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A Flexible Nakagami–Weibull Mixture Cure Model for Survival Data with Long-Term Survivors

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Abstract. Standard parametric survival models typically assume that all individuals will eventually experience the event of interest, an assumption that may be unrealistic in the presence of long-term survivors. To address this limitation, we propose a new parametric cure rate model called the Nakagami–Weibull Mixture Cure Model (NWMCM). The proposed model incorporates the Nakagami–Weibull distribution as the baseline distribution for susceptible individuals within a classical mixture cure framework, providing greater flexibility for modeling survival data with a cure fraction. Parameter estimation is performed using the maximum likelihood method under right-censored data through numerical optimization, while an EM-type algorithm is outlined to facilitate potential computational implementation. The finite-sample performance of the estimators is evaluated through a Monte Carlo simulation study, which demonstrates satisfactory performance in terms of bias and mean squared error. The practical applicability of the proposed model is illustrated using a melanoma survival dataset. The results show that the NWMCM provides an improved goodness-of-fit compared with several existing mixture cure models based on likelihood and information criteria measures. Overall, the proposed model offers a flexible and useful framework for analyzing survival data with long-term survivors.

1. INTRODUCTION

Survival analysis plays a fundamental role in many scientific disciplines, including medicine, epidemiology, reliability engineering, economics, and the social sciences, where the primary objective is to analyze time-to-event data that may be subject to censoring. Classical survival models

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such as the proportional hazards model and accelerated failure time model are widely used because of their interpretability and strong theoretical foundations. However, these models typically assume that all individuals will eventually experience the event of interest if observed for a sufficiently long period of time.

In many real-world applications, particularly in clinical and cancer studies, a proportion of individuals may be effectively cured or become long-term survivors who never experience the event of interest. Ignoring this cured fraction can lead to biased estimation of survival probabilities and misleading statistical inference. To address this issue, cure rate models have been developed to explicitly incorporate long-term survivors into survival analysis.

The earliest cure models were introduced by [1] and later extended by [2], who proposed a two-component mixture formulation for modeling cancer survival data. In this framework, the population is assumed to consist of two latent subpopulations: cured individuals who will never experience the event and susceptible individuals who remain at risk. Since then, mixture cure models have become an important tool for analyzing survival data with long-term survivors [3–5].

Two major classes of cure models have been extensively studied in the literature: mixture cure models and non-mixture (promotion-time) cure models [6]. Mixture cure models explicitly separate the population into cured and susceptible groups, whereas non-mixture models represent the cure fraction implicitly through the hazard structure. Among these approaches, mixture cure models are particularly attractive because they allow direct estimation and interpretation of the cure fraction.

An important component of cure modeling is the choice of the baseline survival distribution for susceptible individuals. Classical distributions such as the Weibull, log-normal, and log-logistic distributions are frequently used in survival analysis. However, these distributions may lack sufficient flexibility when the hazard rate exhibits complex patterns such as increasing, decreasing, unimodal, or bathtub-shaped behavior. Consequently, recent studies have focused on developing more flexible cure rate models based on generalized lifetime distributions [8–12].

Recent developments in cure rate modeling have also emphasized the importance of constructing flexible parametric and semiparametric models capable of capturing complex hazard structures and survival patterns observed in practice [16, 17]. These advances highlight the need for new cure models that combine interpretability with enhanced distributional flexibility.

One widely used approach for generating flexible lifetime distributions is the Marshall–Olkin method for adding parameters to baseline distributions, thereby increasing modeling flexibility [7]. Such generator mechanisms have been successfully applied to construct new families of survival distributions capable of accommodating diverse hazard rate behaviors.

In this context, the Nakagami distribution has emerged as a useful generator for constructing flexible distributional families. Originally introduced in wireless communication theory, the Nakagami distribution provides additional shape flexibility and has been successfully applied in reliability and lifetime modeling. When combined with the Weibull distribution, the resulting

Nakagami–Weibull distribution forms a flexible parametric family capable of modeling a wide range of survival and hazard patterns.

Despite its flexibility and modeling potential, the Nakagami–Weibull distribution has not yet been explored within the mixture cure modeling framework. Incorporating this distribution into a cure rate model may substantially improve the ability to capture heterogeneous survival patterns observed in real datasets, particularly when the hazard structure deviates from standard parametric assumptions.

Motivated by this gap in the literature, this paper proposes a new Nakagami–Weibull Mixture Cure Model (NWMCM) for survival data with long-term survivors. The proposed model combines the flexibility of the Nakagami–Weibull distribution with the interpretability of the mixture cure framework, thereby providing a robust tool for modeling censored survival data. The main contributions of this study are summarized as follows. First, a new mixture cure fraction model based on the Nakagami–Weibull distribution is introduced and its fundamental statistical properties, including the probability density, survival, and hazard functions, are derived. Second, maximum likelihood estimation procedures are developed for parameter estimation under right-censored data. Third, a Monte Carlo simulation study is conducted to evaluate the finite-sample performance of the proposed estimators. Finally, These contributions provide a flexible and robust framework for modeling survival data with cure fractions and complex hazard structures..

The remainder of the paper is organized as follows. Section 2introduces the proposed Nakagami–Weibull mixture cure model and its statistical properties. Section 3 presents the maximum likelihood estimation procedure. Section 4 reports the simulation study. Section 5 presents the real data applications, and Section 6 concludes the paper.

2. The Nakagami–Weibull Mixture Cure Fraction Model

Let T be a non-negative random variable. The Weibull distribution is defined by the cumulative distribution function

$$W(t) = 1 - \exp(-\sigma t^{\alpha}), \quad t \geq 0, \tag{2.1}$$

where $\alpha > 0$ and $\sigma > 0$ denote the shape and scale parameters, respectively.

The Nakagami–Weibull distribution is obtained by applying a Nakagami generator to the Weibull distribution. Its cumulative distribution function is given by

$$F_0(t) = \frac{1}{\Gamma(\Lambda)}\gamma\Big(\Lambda, z(t)\Big), \tag{2.2}$$

where

$$z(t) = \frac{\Lambda}{\xi}\left(e^{\sigma t^{\alpha}} - 1\right)^2,$$

with shape parameters $\Lambda > 0$ and $\xi > 0$. Differentiating (2.2) yields the probability density function

$$f_0(t) = \frac{2\Lambda\sigma\alpha}{\xi\Gamma(\Lambda)}t^{\alpha-1}\Big(e^{\sigma t^{\alpha}} - 1\Big)e^{\sigma t^{\alpha}}z(t)^{\Lambda-1}e^{-z(t)}. \tag{2.3}$$

$$S_0(t) = 1 - \frac{1}{\Gamma(\Lambda)}\gamma\Big(\Lambda, z(t)\Big) \tag{2.4}$$

Let $p \in (0,1)$ denote the cure fraction. The population survival function is defined as

$$S(t) = p + (1-p)S_0(t), \tag{2.5}$$

where $S_0(t)$ is the survival function of susceptible individuals. Substituting Equation (2.4) into Equation (2.5), we obtain

$$S(t) = 1 - \frac{1-p}{\Gamma(\Lambda)}\gamma\Big(\Lambda, z(t)\Big).$$

Hence, population survival function can be written as

$$S(t) = 1 - (1-p)\frac{\gamma\Big(\Lambda, z(t)\Big)}{\Gamma(\Lambda)}. \tag{2.6}$$

An important feature of the model is

$$\lim_{t\to\infty} S(t) = p, \tag{2.7}$$

which represents the long-term survival probability.
The corresponding probability density function is given by

$$f(t) = (1-p)f_0(t). \tag{2.8}$$

Substituting Equation (2.3) into Equation (2.8) gives

$$f(t) = (1-p)\frac{2\Lambda\sigma\alpha}{\xi\Gamma(\Lambda)}t^{\alpha-1}\Big(e^{\sigma t^{\alpha}} - 1\Big)e^{\sigma t^{\alpha}} z(t)^{\Lambda-1}e^{-z(t)}. \tag{2.9}$$

and the hazard rate function is given by

$$h(t) = \frac{f(t)}{S(t)}. \tag{2.10}$$

Substituting Equation (2.9) and (2.6) into (2.10) gives

$$h(t) = \frac{2(1-p)\Lambda\sigma\alpha\, t^{\alpha-1}\Big(e^{\sigma t^{\alpha}} - 1\Big)e^{\sigma t^{\alpha}} z(t)^{\Lambda-1}e^{-z(t)}}{\xi\Big[\Gamma(\Lambda) - (1-p)\gamma\Big(\Lambda, z(t)\Big)\Big]}. \tag{2.11}$$

3. MAXIMUM LIKELIHOOD ESTIMATION

Let (t_i, δ_i), $i = 1, \dots, n$, denote the observed survival times and censoring indicators from a random sample of size n, where $\delta_i = 1$ if the event is observed and $\delta_i = 0$ if the observation is right-censored. Under the mixture cure model framework, the survival and density functions of the proposed model are given by

$$S(t) = p + (1-p)S_0(t), \qquad f(t) = (1-p)f_0(t),$$

where $p \in (0,1)$ represents the cure fraction, and $S_0(t)$ and $f_0(t)$ denote the baseline survival and density functions defined in Equations (2.3) and (2.4).

Based on the observed right-censored sample, the likelihood function of the parameter vector

$$\Theta = (p, \Lambda, \xi, \sigma, \alpha)^\top$$

can be written as

$$L(\Theta) = \prod_{i=1}^{n} [f(t_i)]^{\delta_i} [S(t_i)]^{1-\delta_i} = \prod_{i=1}^{n} [(1-p)f_0(t_i)]^{\delta_i} [p + (1-p)S_0(t_i)]^{1-\delta_i}.$$

Taking the natural logarithm of the likelihood function yields the log-likelihood function

$$\ell(\Theta) = \sum_{i=1}^{n} [\delta_i \log\{(1-p)f_0(t_i)\} + (1-\delta_i)\log\{p + (1-p)S_0(t_i)\}].$$

The maximum likelihood estimators (MLEs) of the parameters are obtained by maximizing the log-likelihood function $\ell(\Theta)$ with respect to Θ. This leads to the likelihood equations

$$\frac{\partial \ell(\Theta)}{\partial p} = 0, \quad \frac{\partial \ell(\Theta)}{\partial \Lambda} = 0, \quad \frac{\partial \ell(\Theta)}{\partial \xi} = 0, \quad \frac{\partial \ell(\Theta)}{\partial \sigma} = 0, \quad \frac{\partial \ell(\Theta)}{\partial \alpha} = 0.$$

Since these equations do not admit closed-form solutions, the parameter estimates are obtained numerically using iterative optimization procedures such as the Newton–Raphson or BFGS algorithm.

Algorithm 1 EM Algorithm for the Nakagami–Weibull Mixture Cure Model (NW–MCM)

```
Input: Observed survival data $(t_i, \delta_i)$ for $i = 1, \dots, n$
Initialize parameter vector $\Theta^{(0)} = (p^{(0)}, \Lambda^{(0)}, \xi^{(0)}, \sigma^{(0)}, \alpha^{(0)})$
Set convergence tolerance $\varepsilon > 0$ and iteration counter $k = 0$
repeat
    E-step: Compute posterior susceptibility probabilities
        $\tau_i^{(k)} = \begin{cases} 1, & \delta_i = 1, \\ \dfrac{(1-p^{(k)})S_0(t_i; \vartheta^{(k)})}{p^{(k)} + (1-p^{(k)})S_0(t_i; \vartheta^{(k)})}, & \delta_i = 0, \end{cases}$
    where $S_0(t_i)$ is the baseline Nakagami–Weibull survival function.
    M-step:
    Update the cure fraction
        $p^{(k+1)} = \frac{1}{n}\sum_{i=1}^{n}(1 - \tau_i^{(k)}).$
    Update baseline parameters $\vartheta = (\Lambda, \xi, \sigma, \alpha)$ by maximizing
        $Q(\vartheta) = \sum_{i=1}^{n} \tau_i^{(k)} [\delta_i \log f_0(t_i; \vartheta) + (1-\delta_i)\log S_0(t_i; \vartheta)].$
    Obtain $\vartheta^{(k+1)}$ using numerical optimization (Newton–Raphson or BFGS).
    Update $\Theta^{(k+1)} = (p^{(k+1)}, \vartheta^{(k+1)})$
    $k \leftarrow k + 1$
until $\|\Theta^{(k)} - \Theta^{(k-1)}\| < \varepsilon$
Output: Maximum likelihood estimates $\hat{\Theta}$
```

4. SIMULATION STUDY

In this section, the performance of the proposed Nakagami–Weibull Mixture Cure Model (NWMCM) is investigated through a Monte Carlo simulation study. The simulations were carried out for different sample sizes $n = 10, 50, 100, 200,$ and 500 to evaluate the finite-sample behavior of the maximum likelihood estimators. These sample sizes were selected to examine the accuracy and stability of the estimators as the sample size increases. The estimation performance was assessed using bias, variance, mean squared error (MSE), and root mean squared error (RMSE). The simulation results are summarized in Table 1. The Monte Carlo simulation results in Table 1 demonstrate the performance of the maximum likelihood estimators for the parameters of the proposed NWMCM. It can be observed that the bias, variance, MSE, and RMSE decrease as the sample size increases, indicating improved estimation accuracy and stability. For larger sample

TABLE 1. Monte Carlo simulation results for the Nakagami–Weibull Mixture Cure Model under different sample sizes.

n	Param	True	Mean	Bias	Var	MSE	RMSE	ConvRate
10	p	0.30	0.33122	0.03122	0.08718	0.08379	0.28947	0.95
	Λ	1.20	1.14677	-0.05323	0.19963	0.19249	0.43873	0.95
	ξ	1.50	1.56306	0.06306	0.14257	0.13942	0.37338	0.95
	σ	1.00	1.02883	0.02883	0.12414	0.11877	0.34463	0.95
	α	2.00	1.97298	-0.02702	0.10699	0.10237	0.31995	0.95
50	p	0.30	0.24853	-0.05147	0.02230	0.02383	0.15437	0.95
	Λ	1.20	1.20200	0.00200	0.01623	0.01542	0.12418	0.95
	ξ	1.50	1.48950	-0.01050	0.02103	0.02009	0.14172	0.95
	σ	1.00	1.05251	0.05251	0.01905	0.02085	0.14441	0.95
	α	2.00	1.99366	-0.00634	0.01464	0.01395	0.11809	0.95
100	p	0.30	0.27589	-0.02411	0.00949	0.00960	0.09796	0.95
	Λ	1.20	1.21808	0.01808	0.00892	0.00880	0.09382	0.95
	ξ	1.50	1.49054	-0.00946	0.01158	0.01109	0.10530	0.95
	σ	1.00	0.95015	-0.04985	0.00621	0.00838	0.09157	0.95
	α	2.00	2.01777	0.01777	0.00975	0.00957	0.09785	0.95
200	p	0.30	0.29927	-0.00073	0.00329	0.00313	0.05590	0.95
	Λ	1.20	1.18805	-0.01195	0.00469	0.00460	0.06780	0.95
	ξ	1.50	1.49888	-0.00112	0.00370	0.00352	0.05933	0.95
	σ	1.00	0.99173	-0.00827	0.00308	0.00300	0.05476	0.95
	α	2.00	1.97483	-0.02517	0.00518	0.00555	0.07451	0.95
500	p	0.30	0.30140	0.00140	0.00224	0.00213	0.04613	0.95
	Λ	1.20	1.20823	0.00823	0.00202	0.00199	0.04457	0.95
	ξ	1.50	1.49052	-0.00948	0.00252	0.00249	0.04986	0.95
	σ	1.00	1.00299	0.00299	0.00275	0.00262	0.05117	0.95
	α	2.00	2.00310	0.00310	0.00170	0.00162	0.04026	0.95

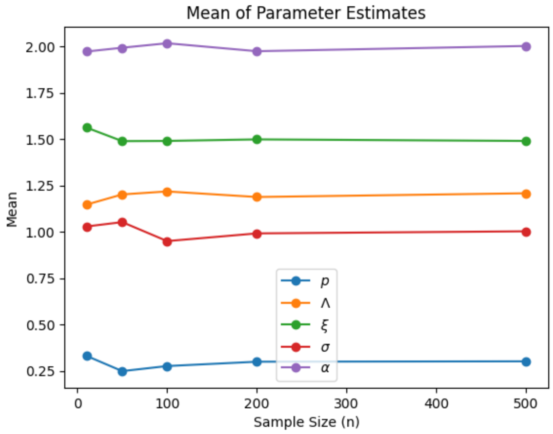

Figure 1. Mean

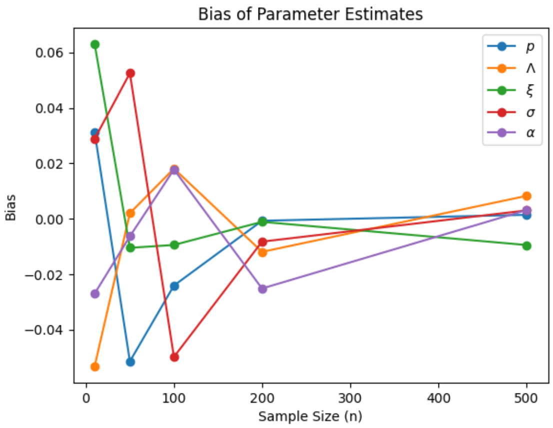

Figure 2. BIAS

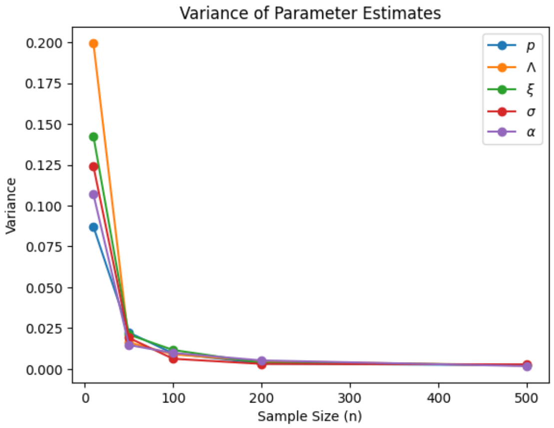

Figure 3. VARIANCE

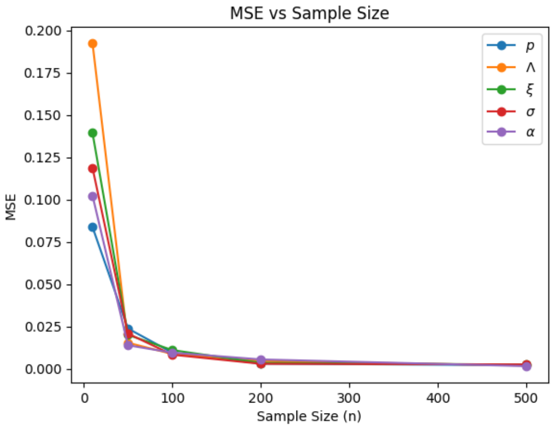

Figure 4. MSE

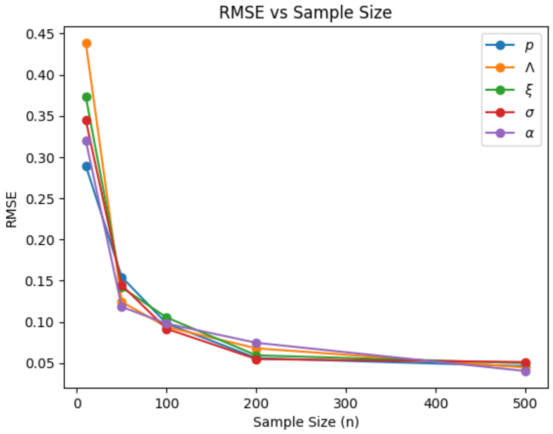

Figure 5. RMSE

sizes ($n = 200$ and $n = 500$), the parameter estimates are very close to the true values with relatively small estimation errors. Moreover, the convergence rate remains consistently high across all sample sizes, suggesting that the estimation procedure is numerically stable. Overall, the results indicate that the estimators perform well and exhibit desirable statistical properties.

5. Real Data Applications

To illustrate the practical usefulness of the proposed Nakagami–Weibull Mixture Cure Model (NWMCM), the melanoma dataset from the Eastern Cooperative Oncology Group (ECOG) phase III clinical trial E1684 was analyzed. The dataset, available in the `smcure` package in R, contains survival information for patients with high-risk melanoma who were randomized either to an observation group or to a treatment group receiving high-dose interferon (IFN). After removing two observations with missing information, the analysis was conducted on 285 patients.

The endpoint considered is relapse-free survival time together with a censoring indicator identifying relapse or death. The Kaplan–Meier survival curve in Figure 6 shows a clear plateau in the tail region, indicating the presence of long-term survivors. Such a pattern suggests that cure rate models are appropriate for analyzing this dataset [13–15].

To evaluate the performance of the proposed model, several competing mixture cure models were fitted to the data, including the generalized exponential mixture (GEM), Burr XII mixture (BXIIM), Burr X mixture (BXM), and Marshall–Olkin Burr X mixture (MOBXM) models. The parameter estimates and goodness-of-fit statistics are presented in Table 2.

The estimated cure fraction is approximately 0.28–0.30 across the fitted models, suggesting that nearly 30% of the patients may be considered long-term survivors. Among the competing models, the proposed NWMCM achieves the highest log-likelihood and the smallest AIC and BIC values, indicating the best overall fit to the melanoma dataset. This result is further supported by the graphical comparison in Figure 6, where the NWMCM curve closely follows the Kaplan–Meier survival estimate.

Table 2. Parameter estimates and goodness-of-fit statistics for the fitted cure models for the melanoma dataset.

Model	$\hat{p}$	$\hat{\Lambda}$	$\hat{\xi}$	$\hat{\sigma}$	$\hat{\alpha}$	LogLik	AIC	BIC
GEM	0.299	–	8.079	–	0.932	-387.645	781.289	792.247
BXIIM	0.294	8.578	0.954	–	–	-384.373	774.746	785.703
BXM	0.299	0.315	0.282	–	–	-404.254	814.508	825.465
MOBXM	0.289	0.645	1.892	19.910	–	-377.733	763.466	778.076
NWMCM	**0.279**	**4554.997**	**0.049**	**0.202**	**0.005**	**-375.906**	**761.812**	**780.074**

Table 2 presents the maximum likelihood estimates and goodness-of-fit statistics for the fitted cure models. The estimated cure fraction p ranges between 0.289 and 0.299 across the competing models, indicating that approximately 29% of the patients may be considered long-term survivors. This finding is consistent with the plateau observed in the Kaplan–Meier survival curve, suggesting the presence of a cured subgroup in the melanoma dataset.In terms of model comparison, the proposed

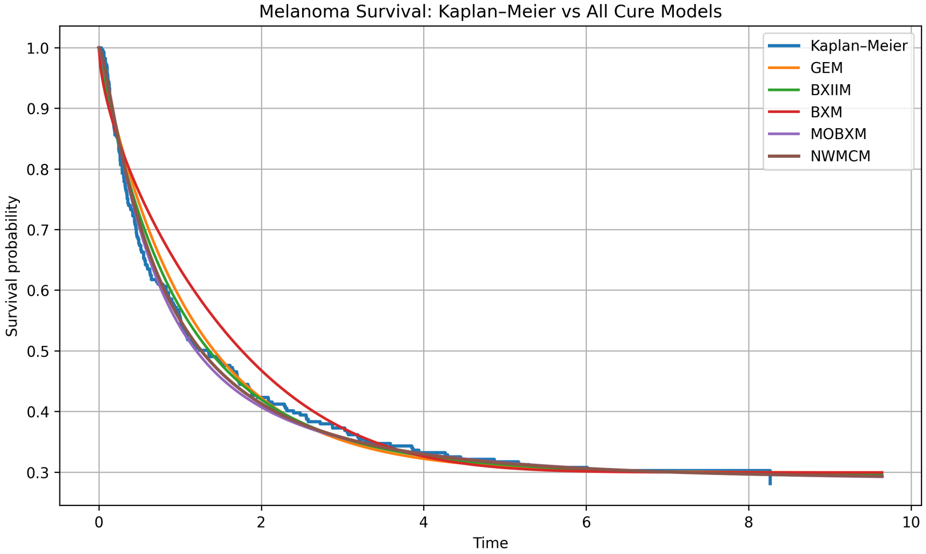

Figure 6. Kaplan–Meier survival curve for the melanoma dataset overlaid with the fitted cure models.

NWMCM produces the highest log-likelihood value and the smallest AIC and BIC values among all the compting models. These results indicate that the proposed model provides the best fit to the data. The improved performance of the NWMCM can be attributed to the additional flexibility introduced by the Nakagami Weibull structure, which allows the model to better capture complex survival patterns and hazard rate behaviors present in the

6. Conclusion

This study introduced a new Nakagami–Weibull Mixture Cure Model (NWMCM) for the analysis of survival data with a cure fraction. By integrating the flexibility of the Nakagami–Weibull distribution within a mixture cure modeling framework, the proposed model is able to accommodate a wide range of hazard rate shapes and survival patterns. The fundamental properties of the model, including the probability density, survival, and hazard functions, were derived, and parameter estimation was carried out using the maximum likelihood method under right-censored data. A Monte Carlo simulation study demonstrated that the estimators perform well, with bias, variance, and mean squared error decreasing as the sample size increases, indicating consistent and efficient estimation. The practical usefulness of the model was illustrated using a melanoma survival dataset, where the estimated cure fraction was approximately 30 percent, confirming the presence of long-term survivors. In comparison with several existing mixture cure models, including the GEM, BXIIM, BXM, and MOBXM models, the proposed NWMCM achieved the highest log-likelihood and the smallest information criteria values, indicating superior model fit. Overall, the proposed model provides a flexible and effective framework for analyzing survival data with cure fractions, and future research may focus on extending the model to include covariate structures, Bayesian estimation approaches, and semiparametric formulations.

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