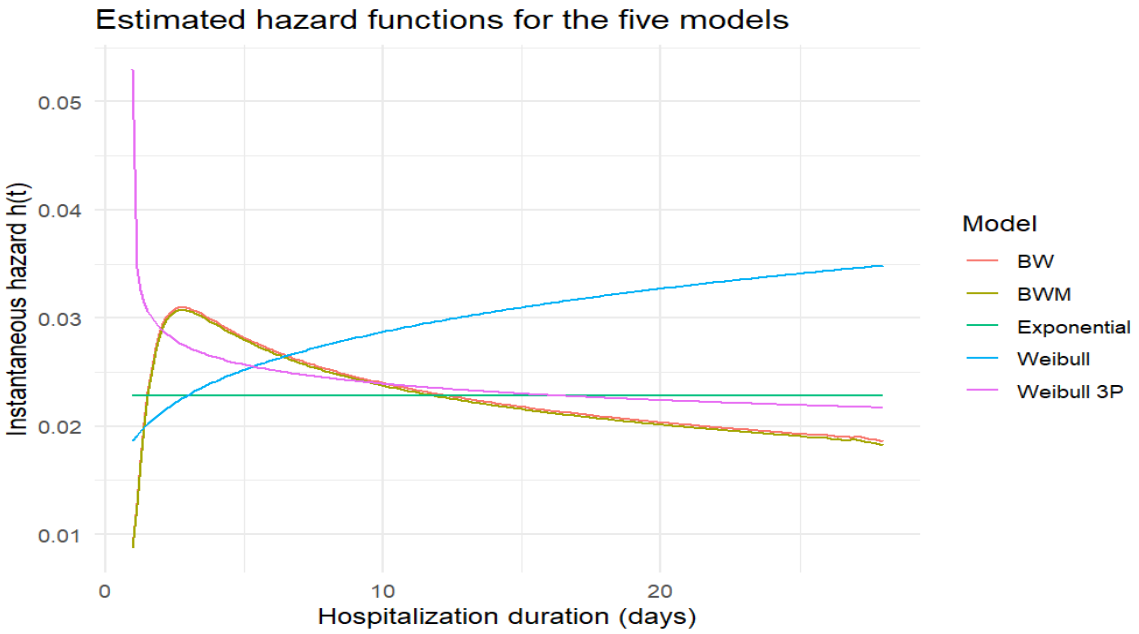

Figure 3: *Estimated hazard functions for the five survival models.*

The three-parameter Weibull model showed a high hazard immediately after the estimated threshold of approximately one day. The hazard then decreased gradually. This pattern indicates that the highest risk occurred during the early phase of hospitalization.

3.6 Clinical factors associated with death

Clinical factors associated with death were investigated using the three-parameter Weibull model under an accelerated failure time (AFT) formulation. This model was selected during the model comparison stage. Univariable analyses were first performed for all available covariates. Variables with a screening threshold of 20% were considered for the multivariable model. Given the 64 observed deaths, a maximum of five covariates was retained. This choice followed the conventional rule of approximately one model parameter per ten events.The multivariable results are presented in Table 7. The time ratio (TR) represents the multiplicative effect of each covariate on survival time. A TR below 1 indicates a shorter survival time. A TR above 1 indicates a longer survival time.

Table 7: *Clinical factors associated with death using the three-parameter Weibull AFT model.*

Covariate	Time ratio	95% CI	p-value
Respiratory distress	0.209	0.117–0.375	< 0.001
Shock	0.147	0.066–0.326	< 0.001
Coma stage	0.420	0.157–1.123	0.084
Spontaneous bleeding	2.065	0.258–16.545	0.495
Lethargy	0.910	0.306–2.706	0.865

Respiratory distress (TR = 0.209; 95% CI: 0.117–0.375; $p < 0.001$) and shock (TR = 0.147; 95% CI: 0.066–0.326; $p < 0.001$) were the factors most strongly associated with shorter survival time. The corresponding reductions in survival time were approximately 79.1% and 85.3%, respectively.Coma stage showed a tendency toward shorter survival (TR = 0.420; $p = 0.084$), but the association was not statistically significant at the 5% level.Spontaneous bleeding and lethargy were not significantly associated with survival time in the multivariable model.The common parameters of the fitted model were $k = 0.944$ and $\tau = 0.999$ days. The value of $k < 1$ indicates a decreasing hazard

after the threshold.

4 Discussion

This study aimed to identify the parametric survival model that best describes hospital mortality among children with severe malaria and to identify clinical factors associated with death. The three-parameter Weibull model provided the best overall fit. Its AIC was 595.11 and its BIC was 607.40. The model also identified a decreasing hazard after a threshold of approximately one day. Respiratory distress and shock were the main prognostic factors. The selection of the three-parameter Weibull model was based on the observed AIC and BIC values. The estimated threshold parameter ($\tau \approx 1$ day) suggests a minimum delay before the event in the fitted model. The estimated shape parameter ($k = 0.912 < 1$) indicates a decreasing hazard after the threshold. Thus, the estimated risk was highest shortly after the threshold and then decreased over time. This pattern is consistent with an acute clinical phase in which the risk of death is concentrated early during hospitalization. Patients who survive this initial phase may subsequently experience a lower risk. The BW and BWM models provided greater theoretical flexibility Famoye et al. (2005); Khan (2015). However, their parameter estimates were unstable. The estimates of a and b were close to the imposed boundaries ($a = 29.642$ and $b = 0.0185$).

The BWM parameter c was estimated at 1.0000. The fitted BWM model therefore reduced effectively to the BW model. These findings indicate limited empirical support for the additional flexibility of the BW and BWM models in this dataset. The limited number of deaths (64) may have contributed to these identifiability problems. The empirical rule of approximately one parameter per ten events would allow no more than six parameters with 64 deaths. The BW and BWM models contain four and five parameters, respectively. Their complexity therefore requires caution, particularly in the presence of parameter instability. The multivariable analysis identified respiratory distress and shock as the factors most strongly associated with shorter survival. Their time ratios were 0.209 and 0.147, respectively. These estimates indicate substantially shorter survival times among children presenting with these clinical signs. The findings are consistent with previous analyses of the same cohort. Dango et al. (2025a) identified respiratory distress and shock as major prognostic factors using a Cox model. The adjusted hazard ratios reported in that study ranged from 2.1 to 4.1. A logistic regression analysis of the same cohort also highlighted the importance of severe clinical signs Dango et al. (2025b).

The agreement between the logistic, Cox, and AFT analyses supports the consistency of the association between severe clinical signs and mortality. Coma stage showed a possible association with shorter survival (TR = 0.420; $p = 0.084$). However, this association did not reach conventional statistical significance. The lack of statistical significance may reflect limited statistical power due to the small number of deaths. Collinearity with other severe clinical signs, such as shock and respiratory distress, may also have reduced the estimated independent effect of coma. Severe anemia was common in the cohort (48.0%) but was not retained in the final multivariable model. Severe anemia is generally considered an important risk factor for malaria mortality. One possible explanation is the clinical management of severe anemia, including blood transfusion when indicated. The proportion of severe anemia was 49.2% among survivors and 40.6% among deaths. However, this observational pattern should not be interpreted as evidence of a protective effect of anemia or transfusion. Treatment information and potential confounding factors should be considered before drawing causal conclusions.

Several limitations should be considered. First, the sample included 444 patients and only 64 deaths. This limited the complexity of the models that could be reliably estimated, particularly for distributions with four or five parameters. Second, the study was conducted at a single hospital. The findings may therefore not generalize to other geographic settings or transmission periods. Third, hospital length of stay was used as a proxy for survival time. This may introduce bias if discharge practices or logistical constraints influence length of stay independently of the underlying

risk of death. These findings have clinical and public health implications. Respiratory distress and shock were strongly associated with shorter survival. Early recognition and prompt management of these signs should therefore remain priorities in severe malaria care. Training healthcare workers to recognize these signs and ensuring access to appropriate supportive care may help improve outcomes in malaria-endemic settings.

Future studies could investigate flexible spline-based survival models, such as the Royston-Parmar framework. Such models may provide an alternative to the BW and BWM distributions for representing complex hazard shapes. Additional biological and socioeconomic covariates could also improve risk stratification. External validation using independent cohorts would further assess the generalizability of the identified prognostic factors.

5 Conclusion

This study showed that the three-parameter Weibull model provided the best fit among the five candidate parametric survival models considered for children hospitalized with severe malaria in Burkina Faso. Its relatively simple parameterization and stable estimation make it particularly suitable for a dataset with a limited number of events. The fitted hazard decreased after an estimated threshold of approximately one day. This pattern suggests that mortality risk was concentrated during the early phase of hospitalization. Respiratory distress and shock were the strongest clinical factors associated with shorter survival. These findings are consistent with previous analyses of the same cohort using Cox and logistic regression models Dango et al. (2025a); Dango et al. (2025b).The BW and BWM models offered greater theoretical flexibility but showed parameter instability and identifiability problems. Their additional complexity did not improve model fit. From a clinical perspective, the findings support early recognition and prompt management of respiratory distress and shock in children with severe malaria.Strengthening clinical training and ensuring the availability of appropriate supportive-care equipment may help reduce malaria-related mortality in hospital settings.

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