

Non–Mixture Cure Fraction Model Based on Fréchet- Weibull Distribution With Application To Cancer Survival Data

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Abstract: Conventional survival models generally assume that all individuals in a study population remain susceptible to the event of interest, an assumption that may be inappropriate for cancer survival data containing a proportion of long-term survivors. This study develops a Fréchet-Weibull Non-Mixture Cure Model (FWDNMCM) to account explicitly for the presence of a cured fraction while retaining the flexibility of the Fréchet-Weibull distribution. The proposed model was formulated by incorporating a cure parameter into the Fréchet-Weibull survival function under the promotion-time framework of Yakovlev et al. (1993). The cumulative distribution function, probability density function, survival function, and hazard function of the proposed model were derived, and the unknown parameters were estimated using the maximum likelihood method. The model was subsequently applied to an acute lymphoblastic leukemia (ALL) survival dataset to evaluate its practical performance and estimate the long-term cured fraction. Kaplan–Meier survival estimates were compared with the fitted survival functions of the conventional Fréchet-Weibull model and the proposed FWDNMCM. The results demonstrate that incorporating a cure parameter provides a positive asymptotic survival probability, thereby allowing the model to distinguish between susceptible patients and long-term survivors. The fitted survival curves further indicate differences in the cured fractions between the treatment groups, with Treatment Group I exhibiting a higher estimated long-term survival proportion than Treatment Group II. The FWDNMCM also provides a better representation of the observed survival pattern than the corresponding baseline Fréchet-

Weibull model, demonstrating the importance of explicitly modelling population heterogeneity. The proposed framework therefore provides a flexible parametric approach for survival data in which a non-negligible proportion of subjects may remain event-free over extended follow-up periods. The model offers potential applications in cancer prognosis and treatment evaluation and provides a basis for future extensions involving covariates and multivariate survival outcomes.

Keywords: *Fréchet-Weibull distribution; non-mixture cure model; cure fraction; cancer survival; Kaplan–Meier estimator; maximum likelihood estimation*

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1.0 Introduction

Survival analysis is an important statistical methodology for investigating the time until the occurrence of a specified event, particularly in medical and epidemiological studies. In cancer research, survival analysis is commonly

used to evaluate the time from diagnosis or treatment to death, relapse, disease progression, or another clinically relevant endpoint. Conventional survival models generally assume that all individuals in the study population remain susceptible to the event of interest and that the event will eventually occur if follow-up is sufficiently long. This assumption may not be appropriate for modern cancer survival data, where improvements in diagnosis, treatment, targeted therapies, and supportive care have resulted in a proportion of patients achieving long-term survival and, in some cases, effectively being cured. Consequently, cancer populations may consist of susceptible individuals who remain at risk of experiencing the event and a nonsusceptible or cured fraction that will never experience the event under consideration. Failure to account for this latent cured fraction can lead to inappropriate estimates of survival probabilities and other model parameters (Omer et al., 2021). Cure models therefore provide an important framework for distinguishing between the long-term survivors and individuals who remain susceptible to the event.

The statistical development of cure models can be traced to the work of Boag (1949), who introduced an early cure-rate formulation for cancer survival data. Subsequent developments led to mixture and non-mixture approaches for incorporating a cured fraction into survival analysis. In particular, Yakovlev et al. (1993) developed the promotion-time or non-mixture cure model, which provides a biologically motivated framework in which the occurrence of a clinical event is associated with latent carcinogenic cells. Under this framework, the number of surviving carcinogenic cells capable of developing into a detectable tumour can be represented using a Poisson mechanism. Unlike conventional survival models, non-mixture cure models allow the population survival function to approach a positive asymptote as time increases, thereby providing

a direct statistical representation of the proportion of individuals who are effectively cured. The increasing availability of long-term follow-up data and the growing number of patients who achieve prolonged survival following cancer treatment have consequently increased the relevance of cure-rate models in contemporary survival analysis. Recent work has continued to examine cure modelling and related survival frameworks for populations containing long-term survivors (Terna & Umar, 2025).

Although cure models provide a mechanism for accounting for long-term survivors, the underlying baseline survival distribution remains an important consideration in determining the flexibility and adequacy of the resulting model. Classical parametric distributions, particularly the exponential and standard Weibull distributions, may be inadequate when survival data exhibit complex or non-monotonic hazard-rate patterns. This limitation has motivated the development of generalized and compound probability distributions capable of providing greater flexibility in describing diverse survival characteristics. For example, Carrasco et al. (2008) proposed the Generalized Modified Weibull distribution, while Ortega et al. (2013) developed the Log-Beta Weibull distribution to provide additional flexibility for modelling lifetime data. Swain et al. (2016) introduced the Generalized Gompertz distribution, and Basheer (2019) developed the Generalized Alpha Power Inverse Weibull distribution. These developments demonstrate the continuing effort to construct flexible parametric distributions that can accommodate survival data exhibiting different levels of skewness, tail behaviour, and hazard-rate shapes.

More recent studies have further explored the combination of Weibull- and Fréchet-type distributions to improve the flexibility of lifetime and survival models. Ibrahim et al. (2025) introduced the Modified Weibull–



Fréchet distribution, while Igiozee et al. (2026) investigated an Exponentiated Fréchet–Weibull distribution. Such developments are important because Fréchet- and Weibull-based distributions can provide alternative representations of survival behaviour that may not be adequately captured by conventional parametric models. In addition, the incorporation of generalized or compound structures can improve model flexibility and statistical fit when the empirical hazard function departs substantially from simple monotonic patterns. Mohammad (2024) emphasized the usefulness of advanced compound and generalized distributions in obtaining improved representations of complex lifetime data. Nevertheless, flexibility in the baseline distribution alone does not resolve the problem of a population containing a permanently cured fraction. A survival distribution may provide an excellent description of the susceptible population while still failing to distinguish adequately between susceptible and cured individuals.

Despite the considerable development of both flexible survival distributions and cure-rate models, an important methodological gap remains in integrating these two areas. Existing studies have introduced numerous generalized Weibull, Fréchet, and related distributions, while non-mixture cure models have traditionally been formulated around selected baseline survival distributions and specific structural assumptions. However, there remains limited development of a non-mixture cure framework based specifically on a Fréchet-Weibull distribution that can simultaneously provide flexible survival behaviour and explicitly account for a long-term cured fraction. This gap is particularly relevant to cancer survival data, where the presence of long-term survivors may produce a survival curve that does not converge to zero within a clinically meaningful follow-up period. A model capable of combining the flexibility of the Fréchet-Weibull distribution

with the asymptotic survival property of a non-mixture cure model may therefore provide a more appropriate representation of such data.

The motivation for developing a Fréchet-Weibull non-mixture cure model is therefore twofold. First, the Fréchet-Weibull distribution provides an extended parametric structure for describing diverse survival and hazard-rate patterns. Second, the non-mixture cure formulation allows the survival function to retain a positive limiting value corresponding to the estimated cured fraction. Combining these features has the potential to produce a model that is more flexible than the conventional Fréchet-Weibull distribution while simultaneously providing clinically interpretable estimates of the proportion of individuals who are unlikely to experience the event of interest. Such a model can also facilitate comparisons between treatment groups by allowing differences in the estimated cured fractions to be evaluated alongside conventional survival characteristics.

Against this background, this study aims to develop a Fréchet-Weibull Non-Mixture Cure Model (FWDNMCM) for survival data containing a potentially cured fraction. Specifically, the study formulates the proposed non-mixture cure model from the Fréchet-Weibull distribution, derives its corresponding likelihood function and parameter estimators using the maximum likelihood method, and evaluates its performance using cancer survival data. The proposed model is subsequently applied to an acute lymphoblastic leukemia (ALL) survival dataset to demonstrate its practical usefulness and to estimate and compare the cured fractions of the relevant treatment groups.

The significance of the study lies in its contribution to the development of flexible parametric cure models for survival analysis. Methodologically, the proposed FWDNMCM extends the Fréchet-Weibull framework by incorporating a cure fraction, thereby providing an alternative to conventional survival models



that implicitly assume eventual occurrence of the event in the entire population. Practically, the model can provide researchers and clinicians with additional information about long-term survival beyond conventional measures such as median survival and hazard rates. In particular, estimation of the cured fraction can provide a more meaningful description of treatment outcomes when a substantial proportion of patients experience prolonged disease-free or event-free survival. The model may therefore serve as a useful statistical tool for analysing cancer survival datasets characterized by heterogeneous susceptibility and long-term survivors. More broadly, the proposed framework provides a foundation for future extensions involving covariates and bivariate or multivariate survival settings.

The remainder of this paper is organized as follows. Section 2 presents the underlying methodology and mathematical formulation of the Fréchet-Weibull distribution and the proposed non-mixture cure framework. Section

3 describes the parameter estimation procedure based on maximum likelihood estimation. Section 4 presents the empirical application of the proposed model to an acute lymphoblastic leukemia survival dataset and discusses the resulting findings. Section 5 summarizes the major conclusions of the study, while Section 6 presents recommendations and directions for future research.

2.0 Methodology

2.1 Fréchet-Weibull Distribution (FWD)

The Fréchet-Weibull Distribution (FWD) proposed by Ieren et al. (2024) is a flexible lifetime distribution that combines characteristics of the Fréchet and Weibull families and can be used to model survival and lifetime data exhibiting different distributional and hazard-rate behaviours. Let $(T>0)$ denote the lifetime or survival time. The cumulative distribution function (CDF) and probability density function (PDF) of the FWD are defined, respectively, as in equations (1) and (2):

$$F(x) = \exp \left\{ - \left(\frac{b}{\alpha} \right)^a x^{-a\beta} \right\} \quad (1)$$

and

$$f(x) = a\beta \left(\frac{b}{\alpha} \right)^a x^{-a\beta-1} \exp \left\{ - \left(\frac{b}{\alpha} \right)^a x^{-a\beta} \right\} \quad (2)$$

where $a, b, \alpha, \beta > 0$ are the parameters of the FWD. Similarly, the corresponding survival function (SF) and hazard function (HF) of FWD are derived respectively as:

$$S(x) = 1 - F(x) = 1 - \exp \left\{ - \left(\frac{b}{\alpha} \right)^a x^{-a\beta} \right\} \quad (3)$$

$$h(x) = \frac{f(x)}{S(x)} = a\beta \left(\frac{b}{\alpha} \right)^a x^{-a\beta-1} \exp \left\{ - \left(\frac{b}{\alpha} \right)^a x^{-a\beta} \right\} \left(1 - \exp \left\{ - \left(\frac{b}{\alpha} \right)^a x^{-a\beta} \right\} \right)^{-1} \quad (4)$$

and

2.2 Non-Mixture Cure Model

The non-mixture cure model, also referred to as the promotion-time cure model, was introduced within the framework developed by Yakovlev et al. (1993). The model provides a mechanism for incorporating a permanently cured fraction into a population in which some individuals

remain susceptible to the event of interest. Its biological motivation is based on the assumption that latent carcinogenic cells surviving treatment may subsequently proliferate and produce a detectable tumour, with the number of such latent cells represented by a Poisson process.



Under this non-mixture (or promotion time) cure framework, the population survival function is defined as:

$$S_T(t) = P^{F(t)} \quad (5)$$

$$F_T(t) = 1 - P^{F(t)} \quad (6)$$

$$f_T(t) = -\ln(P)f(t)P^{F(t)} \quad (7)$$

and

$$h_T(t) = -\ln(P)f(t) \quad (8)$$

$$F(t) = 1 - P^{\left(\exp\left\{-\left(\frac{b}{\alpha}\right)^a t^{-a\beta}\right\}\right)} \quad (9)$$

$$f(t) = -\ln(P)a\beta \left(\frac{b}{\alpha}\right)^a t^{-a\beta-1} \left(\exp\left\{-\left(\frac{b}{\alpha}\right)^a t^{-a\beta}\right\}\right) P^{\left(\exp\left\{-\left(\frac{b}{\alpha}\right)^a t^{-a\beta}\right\}\right)} \quad (10)$$

$$S(t) = P^{\left(\exp\left\{-\left(\frac{b}{\alpha}\right)^a t^{-a\beta}\right\}\right)} \quad (11)$$

and

$$h(t) = -\ln(P)a\beta \left(\frac{b}{\alpha}\right)^a t^{-a\beta-1} \left(\exp\left\{-\left(\frac{b}{\alpha}\right)^a t^{-a\beta}\right\}\right) \quad (12)$$

3.0 Results and Discussion

3.1 Estimation of Parameters of the Non-mixture Model

The Likelihood function is defined by Boag (1949) as

$$L_i = \prod_{i=1}^n [(f(t_i))^{\delta_i} (S(t_i))^{1-\delta_i}] \quad (13)$$

Where $\delta_i = 1$ if failure is observed and $\delta_i = 0$ if the individual is alive.

By, substitution of the non-mixture density in equation (10) and the non-mixture survival function in equation (11) in the standard likelihood function in Equation (13) produces the likelihood for the long-term survivor, non-mixture model as follows:

$$l = r \log[-\log(P)] + r \log a + r \log \beta + a r \log b - a r \log \alpha - r(a\beta + 1) \log t_i - r \left(\frac{b}{\alpha}\right)^a t_i^{-a\beta} + \log(P) \sum_{i=1}^n \left[\exp\left\{-\left(\frac{b}{\alpha}\right)^a t_i^{-a\beta}\right\} \right] \quad (14)$$

$$r = \sum_{i=1}^n \delta_i$$

Therefore, the maximum likelihood estimates for $\theta = (a, b, \alpha, \beta, P)$ denoted by

$\hat{\theta} = (\hat{a}, \hat{b}, \hat{\alpha}, \hat{\beta}, \hat{P})$ are obtained by differentiating l partially w.r.t. a, b, α, β , and P respectively as below;

$$\begin{aligned} \frac{\partial l}{\partial a} = & \frac{r}{a} + r \log \beta - r \log \alpha - r \beta \log t_i - r \left(\frac{b}{\alpha}\right)^a t_i^{-a\beta} \left(\ln \left(\frac{b}{\alpha}\right)^a - \beta \ln(t_i) \right) \\ & + \log(P) \left(\frac{b}{\alpha}\right)^a \sum_{i=1}^n \left[t_i^{-a\beta} \left(\ln \left(\frac{b}{\alpha}\right)^a - \beta \ln(t_i) \right) \left[\exp\left\{-\left(\frac{b}{\alpha}\right)^a t_i^{-a\beta}\right\} \right] \right] \end{aligned} \quad (27)$$

$$\frac{\partial l}{\partial b} = \frac{ar}{b} - rab^{a-1} \alpha^{-a} t_i^{-a\beta} - \log(P) ab^{a-1} \alpha^{-a} \sum_{i=1}^n \left[t_i^{-a\beta} \exp\left\{-\left(\frac{b}{\alpha}\right)^a t_i^{-a\beta}\right\} \right] \quad (28)$$

$$\frac{\partial l}{\partial \alpha} = \frac{ar}{\alpha} + ab^a \alpha^{-a-1} t_i^{-a\beta} + \log(P) ab^a \alpha^{-a-1} \sum_{i=1}^n \left[t_i^{-a\beta} \exp\left\{-\left(\frac{b}{\alpha}\right)^a t_i^{-a\beta}\right\} \right] \quad (29)$$



$$\frac{\partial l}{\partial \beta} = \frac{r}{\beta} - r \log t_i + ar \left(\frac{b}{\alpha}\right)^a t_i^{-a\beta} \ln(t_i) + \log(P) a \left(\frac{b}{\alpha}\right)^a \sum_{i=1}^n \left[t_i^{-a\beta} \ln(t_i) \exp \left\{ - \left(\frac{b}{\alpha}\right)^a t_i^{-a\beta} \right\} \right] \quad (30)$$

and

$$\frac{\partial l}{\partial P} = \frac{r}{P \log(P)} + \frac{1}{P} \sum_{i=1}^n \left[\exp \left\{ - \left(\frac{b}{\alpha}\right)^a t_i^{-a\beta} \right\} \right] \quad (31)$$

Equating the above equations to zero (0) and solving for the solution of the non-linear system of equations produce the maximum likelihood estimates of parameters a , b , α , β , and P under Non-Mixture Cure Model.

3.2 Source of Data

To demonstrate the empirical utility of the proposed model, this study analyzes a clinical dataset of patients with high-risk, refractory acute lymphoblastic leukemia (ALL) who underwent bone marrow transplantation. Originally compiled by Kersey et al. (1987), these data are accessible through the *smcure* package in R (Cai et al., 2012) and have been evaluated in subsequent methodological literature, including works by Cai (2013) and Omer et al. (2021). The cohort comprises 91 patients divided into two treatment arms: 46 patients who received an allogeneic bone marrow transplant and 45 patients who received an autologous transplant.

3.3 Analysis and Discussion of Results

This study utilized a secondary dataset of 91 patients divided into two treatment arms (Group I, $n = 46$; Group II, $n = 45$). Fig. 1

presents the empirical survival profiles of the acute lymphoblastic leukemia (ALL) cohort, estimated non-parametrically using Kaplan–Meier curves. Notably, both curves stabilize into a distinct plateau at the right tail of the distribution, indicating the presence of a non-zero cure fraction in both the allogeneic and autologous treatment groups. This leveling effect underscores the limitations of standard survival models, which fail to accurately accommodate these long-term survivor fractions. Furthermore, the asymptotic plateau for the allogeneic cohort stabilizes at a higher survival probability than that of the autologous cohort. This suggests that allogeneic bone marrow transplantation yields superior long-term survival outcomes, demonstrating a more pronounced therapeutic efficacy compared to the autologous protocol.

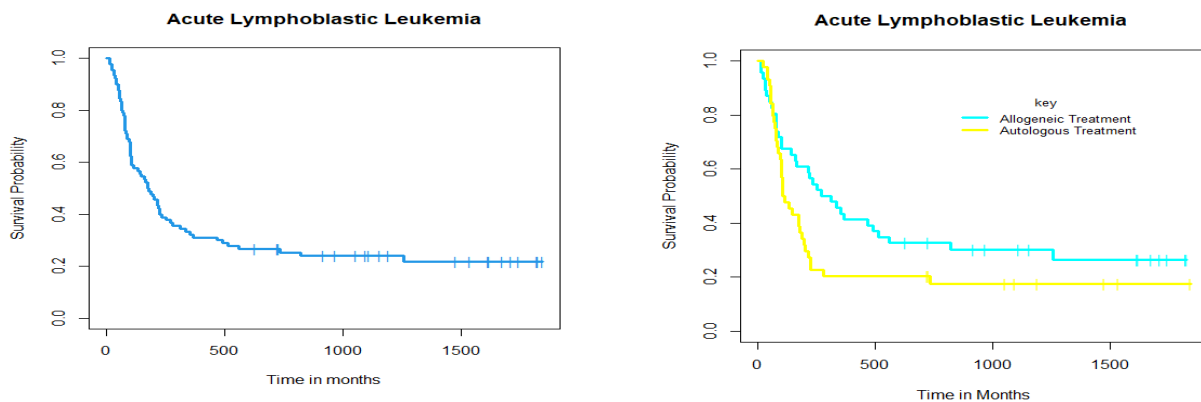


Fig. 1: Kaplan-Meier estimates of overall survival and for each type of Treatment



Table 1: MLEs of the Parameter with Z-values, P-values, AIC and BIC for Treatment Group I (46 Patients)

Parameter	Estimates	Z-value	P-value	AIC	BIC
FWD	$\hat{\alpha} = 0.15252$	0.0196	0.9844	827.2437	834.5482
	$\hat{\beta} = 0.58623$	0.0571	0.9545		
	$\hat{a} = 1.19708$	0.0571	0.9545		
	$\hat{b} = 2.56226$	0.6113	0.5410		
FWDNMCM	$\hat{\alpha} = 1.718e-02$	3.0026e+00	0.002677 **	689.218	698.3612
	$\hat{\beta} = 1.2673$	1.0376e+01	< 2.2e-16 ***		
	$\hat{a} = 7.2983$	1.2895e+05	< 2.2e-16 ***		
	$\hat{b} = 8.0721$	3.6601e+05	< 2.2e-16 ***		
	$\hat{p} = 0.0249$	9.8870e-01	0.322799		

* means significant at 5% level of significance

Table 1 presents the maximum likelihood estimates (MLEs), Z-values, P-values, and information criteria (AIC and BIC) for the Fréchet-Weibull distribution (FWD) and the Fréchet-Weibull non-mixture cure model (FWDNMCM) fitted to treatment group I (46

Patients) of the ALL dataset. Furthermore, the FWDNMCM exhibits marginally lower AIC and BIC values than the baseline FWD. This demonstrates that incorporating a cure parameter substantially improves model fit and explanatory power for this treatment cohort.

Table 2: MLEs of the Parameter with Z-values, P-values, AIC and BIC for Treatment Group II (45 Patients)

Parameter	Estimates	Standard Error	Z-value	P-value	AIC	BIC
FWD	$\hat{\alpha} = 0.22955$	5.67042	0.0405	0.9677	830.2337	834.3704
	$\hat{\beta} = 0.81131$	5.39102	0.1505	0.8804		
	$\hat{a} = 1.40874$	9.36206	0.1505	0.8804		
	$\hat{b} = 9.37931$	0.45986	20.3958	<2e-16 ***		
FWDNMCM	$\hat{\alpha} = 0.021140$	0.036508	0.5790	0.5626	735.0298	743.9507
	$\hat{\beta} = 1.329516$	0.125914	10.5589	< 2.2e-16 ***		
	$\hat{a} = 3.958071$	8.141474	0.4862	0.6269		
	$\hat{b} = 5.520210$	0.967697	5.7045	1.167e-08 ***		
	$\hat{p} = 0.022380$	0.024765	0.9037	0.3662		

* means significant at 5% level of significance



Correspondingly, Table 2 presents the parameter estimates and goodness-of-fit metrics for the two models fitted to treatment group II (45 patients) of the ALL dataset. Based on the information criteria, the FWDNMCM

also yields the lowest AIC and BIC values. This pattern reinforces the finding that incorporating a cure parameter substantially improves model fit compared to the baseline FWD.

Table 3: MLEs of the Parameter with Z-value, P-value, AIC and BIC for the entire ALL Dataset (91 Patients)

Parameter	Estimates	Standard Error	Z-value	P-value	AIC	BIC
FWD	$\hat{\alpha} = 0.115607$	1.089407	0.1061	0.9155	833.2357	837.2329
	$\hat{\beta} = 0.670722$	2.020526	0.3320	0.7399		
	$\hat{a} = 1.249750$	3.764776	0.3320	0.7399		
	$\hat{b} = 2.667089$	0.083904	31.7873	<2e-16 ***		
FWDNMCM	$\hat{\alpha} = 1.7407\text{e-}02$	$5.3581\text{e-}03$	$3.2488\text{e}+00$	0.001159 **	698.8292	711.3283
	$\hat{\beta} = 1.3499$	$1.2326\text{e-}01$	$1.0952\text{e}+01$	< 2.2e-16 ***		
	$\hat{a} = 1.7004\text{e}+01$	$1.1219\text{e-}05$	$1.5157\text{e}+06$	< 2.2e-16 ***		
	$\hat{b} = 1.7044\text{e}+01$	$1.6677\text{e-}05$	$1.0220\text{e}+06$	< 2.2e-16 ***		
	$\hat{p} = 4.8017\text{e-}02$	$2.9500\text{e-}02$	$1.6277\text{e}+00$	0.103586		

* means significant at 5% level of significance

Table 3 presents the parameter estimates and model selection statistics for the FWD and FWDNMCM models fitted to the pooled ALL dataset (91 Patients). The information criteria indicate that the FWDNMCM provides the optimal fit, yielding the lowest AIC and BIC values. This further confirms that accounting for a cured fraction markedly improves model performance when applied to the entire ALL cohort.

4.0 Conclusion

In summary, this study demonstrates that the estimated cured fraction is higher for Group I than for Group II, indicating a superior probability of long-term cure for patients in the former cohort. This finding aligns seamlessly with the empirical survival trajectories depicted in the Kaplan-Meier plots (Figure 1). Furthermore, the non-mixture model (FWDNMCM) yielded higher and more robust

cure parameter estimates than the baseline FWD model. Ultimately, the non-mixture cure formulation substantially outperforms the standard Fréchet-Weibull distribution when analyzing datasets characterized by a cured fraction, underscoring both the statistical and clinical necessity of incorporating cure parameters into survival modeling.

6. Recommendations

1. For survival and lifetime data characterized by long-term survivors, the derivation and implementation of Non - mixture cure model within this distributional framework are recommended. This recommendation is supported by the empirical superiority of the Fréchet-Weibull Non - Mixture cure model (FWDNMCM) over the standard distribution model.



2. Given that this research is restricted to a univariate framework, it is recommended that future studies extend this work to bivariate or multivariate generalizations. Because real-world phenomena are frequently influenced by multiple covariates, such extensions would enable the formulation of parametric regression models capable of handling complex, multi-dimensional datasets.

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Conflict of Interest

The author declared no conflict of interest

Data Availability

Data shall be made available upon request

Ethical Considerations

Not applicable

Author Contributions

The authors jointly conceptualized the study and developed the Fréchet-Weibull non-mixture cure model. Mohammed Saad led the model formulation, mathematical derivations, parameter estimation, and manuscript drafting. A. Bishir, U. F. Abbas, and K. E. Lasisi contributed to methodology development, statistical analysis, interpretation of cancer survival data, validation of results, critical manuscript review, and approval of the final version.

