Effects of knowing the censoring distribution on survival function estimation: a simulation comparison of the Gill and Efron Kaplan-Meier estimators to the S^* estimator

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1 Introduction

Many areas of science and engineering provide a motivation to analyze survival data. In the context of engineering, one may be interested in the expected time to failure of a microchip. In the context of medicine, one may be interested in the expected time to death of a patient in a medical treatment. These examples, among others, motivate the interest to explore time to event data. The general statistical setup is as follows. Survival observations are denoted by the random variable X and we assume $X_1, X_2, ..., X_n \stackrel{iid}{\sim} F$. While our interest is to estimate the distribution F, it becomes difficult to do this with censored observations. Censored observations are denoted by the random variable C and we assume $C_1, C_2, ..., C_n \stackrel{iid}{\sim} G$. Also, we assume that $X_i \perp C_i \ \forall i$. Define $T_i = min(X_i, C_i)$ and $\delta_i = 1$ if $X_i < C_i$, and $\delta_i = 0$ otherwise. The observed data becomes: (T_i, δ_i) with times of death: $t_1, ..., t_k$.

2 Estimators

This report considers the following estimators. The Efron and Gill estimators offer modifications to the Kaplan–Meier estimator (1958). Both modifications attempt to improve the Kaplan–Meier estimator, particularly in cases where the last observation is censored.

Kaplan-Meier estimator

$$\hat{S}_{KM}(t) = \begin{cases} 1 & \text{if } t < t_1 \\ \prod_{t_i \le t} \left(1 - \frac{d_i}{Y_i} \right) & \text{if } t_1 \le t \end{cases}$$

Kaplan–Meier estimator (Efron)

$$\hat{S}_E(t) = \begin{cases} S_{KM}(t) & \text{if } t < t_k \\ 0 & \text{if } t_k \leq t \end{cases}$$

Kaplan-Meier estimator (Gill)

$$\hat{S}_G(t) = \begin{cases} S_{KM}(t) & \text{if } t < t_k \\ S_{KM}(t_k) & \text{if } t_k \le t \end{cases}$$

All the previous estimators assume that neither the censoring distribution or the survival distribution are known. As this report presents several simulations, we can construct an estimator which relies on knowing the distribution of the censoring distribution. This motivates the creation of a new estimator: S^* .

$$P(T > t) = P(\min(X, C) > t) = P(X > t)P(C > t)$$

$$\Leftrightarrow \frac{P(T > t)}{P(C > t)} = P(X > t)$$

We can use the empirical estimators to obtain:

$$S^{*}(t) = \frac{\frac{1}{n} \sum_{i=1}^{n} 1(T_{i} > t)}{P(C > t)}$$

The goal of this project is to compare finite-sample properties of the three estimators, $\hat{S}_E(t)$, $\hat{S}_G(t)$, $S^*(t)$. The $S^*(t)$ would be impossible to obtain in a real-world setting as it required knowledge of the censoring distribution. This is not the case for the Efron and Gill estimators. Comparing all three estimators will allow us to evaluate the effects of knowing the censoring distribution on the survival function estimator. The criteria of bias and mean squared error to compare performance. Note that the All simulations were performed in R. The sample size used was 100 and the number of replications used in each simulation was 10000. In the first part of this project, various distributions of X and C were used to explore these estimators. Additionally, a mixture gamma distribution was considered in the second part of this project.

3 **Part (i)**

The following distributions were chosen for X and C: Exponential($\lambda=0.01$), Weibull($\alpha=2$, $\beta=100$), and Normal($\mu=150$, $\sigma=50$). Exponential, Weibull, and Normal were chosen because of their common use in modeling survival times, and the particular parameters were chosen for each distribution to achieve similar ranges of moderately large values in the simulations

(i.e., sample data that ranged from approximately 0 to 200 or 300). Please see the Appendix for graphs of the bias and MSE in the following settings.

3.1 X is Exp(0.01), C is Exp(0.01)

In this case, the survival times and the censored times are from the same distribution. Bias is near 0 and very similar for the three estimators until around the 80th quantile. After that, the bias of the Gill KM increases exponentially, the bias of the Efron KM becomes negative with increasing magnitude, and the bias of $S^*(t)$ remains near 0. The MSE of $S^*(t)$ is the highest of the estimators for most of the support, with the MSE of the Gill KM surpassing it at the 95th quantile. The $S^*(t)$ MSE increases fairly steadily across the quantiles and may level off around 0.01. The Gill and Efron estimators have the same MSE until the 75th quantile, at which point Efron has higher MSE until the 90th quantile, when Gill increases sharply and Efron decreases sharply. The MSE of all three estimators is low across the quantiles, however, remaining almost entirely below 0.01. Taken together, these results indicate that while $S^*(t)$ is approximately unbiased for S(t), it is more variable than the Gill or Efron KM estimators.

3.2 X is Exp(0.01), C is Weibull(2, 100)

In this case, the CDF of the survival times is above the CDF of the censored times until around time t=100, after which point the CDF of the censored times lies above. The bias of all three estimators is near 0 until the 75th quantile, after which the bias of the Gill KM diverges positively, the bias of the Efron KM diverges negatively, and $S^*(t)$ remains around 0. At the 90th quantile, however, the bias of both the Efron KM and $S^*(t)$ increase. While the MSE for all three estimators is similar and very low for most of the quantiles, the MSE for $S^*(t)$ begins to increase at the 85th quantile and increases dramatically between the 90th and 95th quantiles, almost reaching an MSE of 5 at the 95th quantile and giving an indication that the variance explodes in the later quantiles. This is likely because for the highest quantiles t of the Exp(0.01) distribution, the P(C>t) can be very small, meaning that the value of $S^*(t)$ much higher than 1, the highest value a valid estimator of S(t) should take. For example, in these simulations, the maximum $S^*(t)$ for the 95th quantile time was 78.98371. This in turn contributes to a high variance and MSE for $S^*(t)$ in this setting. Overall, in this setting, $S^*(t)$ provides an improvement over the KM estimators in terms of bias, but has a very high MSE for times in the far right of the tail of the Weibull(2,100) censoring distribution.

3.3 X is Exp(0.01), C is Normal(150, 50)

In this setting, the CDF of the survival times is well above the CDF of the censored times until around time t=200, after which the censored times CDF is slightly above the survival times CDF. Similar to the previous case, this means that P(C>t) can be small for higher values of t, in turn increasing the value of $S^*(t)$. For example, in these simulations, the maximum $S^*(t)$ for the 95th quantile time was 7.20350. The bias of the Gill KM increases and decreases across the quantiles, remaining negative until slightly after the 60th quantile, at which point it becomes positive. At the 90th quantile, the bias begins to increase dramatically. The bias of both the Efron KM and $S^*(t)$ remains near 0 for most of the quantiles, with the bias of the Efron KM becoming negative at the 80th quantile and decreasing sharply between the 85th and 90th quantiles. The bias of $S^*(t)$ also increases slightly between the 90th and 95th quantiles. The MSE behaves similarly to the setting in subsection 2 where $X \sim Exp(0.01)$ and $C \sim Weibull(2,100)$, but on a smaller scale, with the peak MSE, for $S^*(t)$ at the 95th quantile, being slightly under 0.4. Again, similarly to the previous setting, $S^*(t)$ provides an improvement over the KM estimators in terms of bias, but has a very high MSE for times in the far right of the tail of the Normal(150,50) censoring distribution.

3.4 X is Weibull(2, 100), C is Exp(0.01)

In this case, the CDF of the censored times lies above the CDF of the survival times until around time t=100, after which point the CDF of the survival times lies above. This means that the P(C>t) is relatively large compared to the P(X>t), which keeps the value of $S^*(t)$ lower (and, specifically, below 1) as well as keeping the variance of $S^*(t)$ lower. The bias of all three estimators is positive for all the quantiles and very similar until about the 85th quantile. The bias starts around 0.13, peaks around 0.47 at the 35th quantile, and then decreases to less than 0.1 at the 90th quantile. The bias of the Efron KM and $S^*(t)$ decreases to 0.05 at the 95th quantile while the bias of the Gill KM is slightly higher at around 0.08 at the same quantile. The MSE for all three estimates behaves similarly to the bias, increasing until around the 35th and 40th quantiles, peaking around 0.23, then decreasing to less than 0.01 by the 95th quantile. Overall, $S^*(t)$ does not provide improvements over the KM estimators, but it also does not perform worse.

3.5 X is Weibull(2, 100), C is Weibull(2, 100)

Because the survival times and censored times are again from the same distribution, the same patterns hold for the bias and MSE that were described in subsection 1.

3.6 X is Weibull(2, 100), C is Normal(150, 50)

In this setting, the CDF of the survival times lies above the CDF of the censored times for all times until they become equivalent for later times. This means that the P(C>t) is relatively large compared to the P(X>t), which keeps the value of $S^*(t)$ lower (and, specifically, below 1) as well as keeping the variance of $S^*(t)$ lower. The bias and the MSE for all three estimators behave similarly to the setting in subsection 4 where $X\sim Weibull(2,100)$ and $C\sim Exp(0.01)$. The bias peaks at around 0.47 at the 35th quantile and decreases to around 0.05 at the 95th quantile. The MSE peaks at around 0.23 for the 35th and 40th quantiles and decreases to less than 0.005 at the 95th quantile. Because the bias and MSE are very similar among the three estimators for all quantiles, $S^*(t)$ does not provide any improvement over the KM estimators.

3.7 X is Normal(150, 50), C is Exp(0.01)

In this setting, the CDF of the censored times lies above the CDF of the survival times until around time t=200, after which the survival times CDF lies slightly above. This means that for larger times t, the P(C>t) is relatively large compared to P(X>t), which keeps the value of $S^*(t)$ from being so large above 1. Until the 70th quantile, the bias of the KM estimators are near 0 and the bias of $S^*(t)$ is slightly negative. After the 70th quantile, the bias of the Gill KM increases exponentially, reaching around 0.07 at the 95th quantile, the bias of the Efron KM becomes more negative, and the bias of $S^*(t)$ becomes closer to 0. For most of the quantiles, the MSE of $S^*(t)$ is well above the MSE of the KM estimators, peaking slightly above 0.02. By the 95th quantile, the MSE of the Gill KM is closer to 0.01 while the MSE of the Efron KM and $S^*(t)$ is closer to 0.005. While $S^*(t)$ improves on the bias of the KM estimators for larger times t, $S^*(t)$ tends to be more variable than the other estimators in this setting, indicating that, overall, $S^*(t)$ does not improve much on the KM estimators.

3.8 X is Normal(150, 50), C is Weibull(2, 100)

In this setting, the CDF of the censored times lies above the CDF of the survival times for all times until they become equivalent for later times. This means that $P(C>t) \leq P(X>t)$ for larger t, meaning that it is possible for $S^*(t)$ to go above 1. For example, the maximum $S^*(t)$ in this simulation for the 95th quantile time was 4.40017. This in turn contributes to a higher variance for $S^*(t)$ at higher times t. The bias for all three estimators is near 0 until the 50th quantile, after which the Gill KM increases exponentially and the Efron KM becomes increasingly negative until it begins to increase at the 85th quantile. $S^*(t)$ remains near 0 for all the quantiles. The MSE of $S^*(t)$ is higher than the MSE of the KM estimators across all the quantiles, ending around 0.109 at the 95th quantile. The MSE of $S^*(t)$ and the Gill KM increasing as time increases and the MSE of the Efron KM increasing until the 75th quantile, after which it decreases. Overall, in this setting, $S^*(t)$ improves on the KM estimators in terms of bias, but is more variable.

3.9 X is Normal(150, 50), C is Normal(150, 50)

Because the survival times and censored times are again from the same distribution, the same patterns mostly hold for the bias and MSE that were described in subsection 1. One minor difference is that the bias of $S^*(t)$ increases slightly between the 80th and 90th quantile before decreasing again to near 0 by the 95th quantile. For these higher quantiles, the MSE of $S^*(t)$ is also slightly above 0.01.

3.10 General comments

When the censored times and the survival times are from the same distribution, $S^*(t)$ provides some improvement over the KM estimators in terms of bias for higher times t, but performs worse in terms of MSE. This pattern also holds when the survival times come from a Normal(150,50) distribution and the censored times come from either an Exp(0.01) or a Weibull(2,100) distribution. When the survival times come from an Exp(0.01) distribution and the censored times come from either a Weibull(2,100) or a Normal(150,50) distribution, $S^*(t)$ provides a similar improvement in bias over the KM estimators and has low variance for most times t, but the MSE of $S^*(t)$ increases steeply, especially compared to the KM estimators, for times t far in the right tail. When the survival times come from a Weibull(2,100) distribution-

tion and the censored times come from either an Exp(0.01) or a Normal(150, 50) distribution, $S^*(t)$ performs essentially the same as the KM estimators.

4 Part (ii)

The mixture Gamma distribution is highly flexible and readily captures features such as mulitimodality in predictive survival densities. Sometimes, the real life survival datasets are heterogeneous, thus the mixture model is one of the best solutions. Maximum likelihood estimation of the parameters of mixture models were obtained by the EM algorithm.

4.1 Simulation Settings

We use the mixture Gamma distribution for censoring data, the pdf of this mixture model is as follows:

$$f(C) = \sum_{i=1}^{n} p_i f(Y_i | \alpha_i, \beta_i)$$

where $Y_i \sim Gamma(\alpha_i, \beta_i)$ and $\sum_{i=1}^n p_i = 1$. In this project's simulation studies, I use three different mixture Gamma distributions.

1. Mixture Gamma distribution 1:

- $p_1 = 0.1, p_2 = 0.3, p_3 = 0.6$
- $\alpha_1 = 10, \alpha_2 = 20, \alpha_3 = 40$
- $\beta_1 = \beta_2 = \beta_3 = 1.5$
- $E[C] = \mu = \sum_{i=1}^{3} p_i \mu_i = (0.1)(10)(1.5) + (0.3)(20)(1.5) + (0.6)(40)(1.5) = 46.5$
- $Var(C) = \sum_{i=1}^{3} p_i \left(\sigma_i^2 + \mu_i^2 \mu^2\right) = 403.3$

2. Mixture Gamma distribution 2:

- $p_1 = p_2 = p_3 = \frac{1}{3}$
- $\alpha_1 = 10, \alpha_2 = 20, \alpha_3 = 40$
- $\beta_1 = 7, \beta_2 = 2, \beta_3 = 1$
- $E[C] = \mu = \sum_{i=1}^{3} p_i \mu_i = (\frac{1}{3})(10)(7) + (\frac{1}{3})(20)(2) + (\frac{1}{3})(40)(1) = 50$
- $Var(C) = \sum_{i=1}^{3} p_i \left(\sigma_i^2 + \mu_i^2 \mu^2\right) = 360$

3. Mixture Gamma distribution 3:

- $p_1 = 0.5, p_2 = 0.3, p_3 = 0.2$
- $\alpha_1 = 10, \alpha_2 = 20, \alpha_3 = 40$
- $\beta_1 = 6, \beta_2 = 2, \beta_3 = 1$
- $E[C] = \mu = \sum_{i=1}^{3} p_i \mu_i = (0.5)(10)(6) + (0.3)(20)(2) + (0.2)(40)(1) = 50$
- $Var(C) = \sum_{i=1}^{3} p_i \left(\sigma_i^2 + \mu_i^2 \mu^2\right) = 962$

4.2 Simulation Result with Exp(0.02) as the survival pdf

4.2.1 Mixture Gamma Distribution Setting 1

By looking at the cumulative density function comparison plot between exponential distribution with parameter $\lambda=0.02$ and the mixture Gamma distribution (setting 1), before the time point 60, the data is more likely to be the true death time and after that, there is higher possibility that it is the censoring data. Besides, the probability density function of this mixture gamma distribution has two vertexes, so this censoring distribution can handle heterogeneous censoring data.

For the comparison of Efron's KM estimates, Gill's KM estimates and S^* , as the previous section, we calculated the bias and the mean square error for all three estimates. For the bias, the Efron's estimate did a really good job on the first 45^{th} quantile of the time range and it is close to an unbiased estimate. The Gill's estimate behaves the same as the Efron's for the first 45^{th} quantile of the time, and then has a positive bias which matches our expectation, however, the Efron's has a negative bias instead. Since these two estimates diverge at the 45^{th} quantile, the last true death time should be around the 45^{th} quantile, all the data points after that should come from censoring data. Although, the Efron's have a negative bias after 45^{th} quantile, with the time passes, the bias of Efron's is getting large and has a trend to converge to 0. For the S^* , it has negative bias all the time, and before 50^{th} quantile, the bias is decreasing, but afterwards, it is increasing later on. In addition, it is very interesting to see that the Efron's is equivalent to S^* after 60^{th} quantile.

As for the mean square error, the pattern is very similar to the bias plot. Both Efron's and Gill's KM estimates work really well when the time is below the 45^{th} quantile. S*, on the other hand, always has the larger mean square error and it did the worst job on the 50^{th} quantile of the time. It is also interesting to see that the Gill's has lowest MSE among these three estimates before 70^{th} quantile of the time. Later on, the MSE just drop to 0 for both Efron's and S*, but

the Gill's MSE keeps increasing.

4.2.2 Mixture Gamma Distribution Setting 2

For the mixture Gamma distribution cdf comparison plot, before the time point 45, the data is more likely from the true death time and later on, it is more likely from the censoring data. This mixture model actually has three vertexes, so more flexible than what we have in setting 1.

The Efron's and Gill's are both good for bias before 50^{th} quantile, after that, they diverge and the Gill's has the positive bias but the Efron's has the negative bias. Since the pdf of the mixture model has three vertexes, then there is some increases and decreases going on for the S* estimate, but it has the negative bias all the time. After the 75^{th} quantile, the S* and the Efron's have the same bias.

In the MSE plot, the S^* is the worst estimate before the 70^{th} quantile of the time and then it has the same MSE as the Efron's. The Gill's have the same MSE with the Efron's until 55^{th} quantile of the time. After 75^{th} quantile of the time, the Gill's becomes the worst estimates.

4.2.3 Mixture Gamma Distribution Setting 3

The mixture Gamma distribution of setting 3 is very similar to the setting 2, both of then have the three vertexes and the pattern of the cdf is kind of the same as setting 2 as well. Because of these reasons, I will combine the setting 2 and setting 3 together and illustrate the results form this two setting together in the following sections. Overall, it just puts more weights on the Y_1 which follows a Gamma(10, 6). The bias plot and the MSE plot are like setting 2 as well, one thing I noticed is that the MSE of all estimates did slightly worse job than setting 2, if we look at the numerical number of MSE for these two cases.

4.3 Simulation Result with Weibull(0.5, 25) as the survival pdf

4.3.1 Mixture Gamma Distribution Setting 1

From the the cdf comparison plot, the Weibull distribution has a heavier tail than the mixture Gamma model in this setting. Before time point 60, the data is more likely from the true death time and afterwards, the data is more likely to be the censoring data.

Under this simulation setting, for the perspective of bias, all of the estimates seem behave

really well before 30^{th} quantile of the time and then S^* diverges first and has a negative bias. Efron's and Gill's diverge after 65^{th} quantile and as we are expecting, the Gill's has a positive bias and the Efron's has a negative bias. The S^* and Efron's are equivalent after 75^{th} quantile.

For the MSE plot, all of three are equivalent before 30^{th} quantile of the time. From 30^{th} quantile to 65^{th} quantile, the Efron's and Gill's are equally good. After 75^{th} quantile, the Efron's and S^* performs equally again. However, the Gill's is getting worse and worse after 65^{th} quantile.

4.3.2 Mixture Gamma Distribution Setting 2 and Setting 3

In both settings, both cdf comparison plots show that before the time point 60, the data is more likely from the true death time and afterward the censoring data has more chance to be selected.

Both bias plots suggest that the bias of the two KM estimates is close to an unbiased estimates until the 70^{th} quantile of the time, however, the S^* always has the negative bias. After 80^{th} quantile of the time, the S^* and the Efron's are equivalent, and as I mentioned before several times already, after diverging from the Efron's, Gill's then has a positive bias.

For the MSE plots, the S^* is the most unstable estimator and it has larger MSE than Gill's and Efron's until 85^{th} quantile. In practical, I would recommend researcher use KM estimates rather than the S^* since the first 85^{th} quantile of the time, KM are uniformly better.

4.4 Simulation Result with Normal(50, 50) as the survival pdf

4.4.1 Mixture Gamma Distribution Setting 1

The most interesting fact relates to the Normal distribution is that the range of the data is from negative infinity to the positive infinity. The good thing about Normal is that it has a short tail than the exponential and the Weibull distribution we tried. Before the time point 50, the data are more likely to be drawn from the true death time and afterward the censoring data dominates the data.

For the bias plot, For the first 15^{th} quantile of the time, all of the estimates are equally behaved, which might implies that in our simulation, the first 15^{th} quantile of data are all come from the Normal distribution, in another words, from the true death distribution. Besides, the Efron's and the Gill's are diverge from 40^{th} which means our last data point from the Normal

distribution is launched at the 35^{th} quantile of the time.

For the MSE plot, the Efron's and Gill's having the same MSE until 35^{th} quantile and then Efron's will have larger MSE before 65^{th} than Gill's. However, after that point, the Gill's performance is worse. For S^* , it has the worst performance until 45^{th} quantile and then has the same performance with Efron's afterwards.

4.4.2 Mixture Gamma Distribution Setting 2 and Setting 3

As the Weibull cases, for the estimated bias, the S^* performs really bad and always has a negative bias. The two KM estimates have the same performance until 40^{th} quantile and Gill's has a positive bias and Efron's has a negative bias.

For the MSE plot, the Efron's and Gill's having the same MSE until 45^{th} quantile and then Efron's will have larger MSE before 70^{th} than Gill's. However, after that point, the Gill's performance is worse. For S^* , it has the worst performance until 60^{th} quantile and then has the same performance with Efron's afterwards.

4.5 Overall Conclusion

For the bias, the S^* is always negative for all my cases, and is the worst estimate based on my simulation. The Efron's and the Gill's are somewhat similar with each other at the begining and as time pass by, they will diverge eventually, and Gill's always has positive bias and Efron's has negative bias. The Efron's estimate sort of converge to zero as time pass by.

Since the bias of S^* is relevantly larger than other two estimates at the beginning, it did a bad job on MSE at the beginning as well. However, after some point, the performance of this estimate is equivalently to the Efron's. The Gill's always behave really good at early stage, but after more late censoring data are drawn, it acts poorly.

5 Discussion and Conclusions

From class, we expected the Gill modification to have positive bias and the Efron modification to have negative bias. In certain settings, the S^* estimator provided improvement in bias, but was often more variable; in other settings, the S^* performed essentially the same as the Kaplan-Meier estimators. The improvement, or lack thereof, of the S^* estimator in comparison to the KM estimators depended on the chosen survival and censoring distributions. One

might expect that knowing the distribution of C, the censoring distribution, may contribute to estimators with lower bias and MSE, but that was not the case with these simulations.

For the future work, we can explore this mixture model more by adding more components $(Y_i s)$. Also, we could set the $\alpha_i s$ and $\beta_i s$ very different, so that the mixture distribution has more vertexes and more flexible. Besides, another idea would be to mix different distributions together, e.g., we can mix Normal, Exponential, and Weibull together and put different weights on them.

6 References

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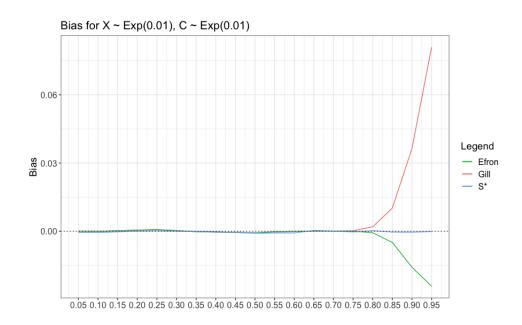
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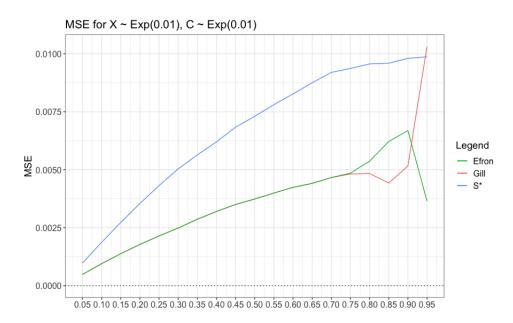
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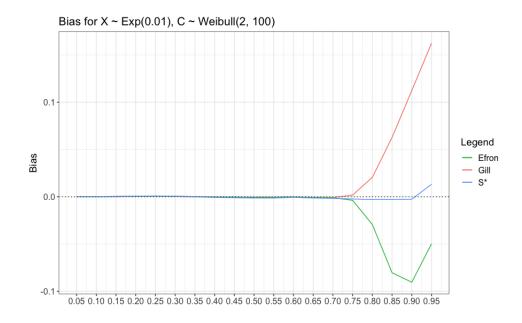
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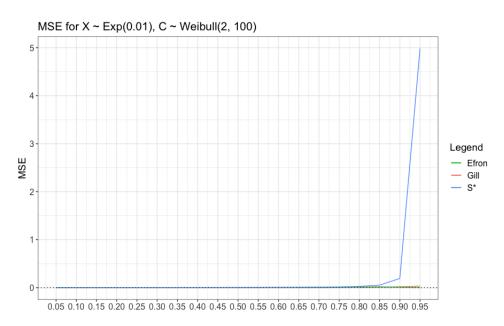
7 Appendix

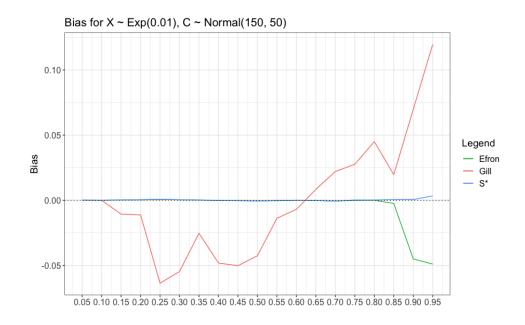
7.1 Part (i) Bias and MSE plots

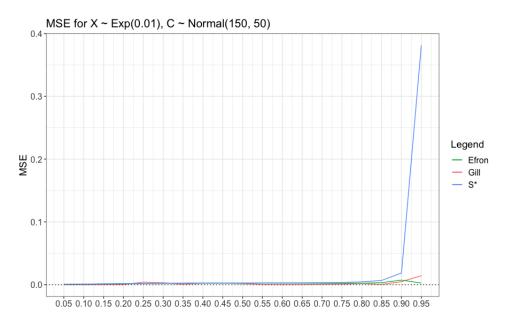


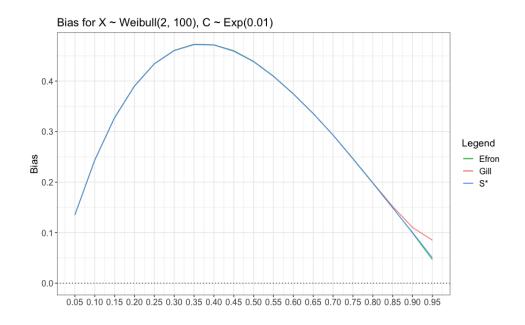


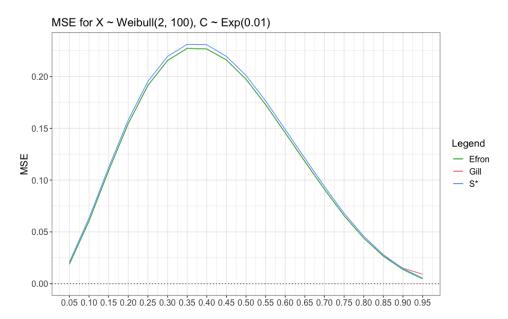


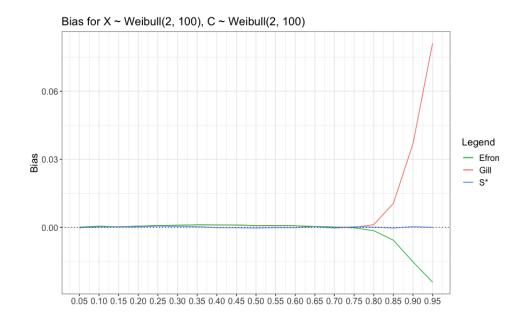




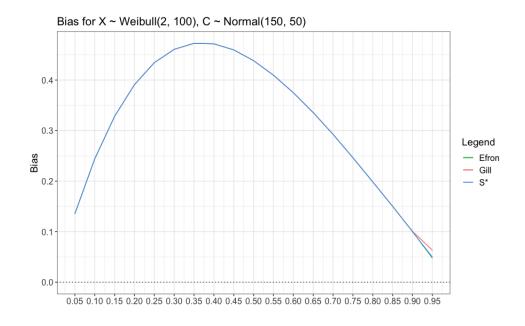


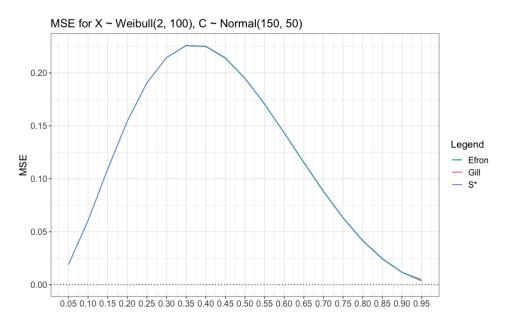


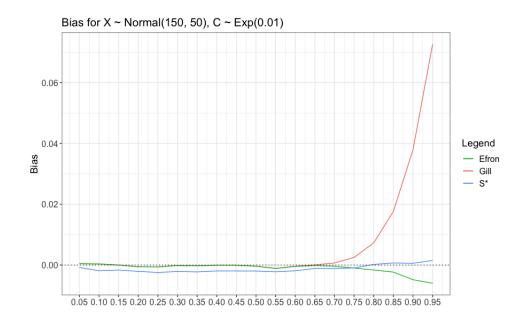


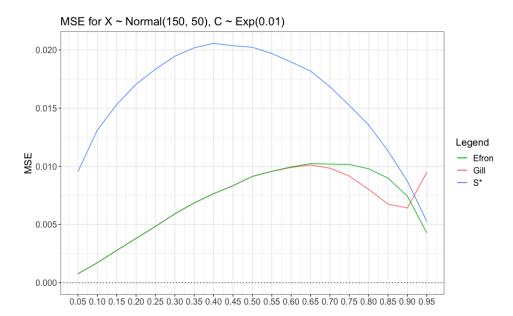


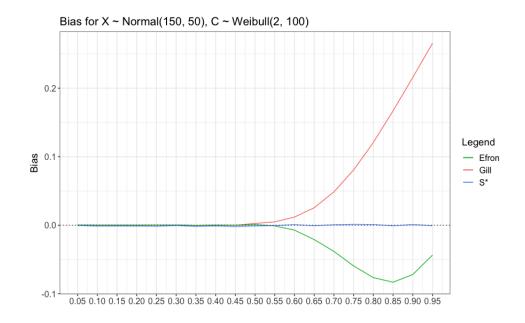


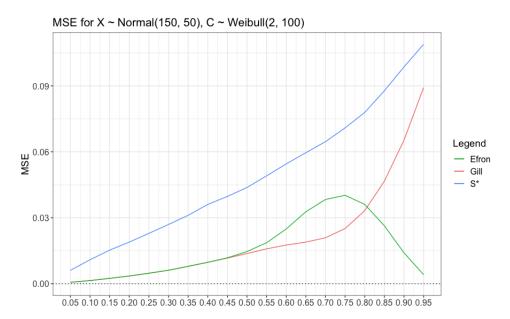


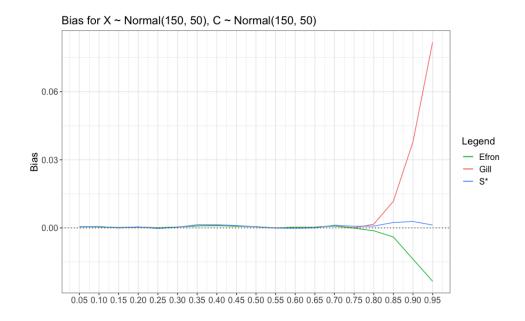


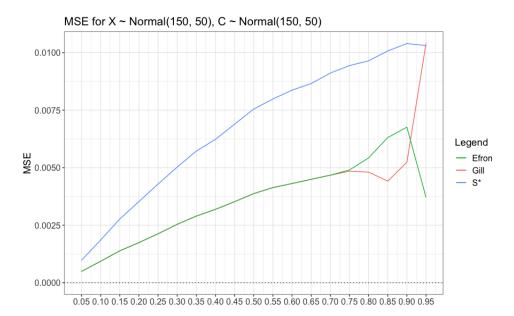




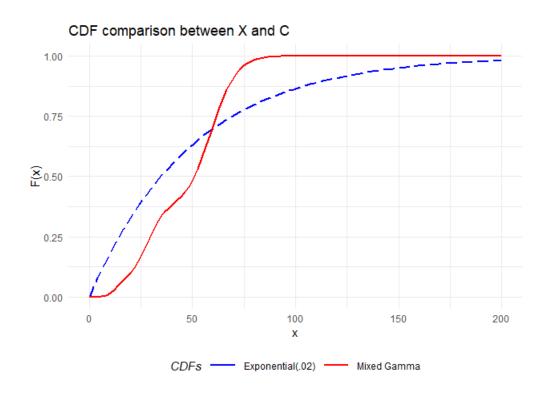


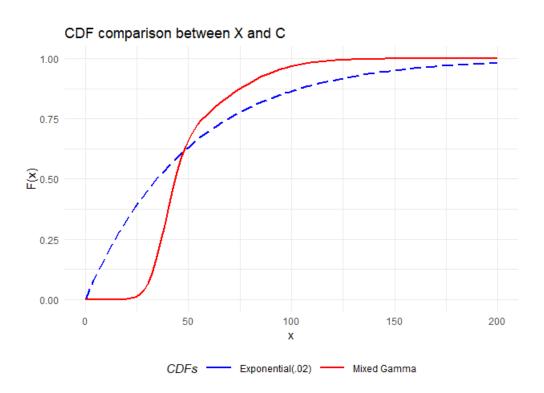


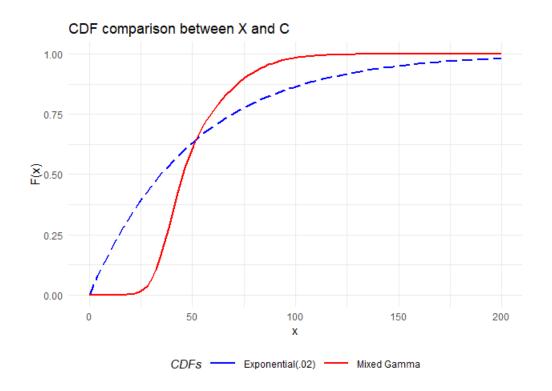


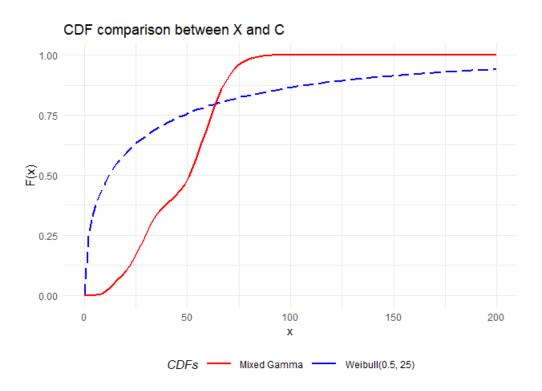


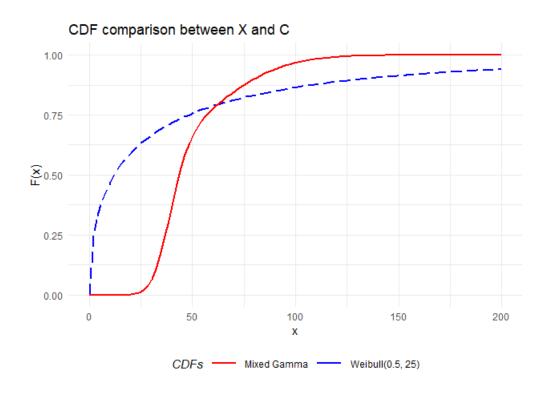
7.2 Part (ii) cdf plots

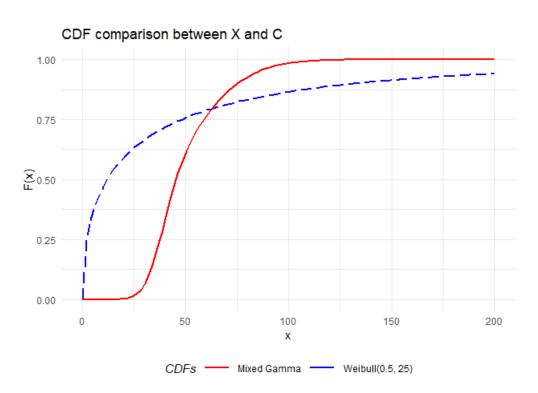


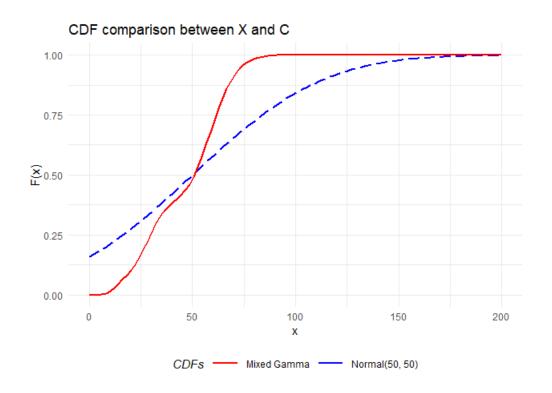


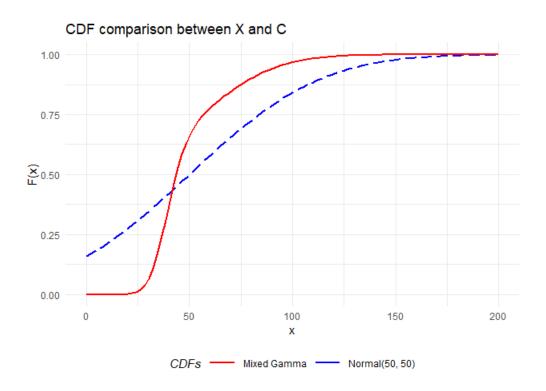


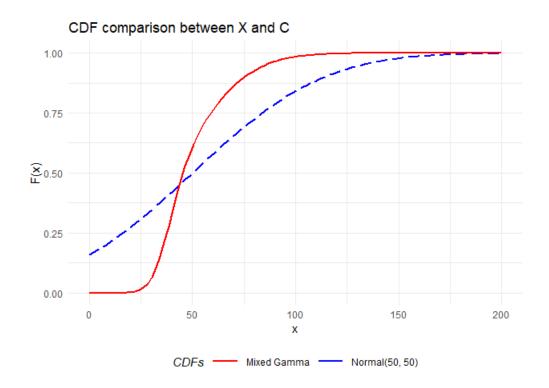












7.3 Part (ii) Bias and MSE plots

