Survival extrapolation - Supplementary Appendix

NCPE

October 2024

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`.

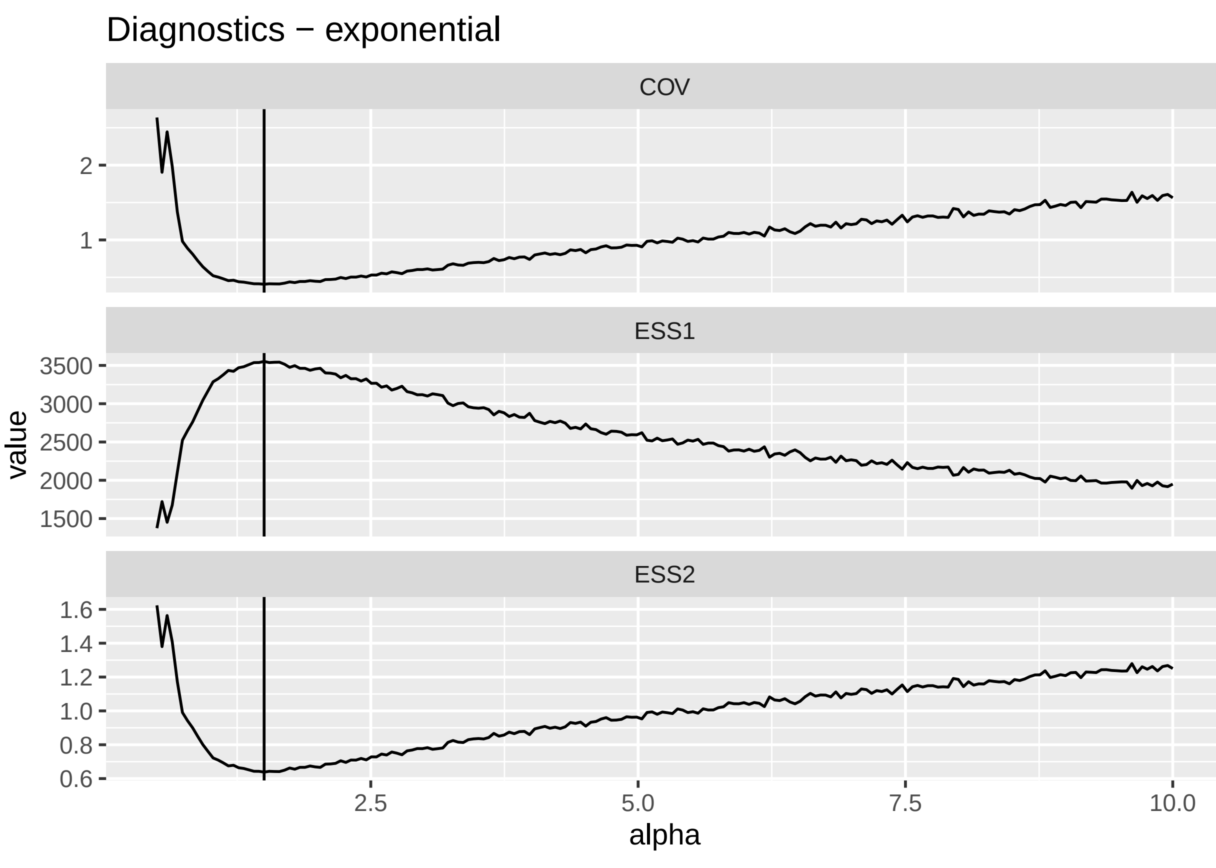

Figure 1: Importance sampling diagnostics: coefficient of variation (COV) and effective sample size (ESS) as functions of the tempering parameter alpha, Exponential distribution. The vertical line shows the optimal value of alpha identified by the algorithm.

Table 1: Parameter estimates obtained using trial data only (left) and combining trial data with external information (right): Exponential distribution.

x	x
-4.562874	-4.467088

Table 2: Covariance matrices obtained using trial data only (left) and combining trial data with external information (right): Exponential distribution.

0.0138444

	rate
rate	0.0169491

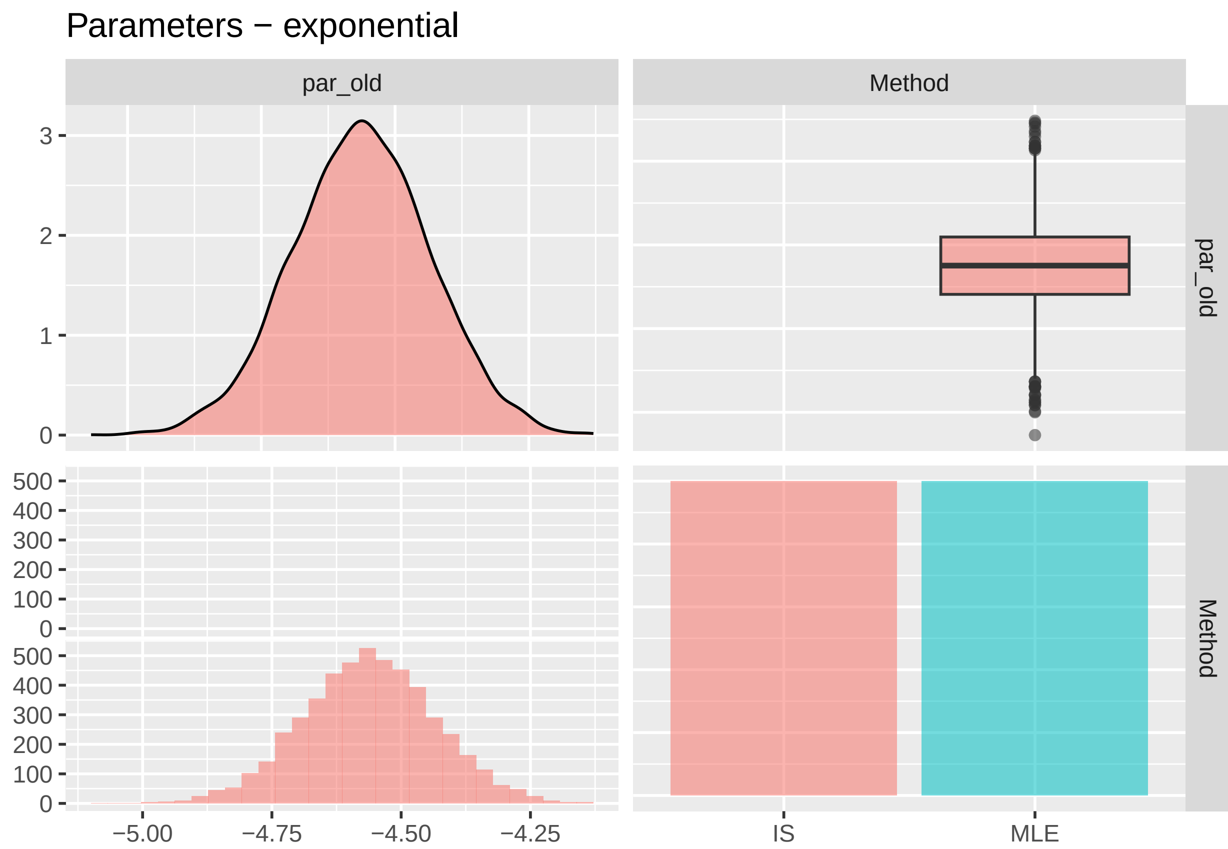

Figure 2: Survival curve parameter distributions and covariance estimates obtained using trial data only (MLE) and combining trial data with external information (IS), Exponential distribution

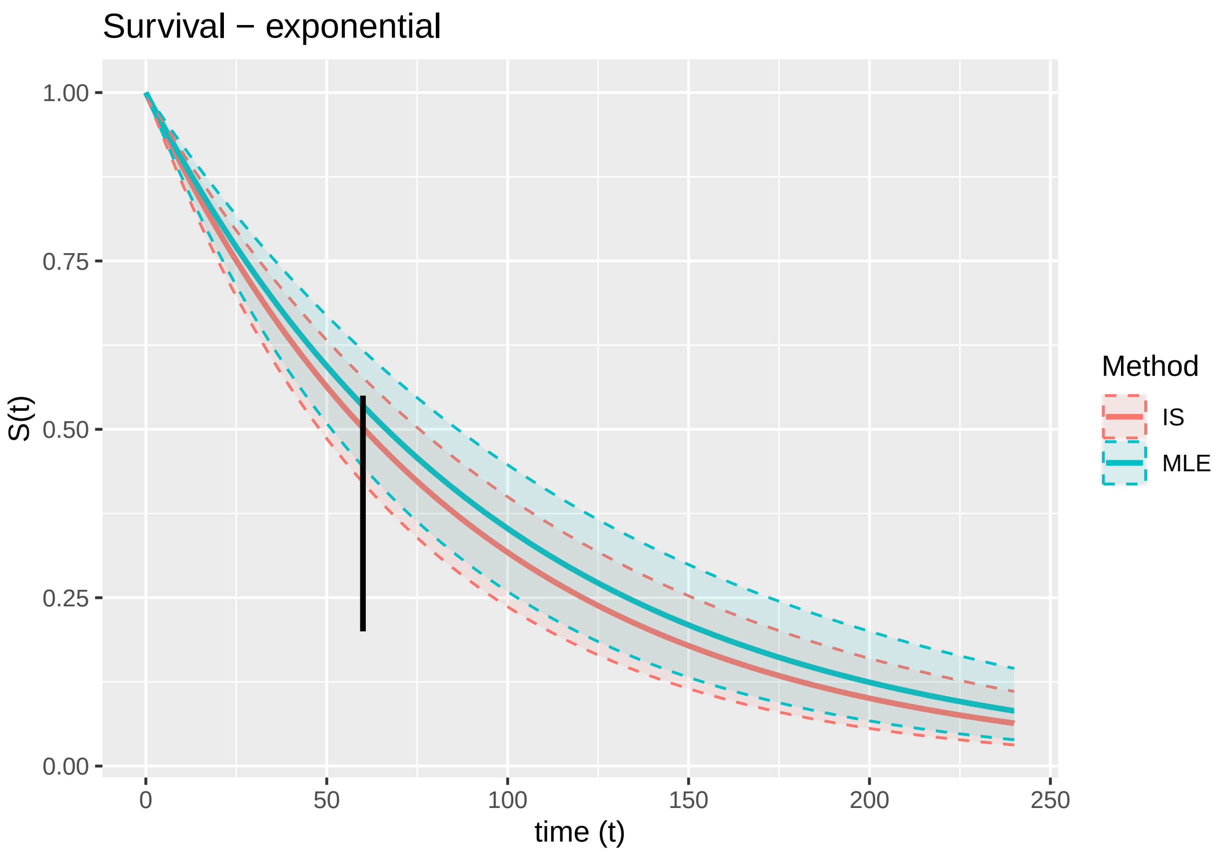

Figure 3: Survival curves (median and 95% confidence intervals) obtained using trial data only (MLE) and combining trial data with external information (IS), Exponential distribution

Table 3: Parameter estimates obtained using trial data only (left) and combining trial data with external information (right): Weibull distribution.

	x
shape	0.2028128
scale	4.2127617

	x
shape	0.2199019
scale	4.1750757

Table 4: Covariance matrices obtained using trial data only (left) and combining trial data with external information (right): Weibull distribution.

	shape	scale
shape	0.0094518	-0.0118402
scale	-0.0118402	0.0235769

	shape	scale
shape	0.0147844	-0.0228526
scale	-0.0228526	0.0466213

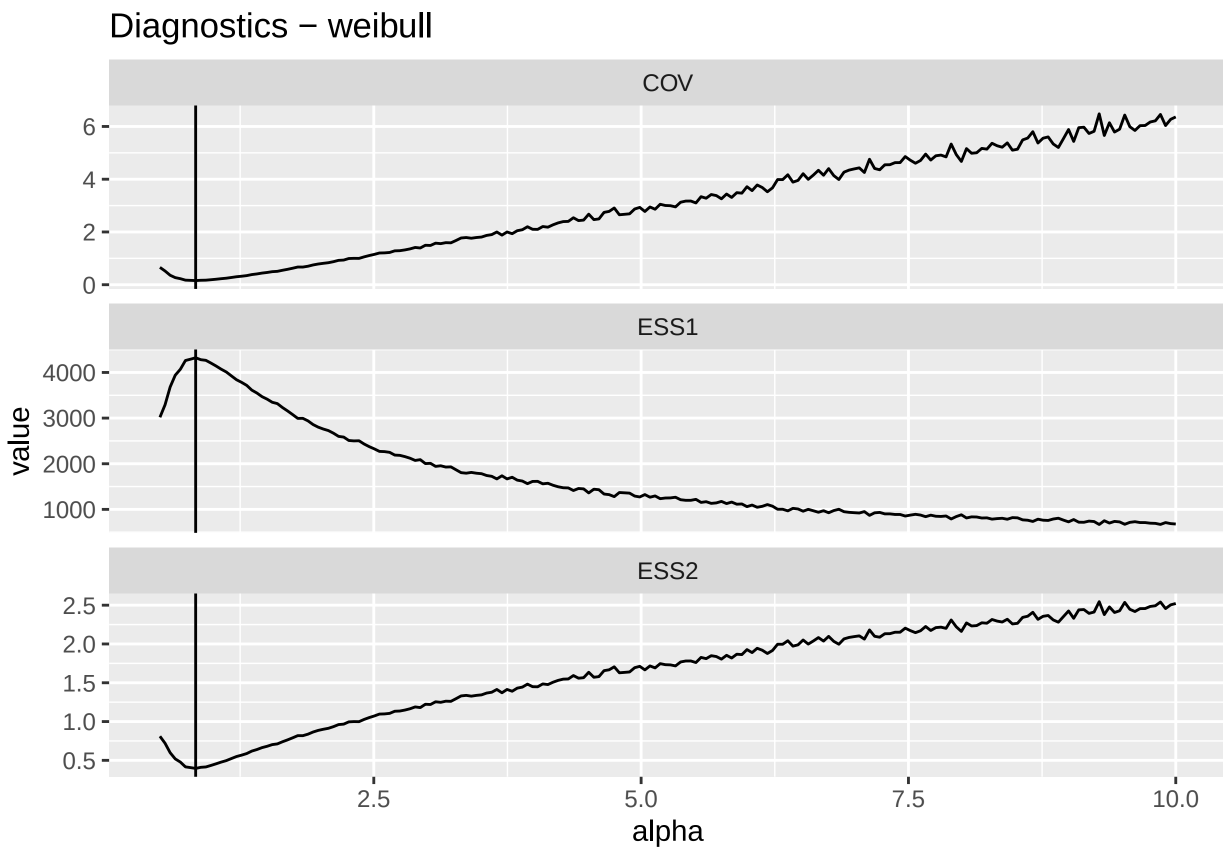

Figure 4: Importance sampling diagnostics: coefficient of variation (COV) and effective sample size (ESS) as functions of the tempering parameter alpha, Weibull distribution. The vertical line shows the optimal value of alpha identified by the algorithm.

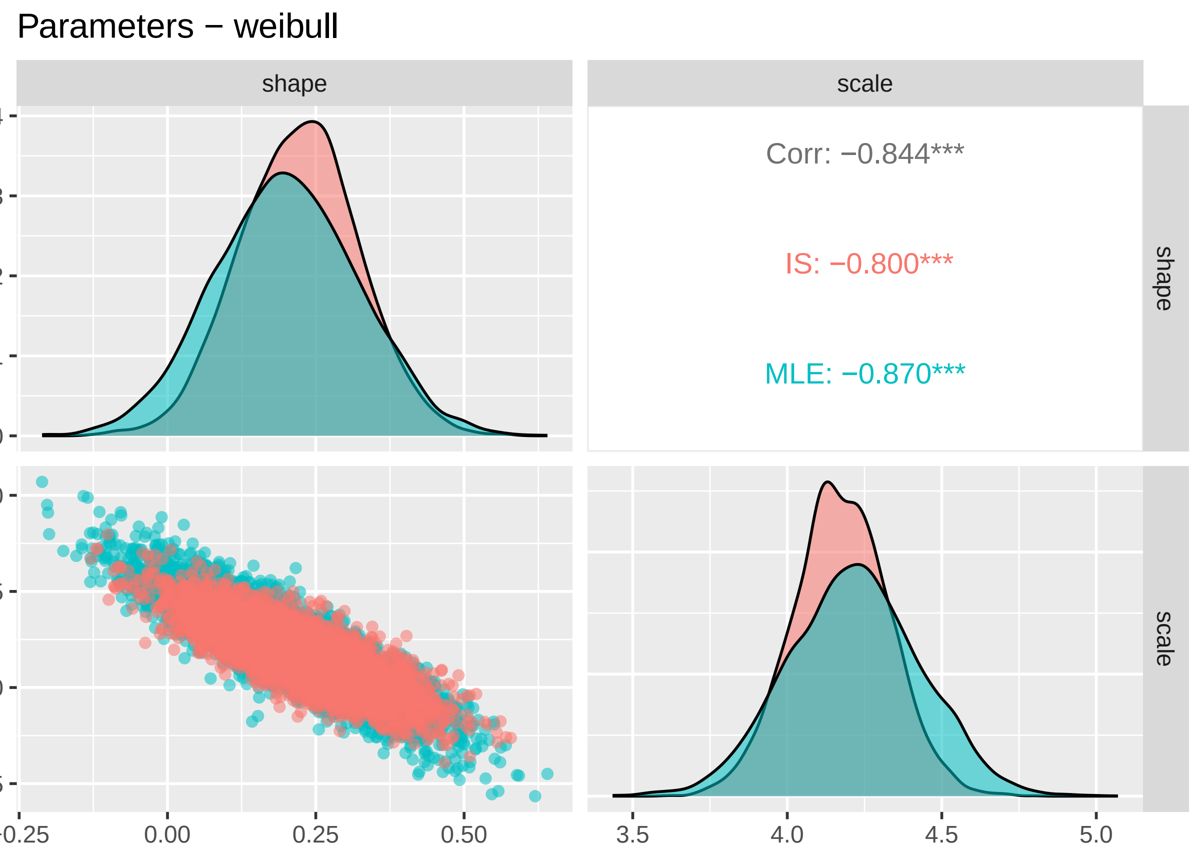

Figure 5: Survival curve parameter distributions and covariance estimates obtained using trial data only (MLE) and combining trial data with external information (IS), Weibull distribution

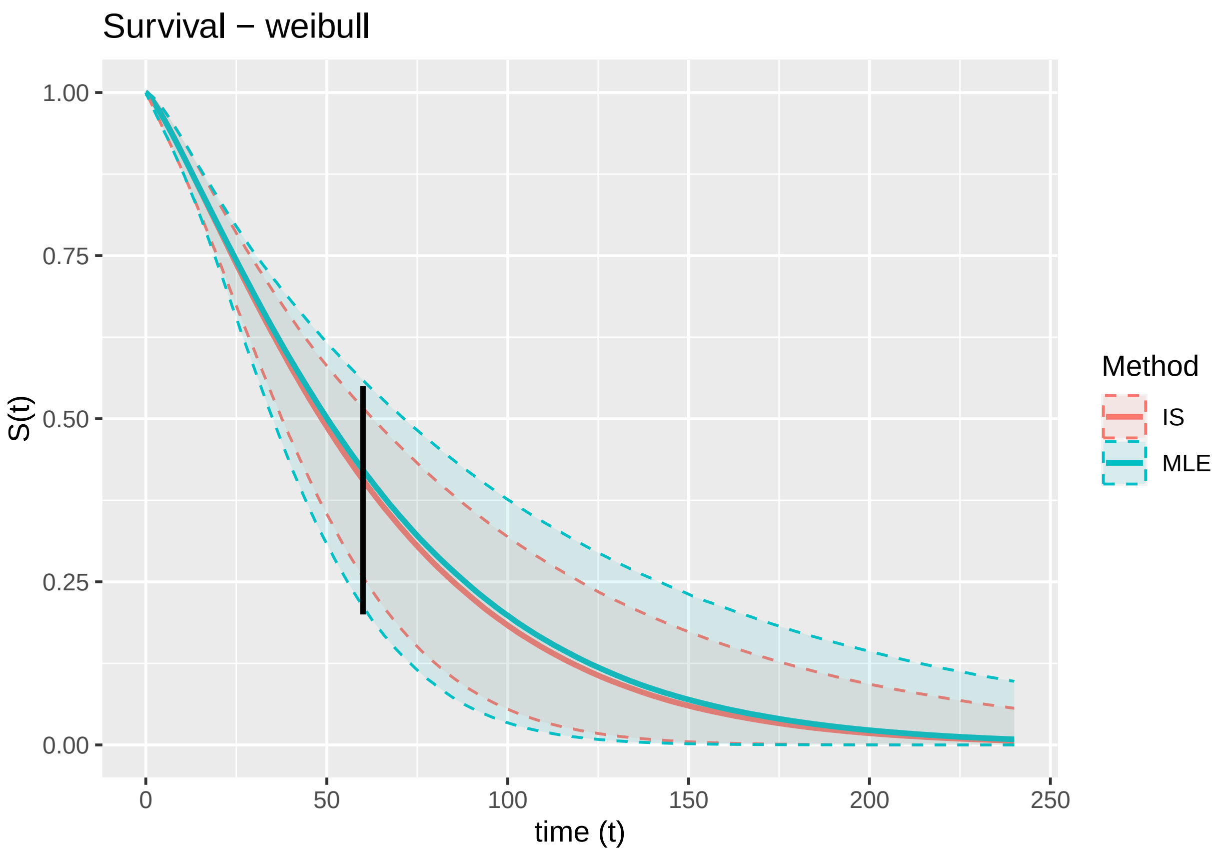

Figure 6: Survival curves (median and 95% confidence intervals) obtained using trial data only (MLE) and combining trial data with external information (IS), Weibull distribution

Table 5: Parameter estimates obtained using trial data only (left) and combining trial data with external information (right): Gompertz distribution.

	x
shape	0.0389625
rate	-4.8682858

	x
shape	0.0197027
rate	-4.7220927

Table 6: Covariance matrices obtained using trial data only (left) and combining trial data with external information (right): Gompertz distribution.

	shape	rate
shape	0.0000970	-0.0013281
rate	-0.0013281	0.0316264

	shape	rate
shape	0.0006747	-0.0056125
rate	-0.0056125	0.0636359

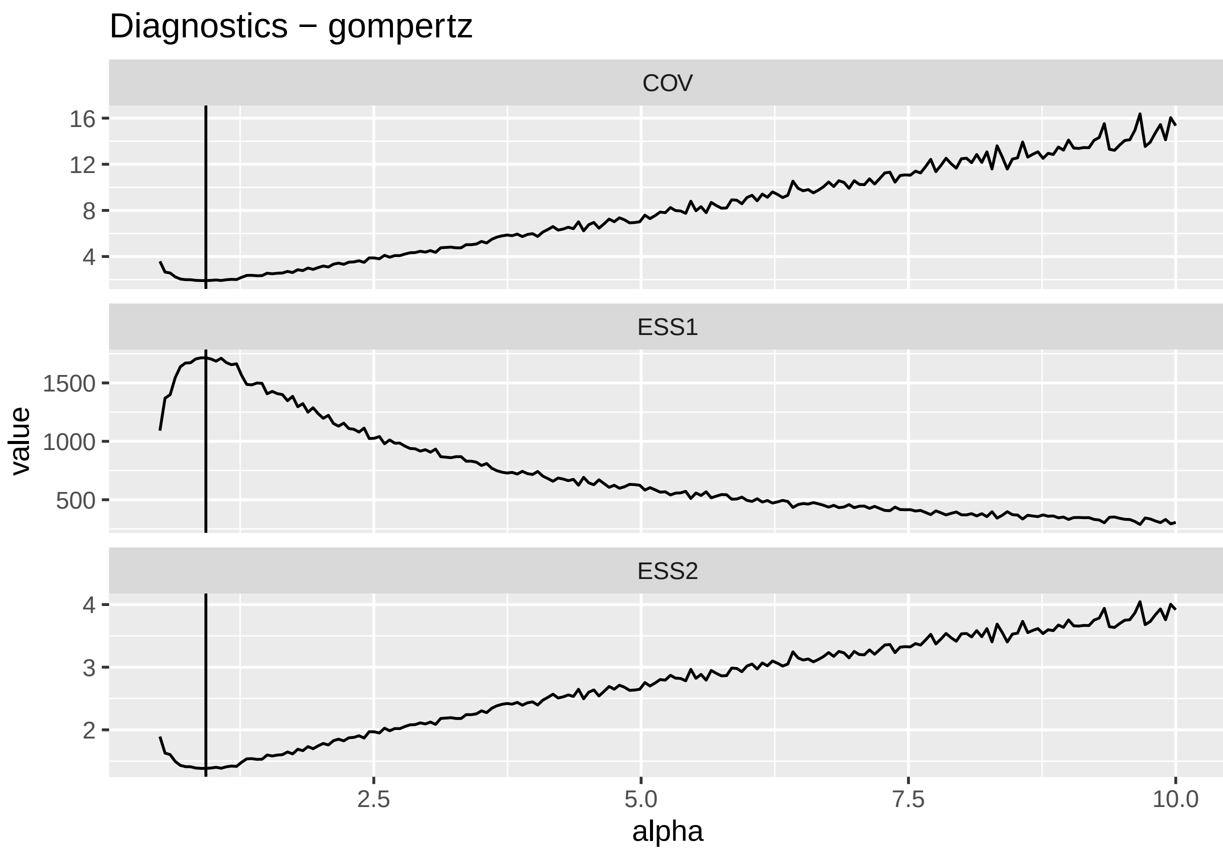

Figure 7: Importance sampling diagnostics: coefficient of variation (COV) and effective sample size (ESS) as functions of the tempering parameter alpha, Log-normal distribution. The vertical line shows the optimal value of alpha identified by the algorithm.

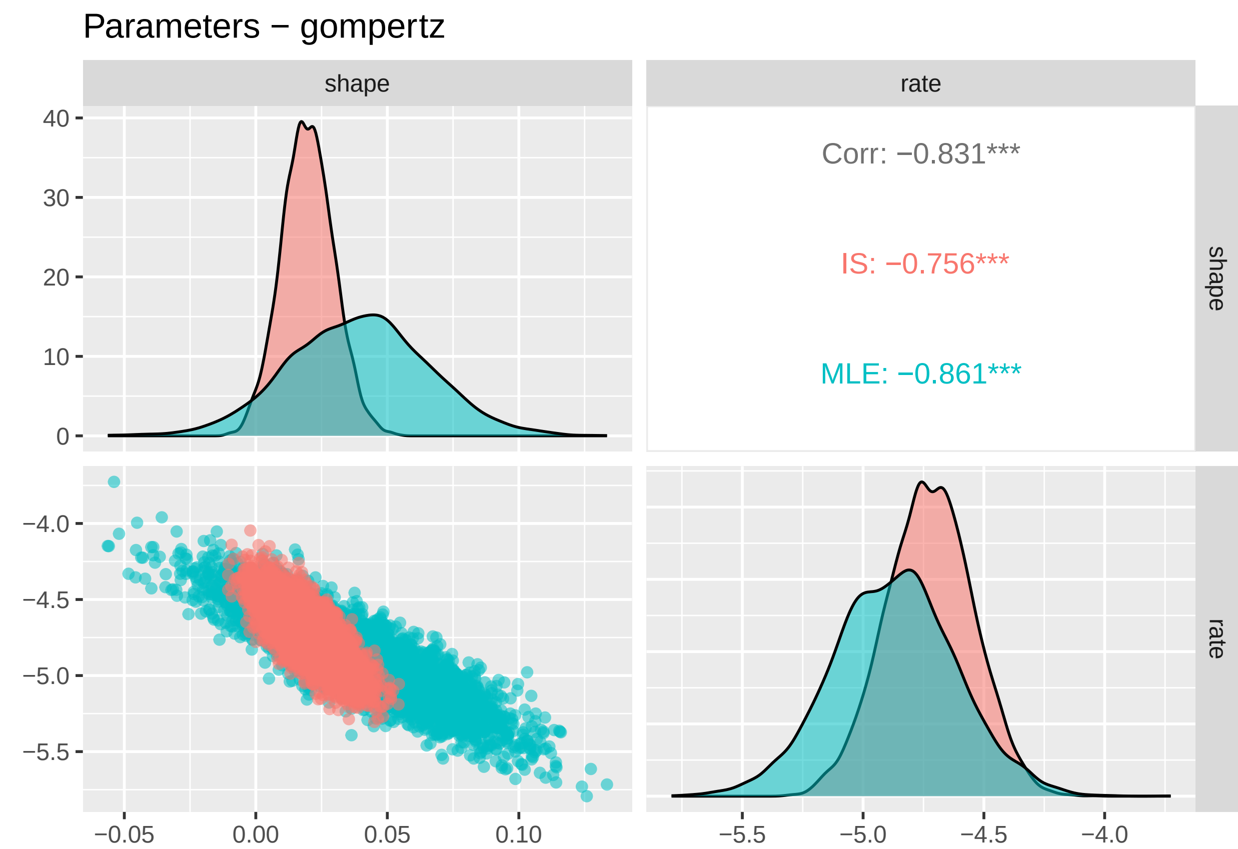

Figure 8: Survival curve parameter distributions and covariance estimates obtained using trial data only (MLE) and combining trial data with external information (IS), Log-normal distribution

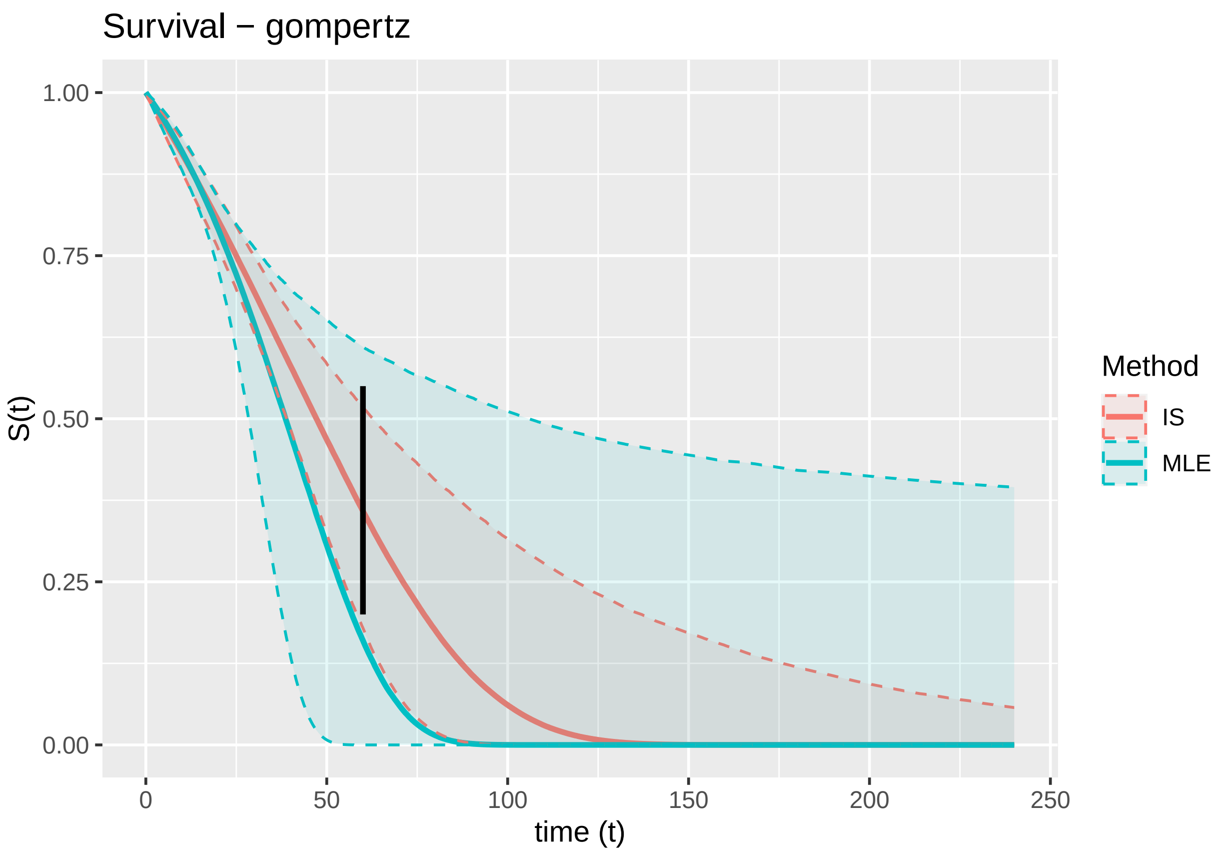

Figure 9: Survival curves (median and 95% confidence intervals) obtained using trial data only (MLE) and combining trial data with external information (IS), Log-normal distribution

Table 7: Parameter estimates obtained using trial data only (left) and combining trial data with external information (right): Log-normal distribution.

	x
meanlog	4.5379239
sdlog	0.5475716

	x
meanlog	4.2299230
sdlog	0.4404943

Table 8: Covariance matrices obtained using trial data only (left) and combining trial data with external information (right): Log-normal distribution.

	meanlog	sdlog
meanlog	0.0545435	0.0201378
sdlog	0.0201378	0.0100655

	meanlog	sdlog
meanlog	0.0696811	0.0247171
sdlog	0.0247171	0.0114622

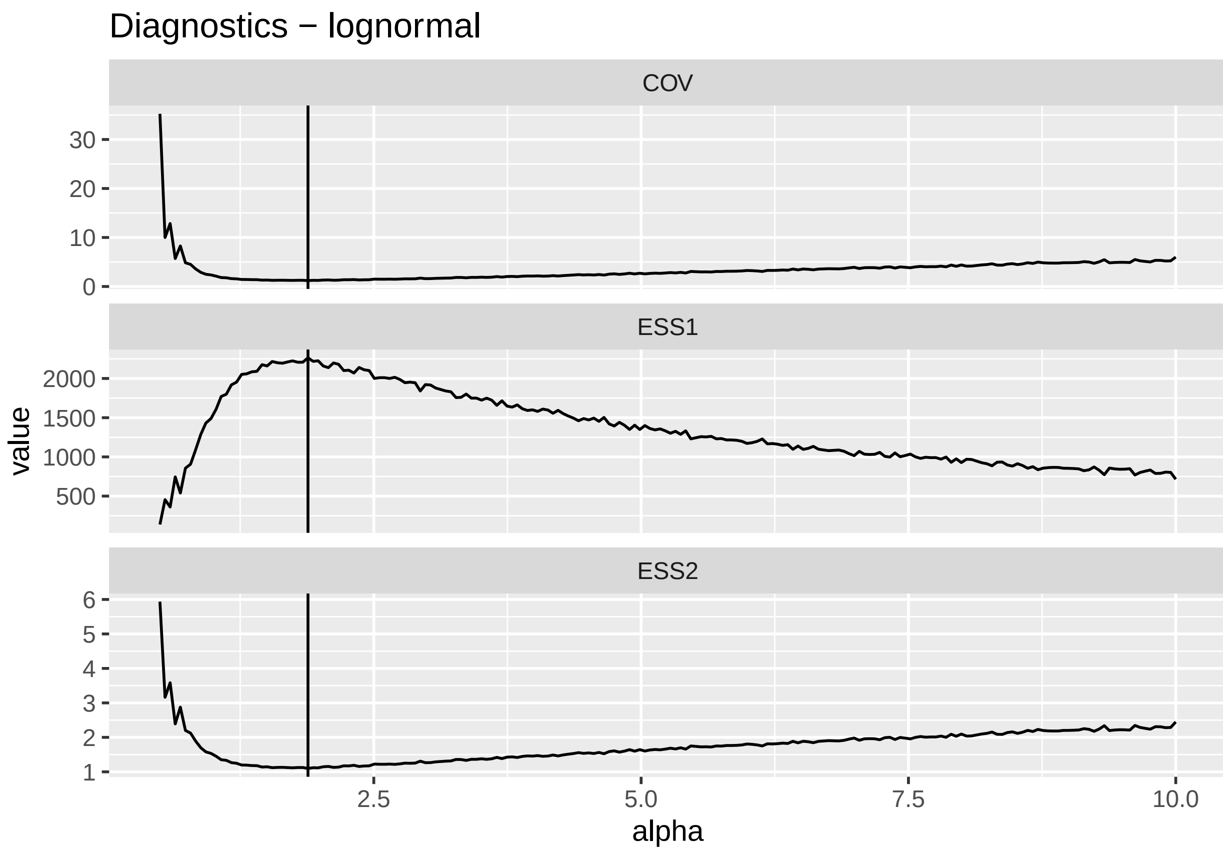

Figure 10: Importance sampling diagnostics: coefficient of variation (COV) and effective sample size (ESS) as functions of the tempering parameter alpha, Log-logistic distribution. The vertical line shows the optimal value of alpha identified by the algorithm.

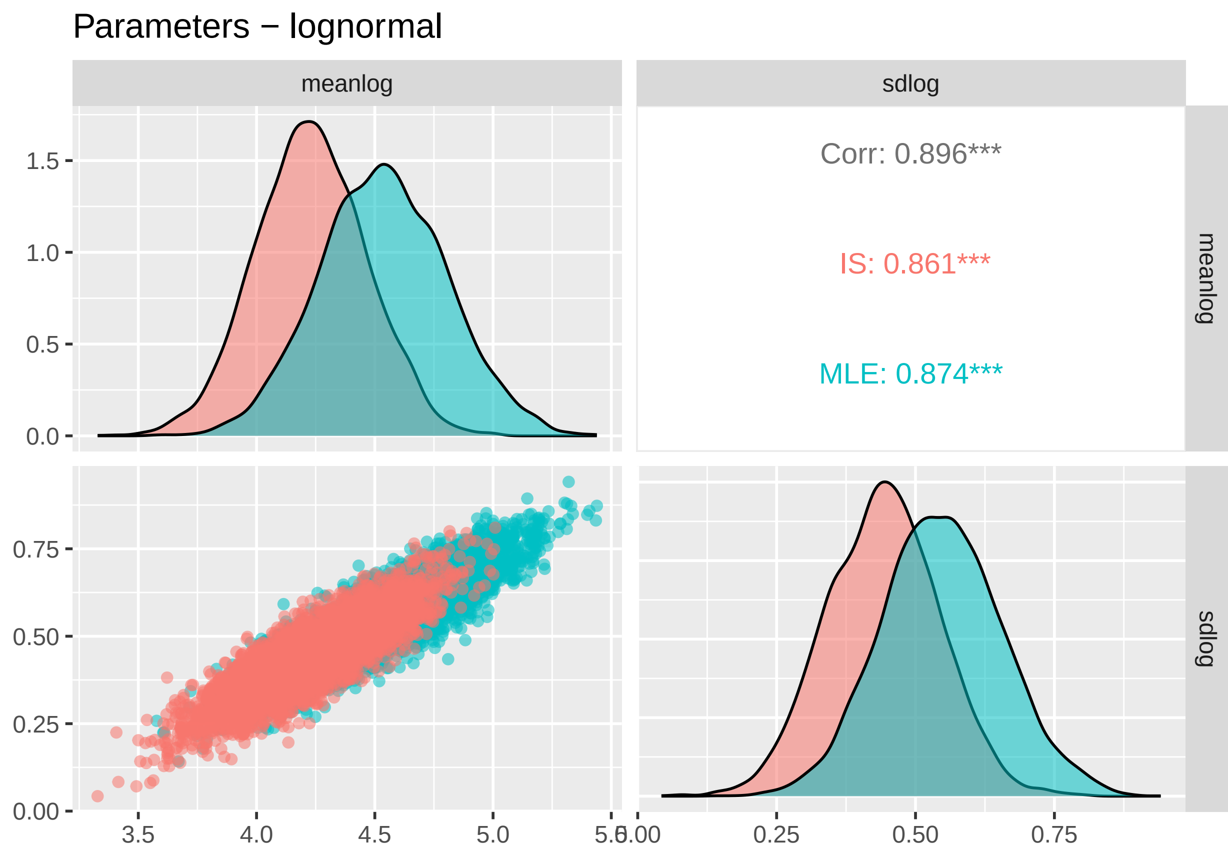

Figure 11: Survival curve parameter distributions and covariance estimates obtained using trial data only (MLE) and combining trial data with external information (IS), Log-logistic distribution

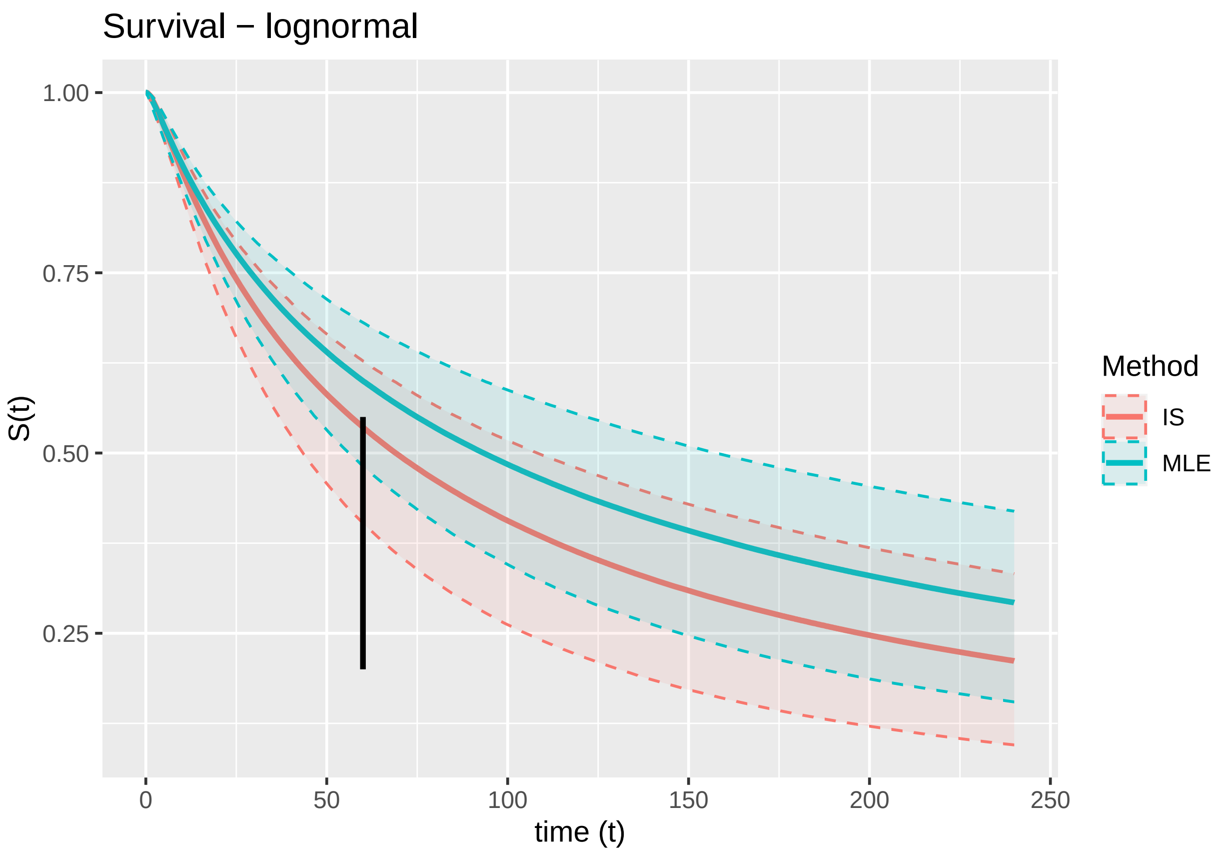

Figure 12: Survival curves (median and 95% confidence intervals) obtained using trial data only (MLE) and combining trial data with external information (IS), Log-logistic distribution

Table 9: Parameter estimates obtained using trial data only (left) and combining trial data with external information (right): Log-logistic distribution.

	x
shape	0.2450539
scale	4.0866467

	x
shape	0.3103417
scale	3.9558382

Table 10: Covariance matrices obtained using trial data only (left) and combining trial data with external information (right): Log-logistic distribution.

	shape	scale
shape	0.0111243	-0.0139385
scale	-0.0139385	0.0276608

	shape	scale
shape	0.0144928	-0.0213001
scale	-0.0213001	0.0434079

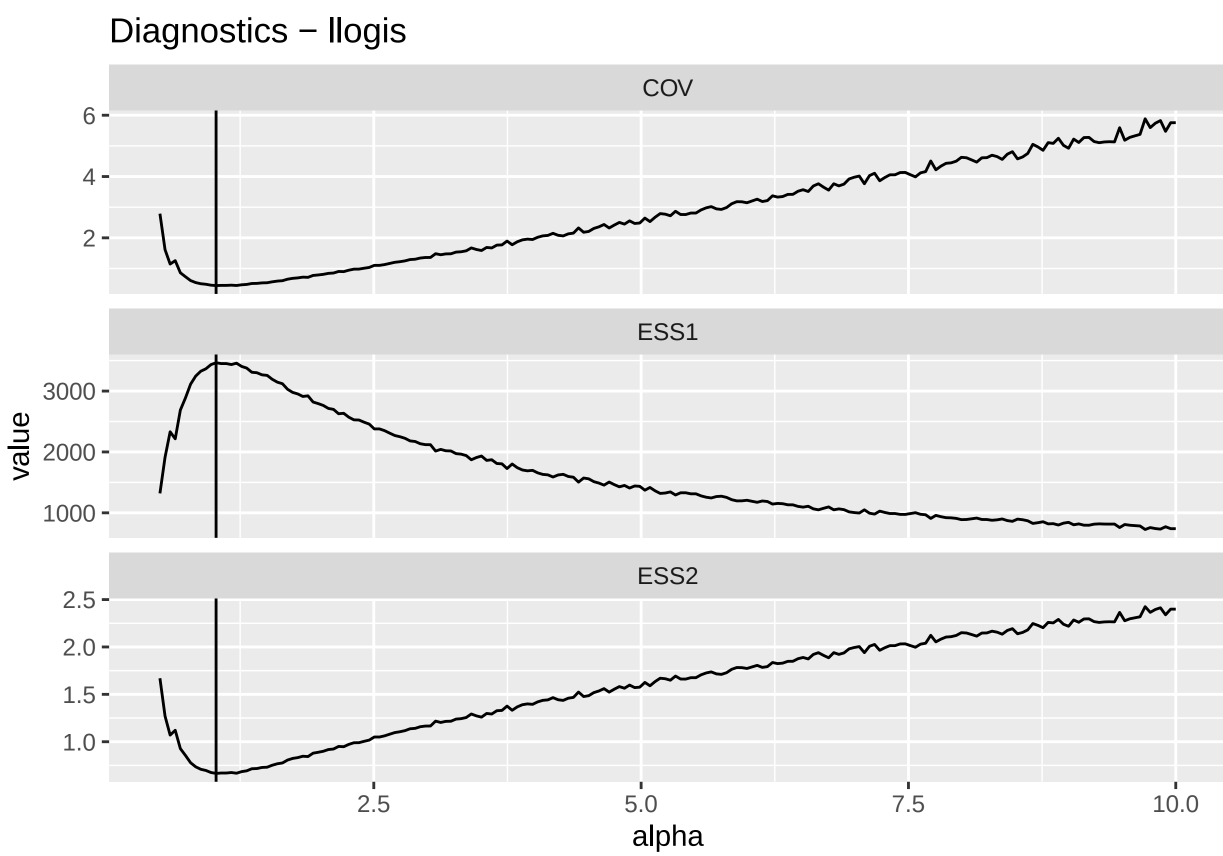

Figure 13: Importance sampling diagnostics: coefficient of variation (COV) and effective sample size (ESS) as functions of the tempering parameter alpha, Gompertz distribution. The vertical line shows the optimal value of alpha identified by the algorithm.

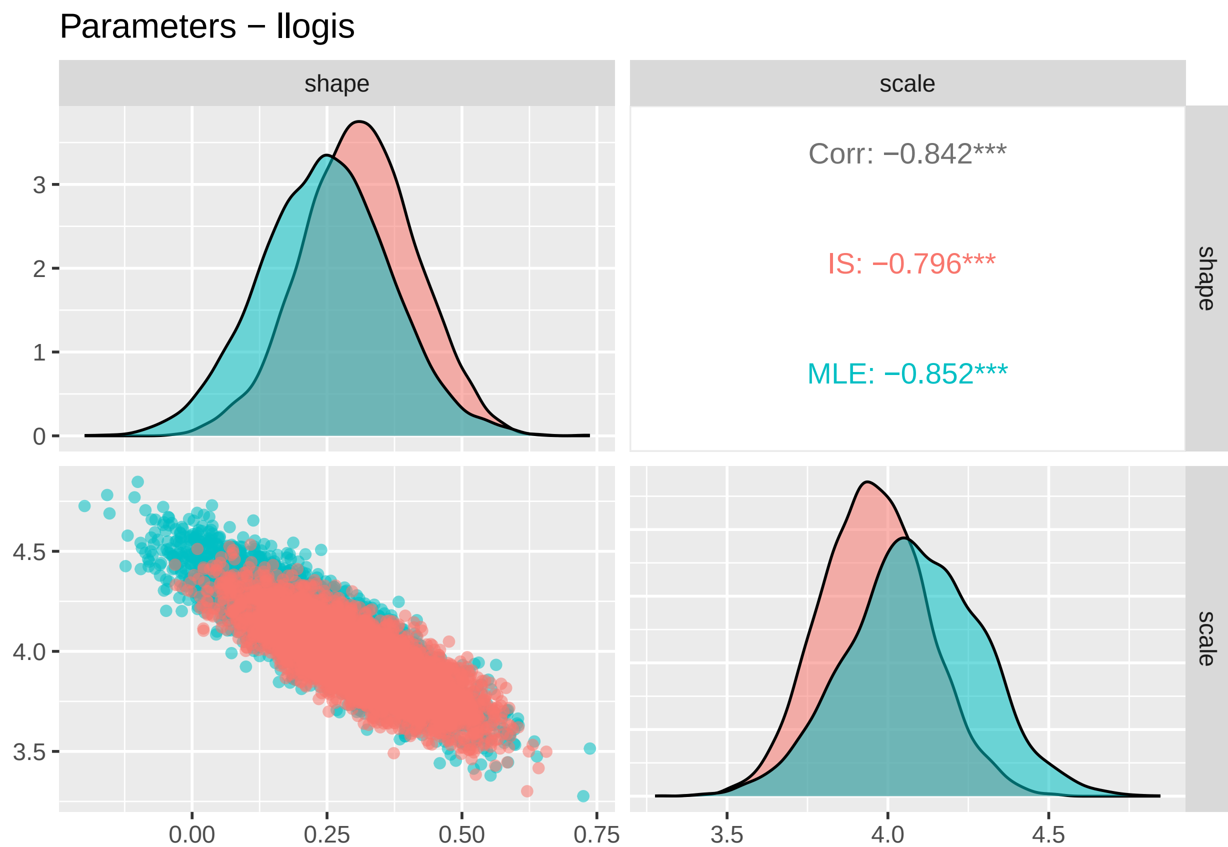

Figure 14: Survival curve parameter distributions and covariance estimates obtained using trial data only (MLE) and combining trial data with external information (IS), Gompertz distribution

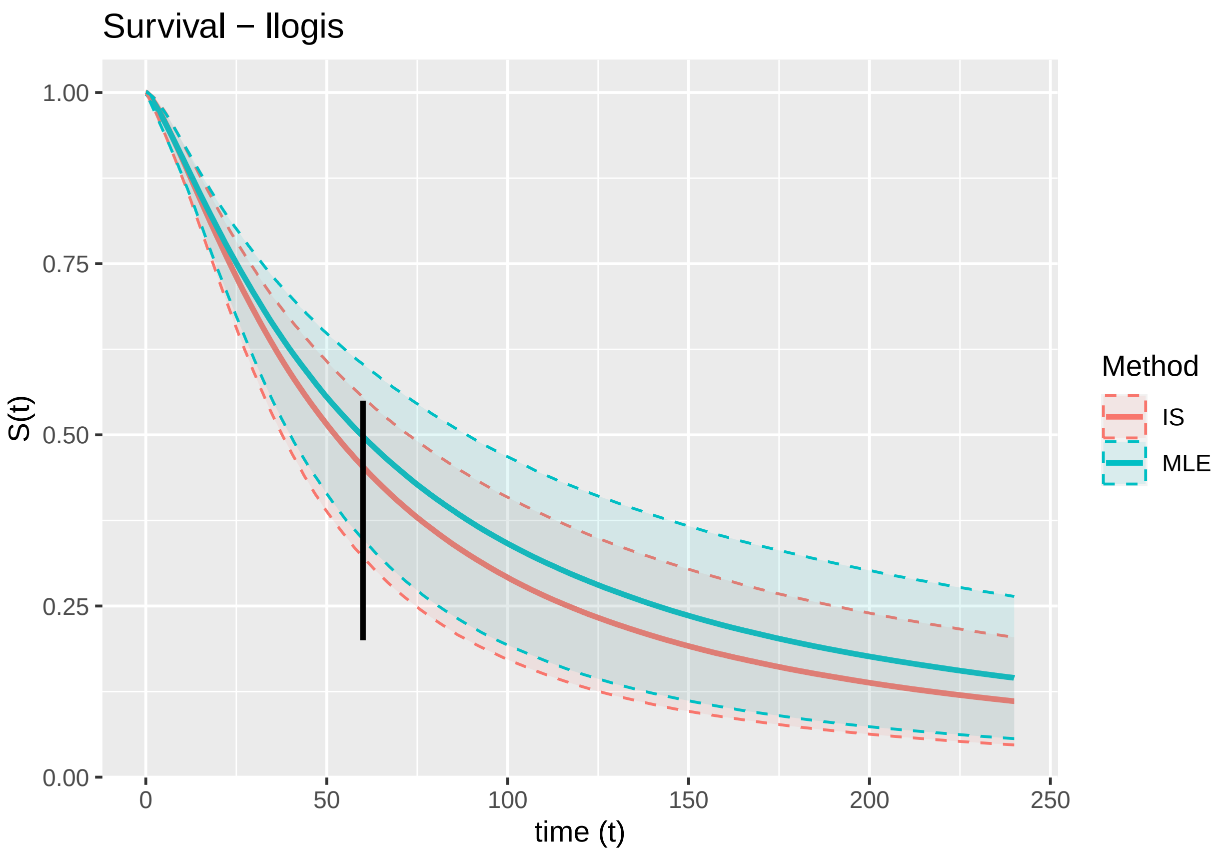

Figure 15: Survival curves (median and 95% confidence intervals) obtained using trial data only (MLE) and combining trial data with external information (IS), Gompertz distribution

Table 11: Parameter estimates obtained using trial data only (left) and combining trial data with external information (right): Gen. Gamma distribution.

	x
mu	4.1703317
sigma	-0.3599072
Q	1.2031485

	x
mu	4.1857610
sigma	-0.3818327
Q	1.2508022

Table 12: Covariance matrices obtained using trial data only (left) and combining trial data with external information (right): Gen. Gamma distribution.

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

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

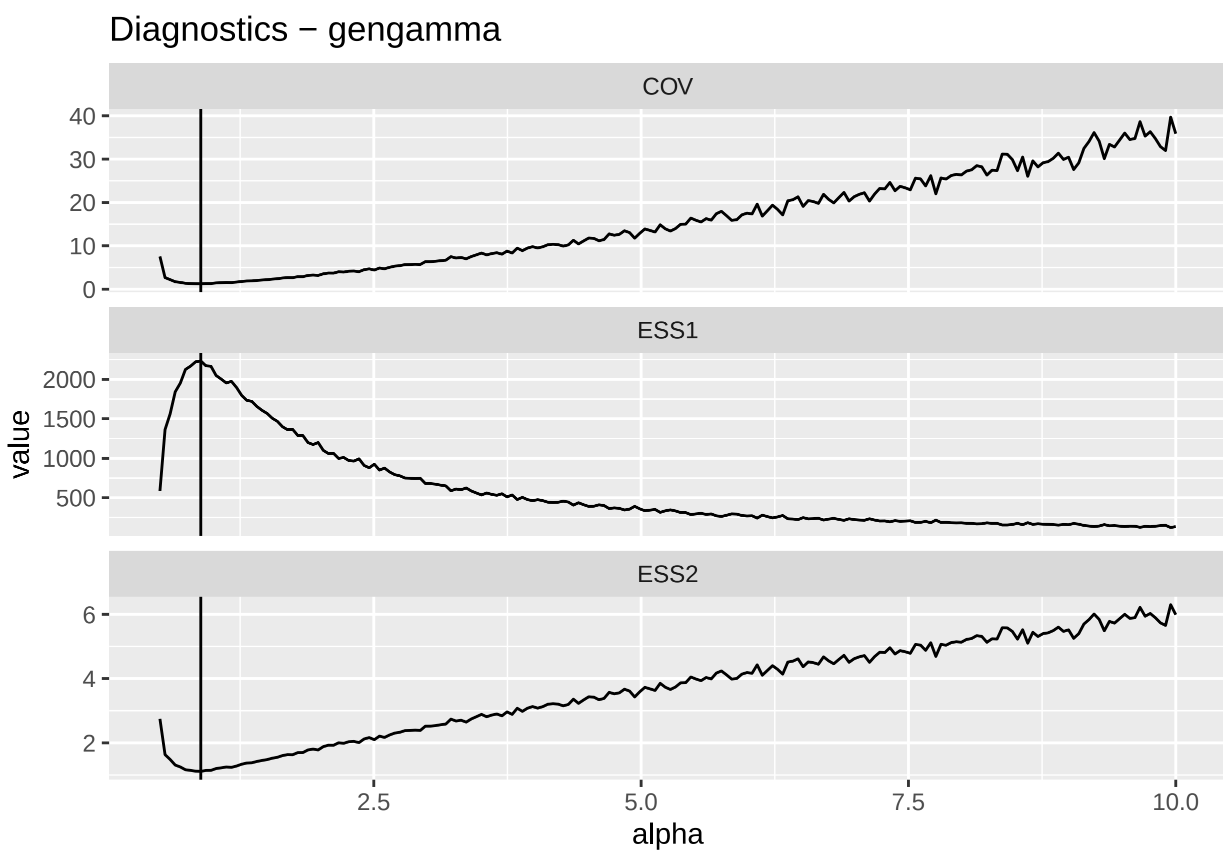

Figure 16: Importance sampling diagnostics: coefficient of variation (COV) and effective sample size (ESS) as functions of the tempering parameter alpha, Gen. Gamma distribution. The vertical line shows the optimal value of alpha identified by the algorithm.

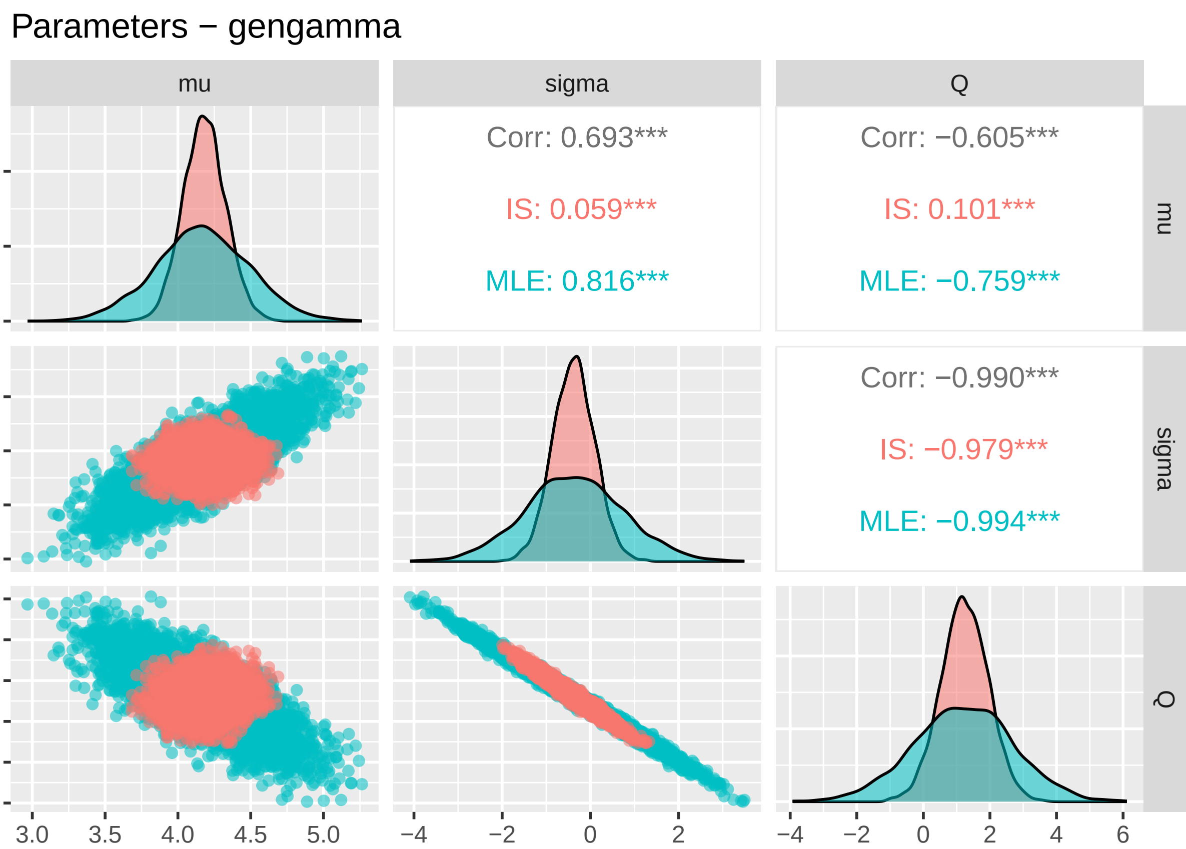

Figure 17: Survival curve parameter distributions and covariance estimates obtained using trial data only (MLE) and combining trial data with external information (IS), Gen. Gamma distribution

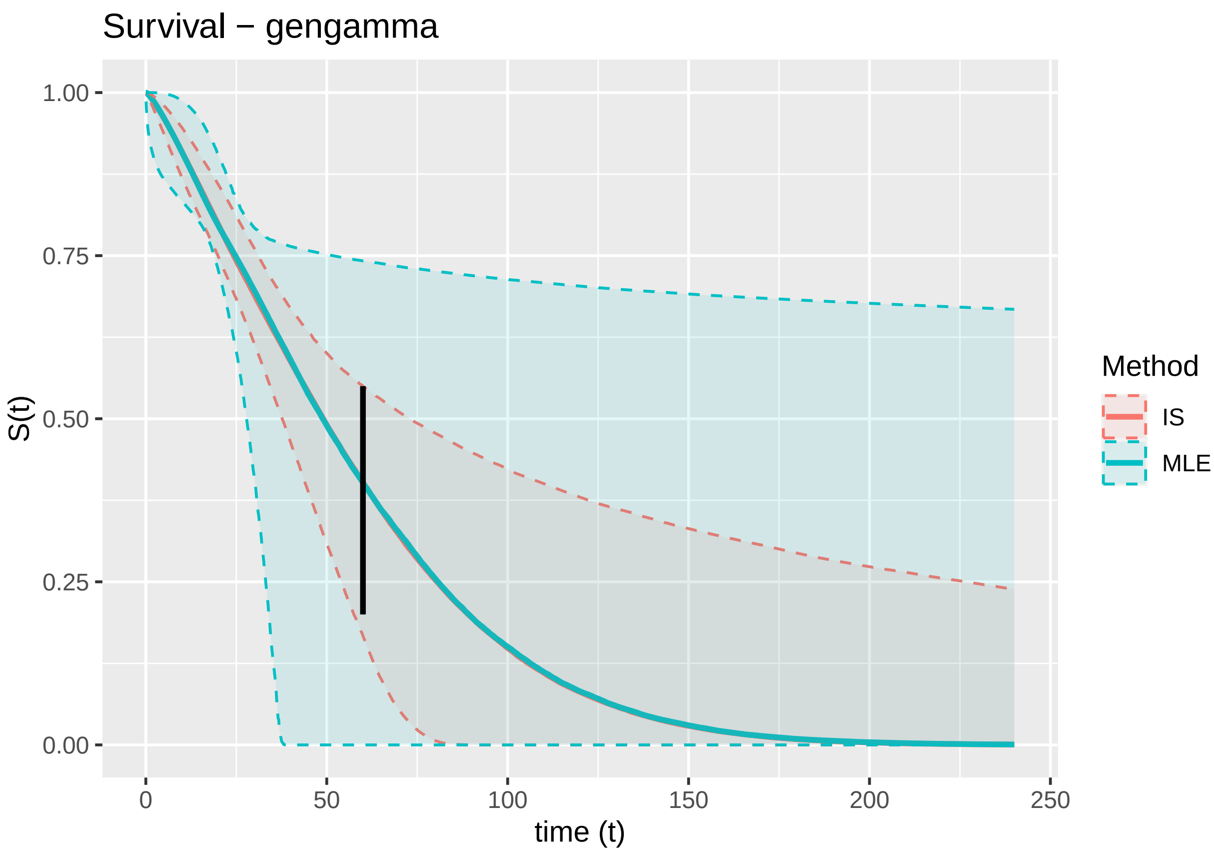

Figure 18: Survival curves (median and 95% confidence intervals) obtained using trial data only (MLE) and combining trial data with external information (IS), Gen. Gamma distribution

Parameter variability

The table below shows 'Generalised variance,' i.e., determinants of variance-covariance matrices, of the parameter estimates obtained using trial data only (MLE) and combining trial data withe external information (IS). Formally, the generalised variance gives the area of the 95% highest density ellipse and can be interpreted as a 1-parameter measure of parameter uncertainty, see e.g., https://stats.stackexchange.com/questions/12762/measure-of-spread-of-a-multivariate-normal-distribution .

Table 13: Generalised variance of model parameter distributions. Comparison between parameter estimates obtained using trial data only (MLE) and combining trial data with external information (IS).

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

Comparisons of survival curves (median and 95% confidence/credible intervals) obtained from the importance sampling method described in the paper, with those obtained from the fully Bayesian approach of Cooney & White implemented in the expertsurv package.

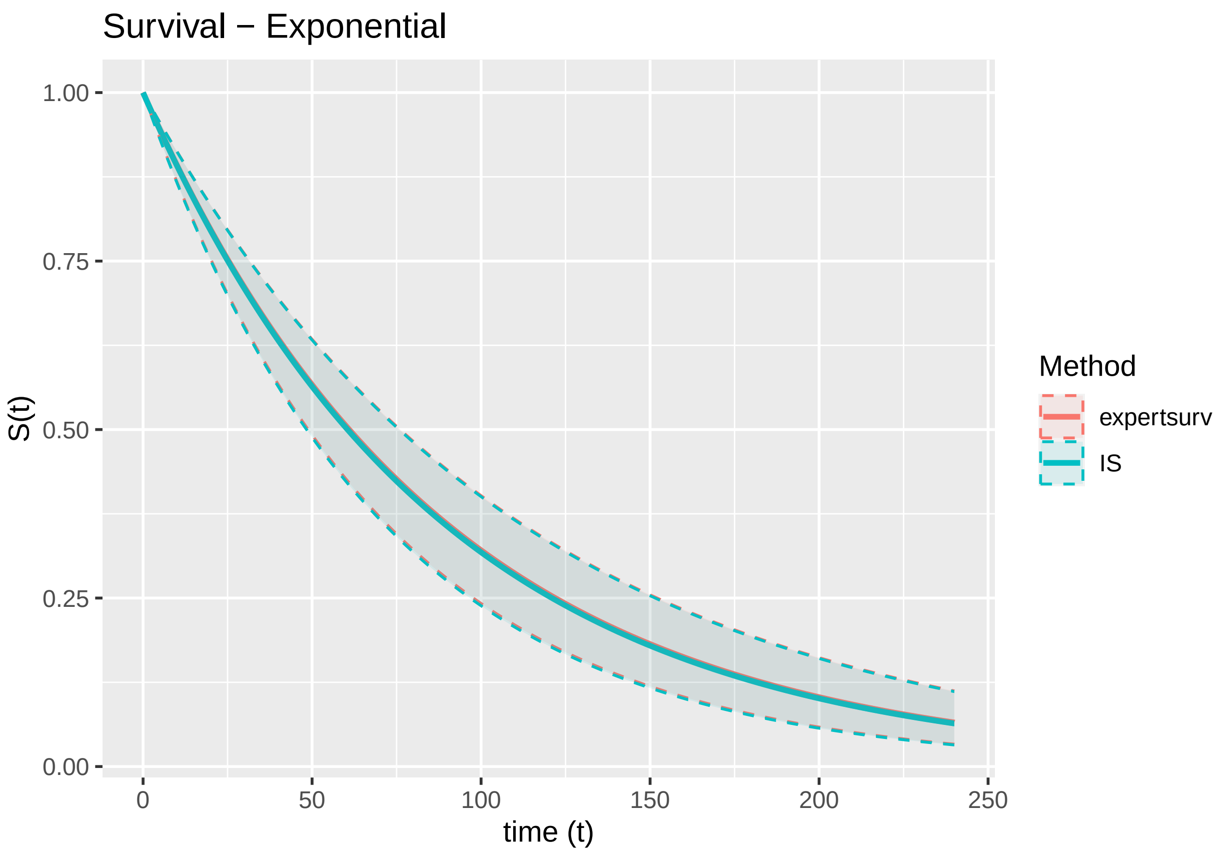

Figure 19: Survival curves (median and 95% confidence intervals) obtained by combining trial data with external information using the importance sampling (IS) and expertsurv methods, Exponential distribution

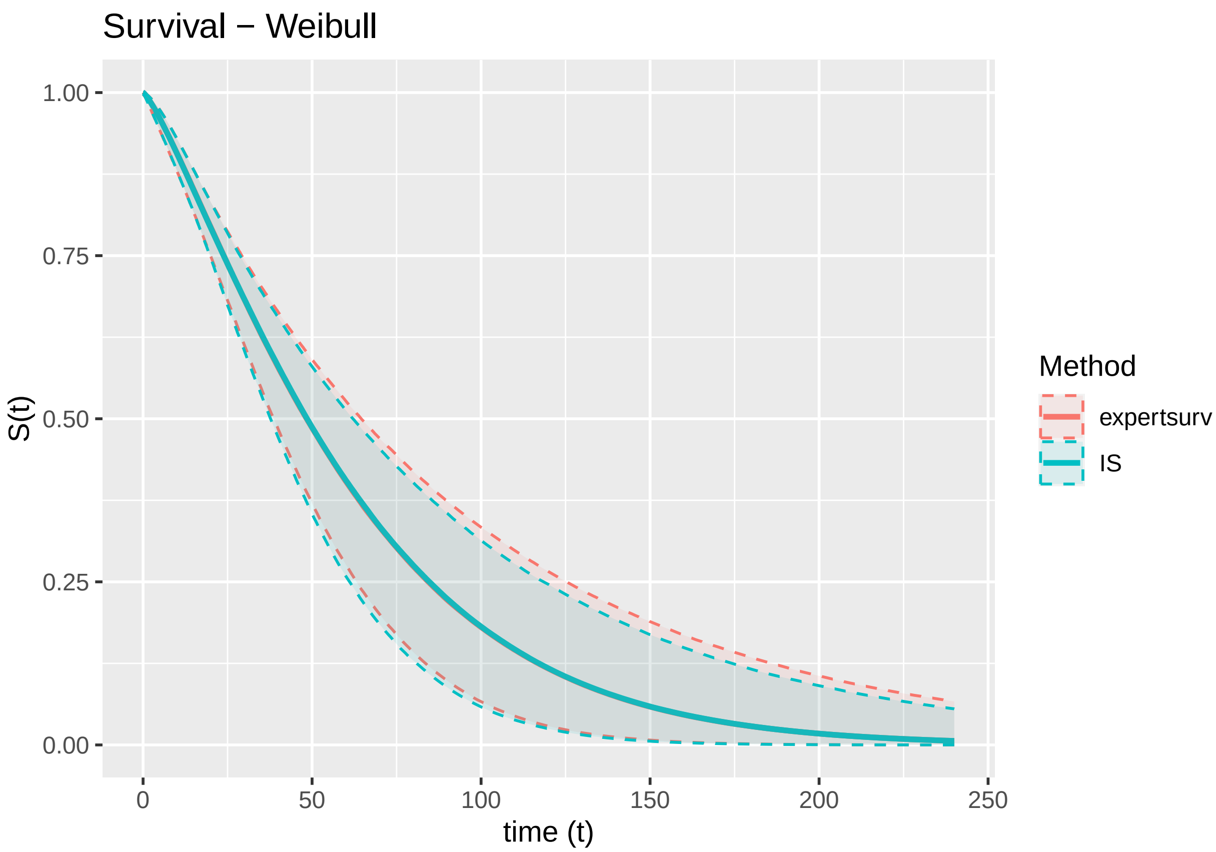

Figure 20: Survival curves (median and 95% confidence intervals) obtained by combining trial data with external information using the importance sampling (IS) and expertsurv methods, Weibull distribution

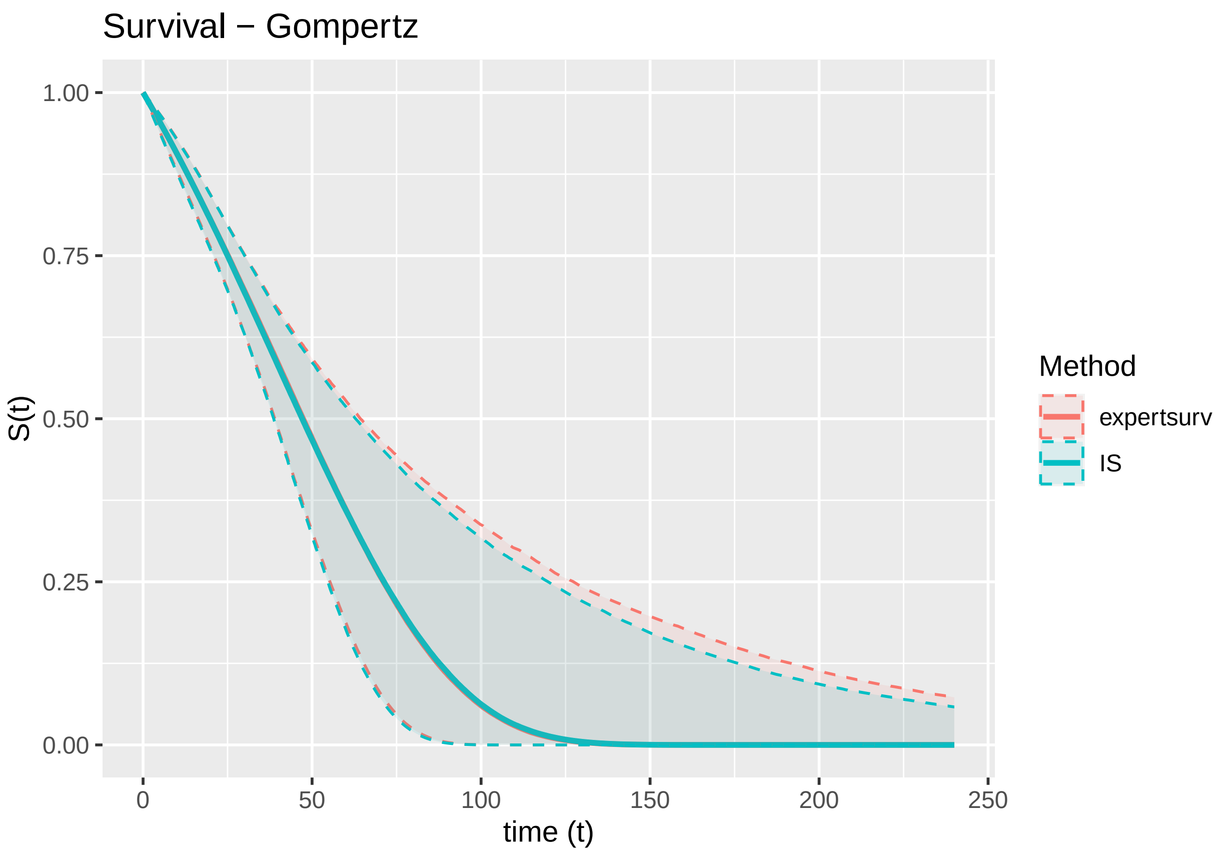

Figure 21: Survival curves (median and 95% confidence intervals) obtained by combining trial data with external information using the importance sampling (IS) and expertsurv methods, Log-normal distribution

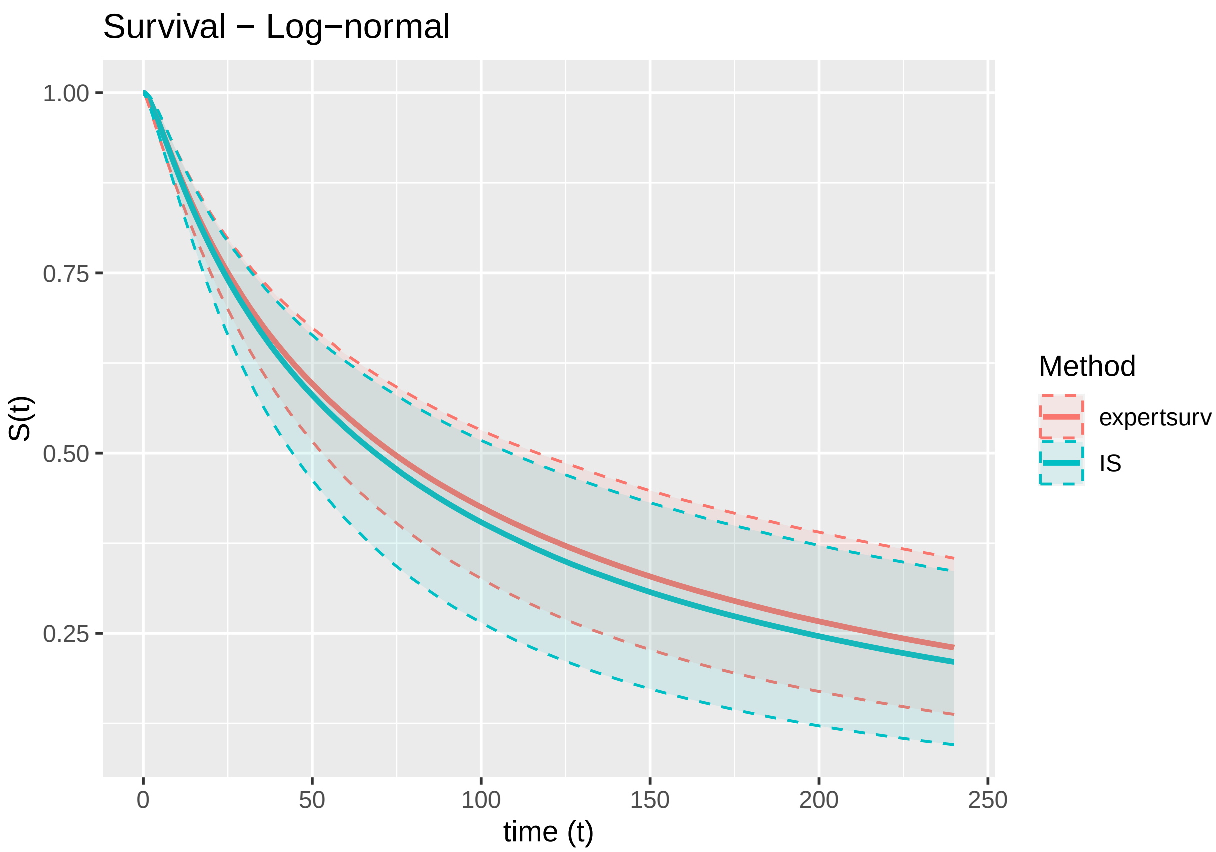

Figure 22: Survival curves (median and 95% confidence intervals) obtained by combining trial data with external information using the importance sampling (IS) and expertsurv methods, Log-logistic distribution

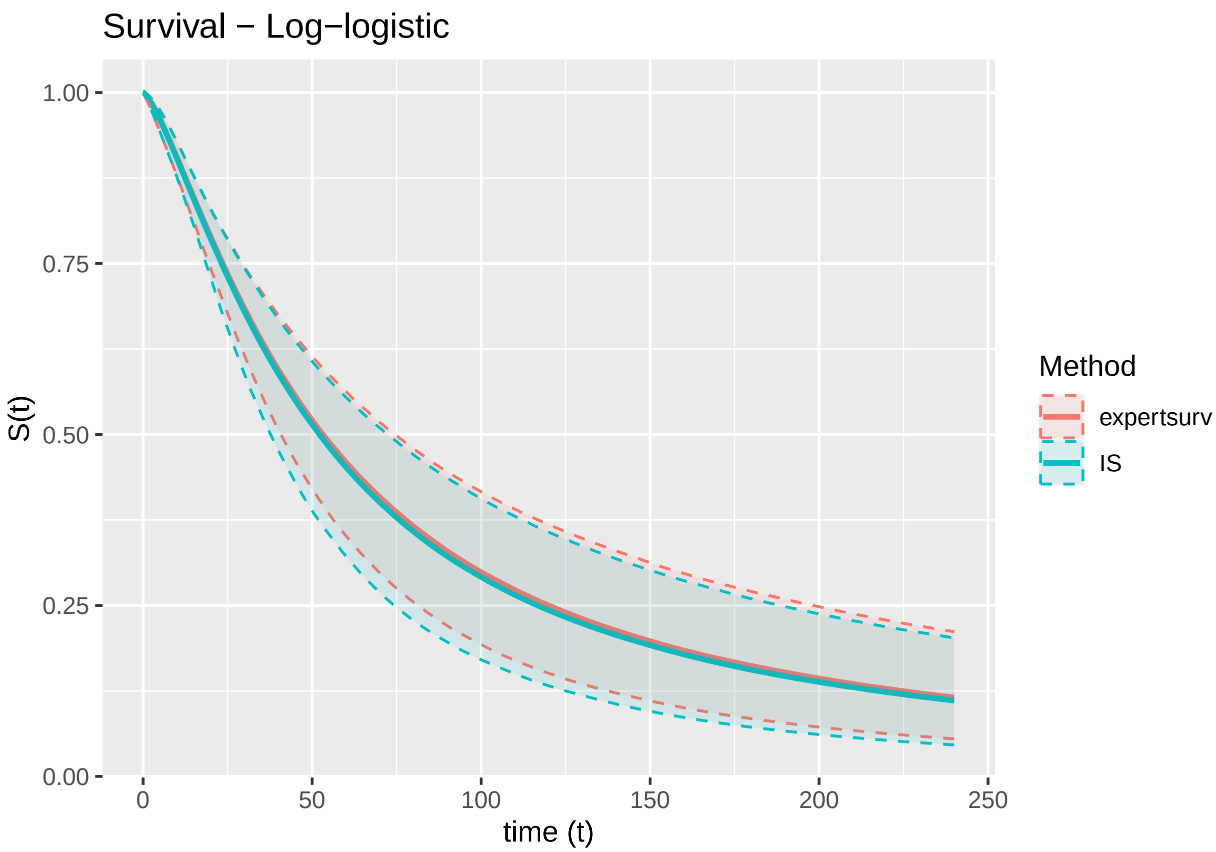

Figure 23: Survival curves (median and 95% confidence intervals) obtained by combining trial data with external information using the importance sampling (IS) and expertsurv methods, Gompertz distribution

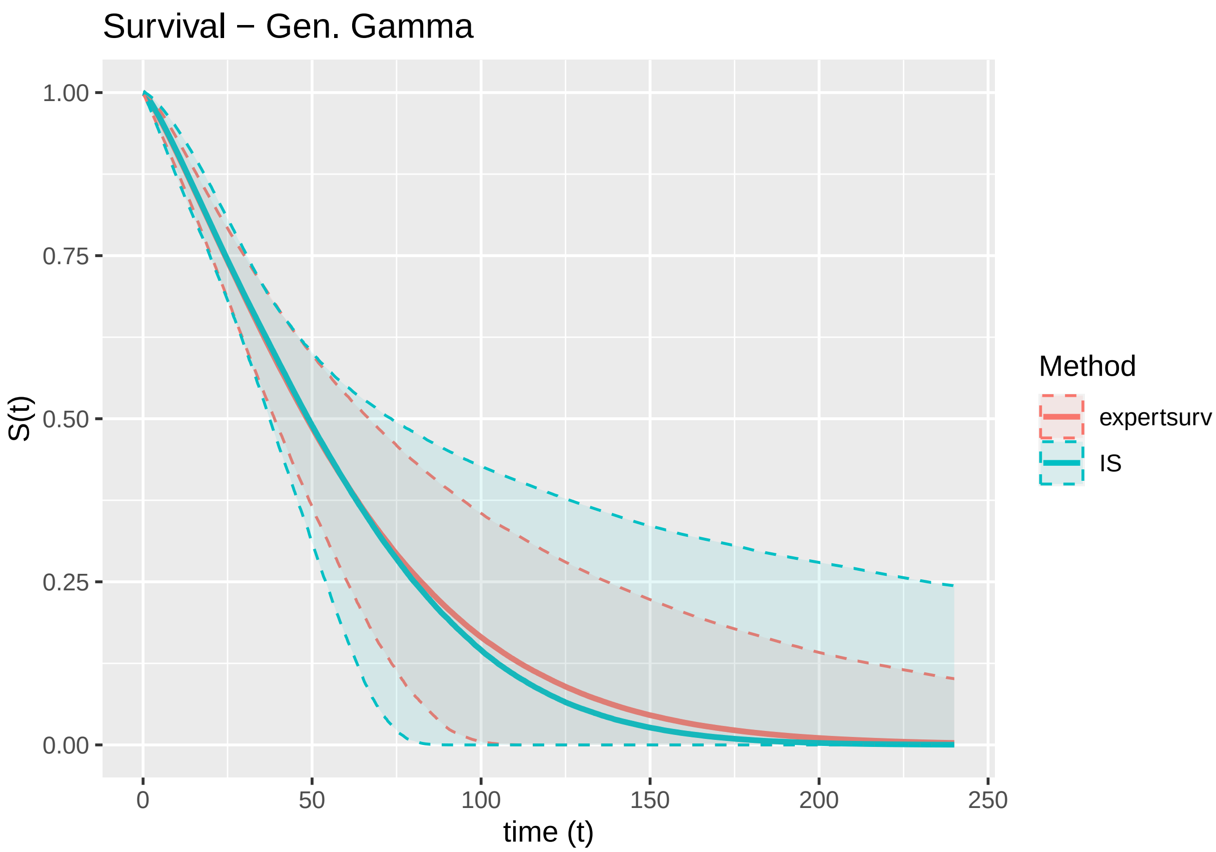

Figure 24: Survival curves (median and 95% confidence intervals) obtained by combining trial data with external information using the importance sampling (IS) and expertsurv methods, Gen. Gamma distribution

Comparisons of parameter distributions

Comparisons of survival curve parameter distributions obtained from the importance sampling method described in the paper, with those obtained from the fully Bayesian approach of Cooney & Whilte implemented in the expertsurv package.

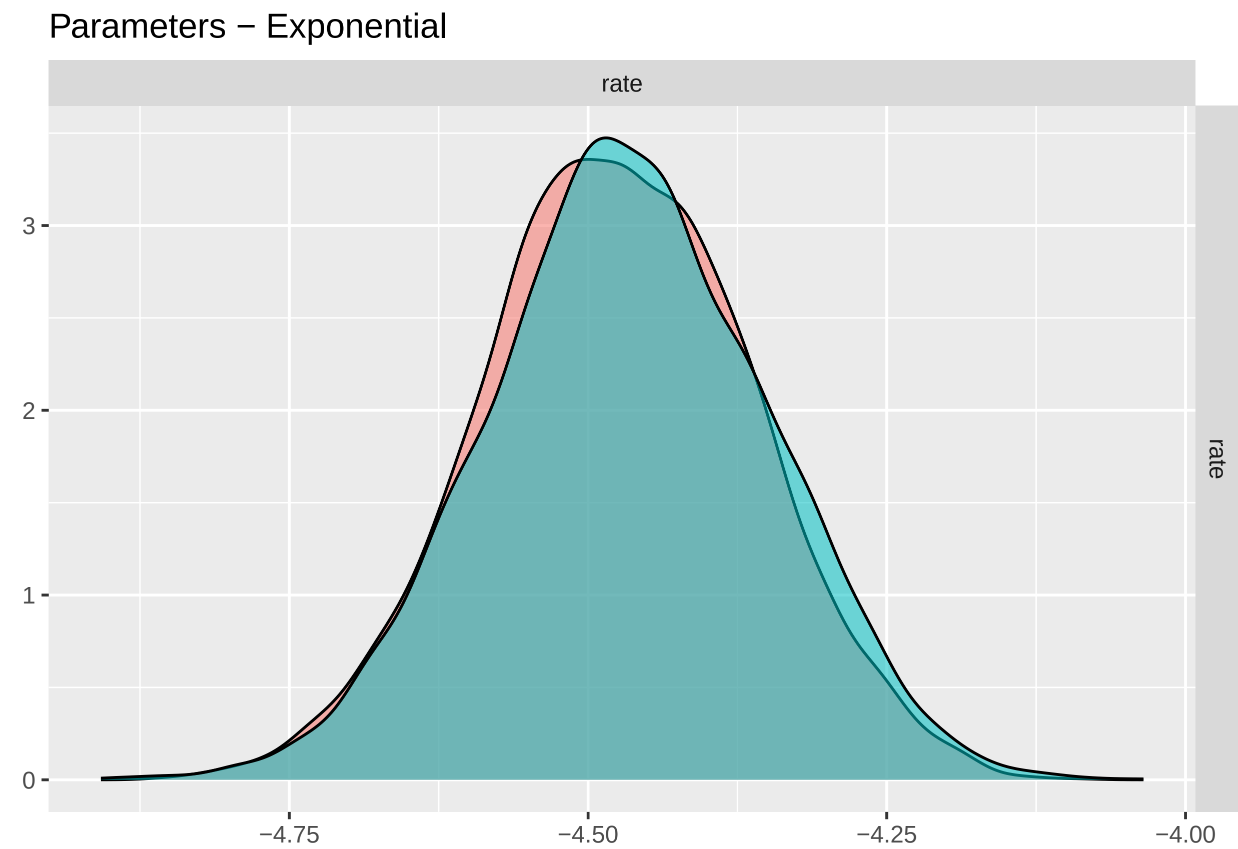

Figure 25: Survival curve parameter distributions and covariance estimates obtainedby combining trial data with external information using the importance sampling (IS) and expertsurv methods, Exponential distribution

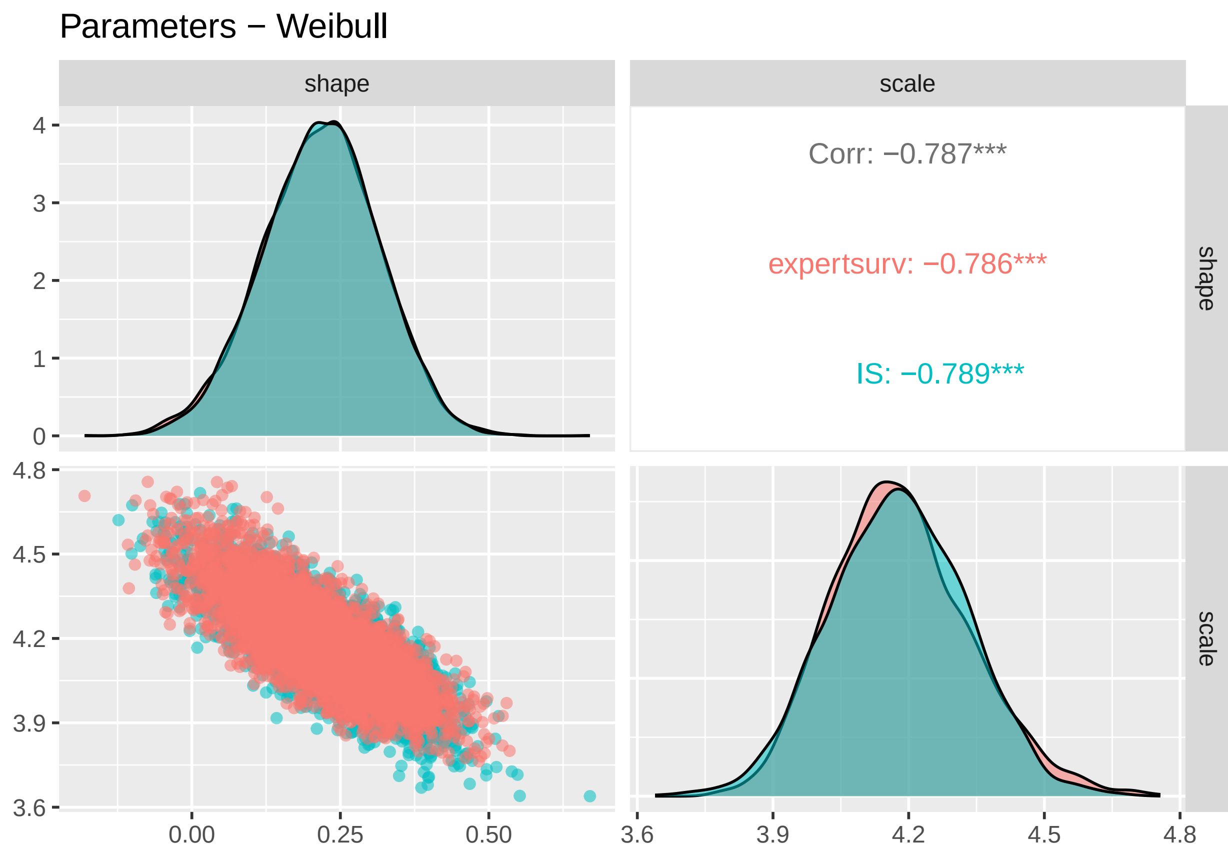

Figure 26: Survival curve parameter distributions and covariance estimates obtainedby combining trial data with external information using the importance sampling (IS) and expertsurv methods, Weibull distribution

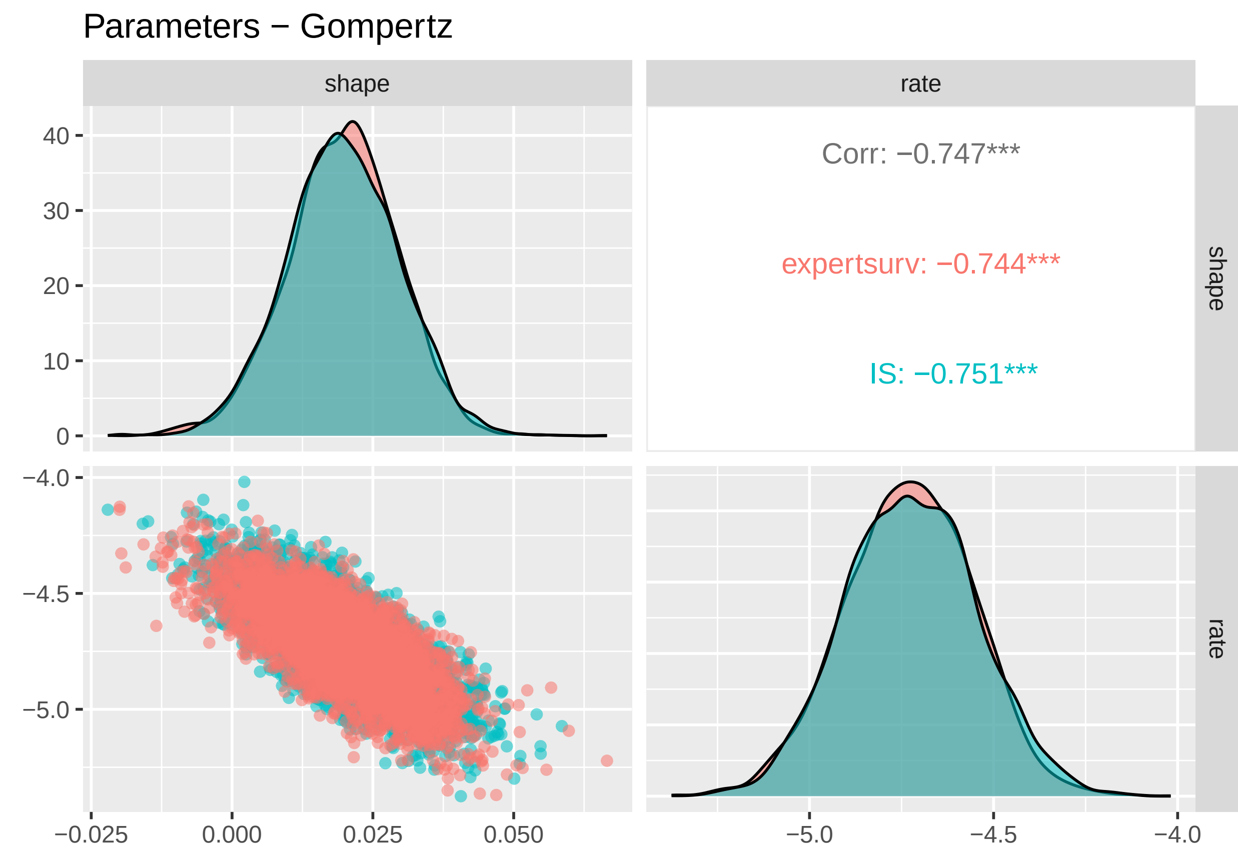

Figure 27: Survival curve parameter distributions and covariance estimates obtainedby combining trial data with external information using the importance sampling (IS) and expertsurv methods, Log-normal distribution

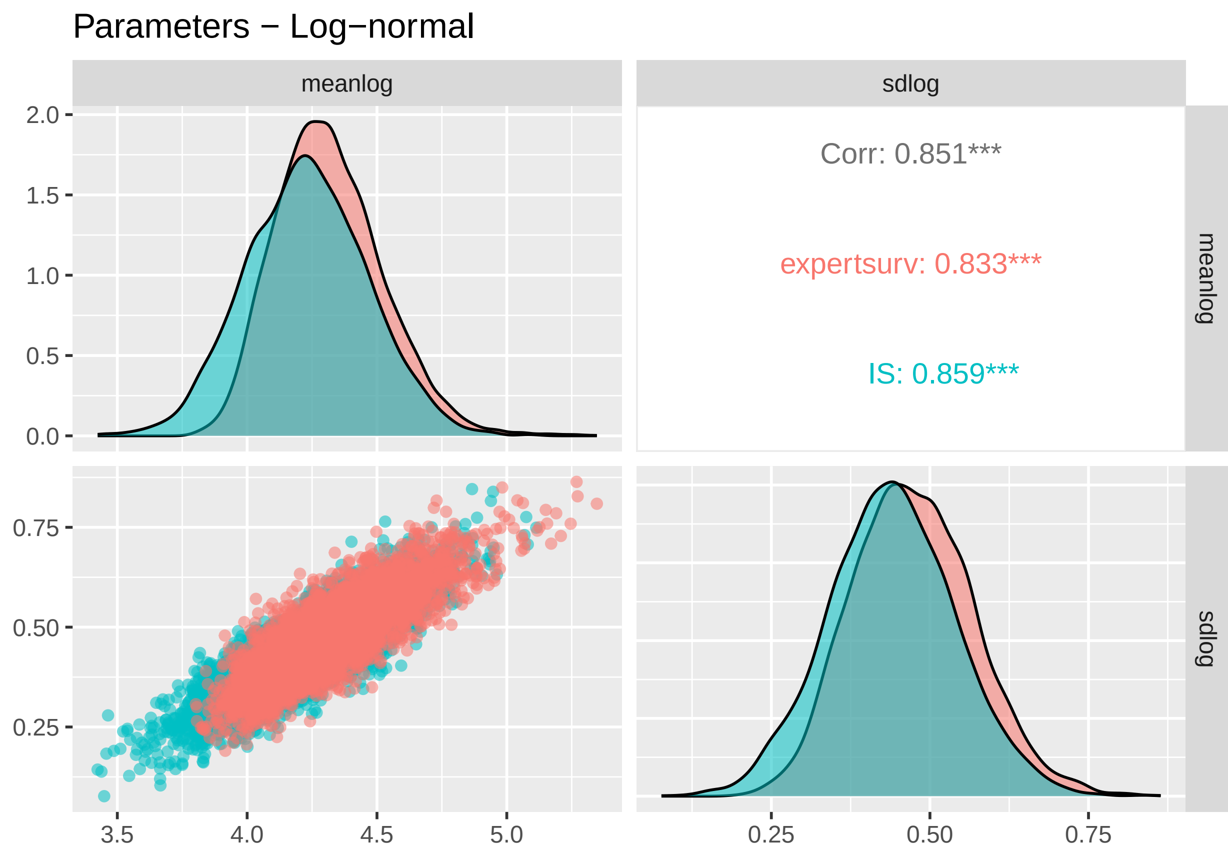

Figure 28: Survival curve parameter distributions and covariance estimates obtainedby combining trial data with external information using the importance sampling (IS) and expertsurv methods, Log-logistic distribution

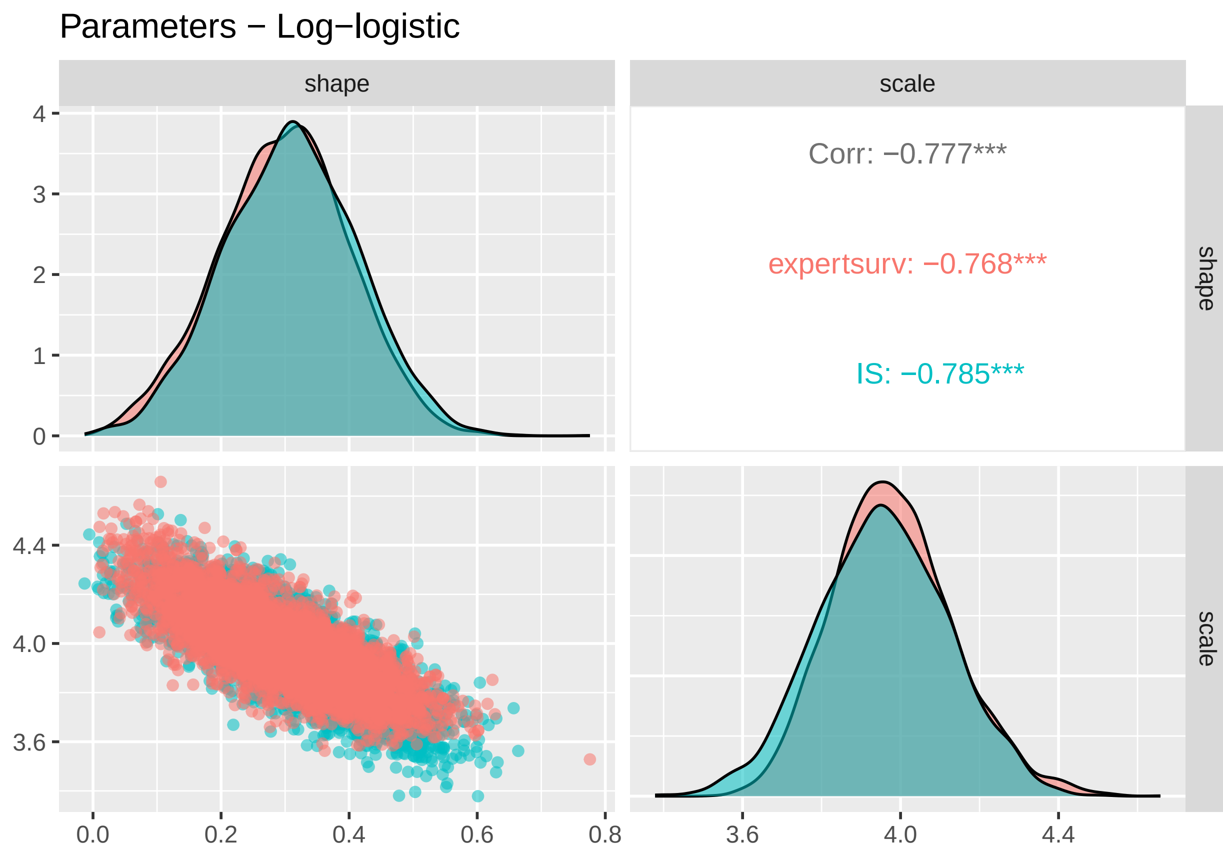

Figure 29: Survival curve parameter distributions and covariance estimates obtainedby combining trial data with external information using the importance sampling (IS) and expertsurv methods, Gompertz distribution

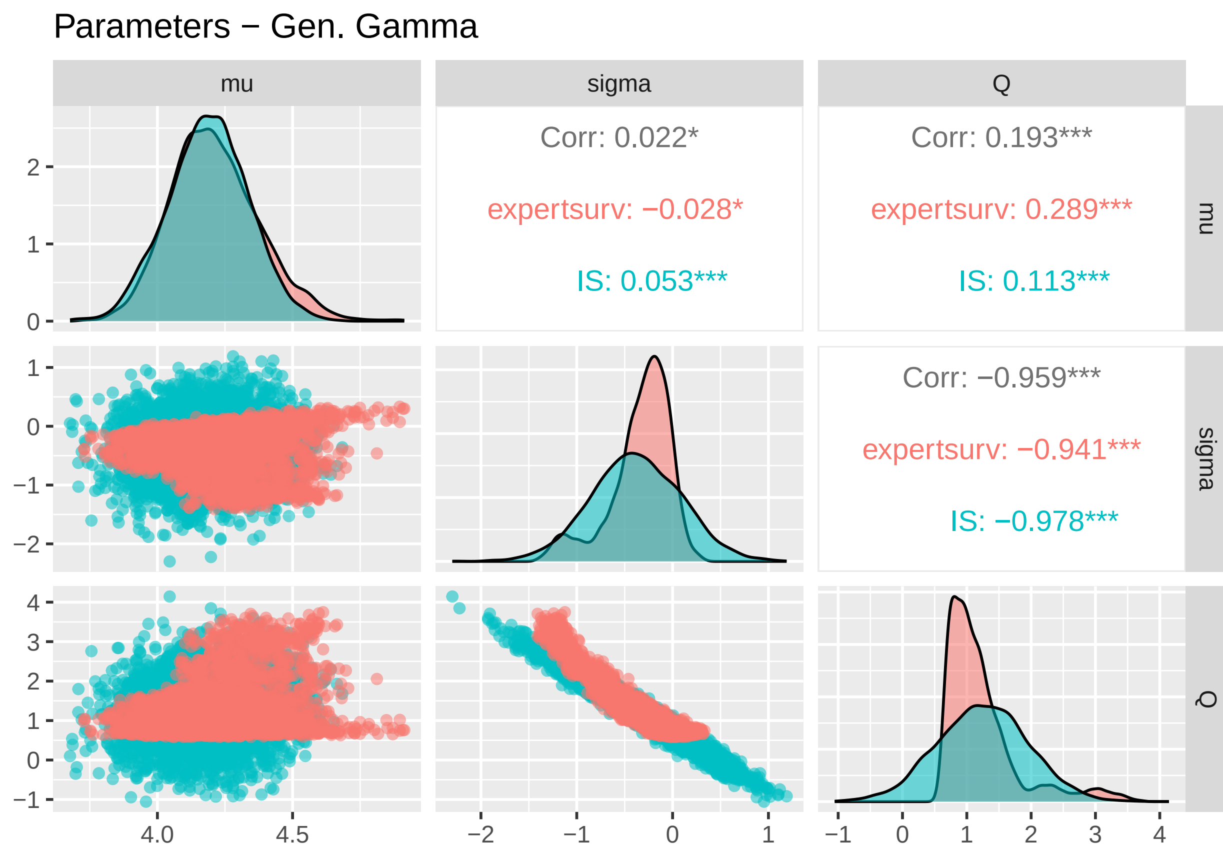

Figure 30: Survival curve parameter distributions and covariance estimates obtainedby combining trial data with external information using the importance sampling (IS) and expertsurv methods, Gen. Gamma distribution

Comparisons of AUC distributions

Area under the curve measures mean survival extrapolated over a lifetime (in these examples survival is capped at 100 years since some curves plateau).

Table 14: Comparison of probabilistic total area under the curve (mean lifetime OS) estimates, obtained from combining trial data with external information using the importance sampling (IS) method described in the paper, and with the fully Bayesian method of Cooney and White implemented in the expertsurv package. Values shown are probabilstic mean and 95% confidence/credible intervals.

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

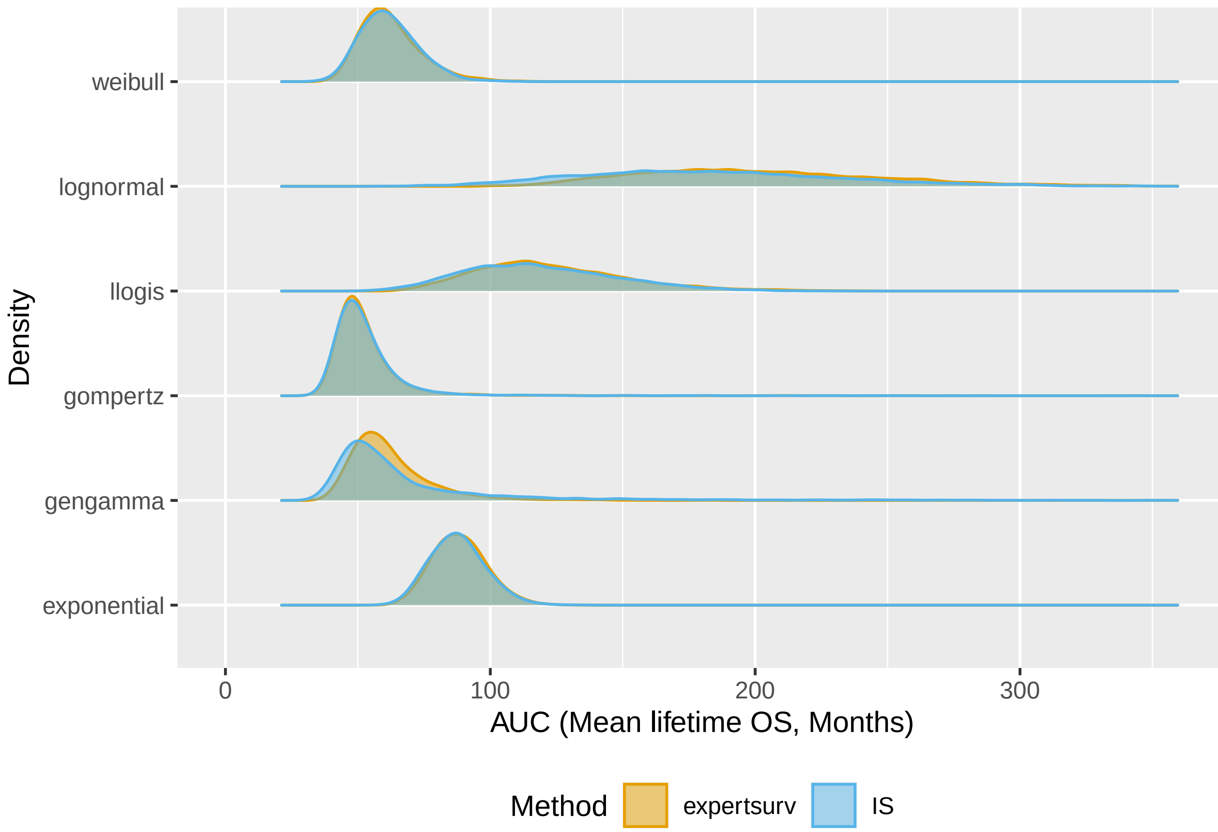

Figure 31: Density plots comparing probabilistic total area under the curve (mean OS) distributions obtained from combining trial data with external information using the importance sampling (IS) method described in the paper, with those obtained from the fully Bayesian method of Cooney and White implemented in the expertsurv package.

Comparisons of 5-year OS

Given that the external information concerns OS at 5 years, we compare estimates of 5-year OS obtained from the two methods.

Table 15: Comparison of 5-year OS estimates, obtained from combining trial data with external information using the importance sampling (IS) method described in the paper, with the fully Bayesian method of Cooney and White implemented in the expertsurv package.

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%

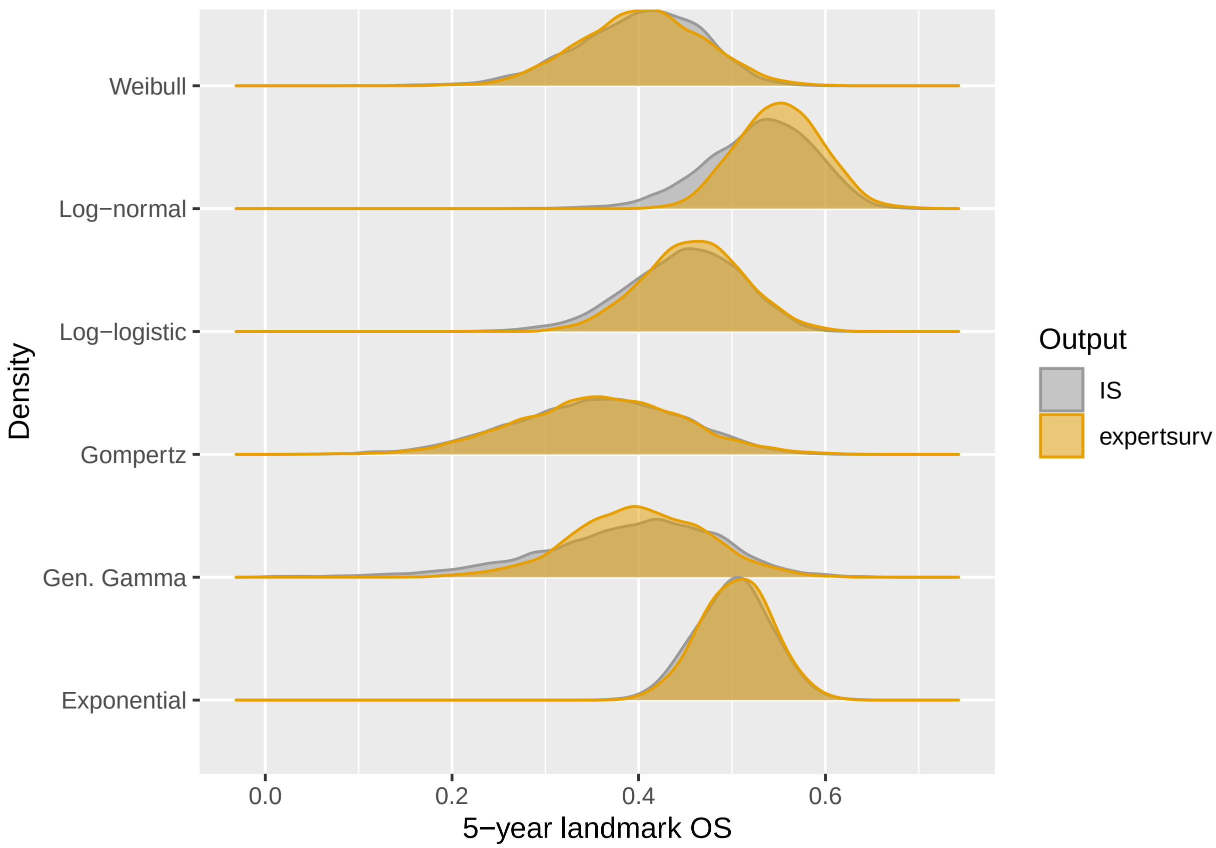

Figure 32: Density plots comparing 5-year OS estimates, obtained from combining trial data with external information using the importance sampling (IS) method described in the paper, with those obtained from the fully Bayesian method of Cooney and White implemented in the expertsurv package.