

# Survival extrapolation - Supplementary Appendix

NCPE

October 2024

## Expert opinion and construction of a prior distribution

Published NICE committee slides, see slide 24 of <https://www.nice.org.uk/guidance/ta650/documents/1>, provides a summary of clinical experts' opinion on 5-year OS:

- Company: 50%
- ERG: 50% is optimistic
- NICE technical team: 30%

For the NCPE assessment (data on file), experts were presented with OS predictions from the six standard parametric distributions and asked to comment on their plausibility:

- Expert 1 stated that the curves giving estimates of 20% and 39% were plausible, said nothing about model 3 (45%), and considered all higher estimates of 5-year OS to be implausible.
- Expert 2 identified the curve giving a 5-year OS of 45% as the most appropriate, with other 'plausible' curves giving a range of 20% to 54%.

The authors considered a range of 20% to 55% to give a reasonable summary of experts' expectations of 5-year overall survival. For simplicity, a normal distribution was selected for the prior, with 95% prior density contained in the range 20% to 55%.

## Importance sampling: model diagnostics, parameter distributions, and survival estimates

We can now examine importance sampling diagnostics, comparisons of likelihood and posterior parameter distributions, and survival time distributions, using the function `expert_surv_viz_gg`.

Table 1: MLE Parameter Estimates

x
-4.562874

Table 2: MLE Covariance Matrix

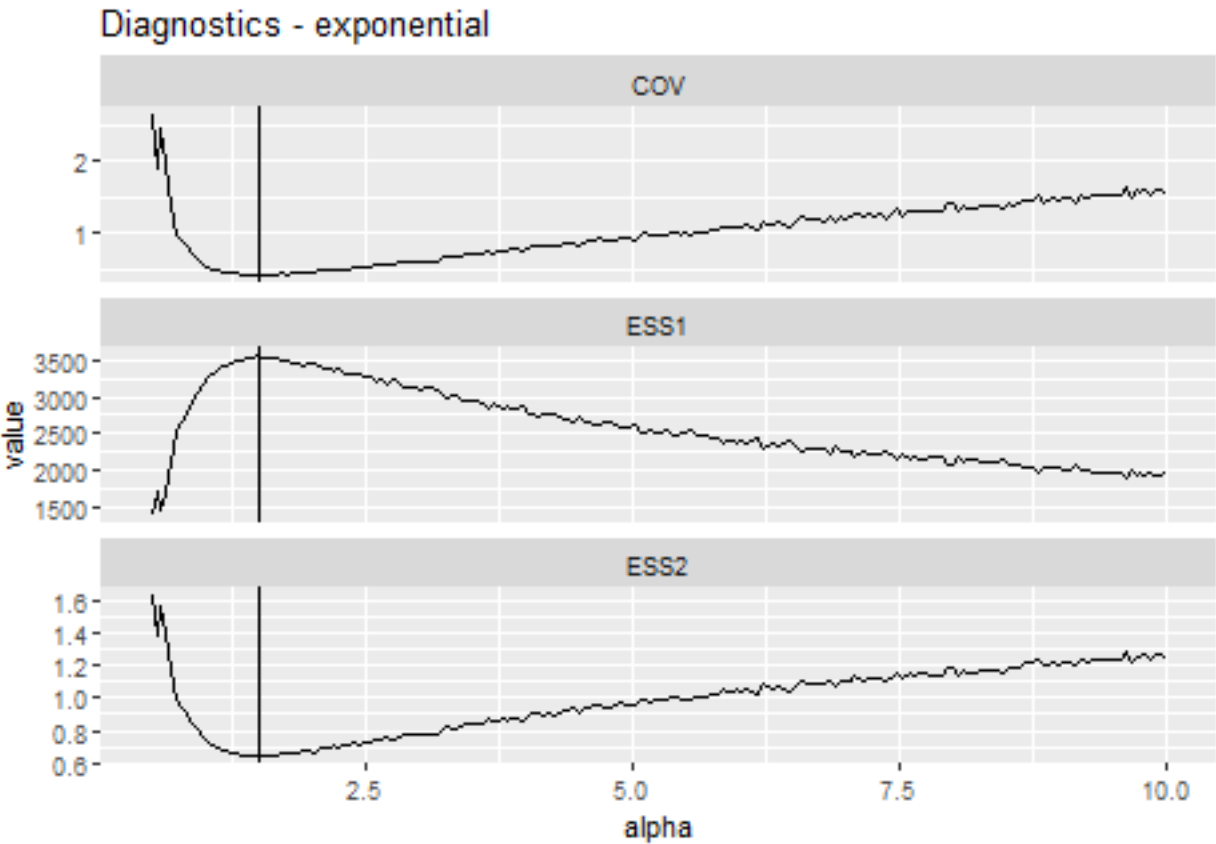
rate	rate
rate	0.0169491

Table 3: IS Parameter Estimates

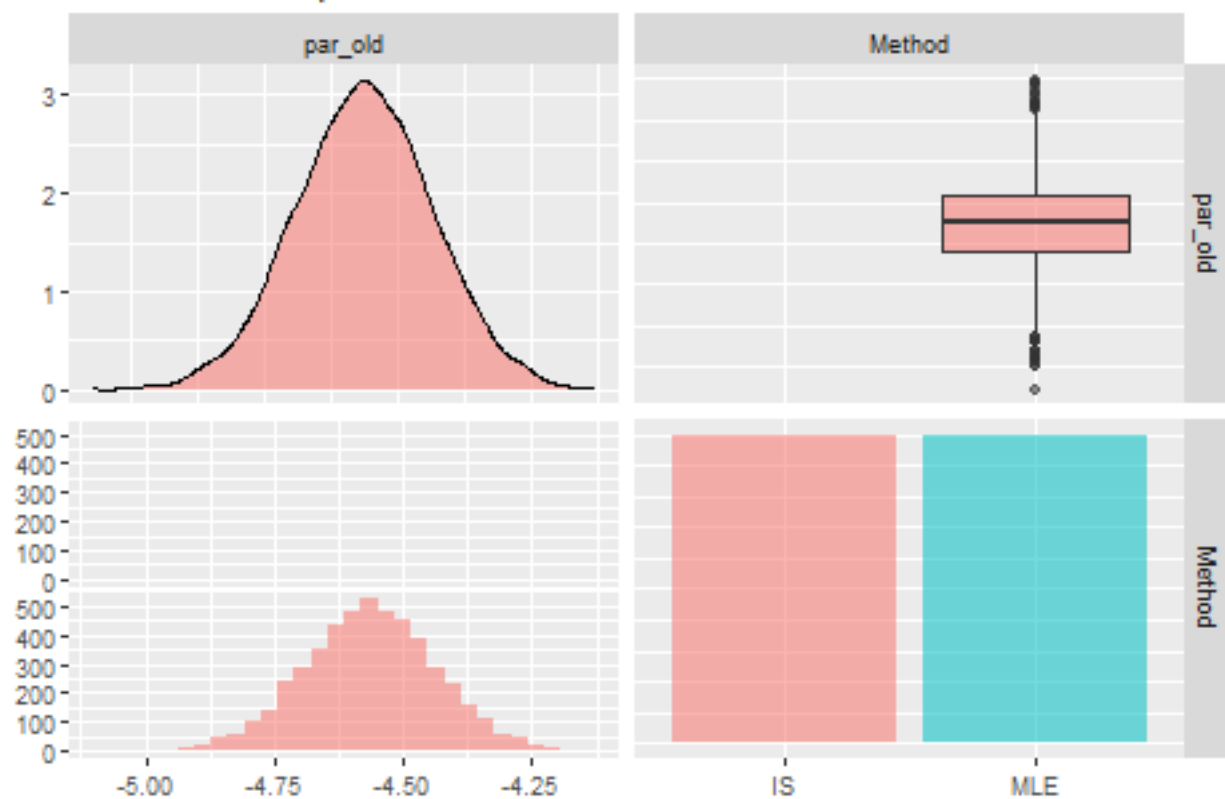
$x$
-4.467088

Table 4: IS Covariance Matrix

0.0138444
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### Parameters - exponential



### Survival - exponential

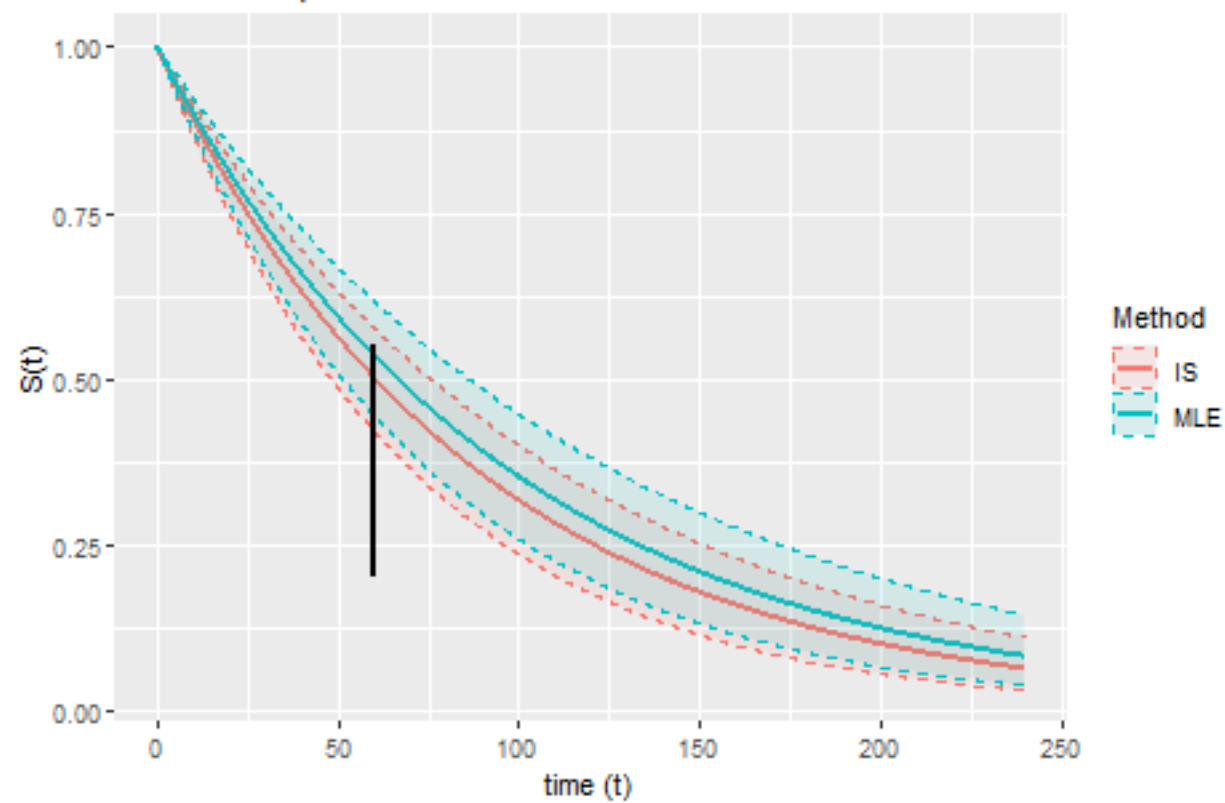


Table 5: MLE Parameter Estimates

	x
shape	0.2028128
scale	4.2127617

Table 6: MLE Covariance Matrix

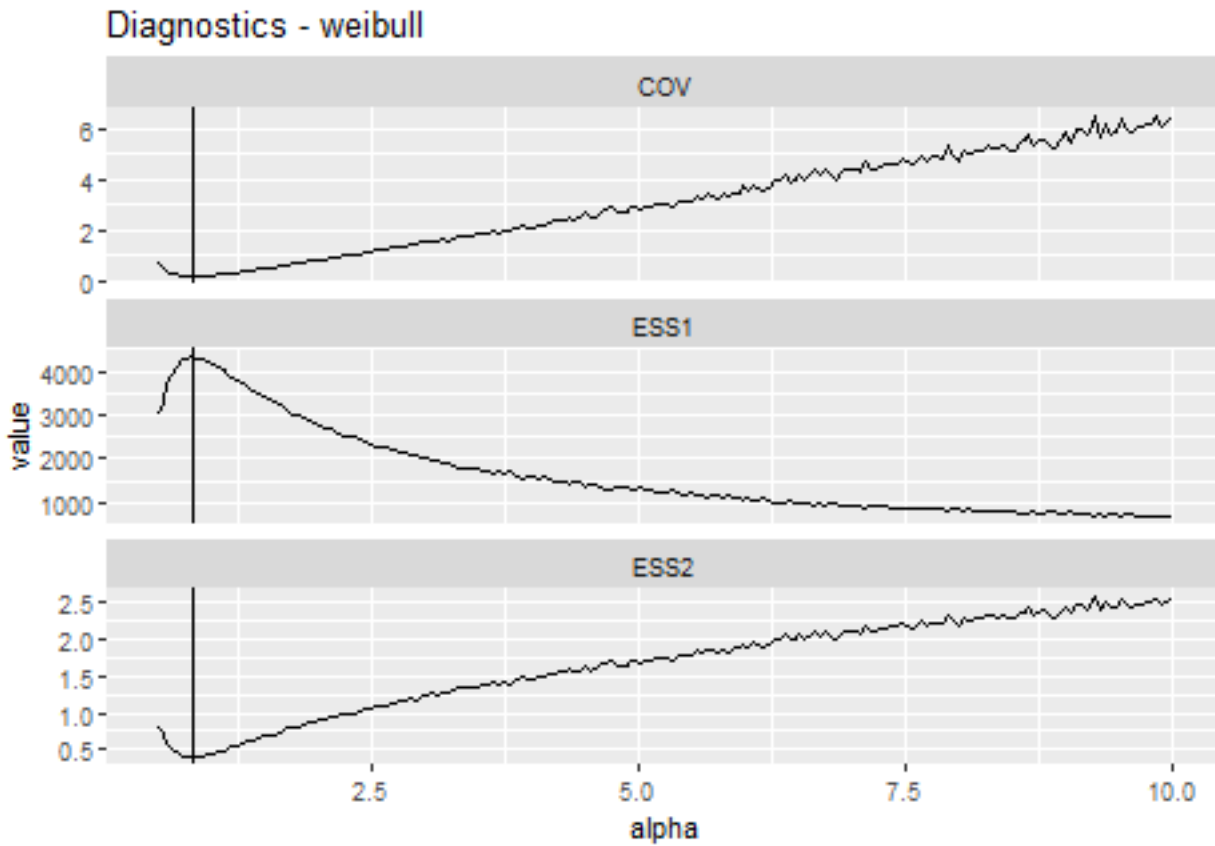
	shape	scale
shape	0.0147844	-0.0228526
scale	-0.0228526	0.0466213

Table 7: IS Parameter Estimates

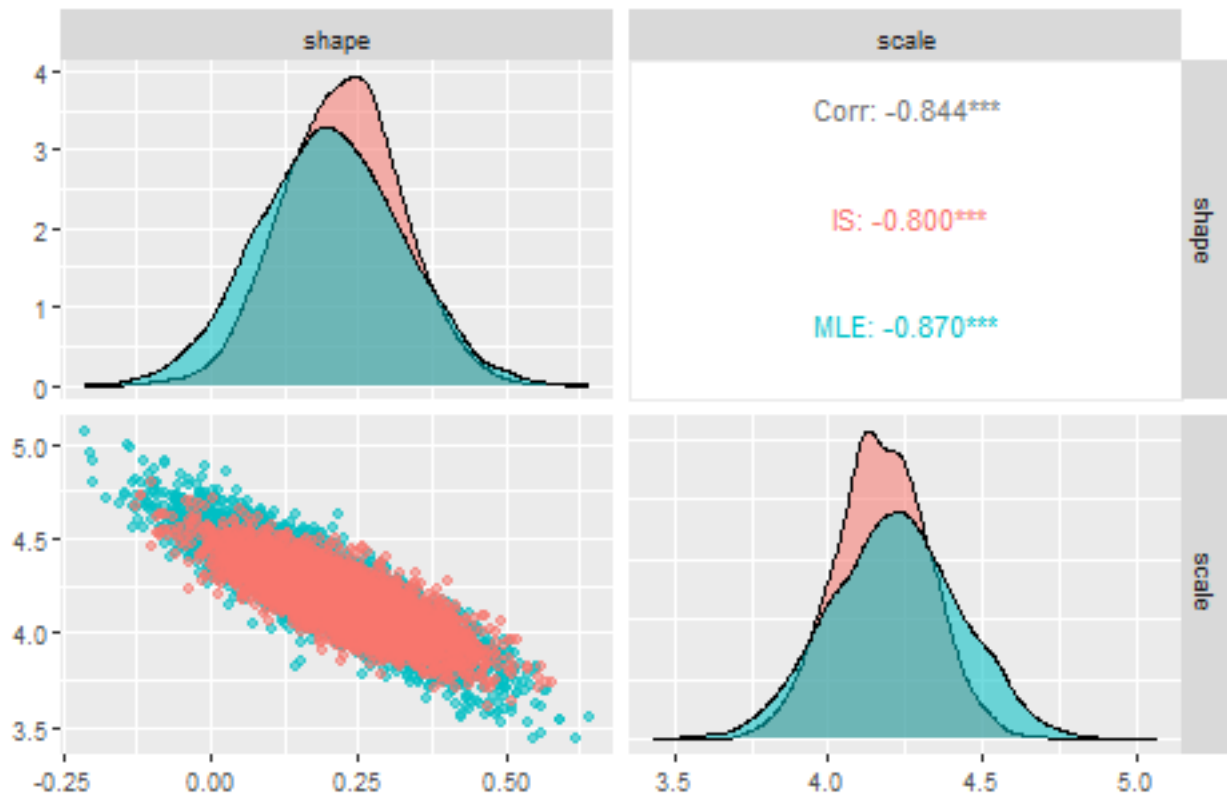
	x
shape	0.2199019
scale	4.1750757

Table 8: IS Covariance Matrix

	shape	scale
shape	0.0094518	-0.0118402
scale	-0.0118402	0.0235769



### Parameters - weibull



### Survival - weibull

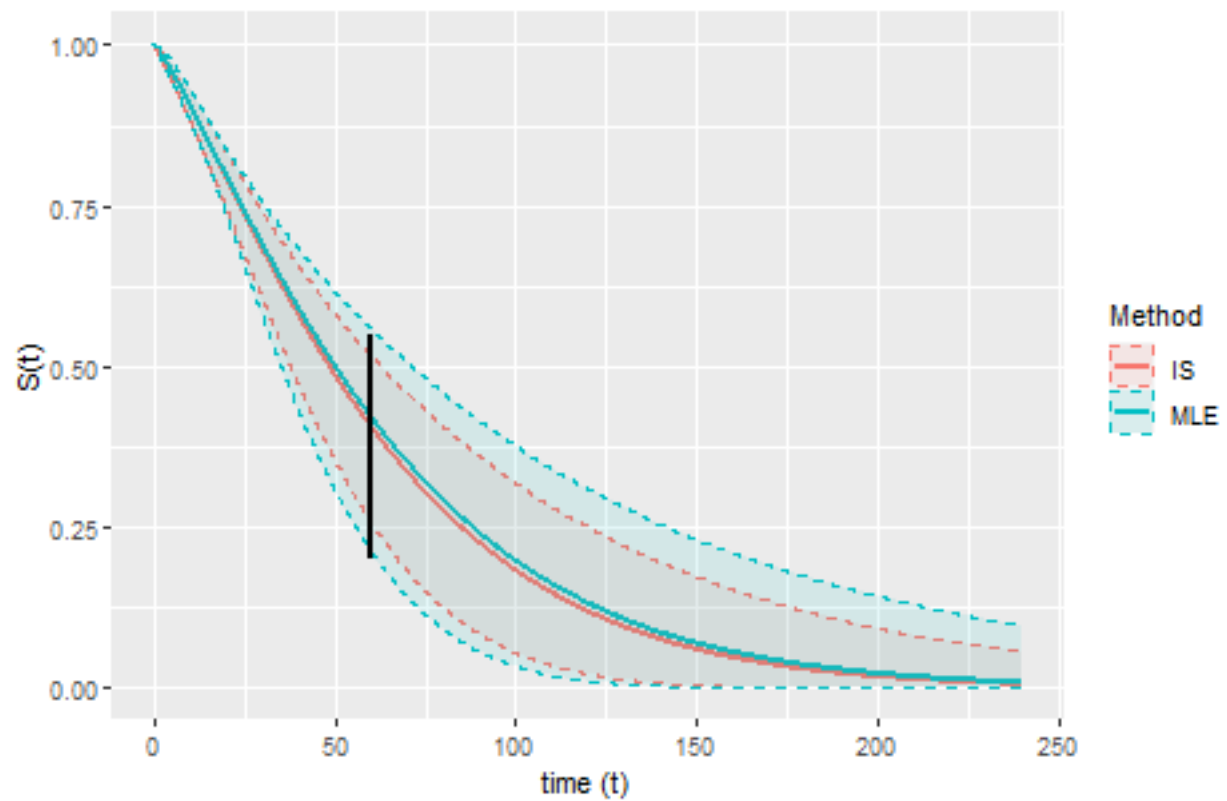


Table 9: MLE Parameter Estimates

	x
shape	0.0389625
rate	-4.8682858

Table 10: MLE Covariance Matrix

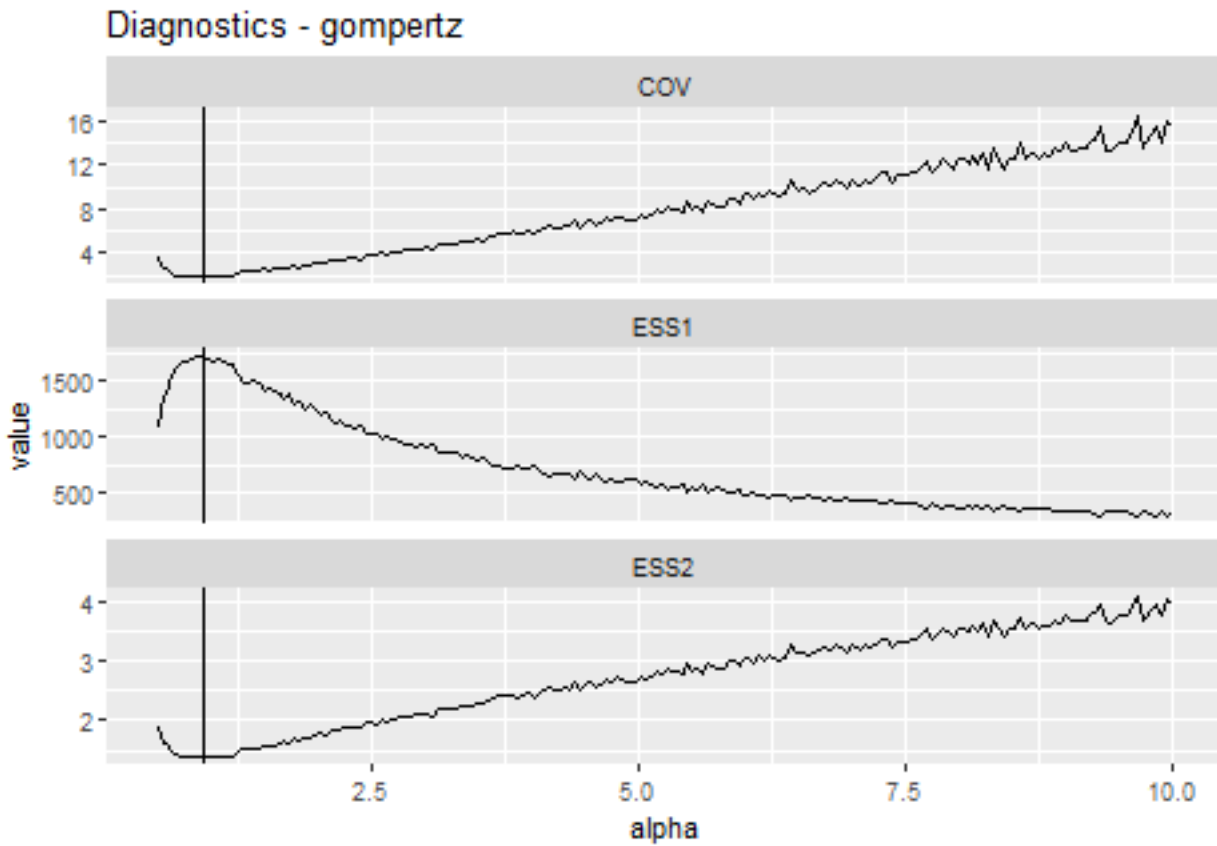
	shape	rate
shape	0.0006747	-0.0056125
rate	-0.0056125	0.0636359

Table 11: IS Parameter Estimates

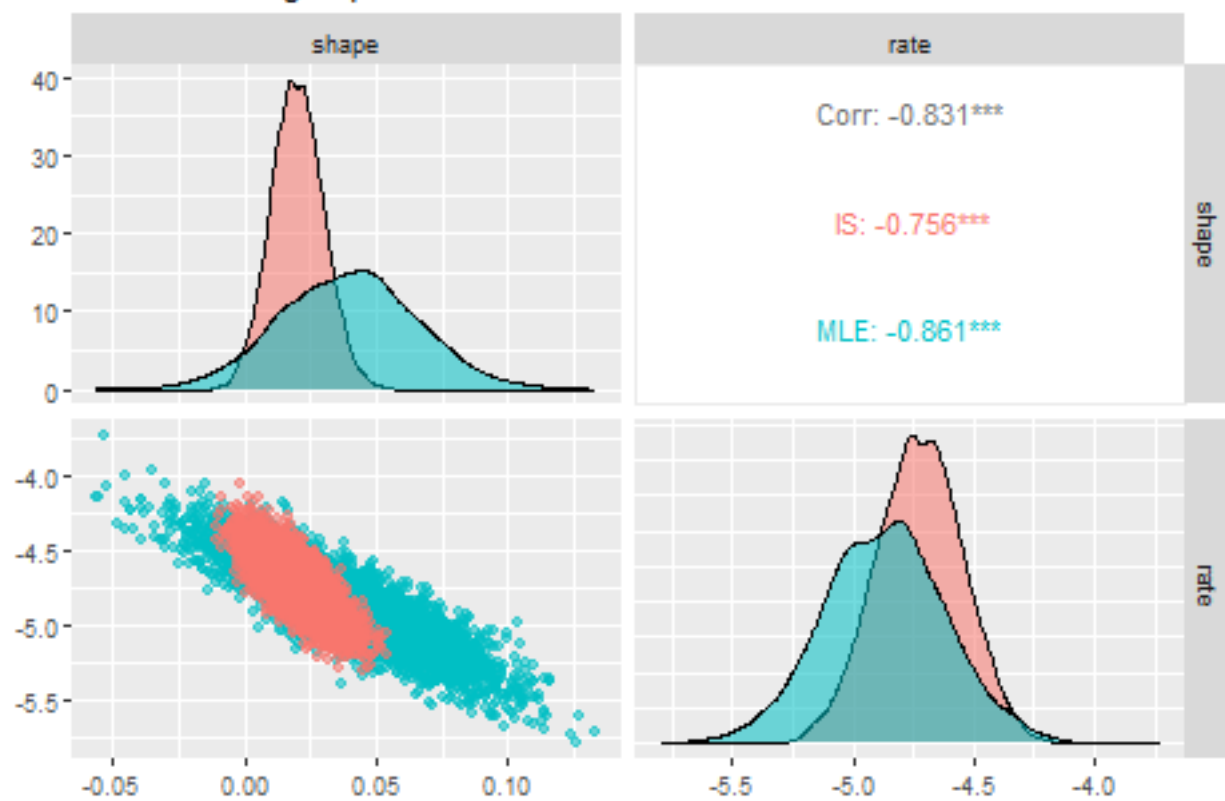
	x
shape	0.0197027
rate	-4.7220927

Table 12: IS Covariance Matrix

	shape	rate
shape	0.0000970	-0.0013281
rate	-0.0013281	0.0316264



## Parameters - gompertz



## Survival - gompertz

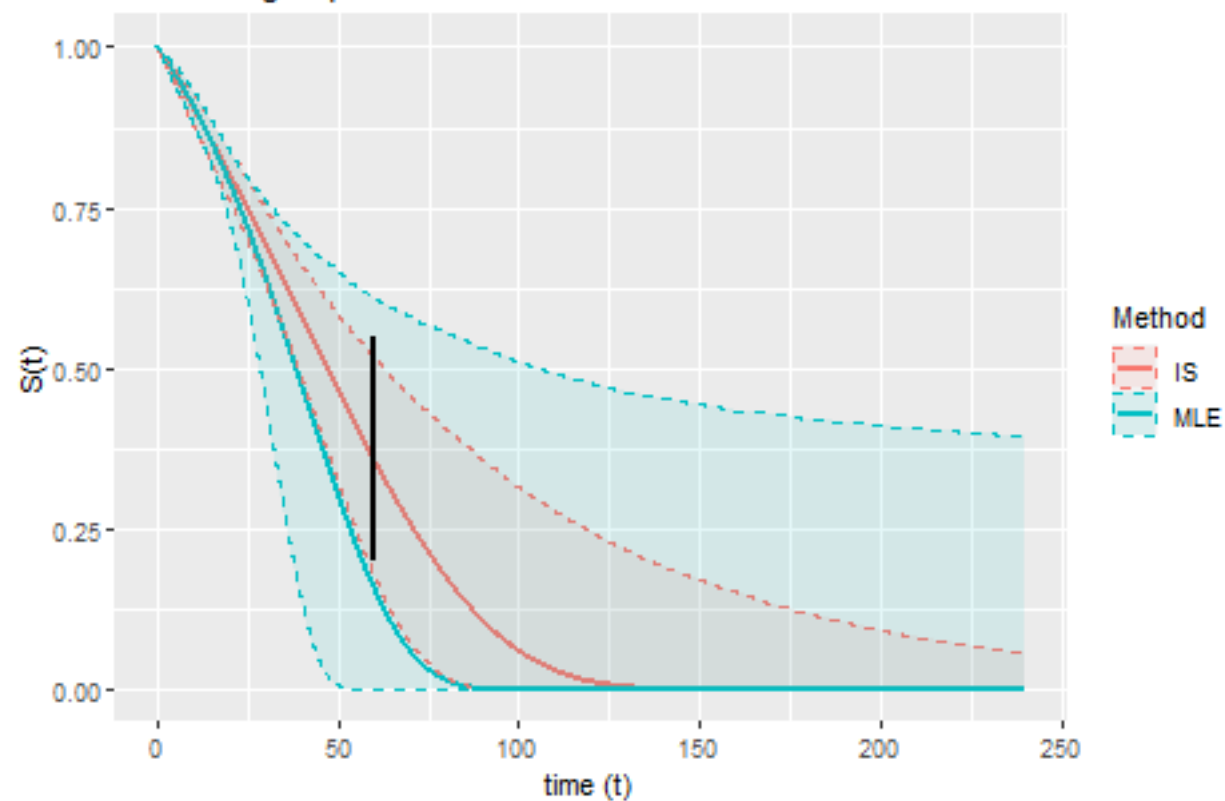


Table 13: MLE Parameter Estimates

	x
meanlog	4.5379239
sdlog	0.5475716

Table 14: MLE Covariance Matrix

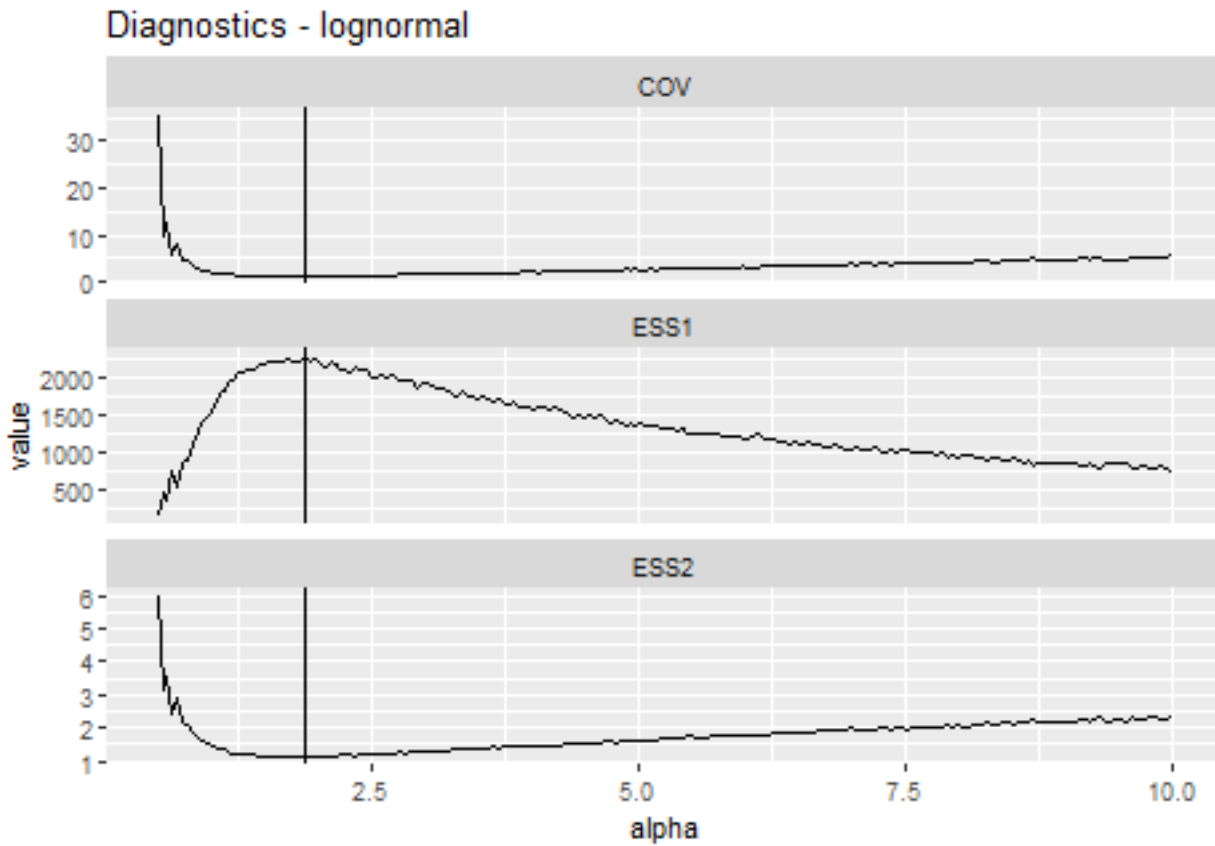
	meanlog	sdlog
meanlog	0.0696811	0.0247171
sdlog	0.0247171	0.0114622

Table 15: IS Parameter Estimates

	x
meanlog	4.2299230
sdlog	0.4404943

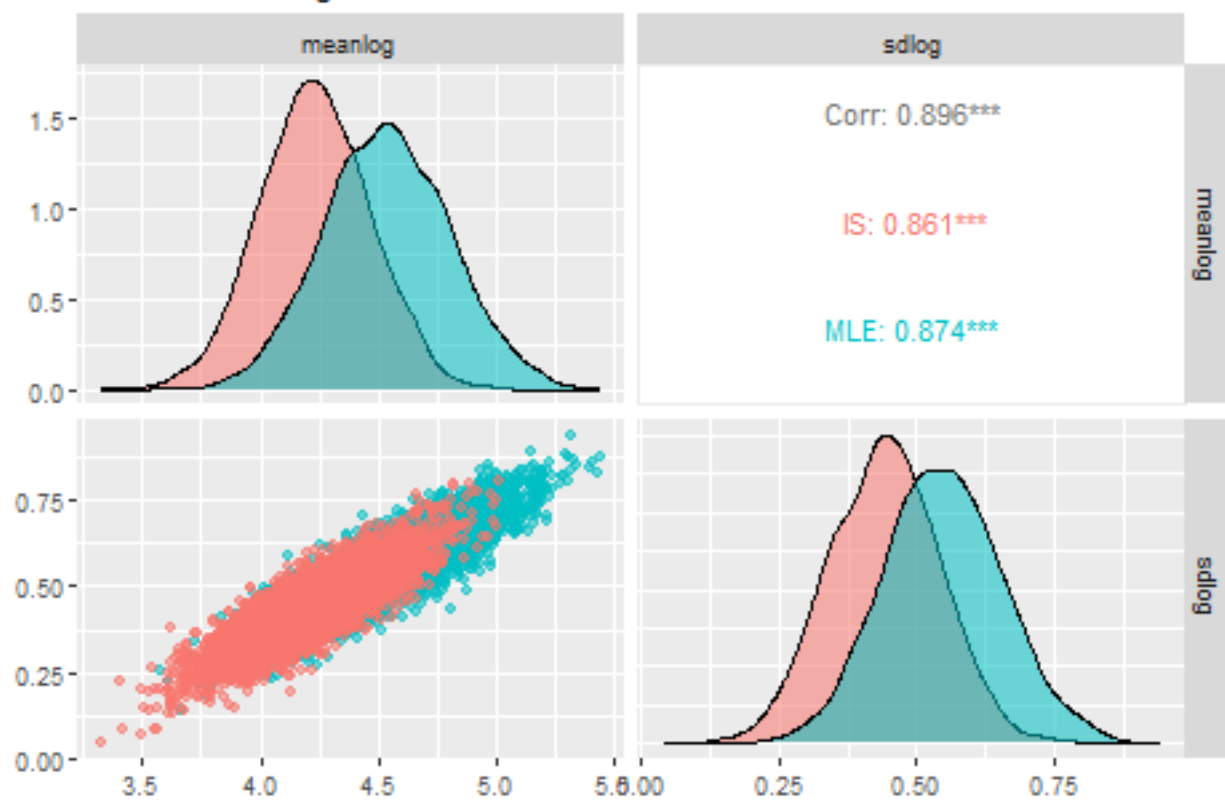
Table 16: IS Covariance Matrix

	meanlog	sdlog
meanlog	0.0545435	0.0201378
sdlog	0.0201378	0.0100655





## Parameters - lognormal



## Survival - lognormal

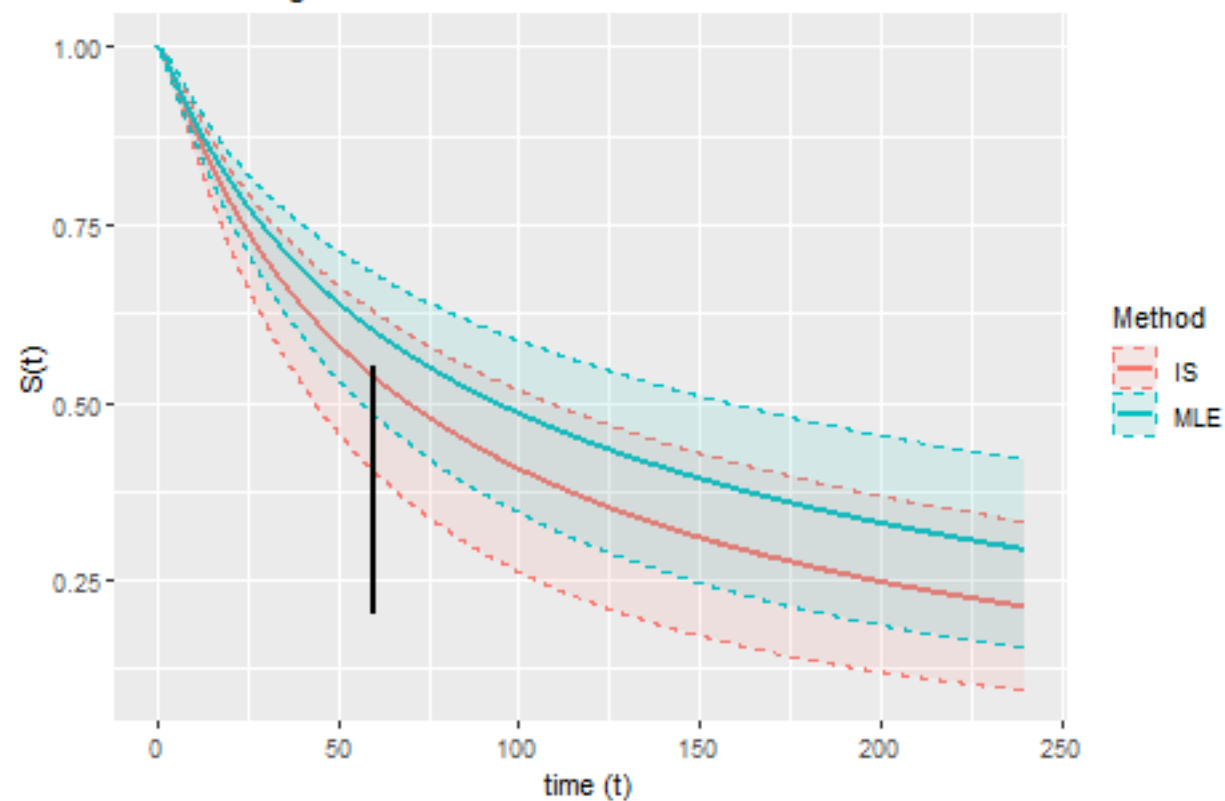


Table 17: MLE Parameter Estimates

	x
shape	0.2450539
scale	4.0866467

Table 18: MLE Covariance Matrix

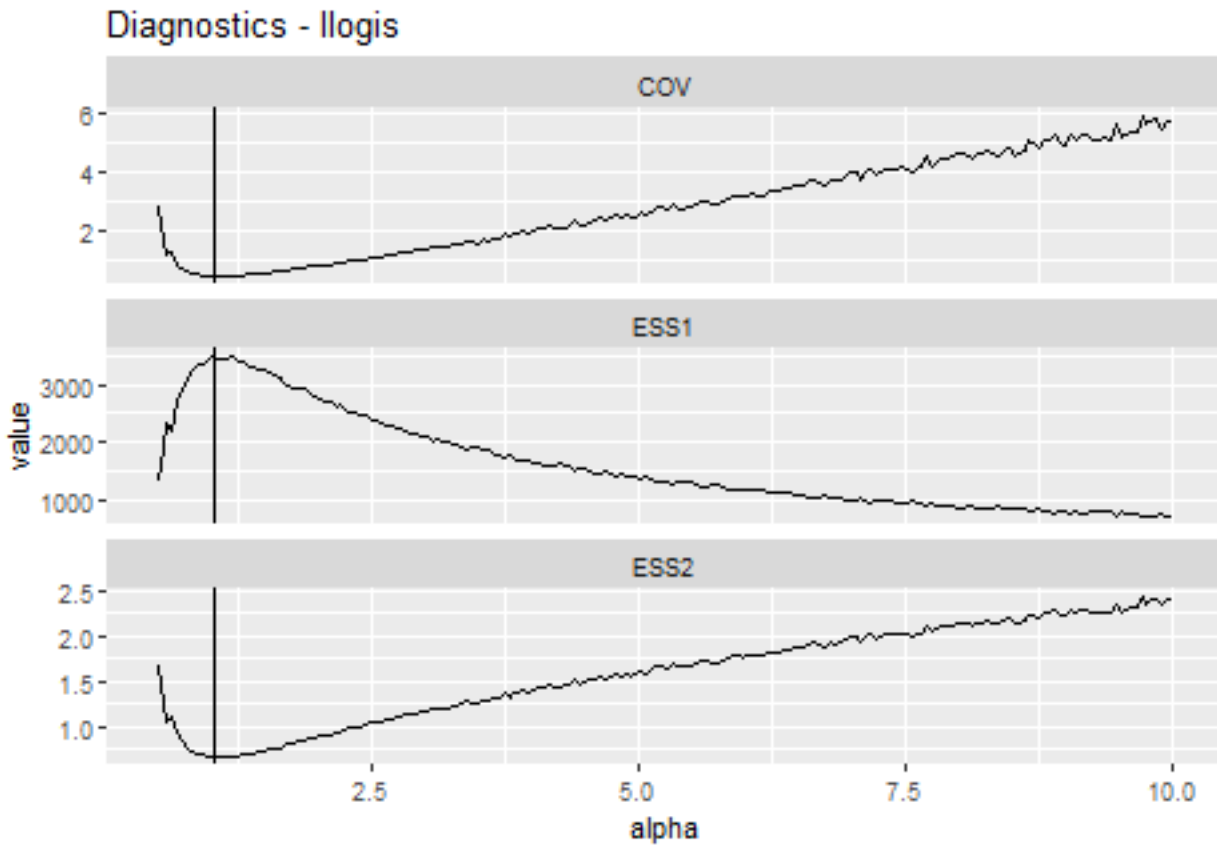
	shape	scale
shape	0.0144928	-0.0213001
scale	-0.0213001	0.0434079

Table 19: IS Parameter Estimates

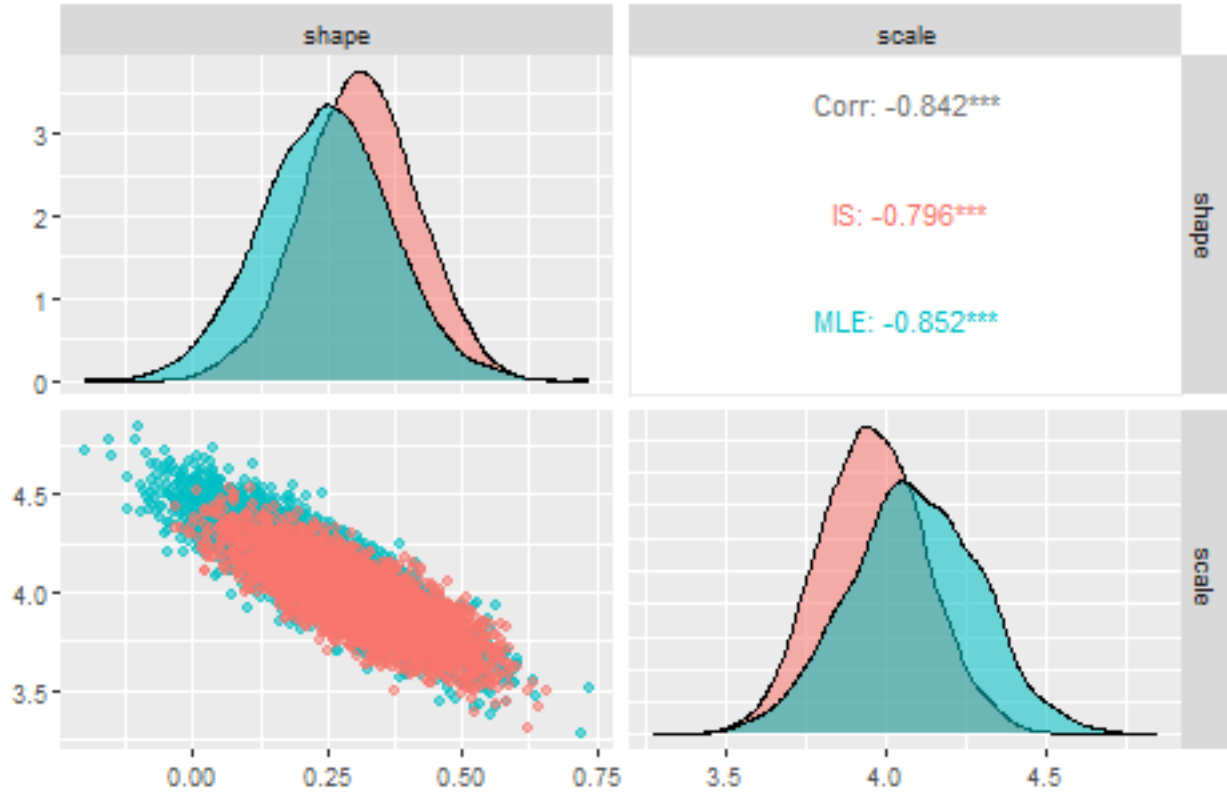
	x
shape	0.3103417
scale	3.9558382

Table 20: IS Covariance Matrix

	shape	scale
shape	0.0111243	-0.0139385
scale	-0.0139385	0.0276608



### Parameters - llogis



### Survival - llogis

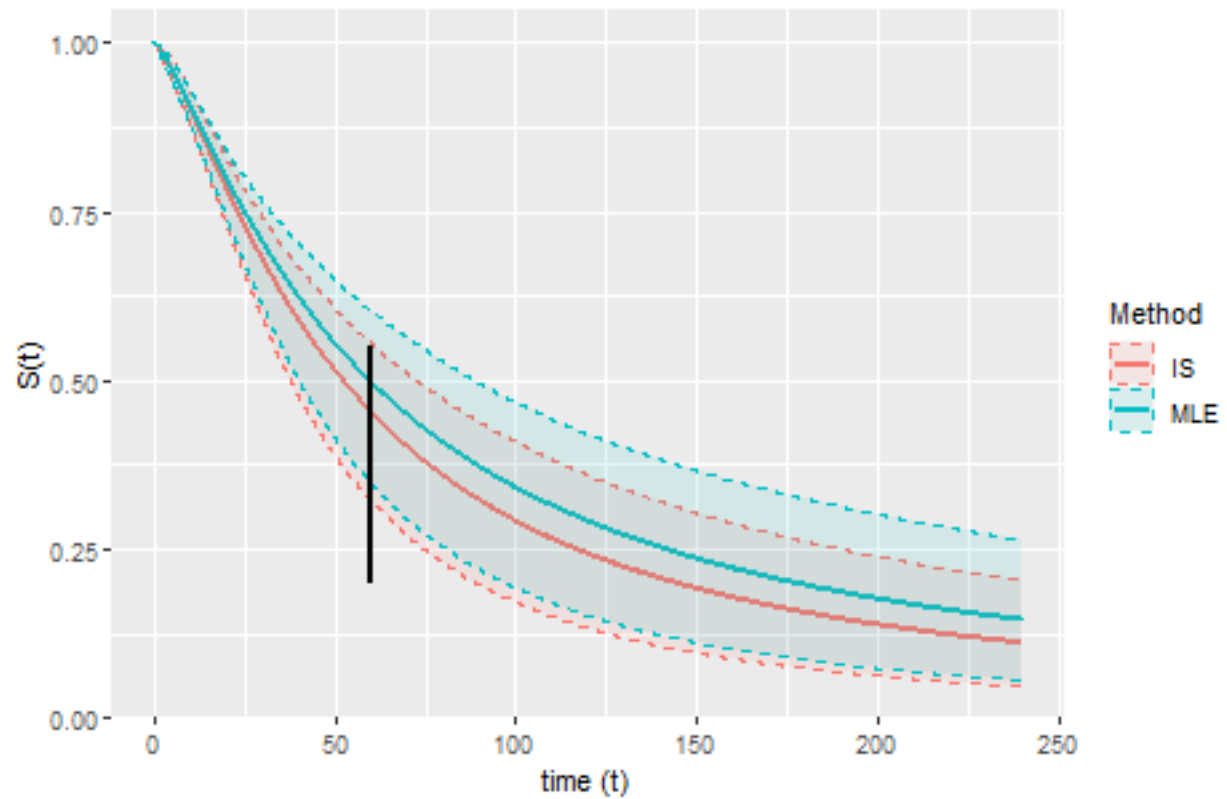


Table 21: MLE Parameter Estimates

	x
mu	4.1703317
sigma	-0.3599072
Q	1.2031485

Table 22: MLE Covariance Matrix

	mu	sigma	Q
mu	0.1026807	0.2899736	-0.3589428
sigma	0.2899736	1.2303463	-1.6290913
Q	-0.3589428	-1.6290913	2.1837103

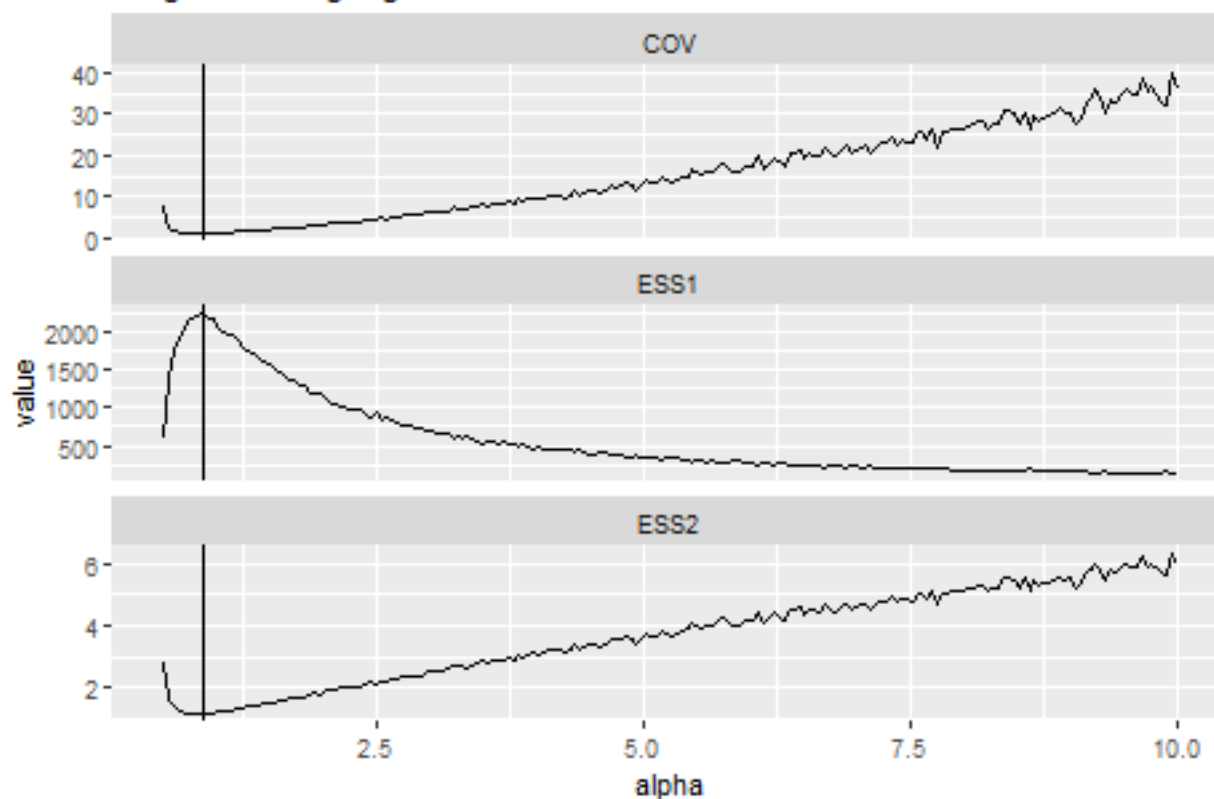
Table 23: IS Parameter Estimates

	x
mu	4.1857610
sigma	-0.3818327
Q	1.2508022

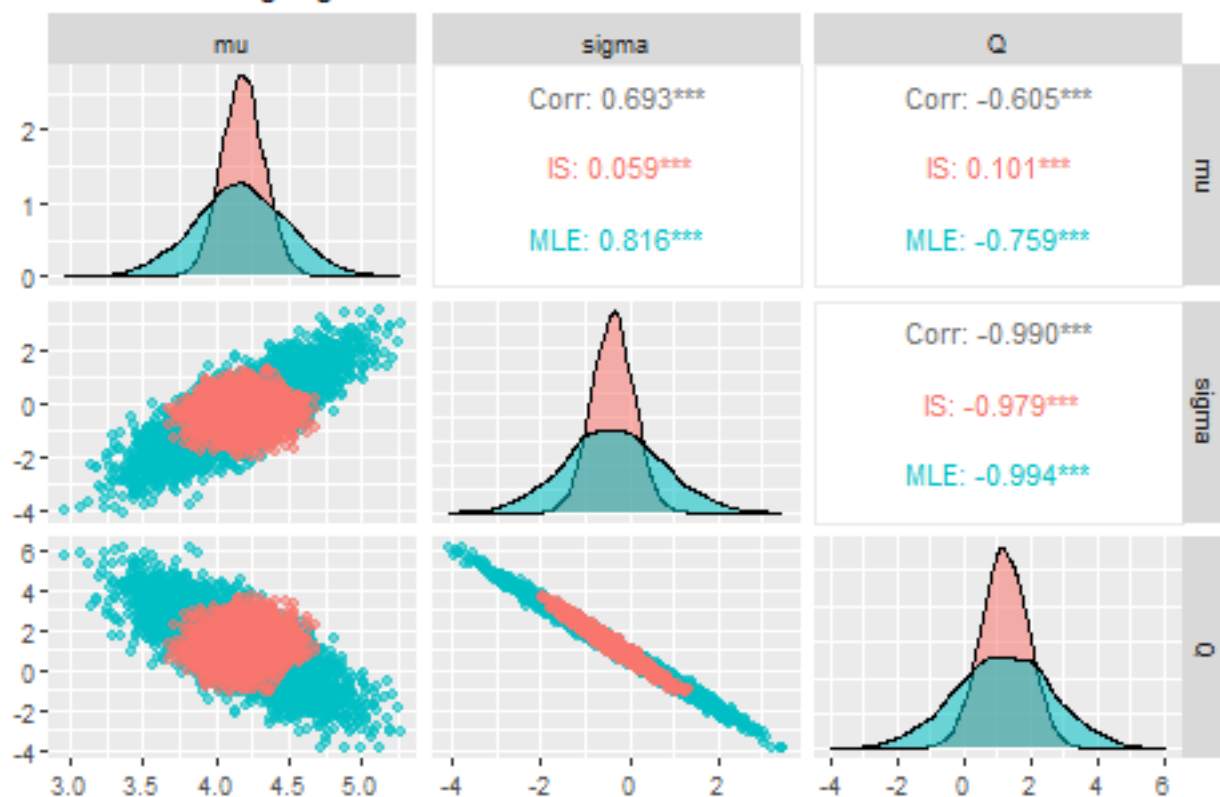
Table 24: IS Covariance Matrix

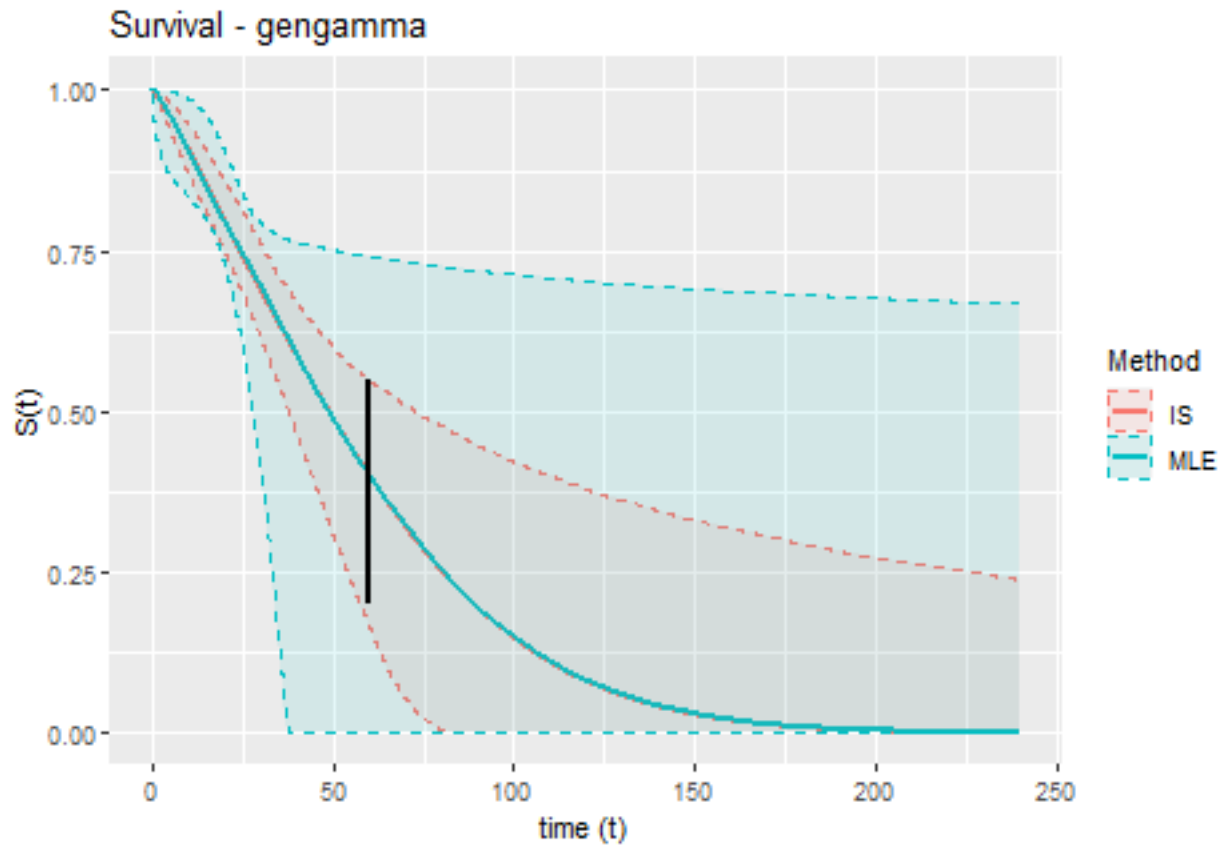
	mu	sigma	Q
mu	0.0219135	0.0031467	0.0125013
sigma	0.0031467	0.2238160	-0.3291366
Q	0.0125013	-0.3291366	0.5057176

## Diagnostics - gengamma



## Parameters - gengamma





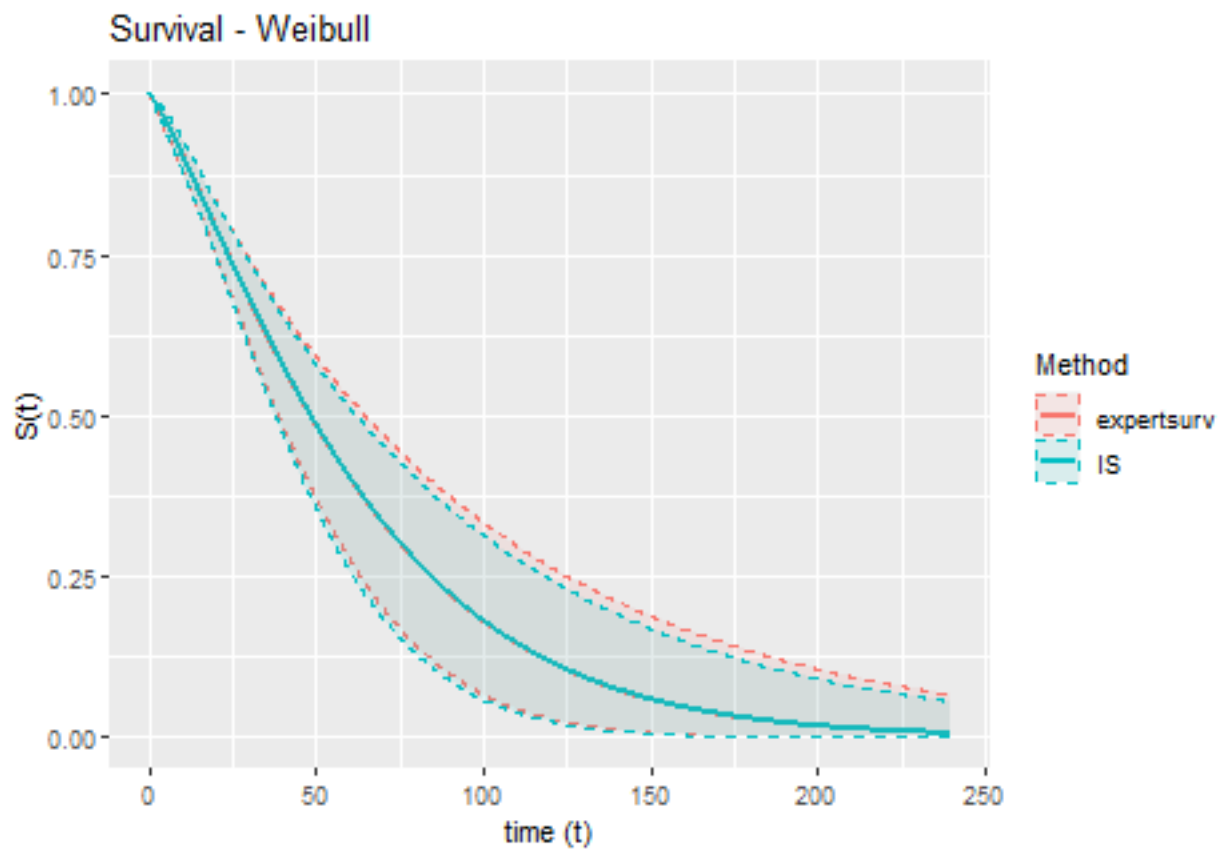
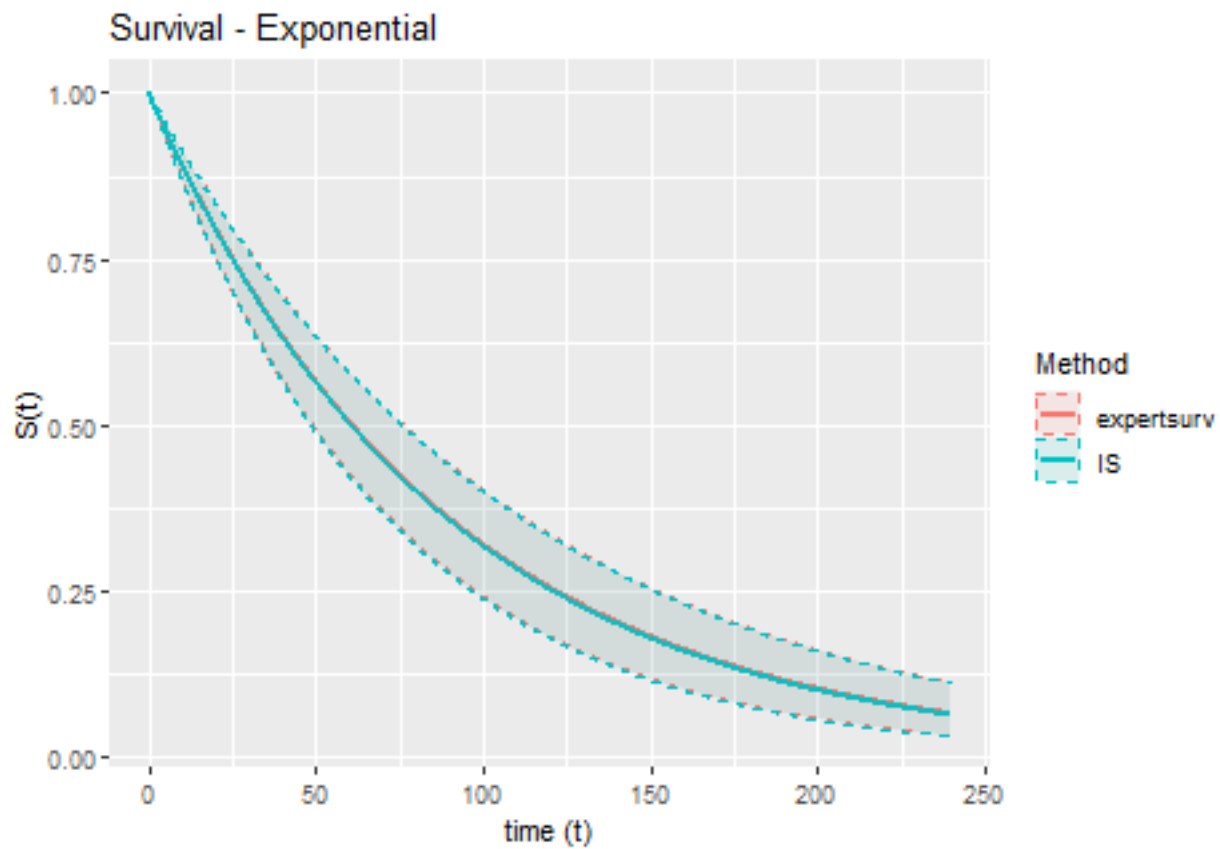
## Parameter variability

Compare ‘Generalised variance,’ i.e., determinants of variance-covariance matrices. This gives the area of the 95% highest density ellipse and can be interpreted as a 1-parameter measure of parameter uncertainty. See <https://stats.stackexchange.com/questions/12762/measure-of-spread-of-a-multivariate-normal-distribution> .

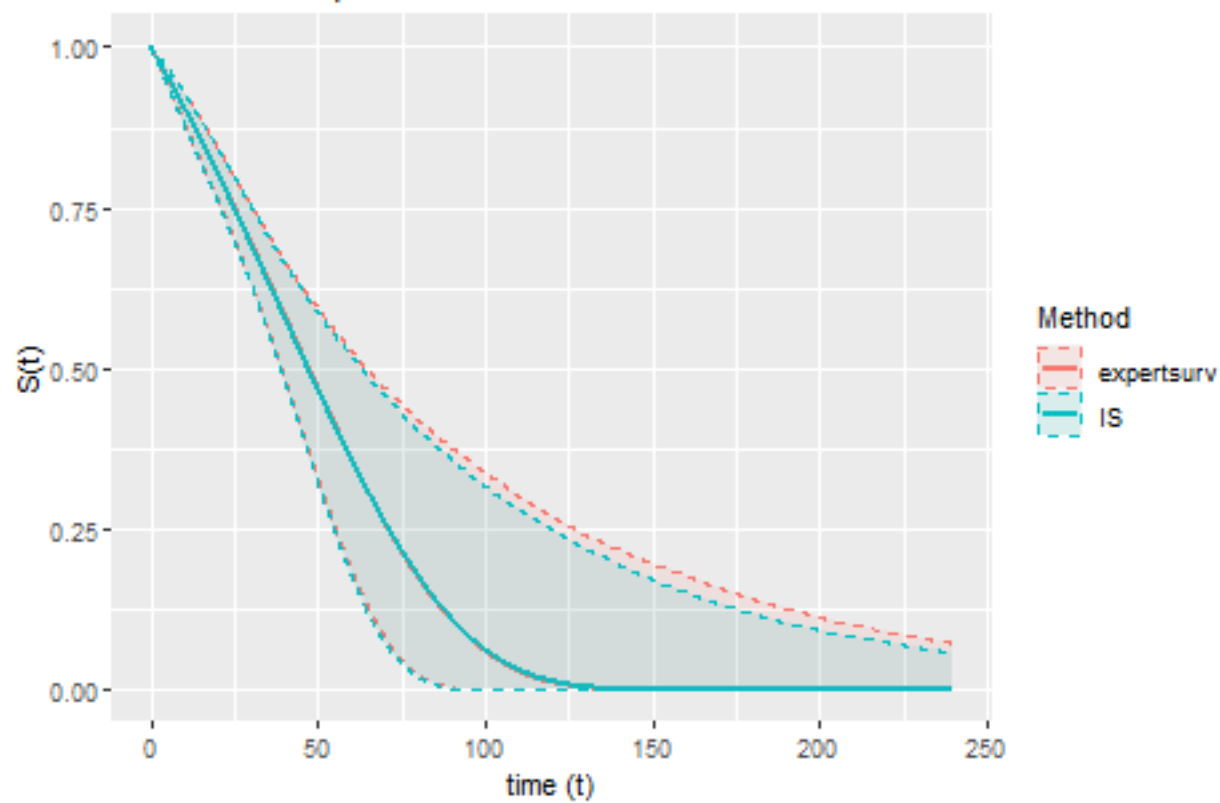
Distribution	Distance	MLE.Variance	IS.Variance	Ratio
exponential	0.0957855	0.0169491	0.0138444	0.8168193
weibull	0.0413796	0.0001670	0.0000827	0.4948566
gompertz	0.1474564	0.0000114	0.0000013	0.1140791
lognormal	0.3260830	0.0001878	0.0001435	0.7641277
llogis	0.1461963	0.0001754	0.0001134	0.6466355
gengamma	0.0546778	0.0003562	0.0000405	0.1138456

## Comparison with expertsurv output

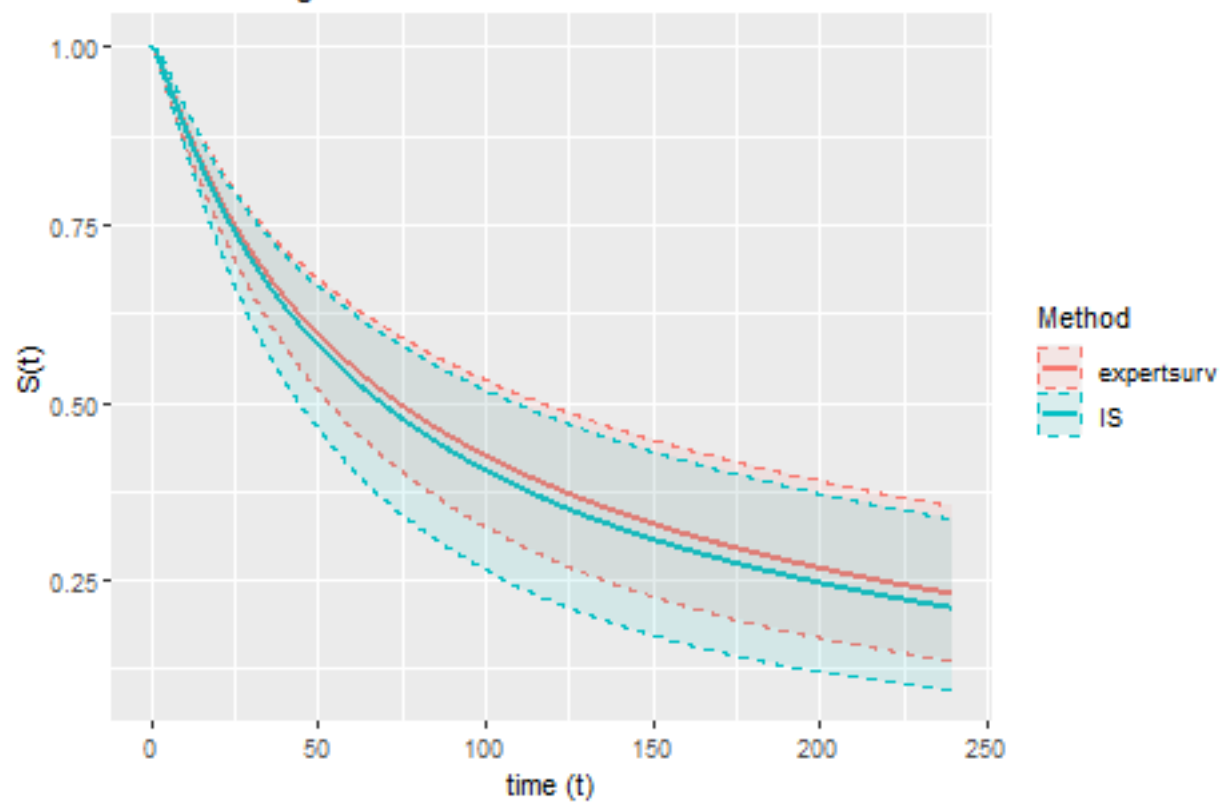
Plots of survival curves over time



Survival - Gompertz

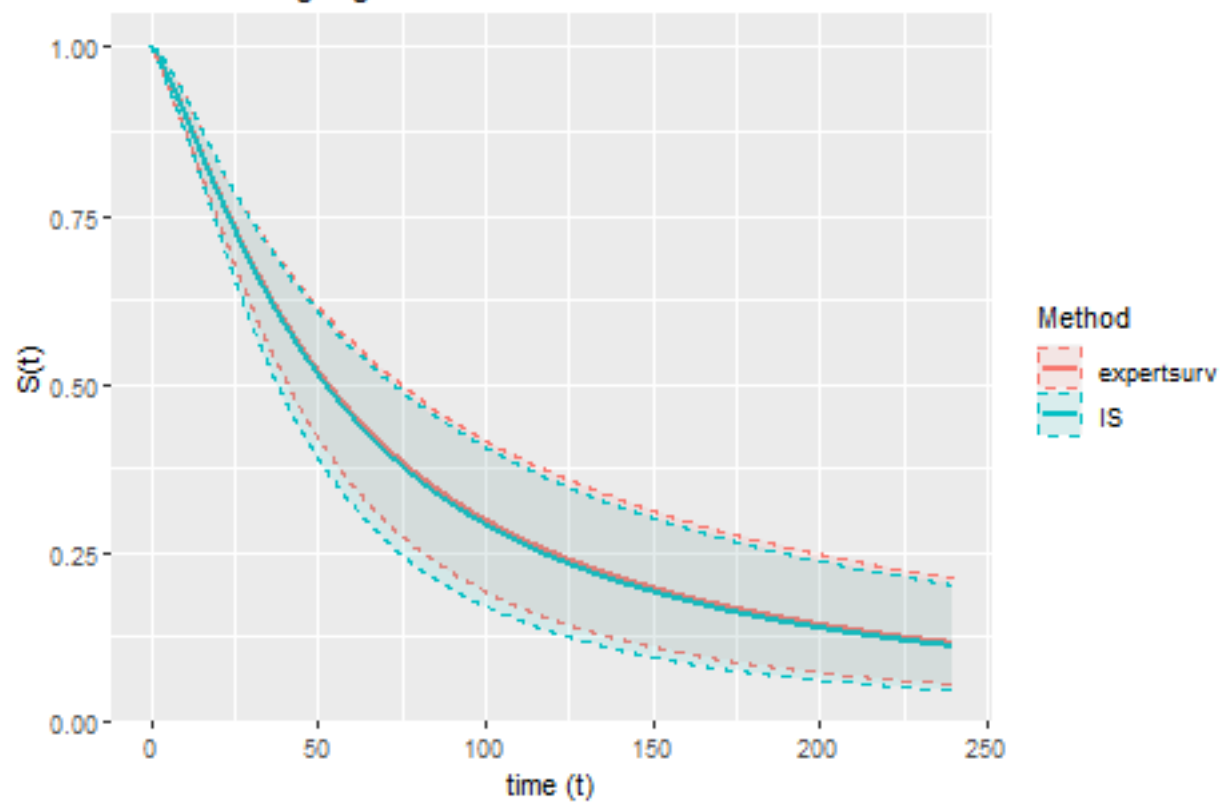


Survival - Log-normal

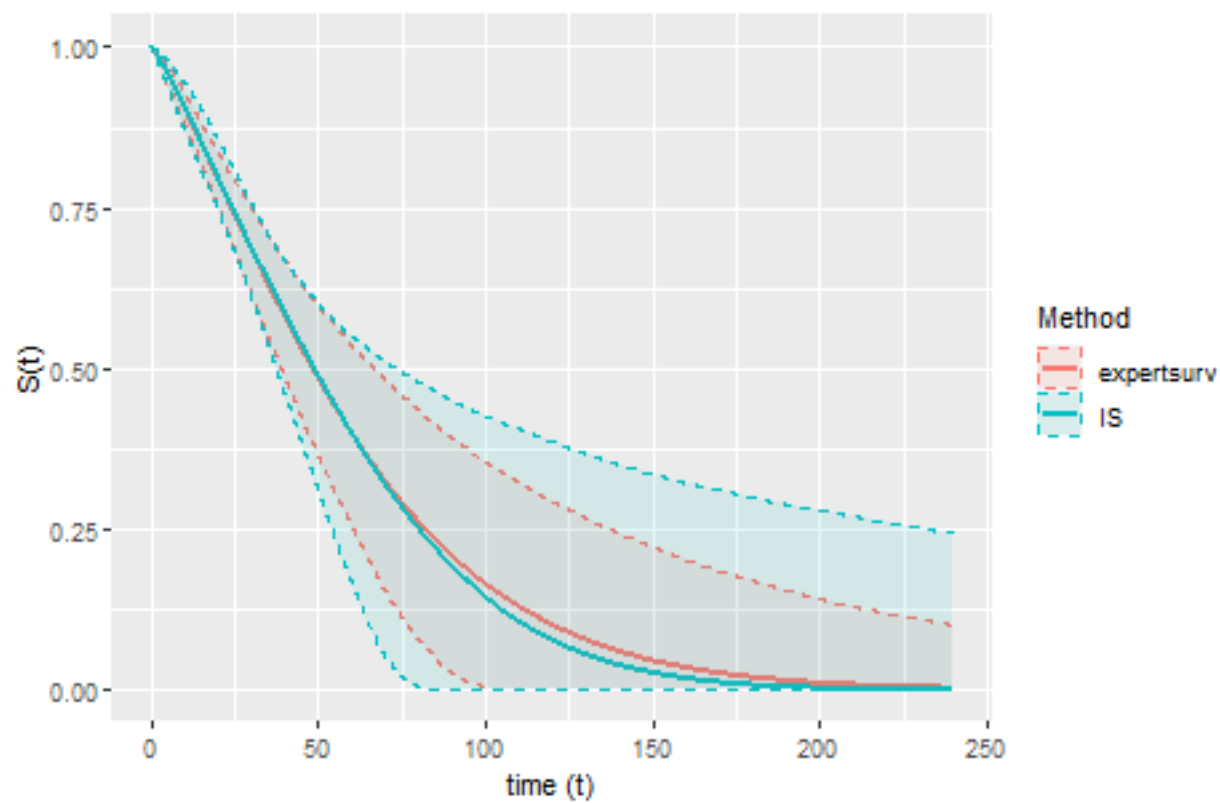




Survival - Log-logistic

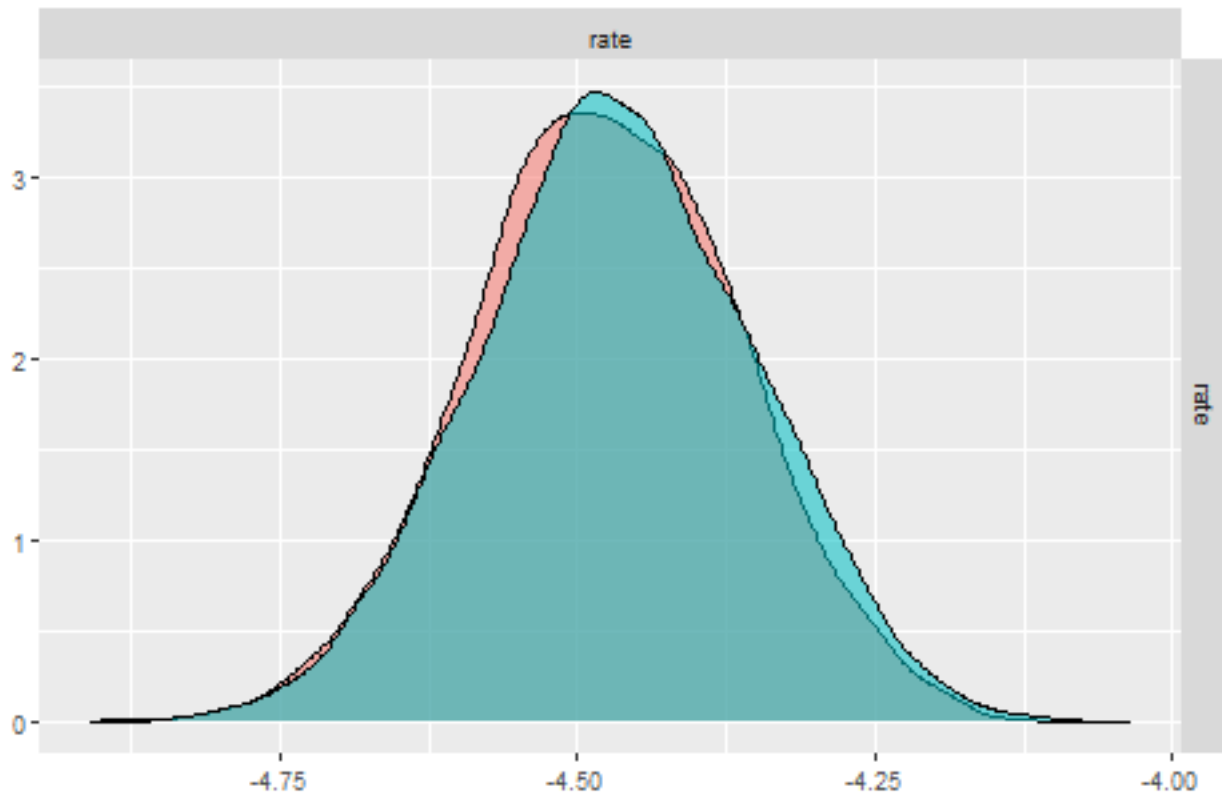


Survival - Gen. Gamma

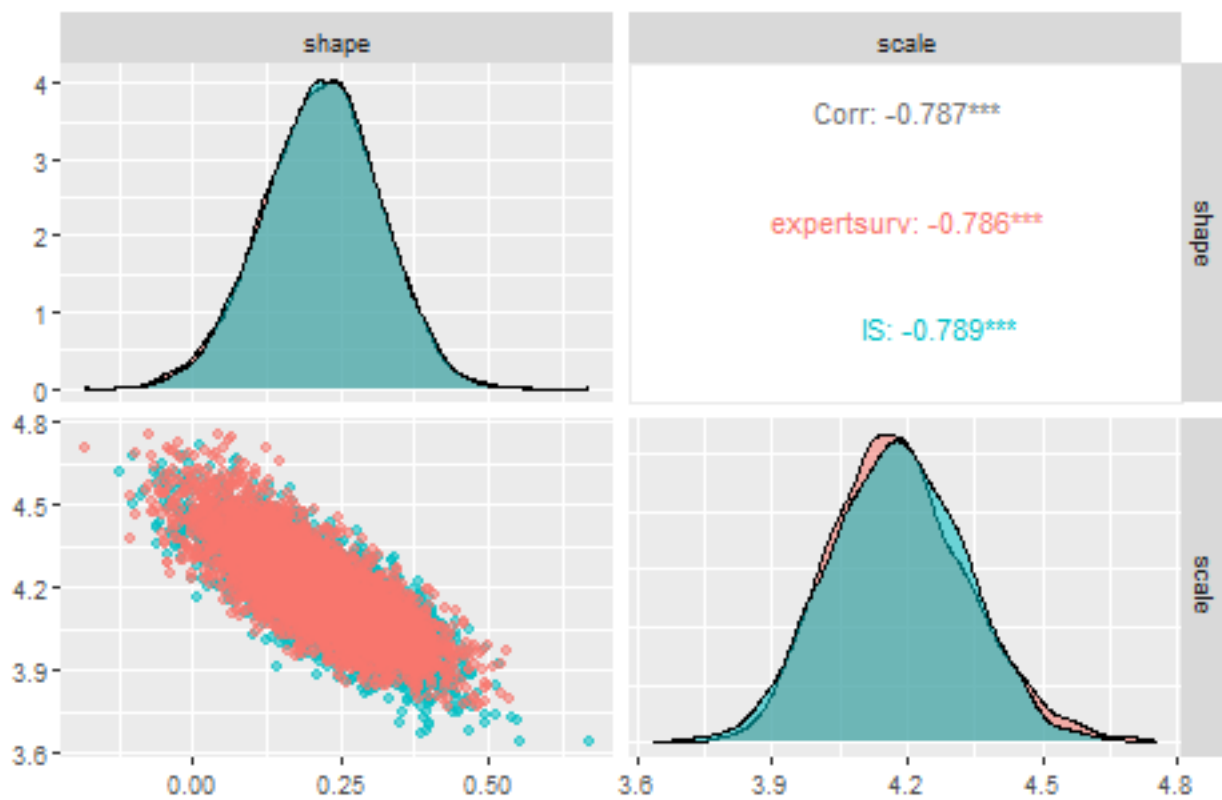


## Comparisons of parameter distributions

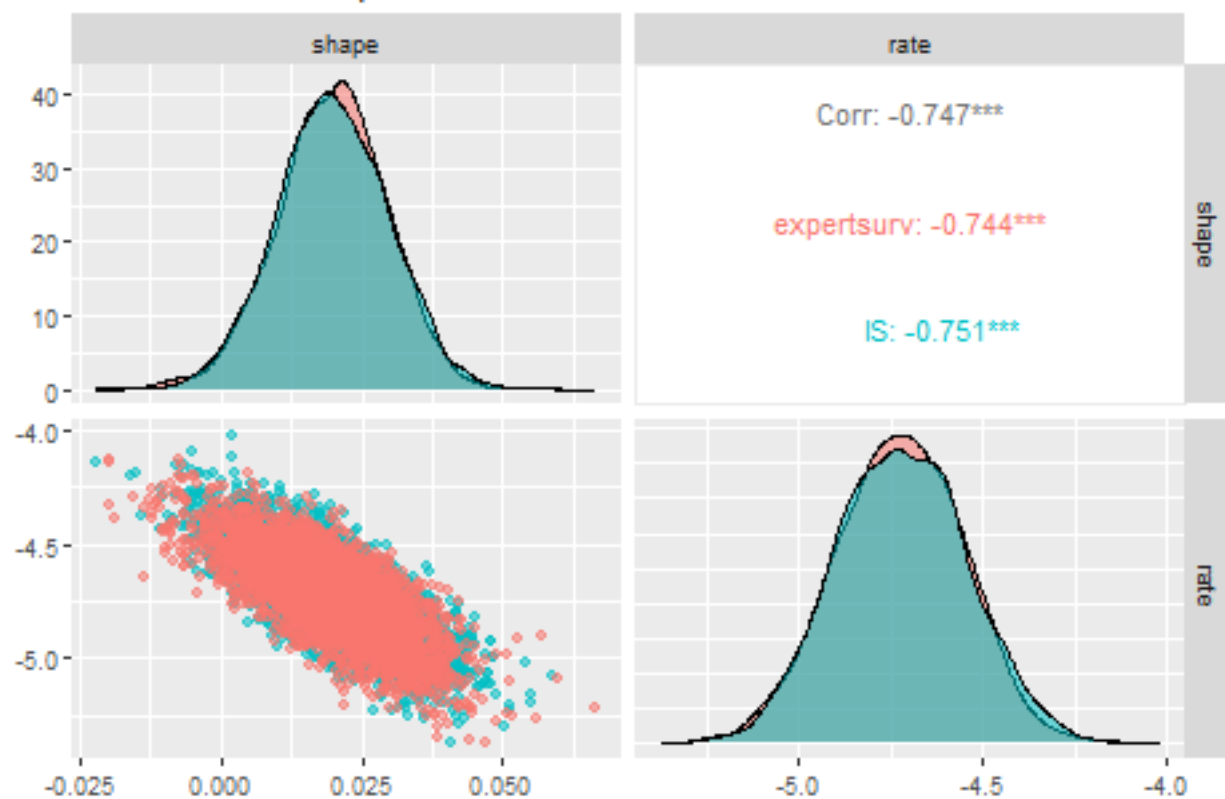
### Parameters - Exponential



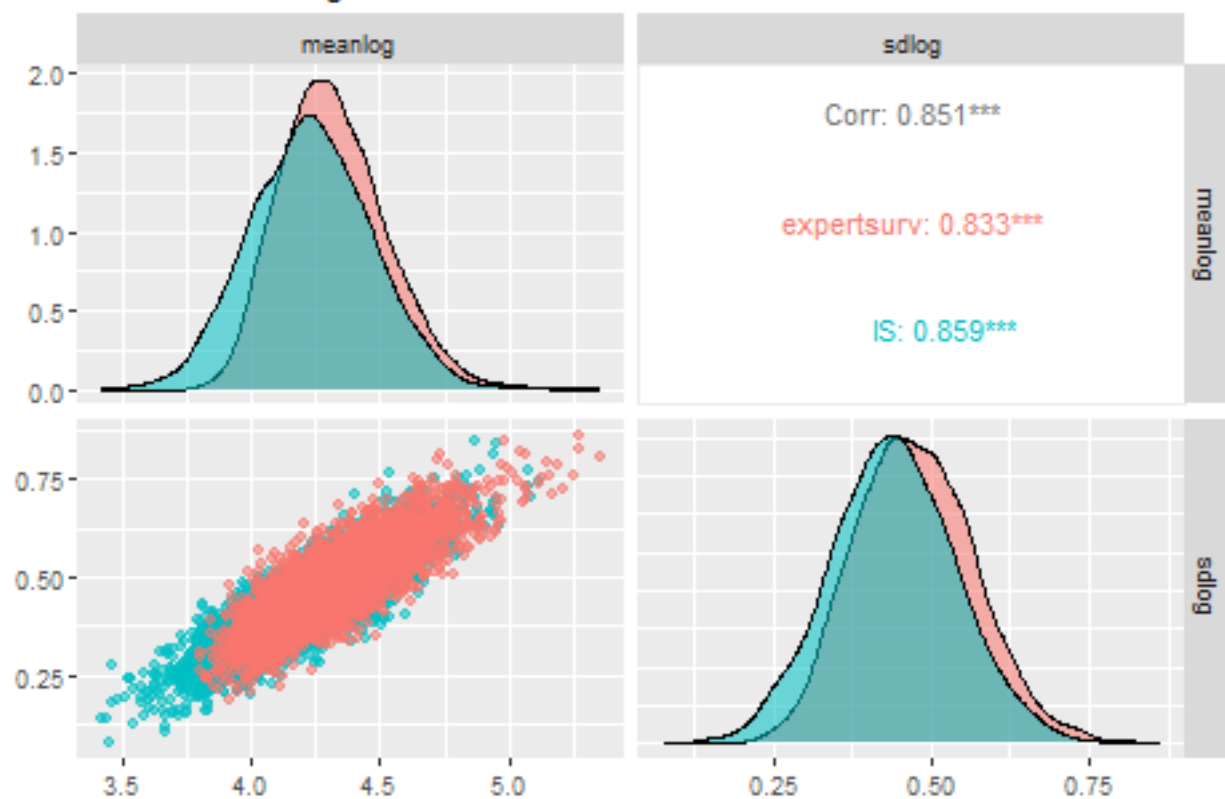
### Parameters - Weibull



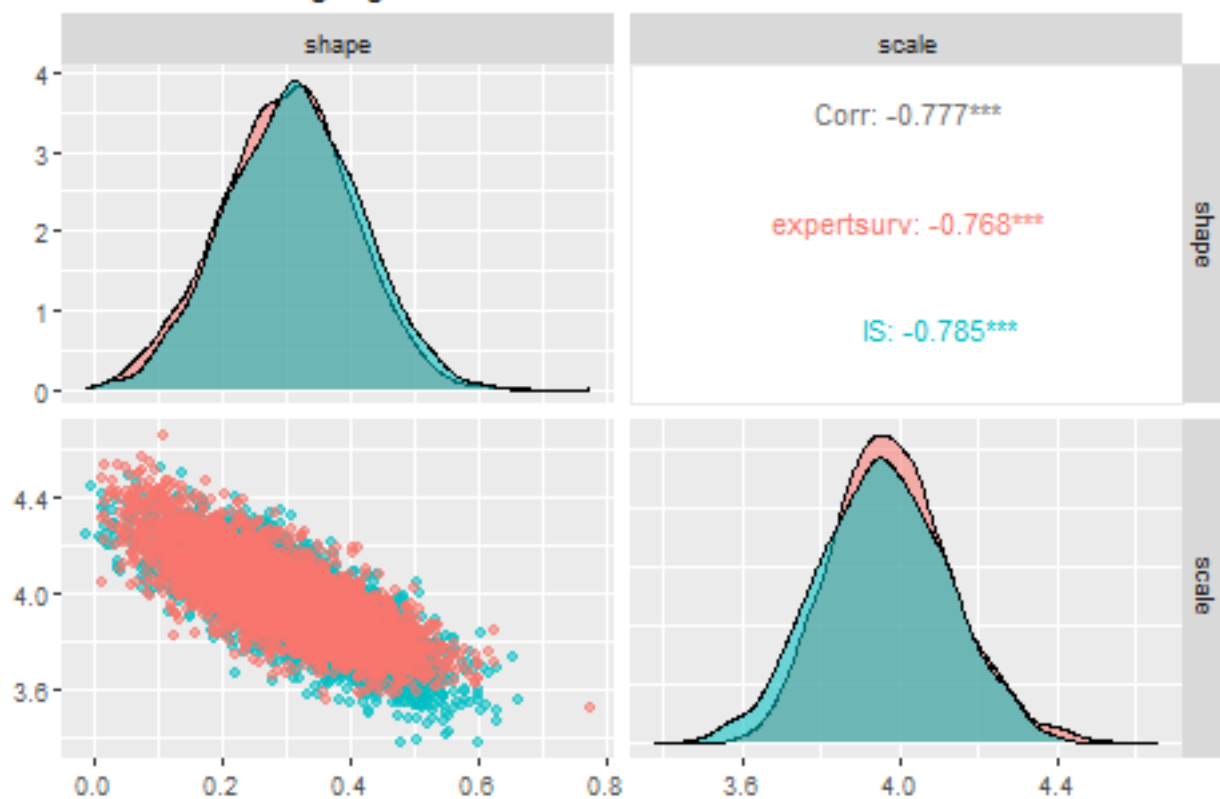
## Parameters - Gompertz



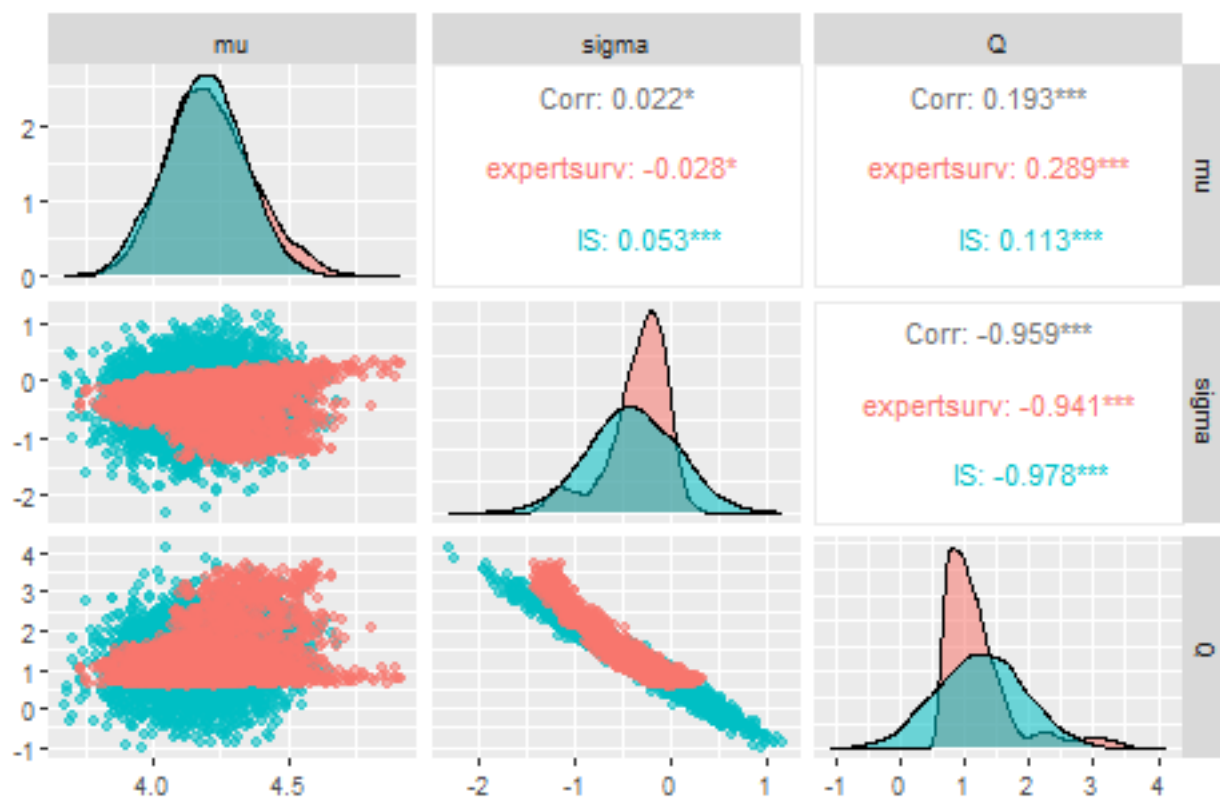
## Parameters - Log-normal



## Parameters - Log-logistic

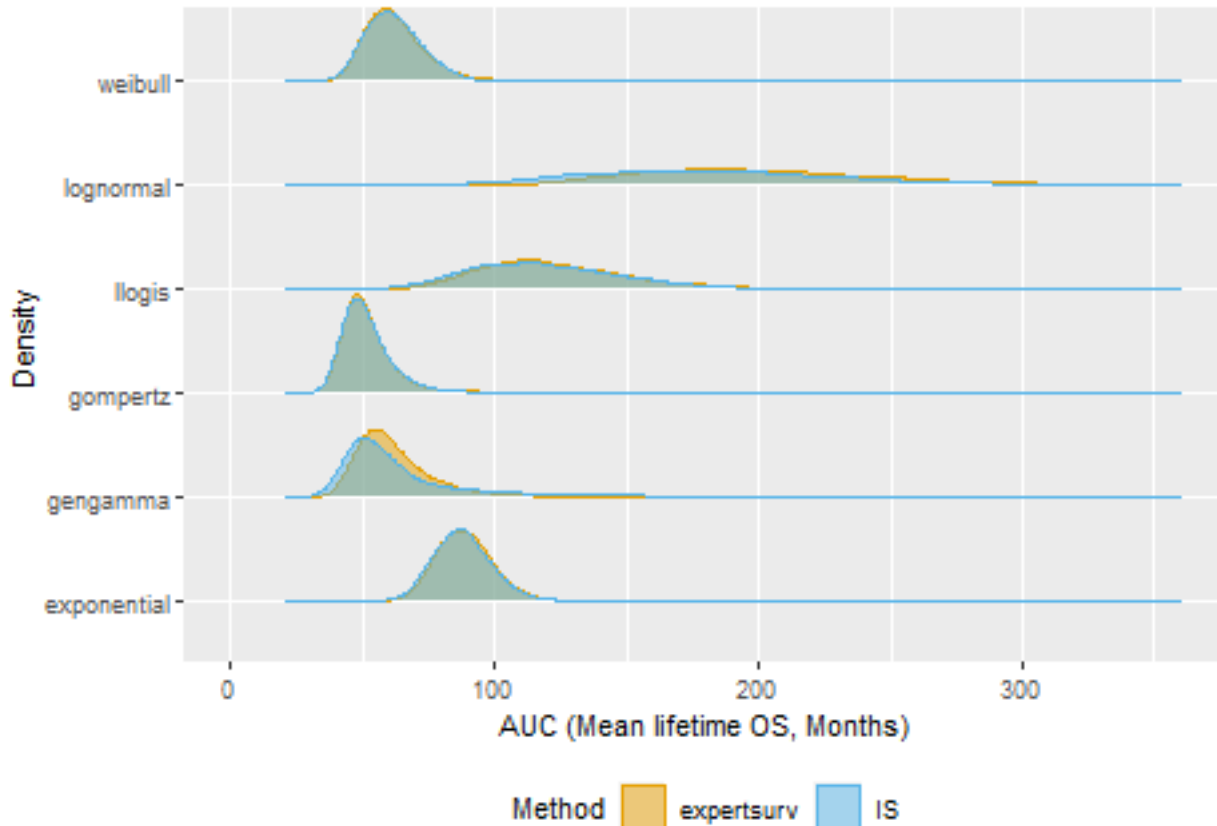


## Parameters - Gen. Gamma



## Comparisons of AUC distributions

Distribution	expertsurv	IS	Mean.Diff	Var.Ratio
Exponential	88.48 (70.48, 109.73)	87.74 (69.78, 109.28)	-0.74	1.06
Gen. Gamma	62.23 (42.85, 103.18)	71.11 (38.84, 216.27)	8.88	8.73
Gompertz	55.85 (39.56, 92.84)	53.89 (39.24, 85.24)	-1.96	0.44
Log-logistic	123.17 (77.65, 189.59)	119.06 (71.11, 181.96)	-4.11	1.01
Log-normal	202.54 (126.08, 311.84)	183.80 (97.93, 295.22)	-18.74	1.07
Weibull	62.43 (45.73, 90.16)	61.93 (44.18, 85.17)	-0.50	0.90



## Comparisons of 5-year OS

Distribution	Output	mean	median	sd	lwr.95	upr.95
Exponential	IS	50.16%	50.28%	4.03%	42.32%	57.75%
Exponential	expertsurv	50.47%	50.56%	3.87%	42.68%	57.88%
Gen. Gamma	IS	38.94%	40.11%	9.74%	16.65%	55.04%
Gen. Gamma	expertsurv	40.08%	40.03%	7.12%	25.45%	53.88%
Gompertz	IS	35.63%	35.98%	8.87%	17.68%	51.87%
Gompertz	expertsurv	35.89%	36.01%	8.71%	18.84%	52.77%
Log-logistic	IS	44.89%	45.25%	5.98%	32.21%	55.46%
Log-logistic	expertsurv	45.88%	45.95%	5.37%	35.19%	56.30%
Log-normal	IS	52.94%	53.44%	5.72%	40.77%	62.69%
Log-normal	expertsurv	55.11%	55.20%	4.50%	46.42%	63.67%
Weibull	IS	40.05%	40.56%	6.65%	25.86%	51.30%

Distribution	Output	mean	median	sd	lwr.95	upr.95
Weibull	expertsurv	40.32%	40.41%	6.53%	27.64%	52.69%

