# 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`.

Table 1: Parameter estimates obtained via MLE: Exponential

| x |
|---|
| -4.562874 |

Table 2: Covariance matrix obtained via MLE: Exponential

| | rate |
|---|---|
| rate | 0.0169491 |

Table 3: Parameter estimates obtained via Importance Sampling: Exponential

| x |
|---|
| -4.467088 |

Table 4: Covariance matrix obtained via Importance Sampling: Exponential

| |
|---|
| 0.0138444 |

Table 5: Parameter estimates obtained via MLE: Weibull

| | x |
|---|---|
| shape | 0.2028128 |
| scale | 4.2127617 |

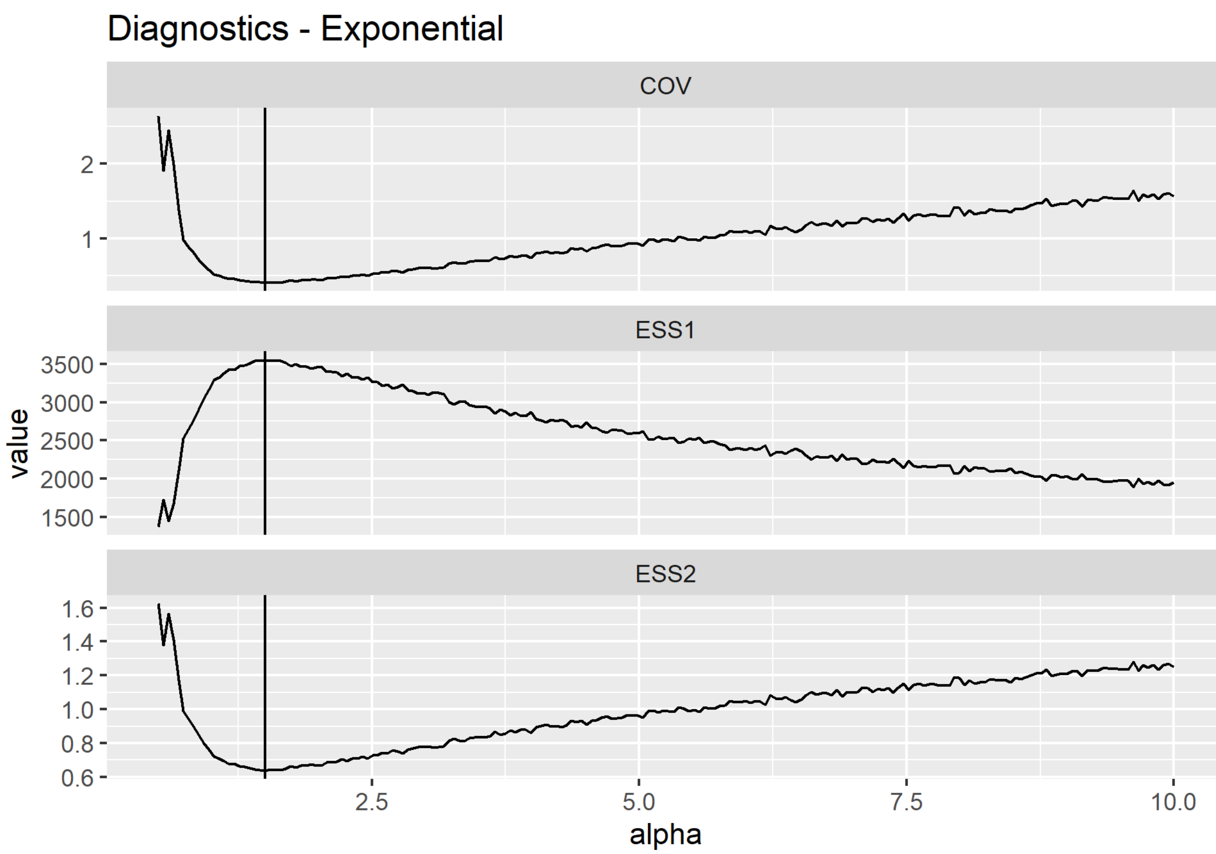


Figure 1: Importance sampling diagnostics: coefficient of variation (COV) and effective sample size (ESS) as functions of the tempering parameter alpha, Exponential distribution. The vertical line shows the optimal value of alpha identified by the algorithm.

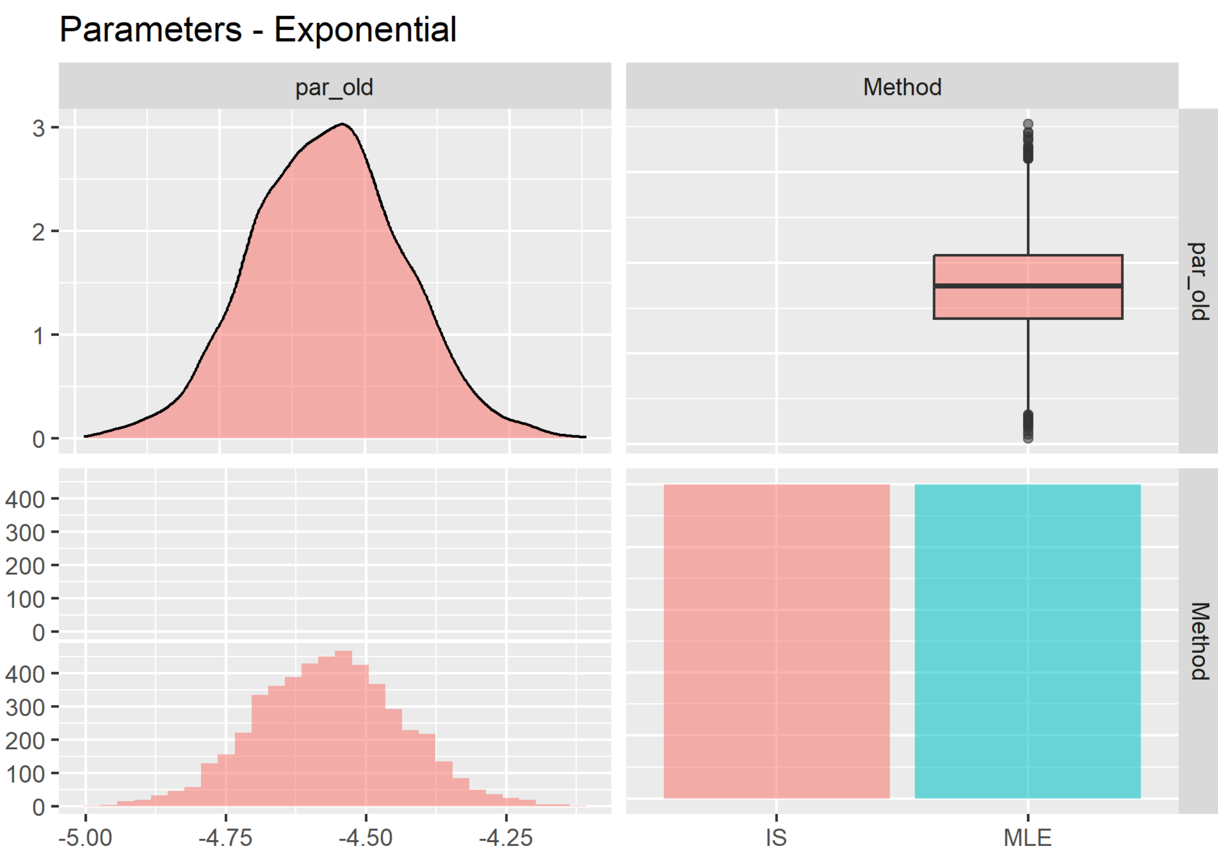


Figure 2: Survival curve parameter distributions and covariance estimates obtained using trial data only (MLE) and combining trial data with external information (IS), Exponential distribution

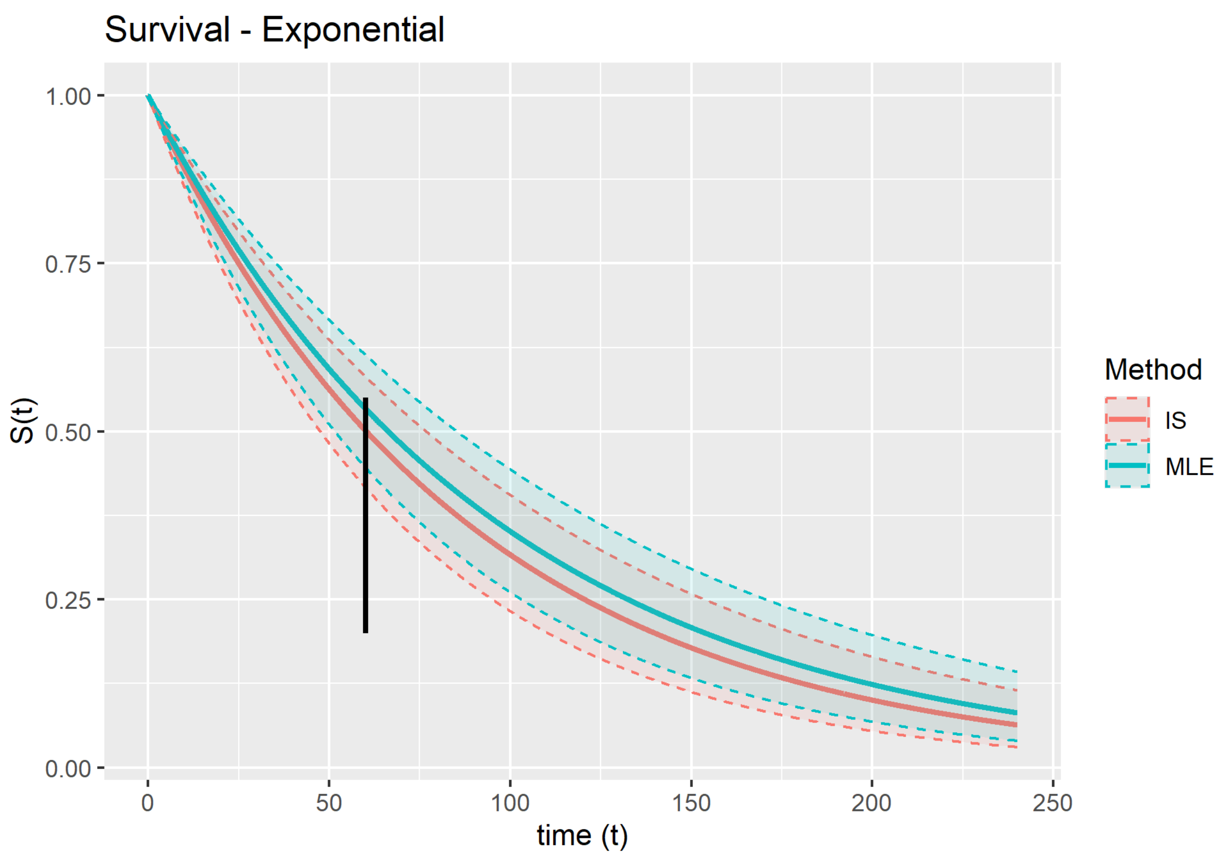


Figure 3: Survival curves (median and 95% confidence intervals) obtained using trial data only (MLE) and combining trial data with external information (IS), Exponential distribution

Table 6: Covariance matrix obtained via MLE: Weibull

| | shape | scale |
|---|---|---|
| shape | 0.0147844 | -0.0228526 |
| scale | -0.0228526 | 0.0466213 |

Table 7: Parameter estimates obtained via Importance Sampling: Weibull

| | x |
|---|---|
| shape | 0.2199019 |
| scale | 4.1750757 |

Table 8: Covariance matrix obtained via Importance Sampling: Weibull

| | shape | scale |
|---|---|---|
| shape | 0.0094518 | -0.0118402 |
| scale | -0.0118402 | 0.0235769 |

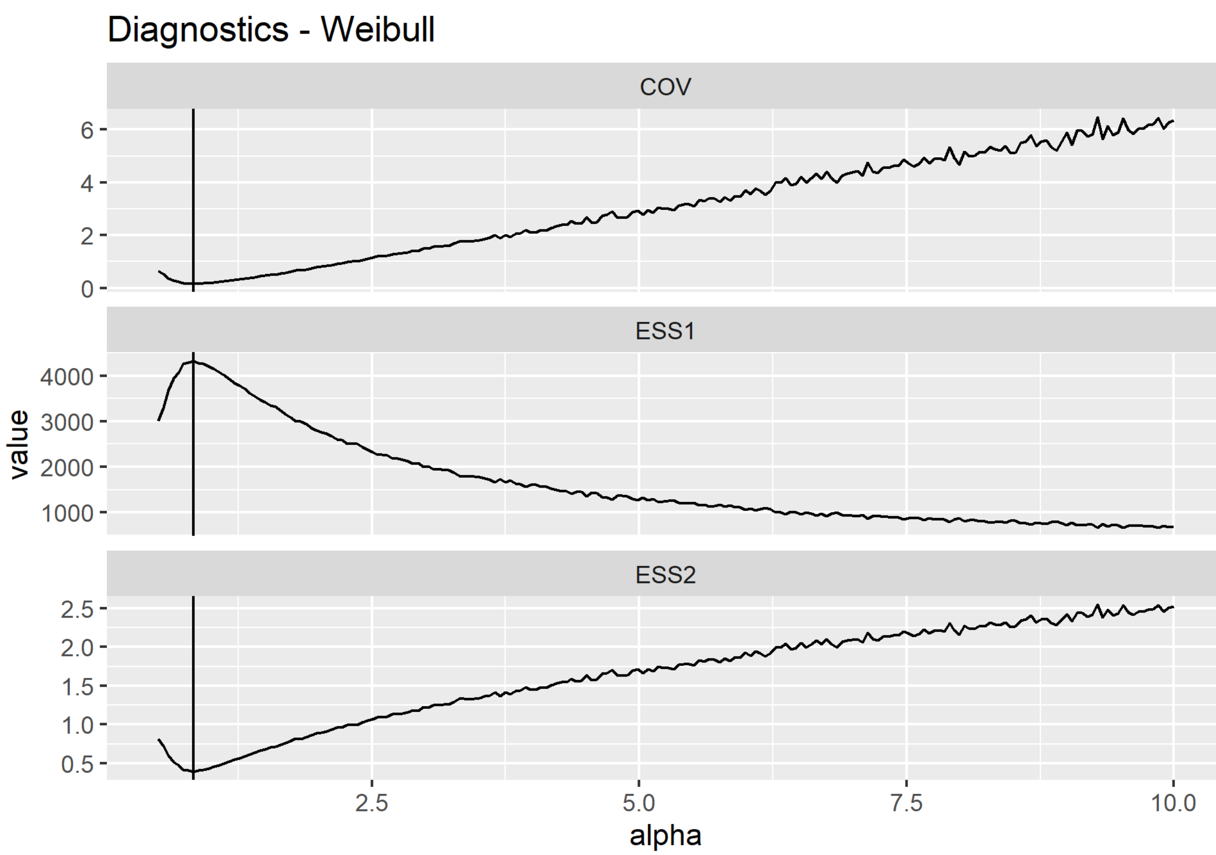


Figure 4: Importance sampling diagnostics: coefficient of variation (COV) and effective sample size (ESS) as functions of the tempering parameter alpha, Weibull distribution. The vertical line shows the optimal value of alpha identified by the algorithm.

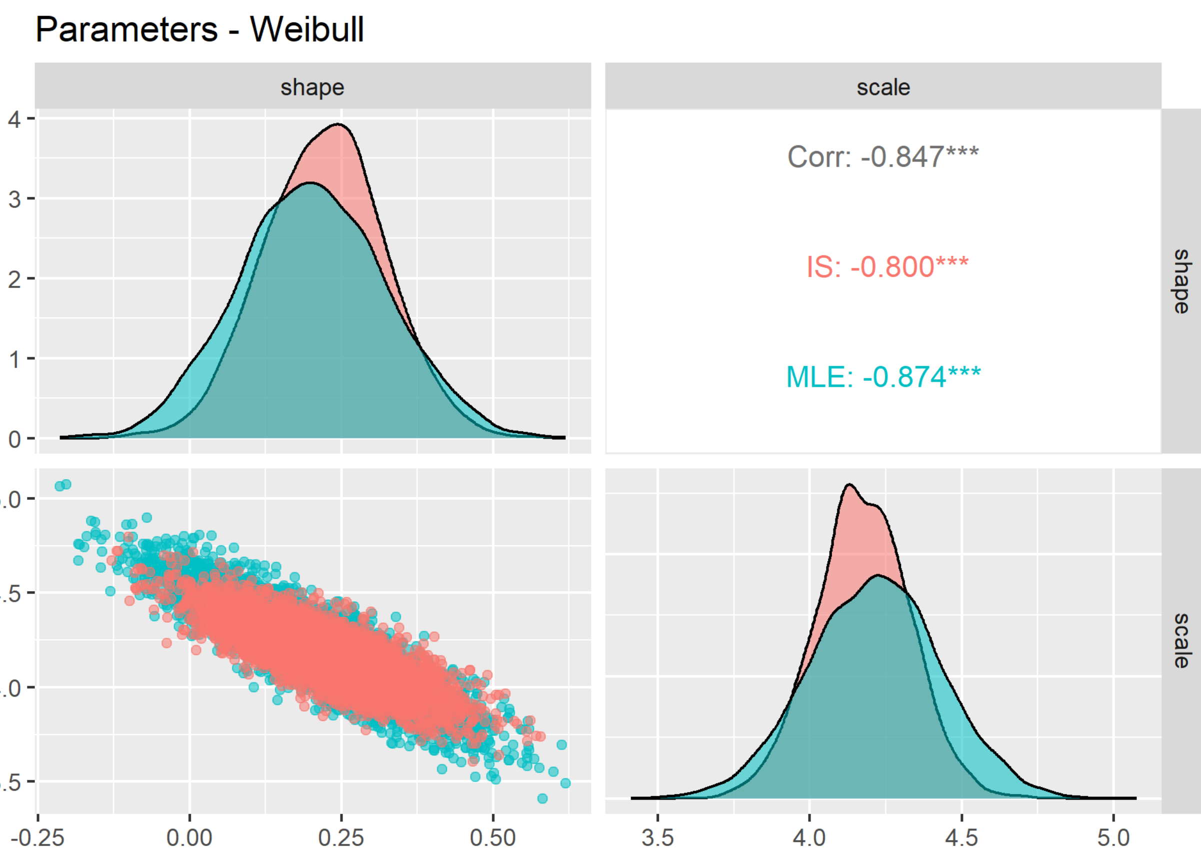


Figure 5: Survival curve parameter distributions and covariance estimates obtained using trial data only (MLE) and combining trial data with external information (IS), Weibull distribution

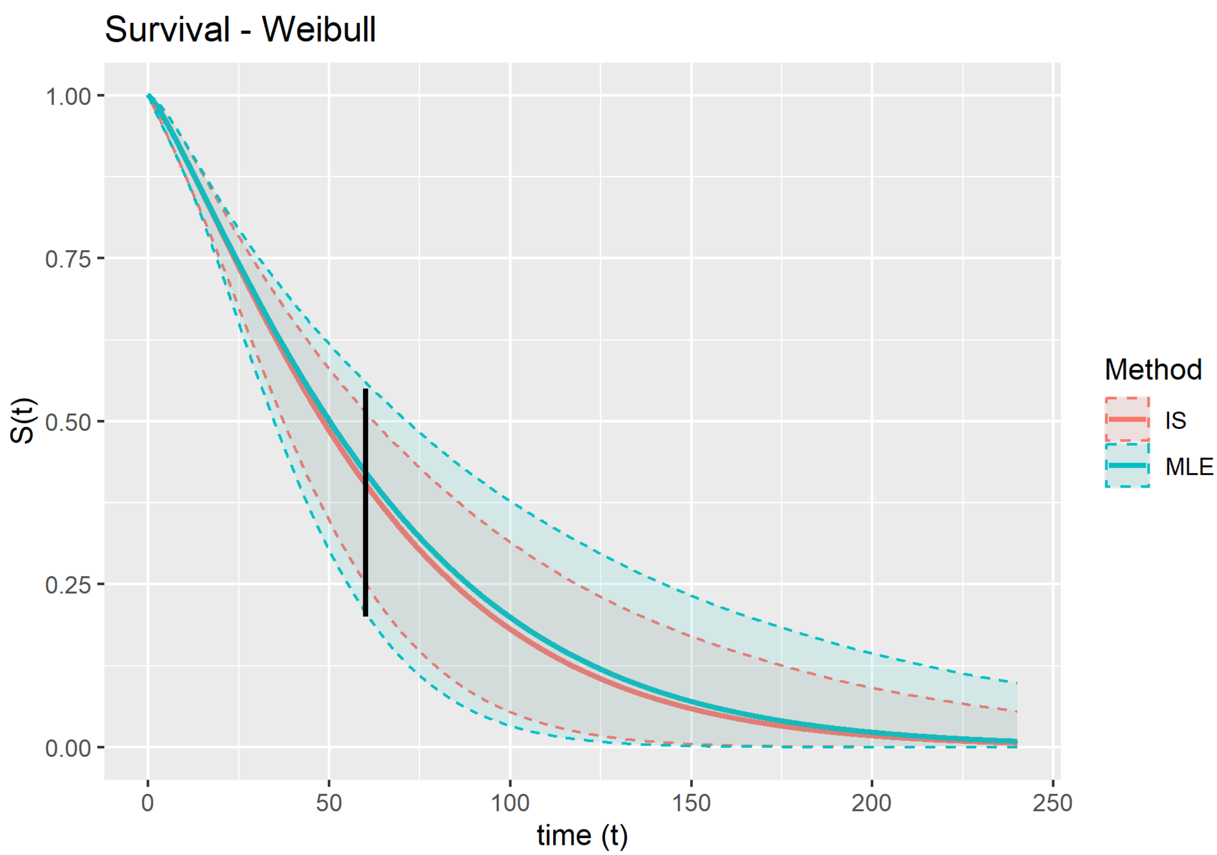


Figure 6: Survival curves (median and 95% confidence intervals) obtained using trial data only (MLE) and combining trial data with external information (IS), Weibull distribution

Table 9: Parameter estimates obtained via MLE: Gompertz

| | x |
|---|---|
| shape | 0.0389625 |
| rate | -4.8682858 |

Table 10: Covariance matrix obtained via MLE: Gompertz

| | shape | rate |
|---|---|---|
| shape | 0.0006747 | -0.0056125 |
| rate | -0.0056125 | 0.0636359 |

Table 11: Parameter estimates obtained via Importance Sampling: Gompertz

| | x |
|---|---|
| shape | 0.0197027 |
| rate | -4.7220927 |

Table 12: Covariance matrix obtained via Importance Sampling: Gompertz

| | shape | rate |
|---|---|---|
| shape | 0.0000970 | -0.0013281 |
| rate | -0.0013281 | 0.0316264 |

Table 13: Parameter estimates obtained via MLE: Log-normal

| | x |
|---|---|
| meanlog | 4.5379239 |
| sdlog | 0.5475716 |

Table 14: Covariance matrix obtained via MLE: Log-normal

| | meanlog | sdlog |
|---|---|---|
| meanlog | 0.0696811 | 0.0247171 |
| sdlog | 0.0247171 | 0.0114622 |

Table 15: Parameter estimates obtained via Importance Sampling: Log-normal

| | x |
|---|---|
| meanlog | 4.2299230 |
| sdlog | 0.4404943 |

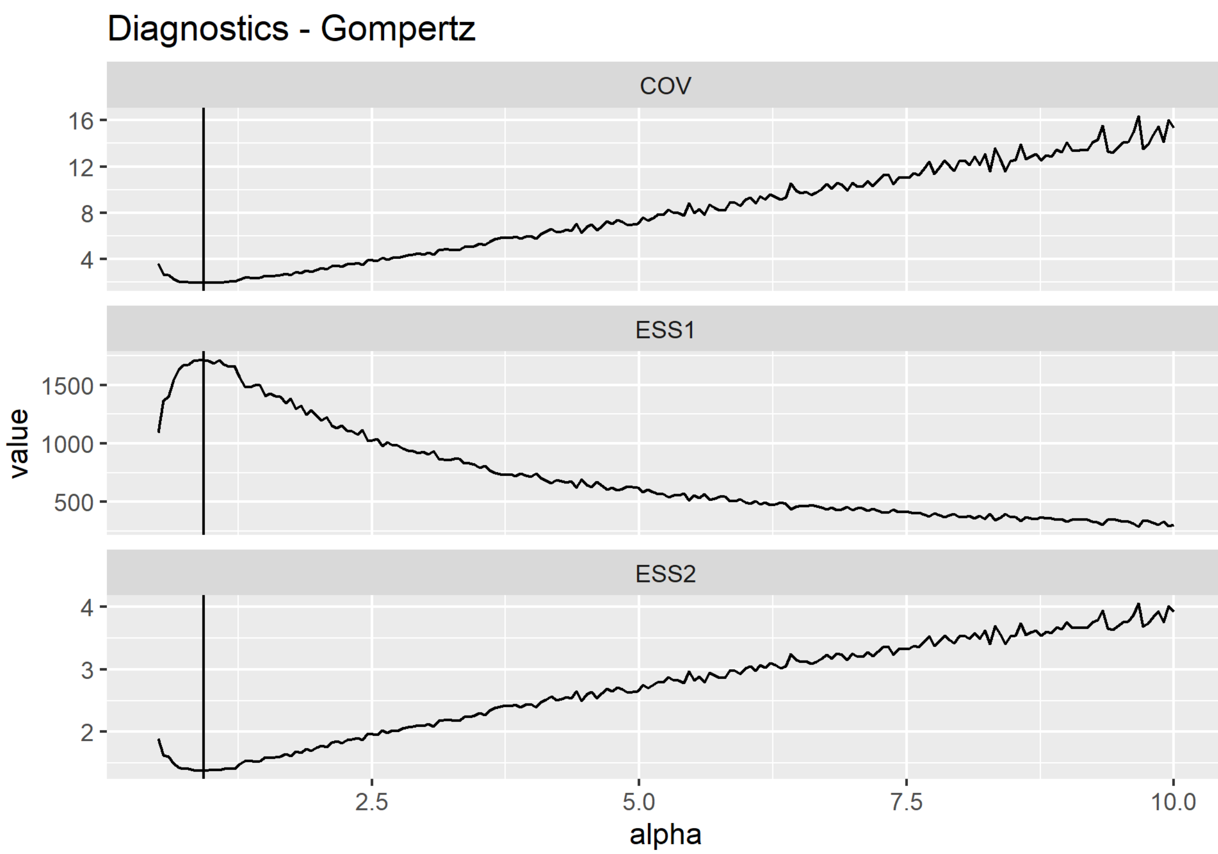


Figure 7: Importance sampling diagnostics: coefficient of variation (COV) and effective sample size (ESS) as functions of the tempering parameter alpha, Log-normal distribution. The vertical line shows the optimal value of alpha identified by the algorithm.

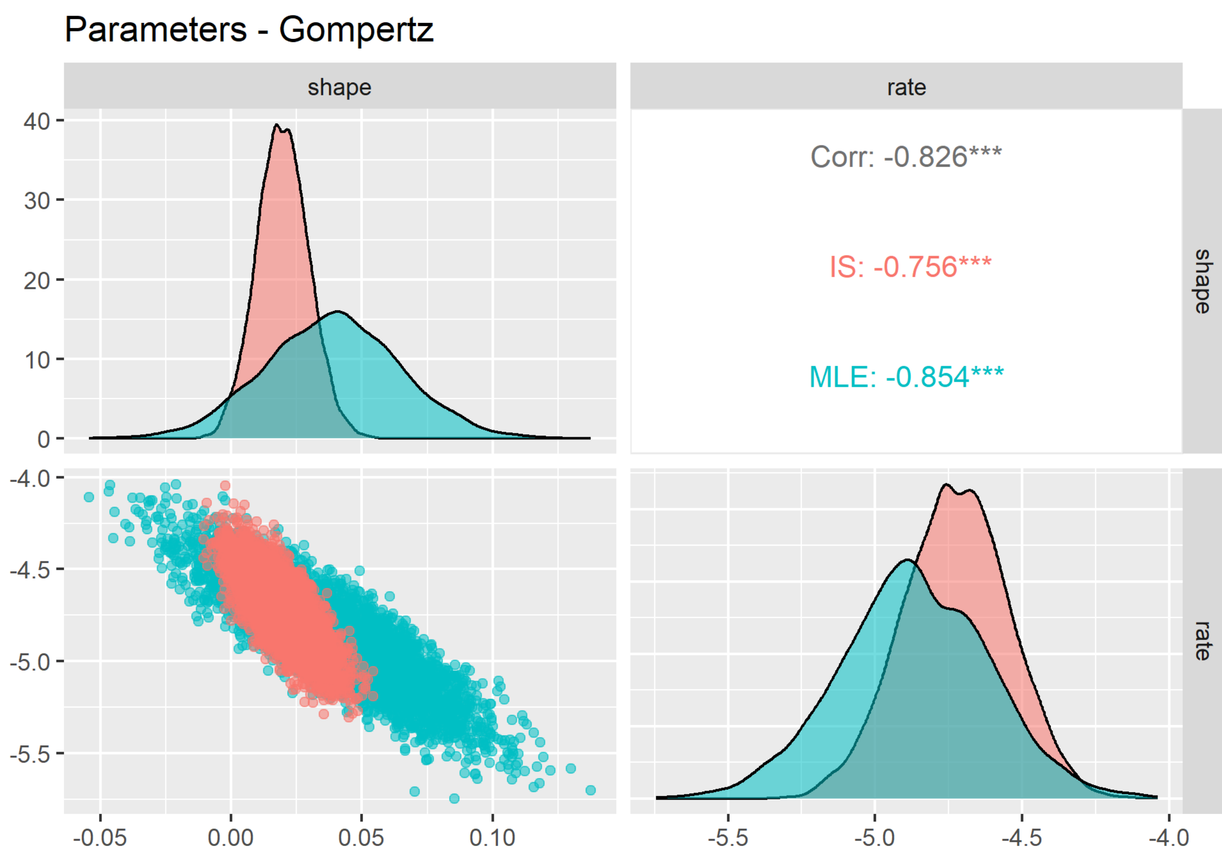


Figure 8: Survival curve parameter distributions and covariance estimates obtained using trial data only (MLE) and combining trial data with external information (IS), Log-normal distribution

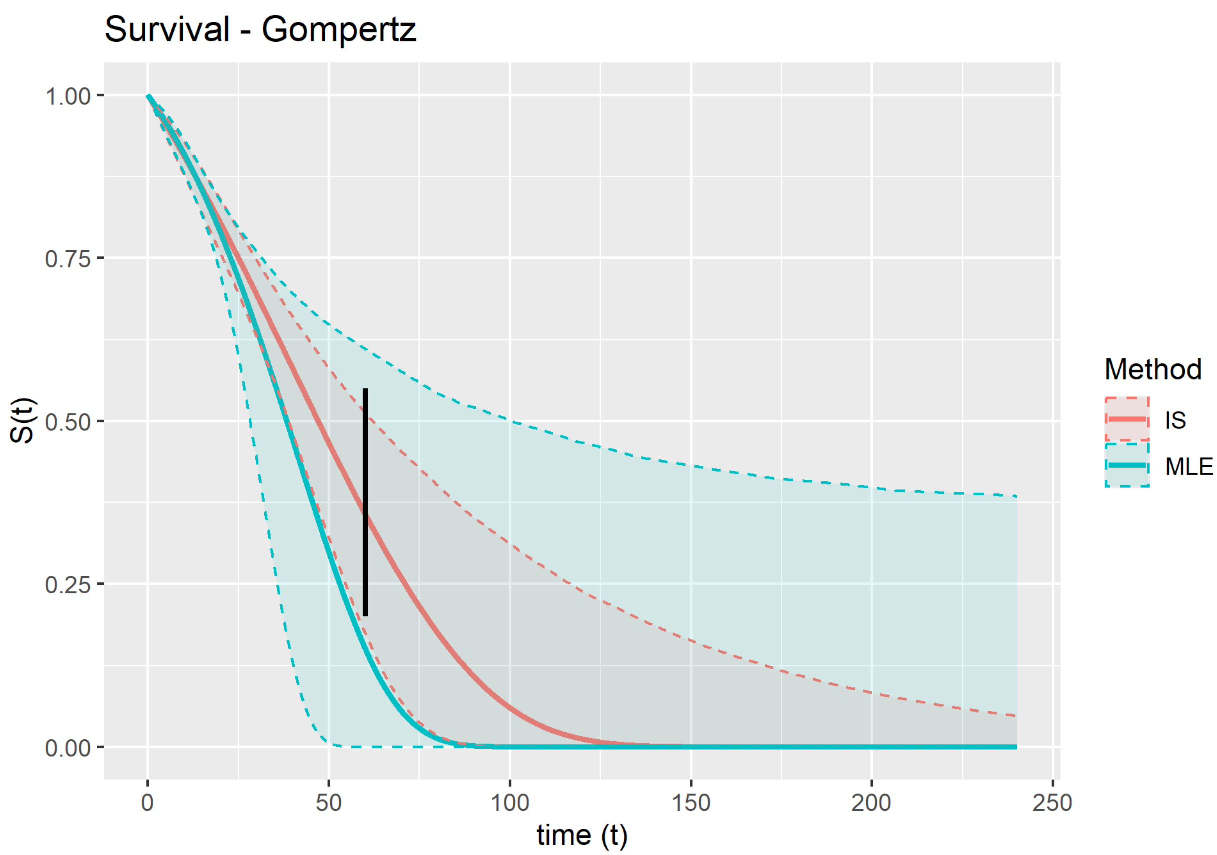


Figure 9: Survival curves (median and 95% confidence intervals) obtained using trial data only (MLE) and combining trial data with external information (IS), Log-normal distribution

Table 16: Covariance matrix obtained via Importance Sampling: Log-normal

| | meanlog | sdlog |
|---|---|---|
| meanlog | 0.0545435 | 0.0201378 |
| sdlog | 0.0201378 | 0.0100655 |

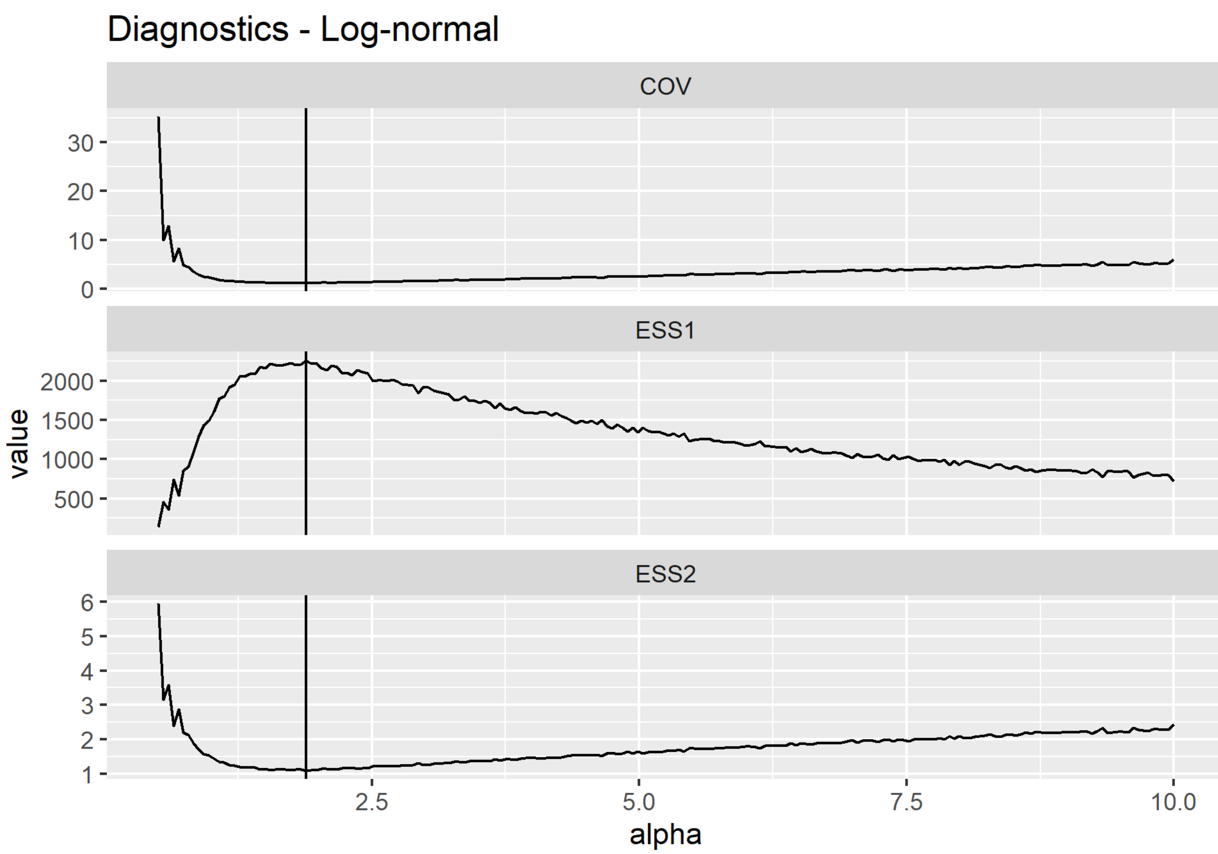


Figure 10: Importance sampling diagnostics: coefficient of variation (COV) and effective sample size (ESS) as functions of the tempering parameter alpha, Log-logistic distribution. The vertical line shows the optimal value of alpha identified by the algorithm.

Table 17: Parameter estimates obtained via MLE: Log-logistic

| | x |
|---|---|
| shape | 0.2450539 |
| scale | 4.0866467 |

Table 18: Covariance matrix obtained via MLE: Log-logistic

| | shape | scale |
|---|---|---|
| shape | 0.0144928 | -0.0213001 |
| scale | -0.0213001 | 0.0434079 |

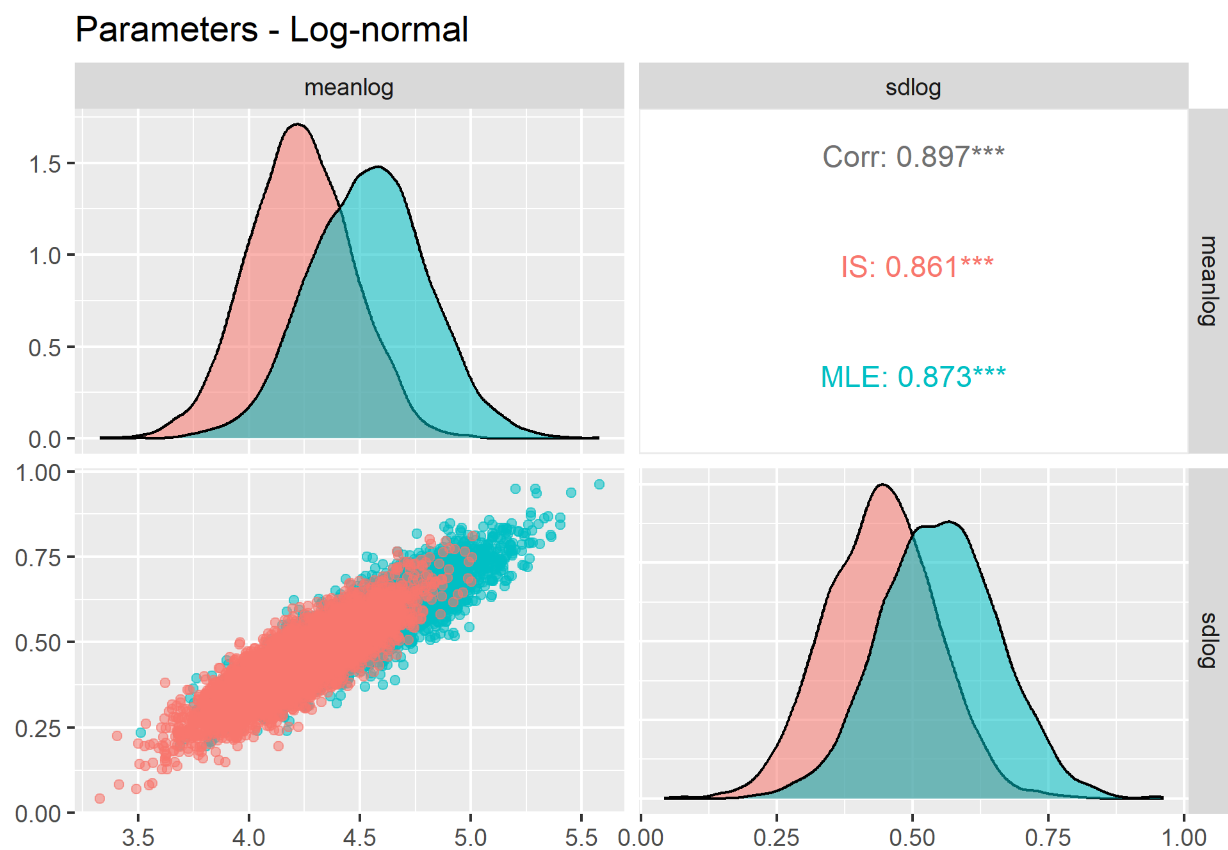


Figure 11: Survival curve parameter distributions and covariance estimates obtained using trial data only (MLE) and combining trial data with external information (IS), Log-logistic distribution

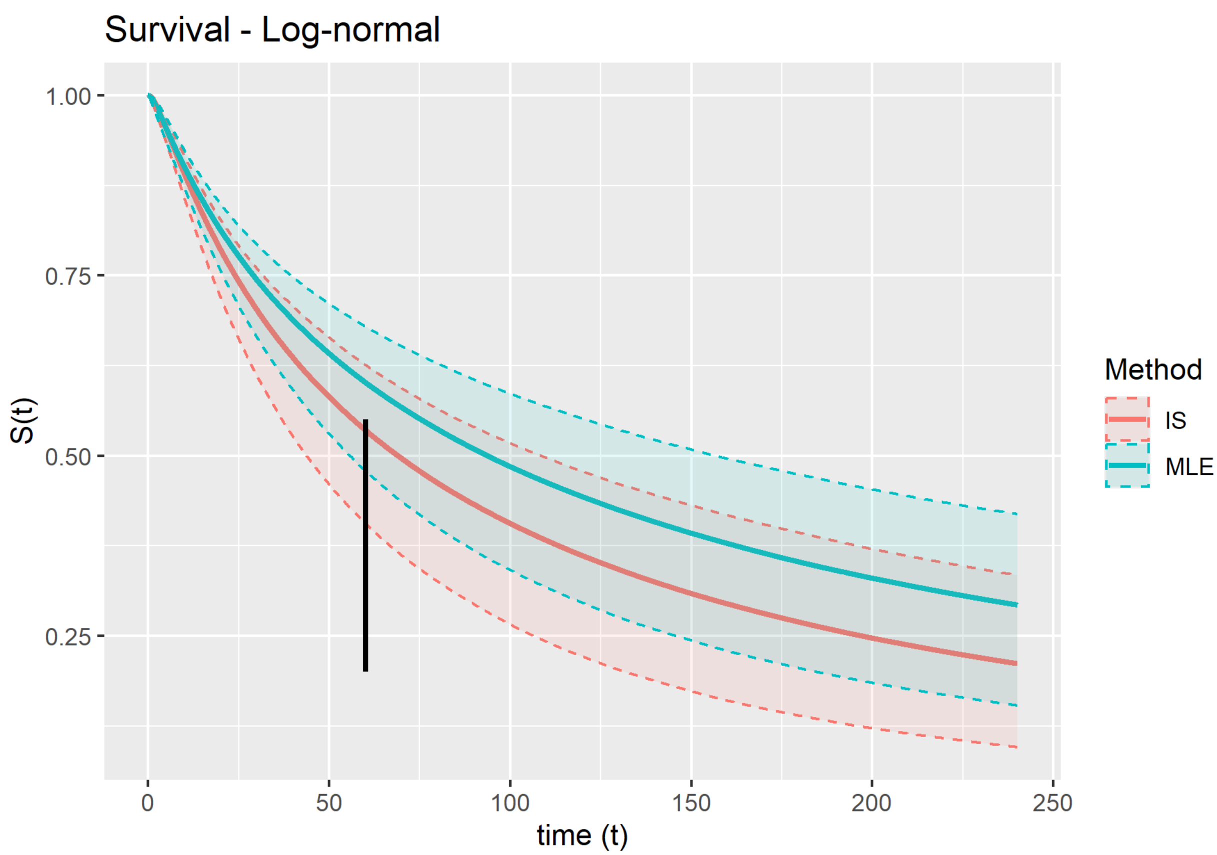


Figure 12: Survival curves (median and 95% confidence intervals) obtained using trial data only (MLE) and combining trial data with external information (IS), Log-logistic distribution

Table 19: Parameter estimates obtained via Importance Sampling: Log-logistic

| | x |
|---|---:|
| shape | 0.3103417 |
| scale | 3.9558382 |

Table 20: Covariance matrix obtained via Importance Sampling: Log-logistic

| | shape | scale |
|---|---:|---:|
| shape | 0.0111243 | -0.0139385 |
| scale | -0.0139385 | 0.0276608 |

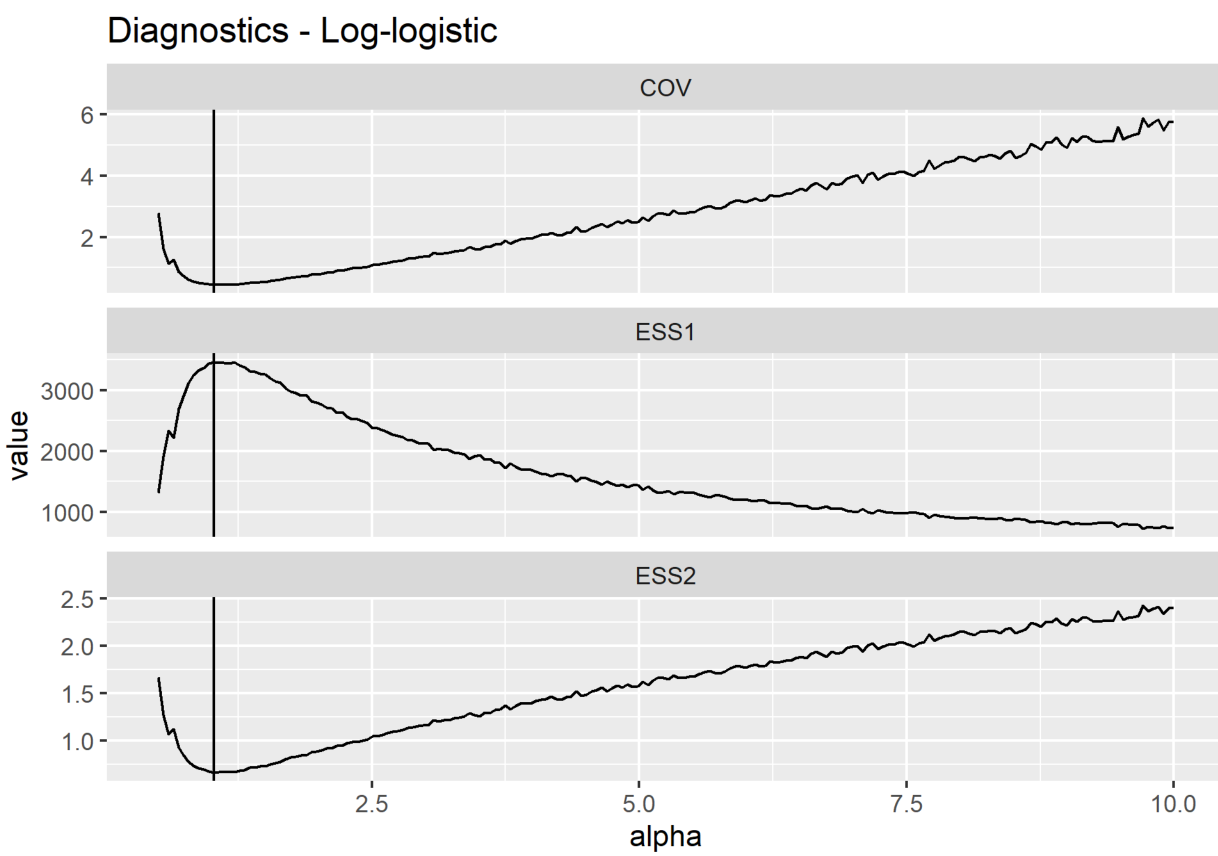


Figure 13: Importance sampling diagnostics: coefficient of variation (COV) and effective sample size (ESS) as functions of the tempering parameter alpha, Gompertz distribution. The vertical line shows the optimal value of alpha identified by the algorithm.

Table 21: Parameter estimates obtained via MLE: Gen. Gamma

| | x |
|---|---:|
| mu | 4.1703317 |
| sigma | -0.3599072 |
| Q | 1.2031485 |

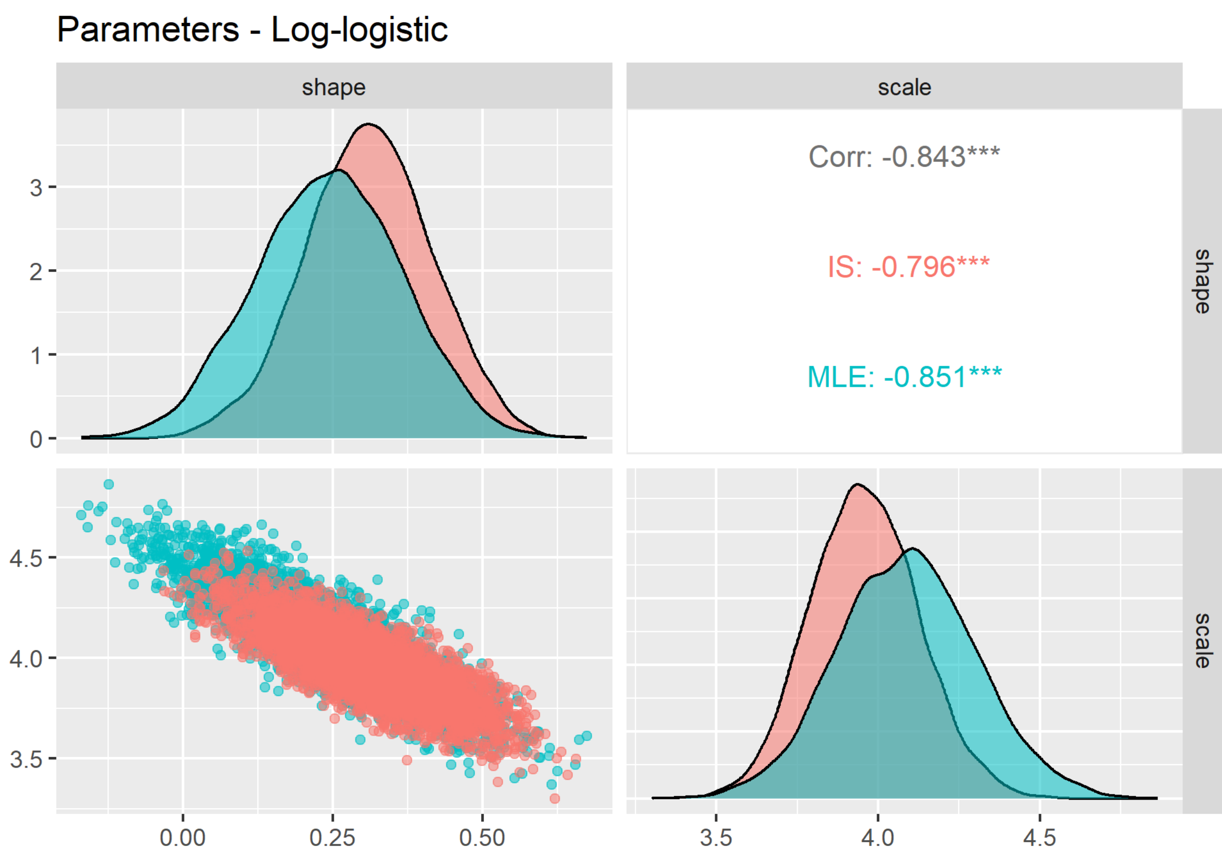


Figure 14: Survival curve parameter distributions and covariance estimates obtained using trial data only (MLE) and combining trial data with external information (IS), Gompertz distribution

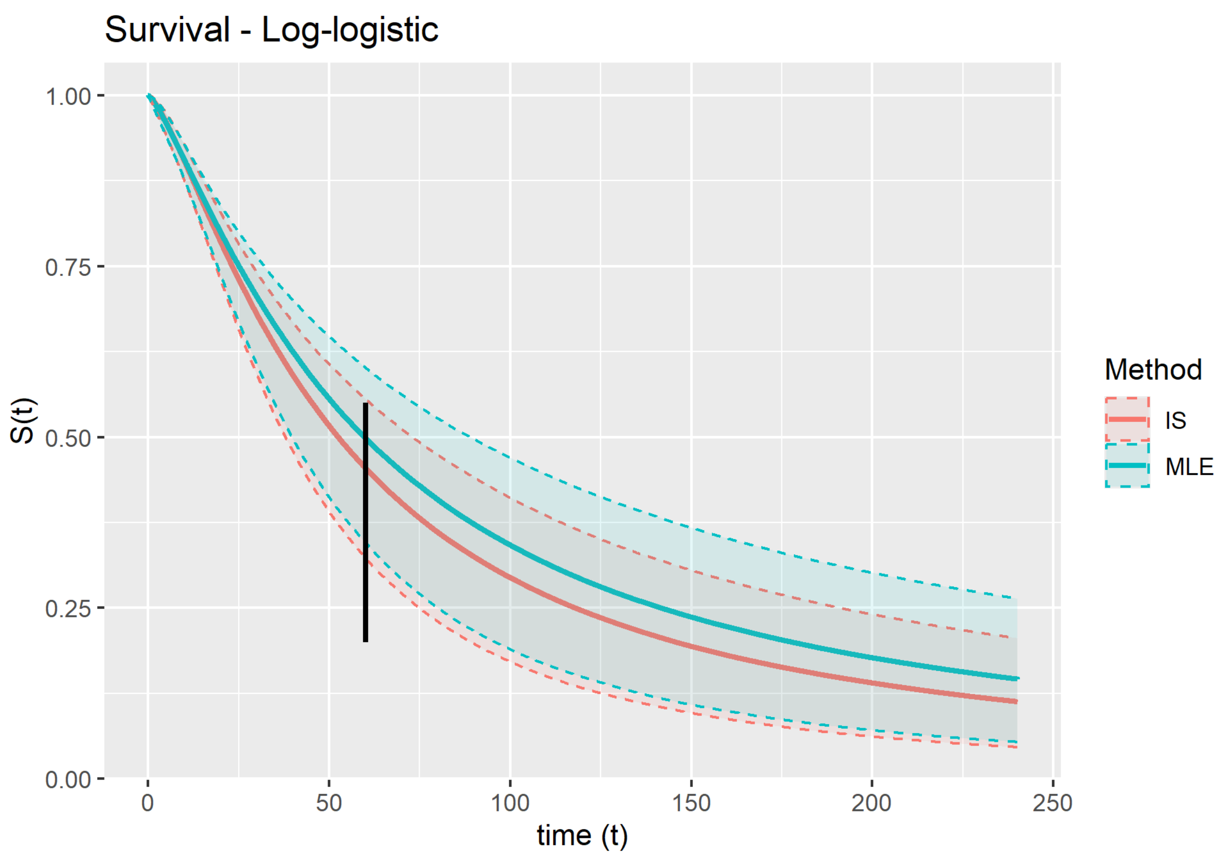


Figure 15: Survival curves (median and 95% confidence intervals) obtained using trial data only (MLE) and combining trial data with external information (IS), Gompertz distribution

Table 22: Covariance matrix obtained via MLE: Gen. Gamma

| | 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: Parameter estimates obtained via Importance Sampling: Gen. Gamma

| | x |
|---|---|
| mu | 4.1857610 |
| sigma | -0.3818327 |
| Q | 1.2508022 |

Table 24: Covariance matrix obtained via Importance Sampling: Gen. Gamma

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

### 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 25: 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 & Whilte

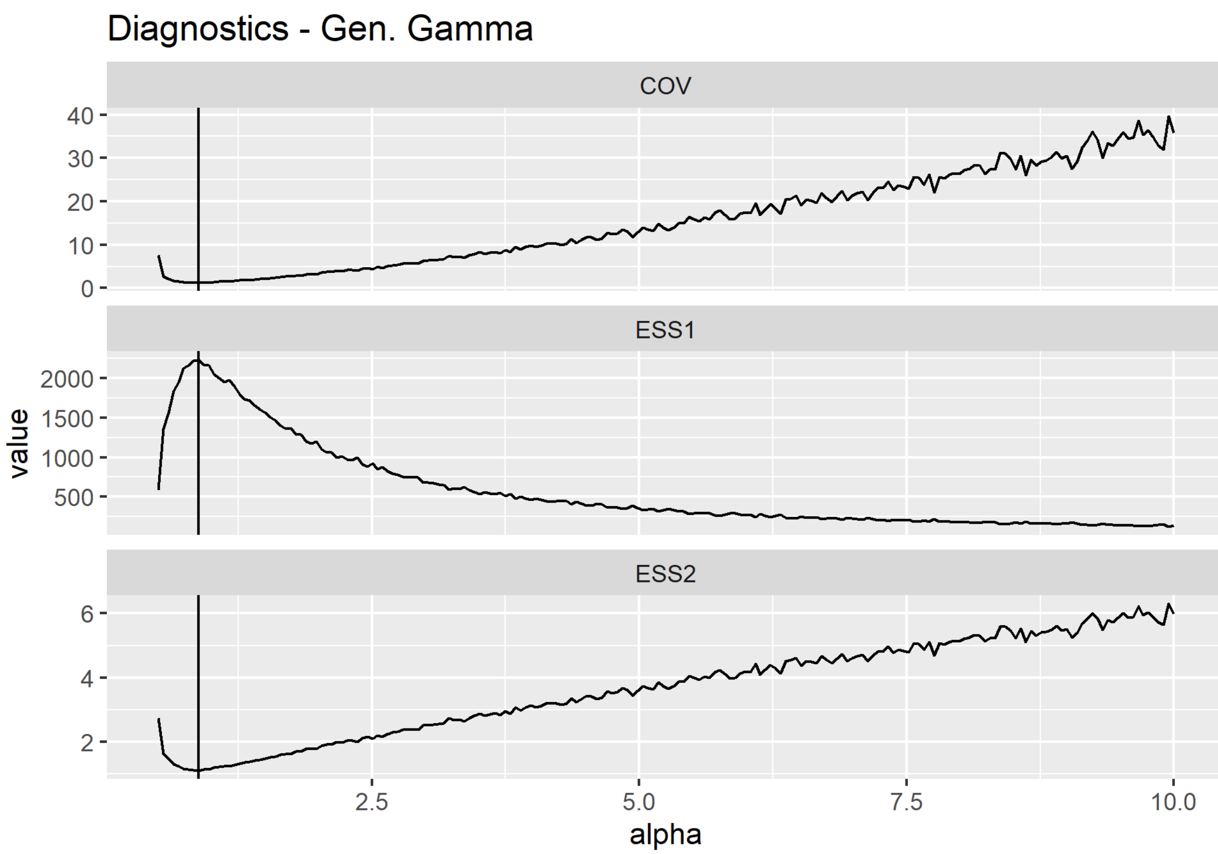


Figure 16: Importance sampling diagnostics: coefficient of variation (COV) and effective sample size (ESS) as functions of the tempering parameter alpha, Gen. Gamma distribution. The vertical line shows the optimal value of alpha identified by the algorithm.

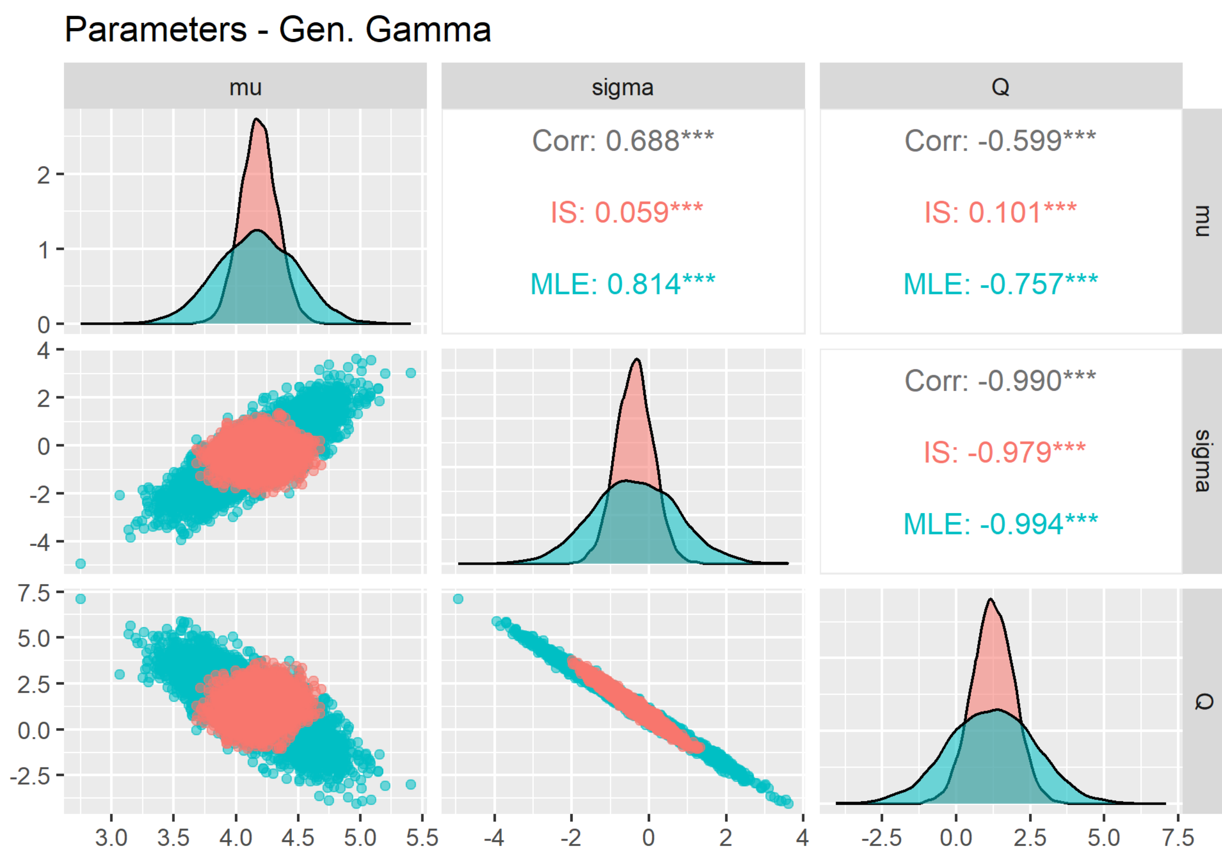


Figure 17: Survival curve parameter distributions and covariance estimates obtained using trial data only (MLE) and combining trial data with external information (IS), Gen. Gamma distribution

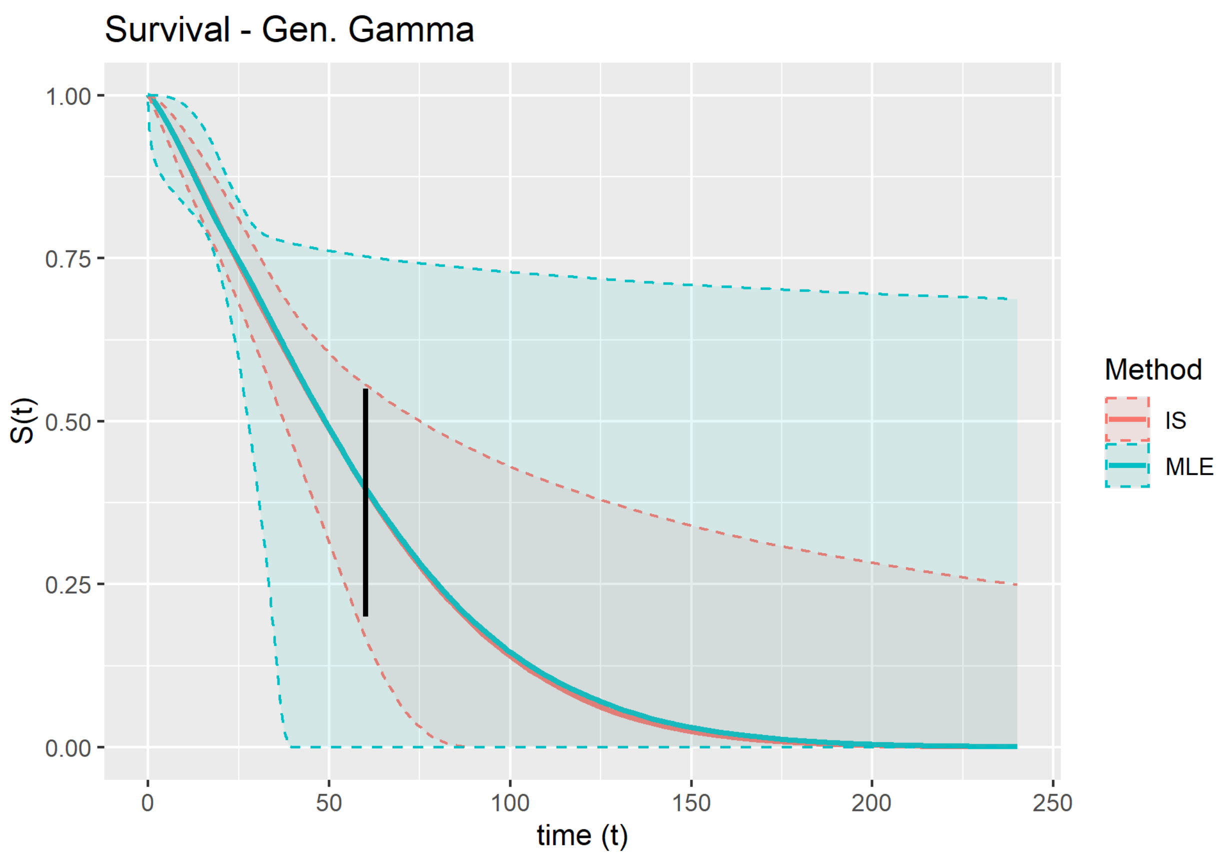


Figure 18: Survival curves (median and 95% confidence intervals) obtained using trial data only (MLE) and combining trial data with external information (IS), Gen. Gamma distribution

implemented in the expertsurv package.

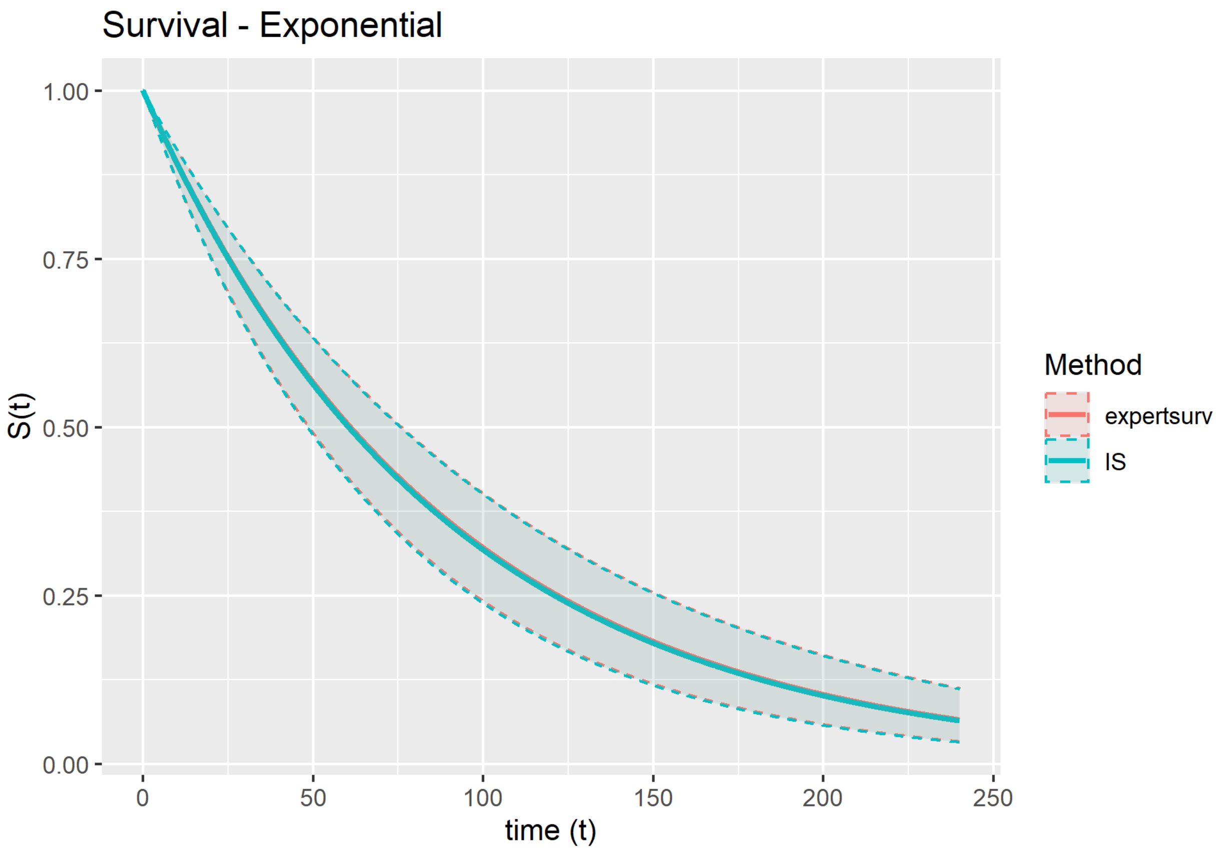


Figure 19: Survival curves (median and 95% confidence intervals) obtained by combining trial data with external information using the importance sampling (IS) and expertsurv methods, Exponential distribution

#### 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.

### 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 26: 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 & 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 |

| Distribution | expertsurv | IS | Mean.Diff | Var.Ratio |
|---|---|---|---|---|
| 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

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

Table 27: 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 & 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% |
| Weibull | expertsurv | 40.32% | 40.41% | 6.53% | 27.64% | 52.69% |

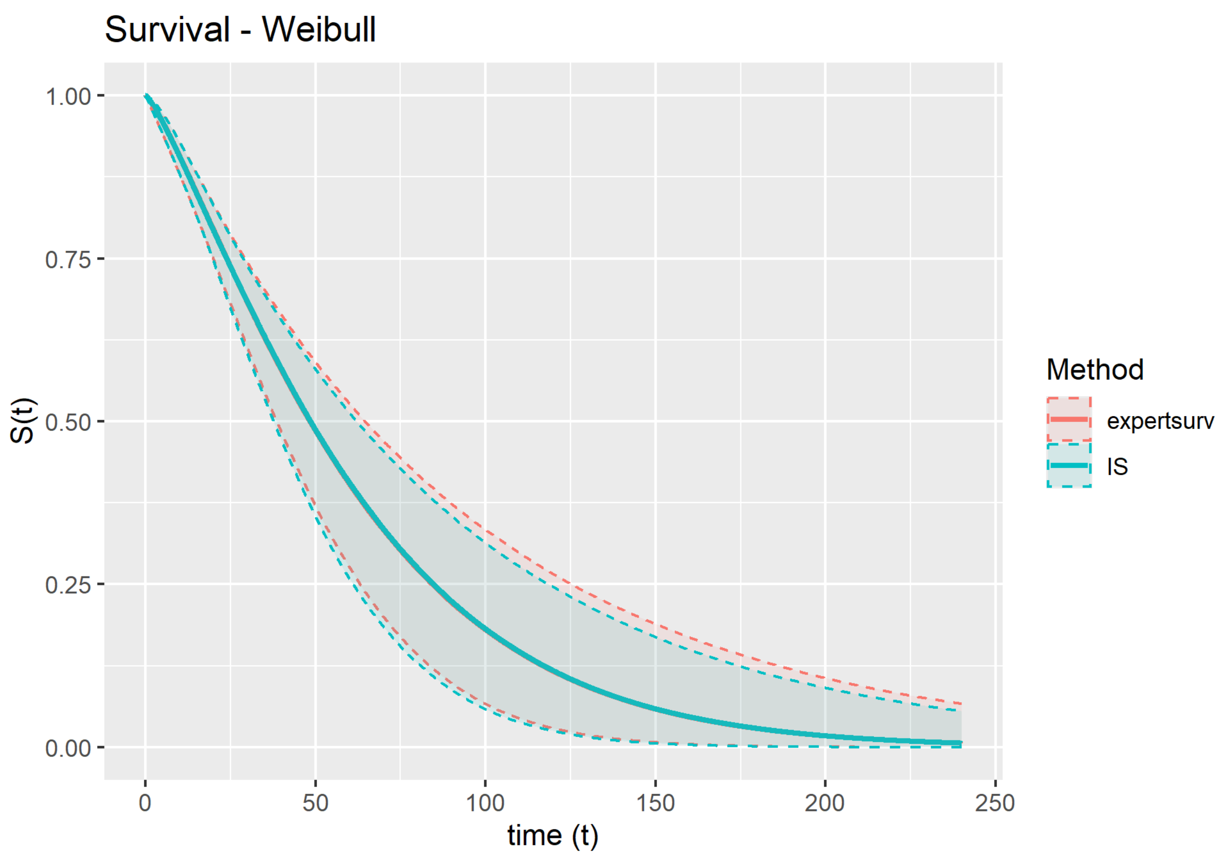


Figure 20: Survival curves (median and 95% confidence intervals) obtained by combining trial data with external information using the importance sampling (IS) and expertsurv methods, Weibull distribution

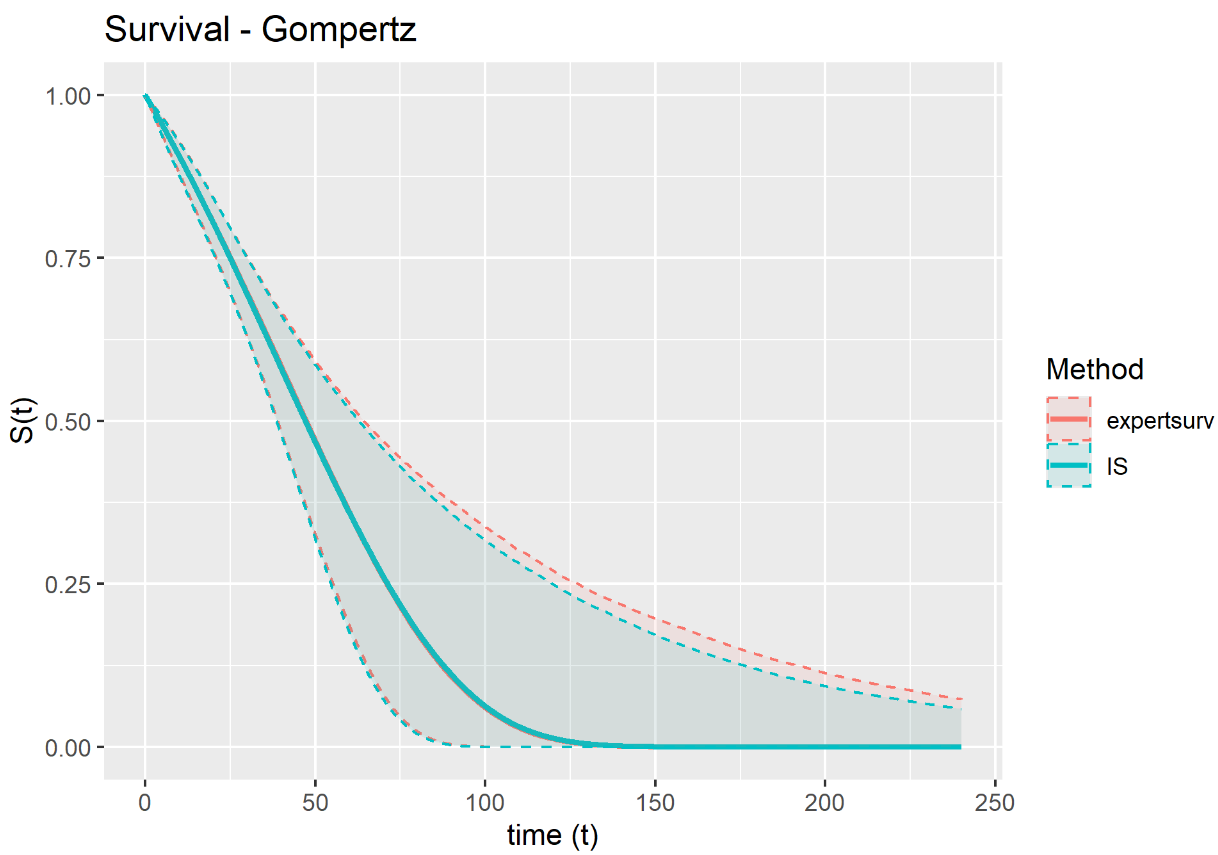


Figure 21: Survival curves (median and 95% confidence intervals) obtained by combining trial data with external information using the importance sampling (IS) and expertsurv methods, Log-normal distribution

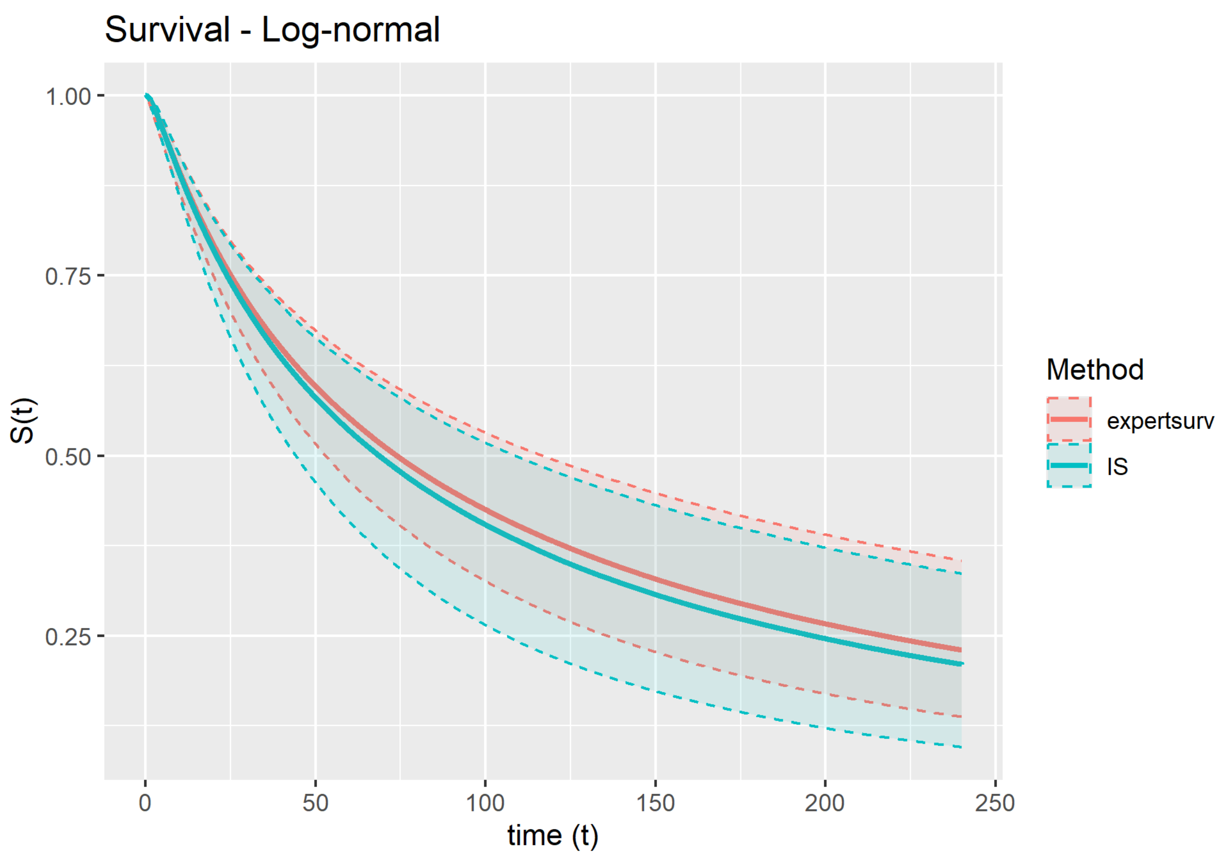


Figure 22: Survival curves (median and 95% confidence intervals) obtained by combining trial data with external information using the importance sampling (IS) and expertsurv methods, Log-logistic distribution

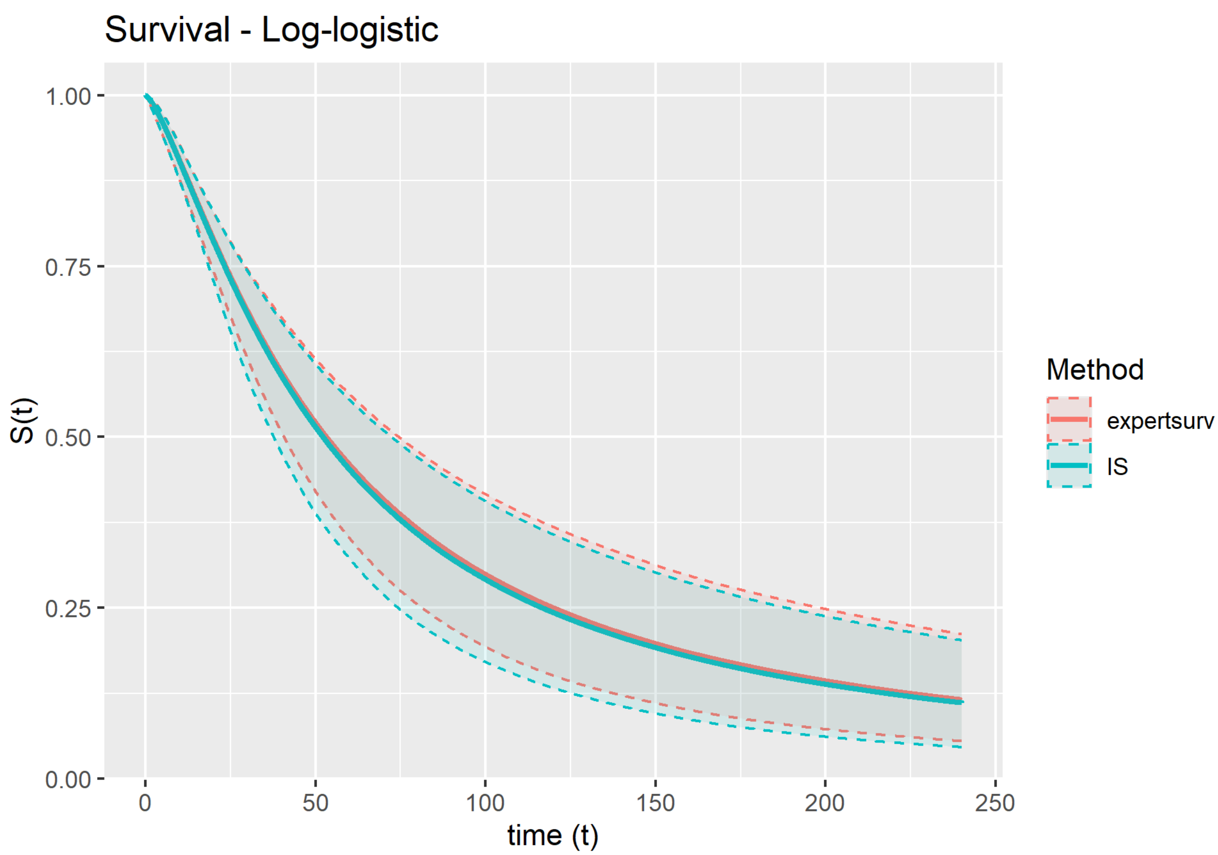


Figure 23: Survival curves (median and 95% confidence intervals) obtained by combining trial data with external information using the importance sampling (IS) and expertsurv methods, Gompertz distribution

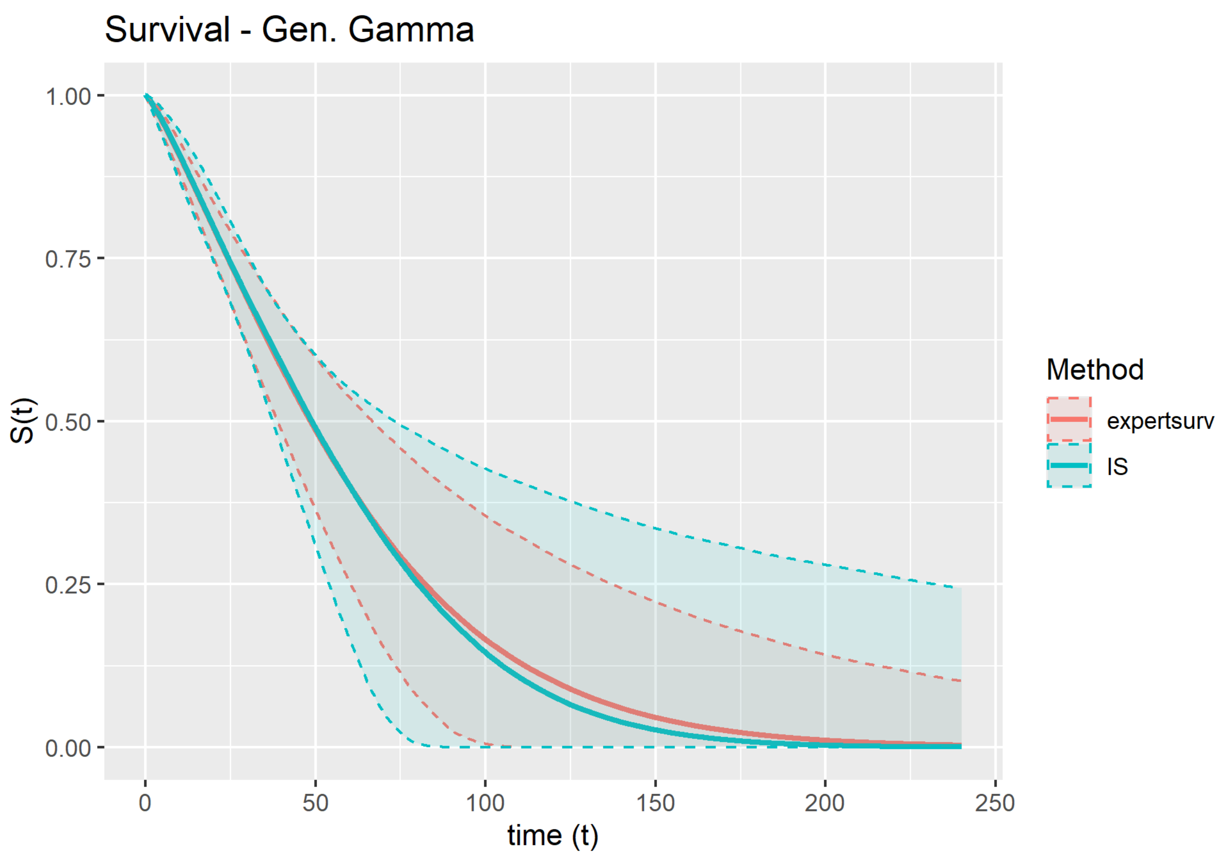


Figure 24: Survival curves (median and 95% confidence intervals) obtained by combining trial data with external information using the importance sampling (IS) and expertsurv methods, Gen. Gamma distribution

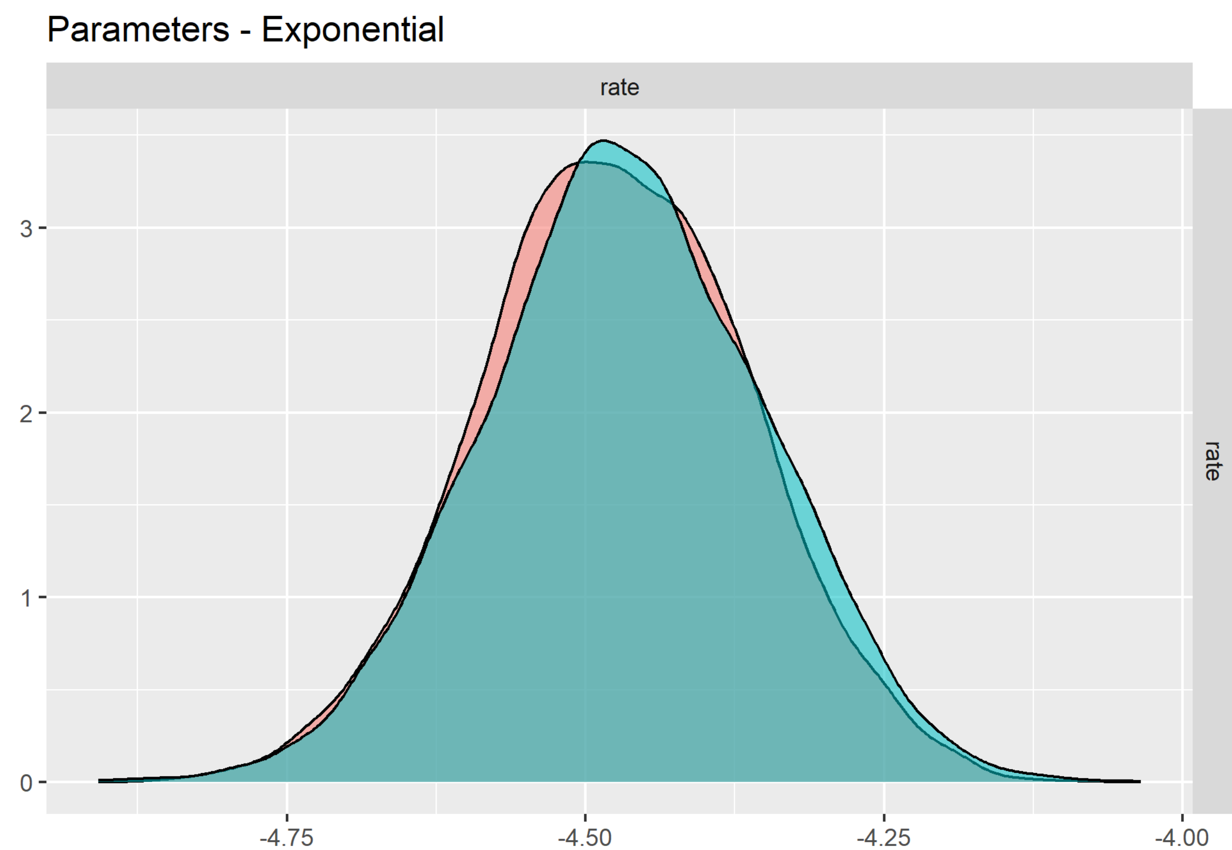


Figure 25: Survival curve parameter distributions and covariance estimates obtainedby combining trial data with external information using the importance sampling (IS) and expertsurv methods, Exponential distribution

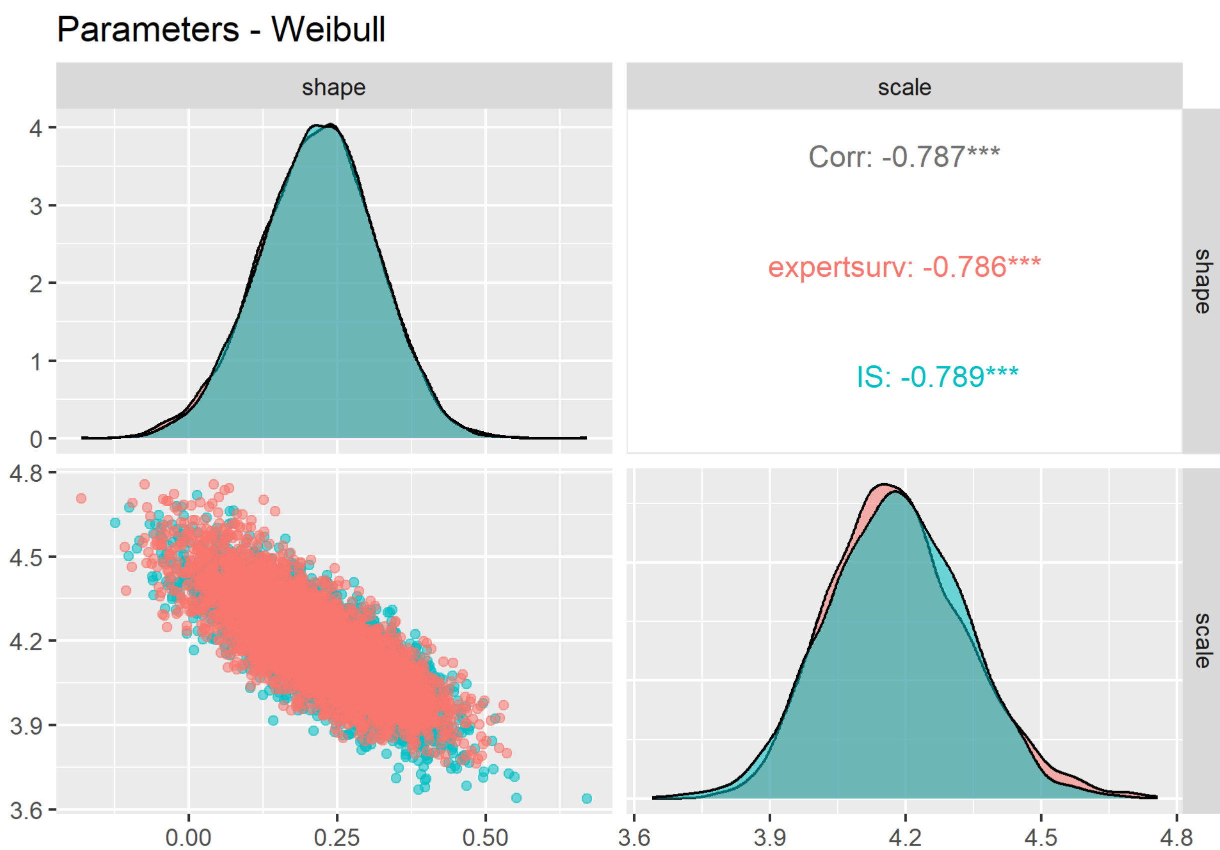


Figure 26: Survival curve parameter distributions and covariance estimates obtainedby combining trial data with external information using the importance sampling (IS) and expertsurv methods, Weibull distribution

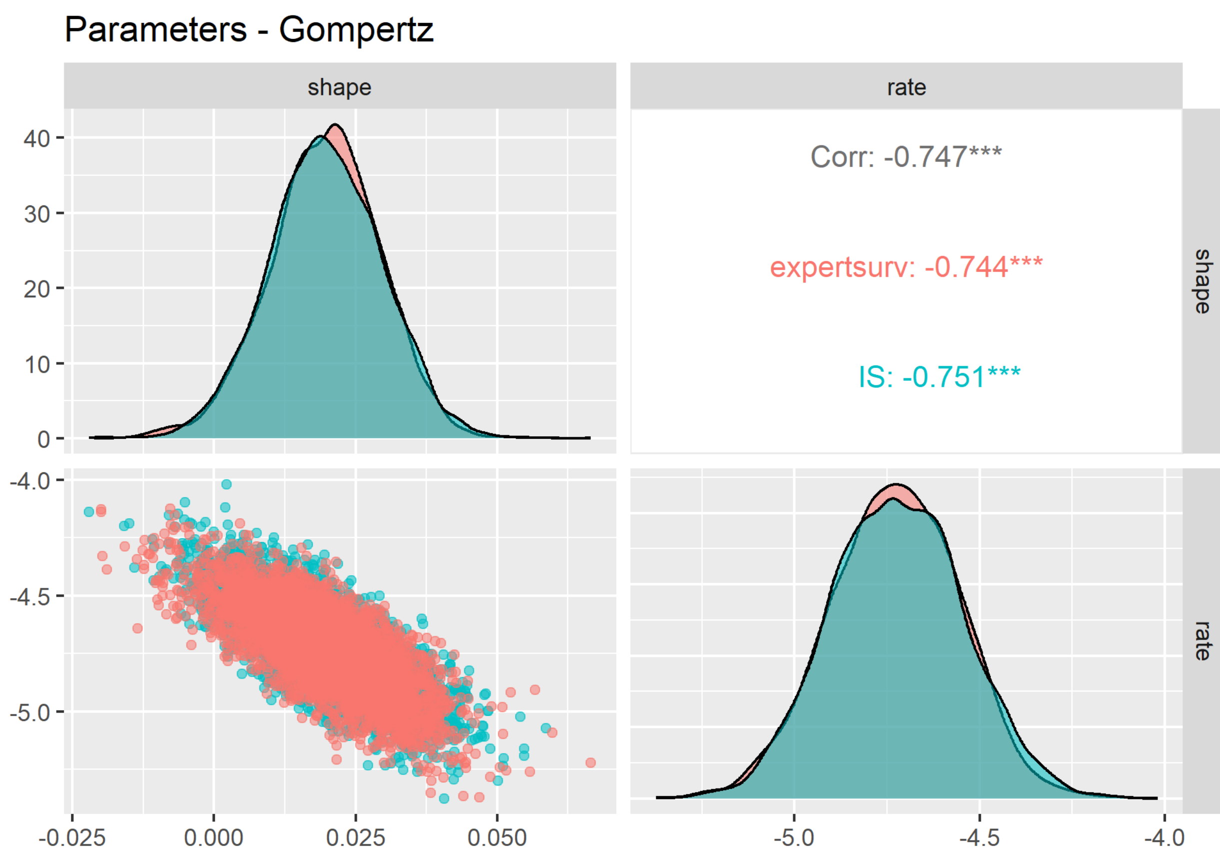


Figure 27: Survival curve parameter distributions and covariance estimates obtainedby combining trial data with external information using the importance sampling (IS) and expertsurv methods, Log-normal distribution

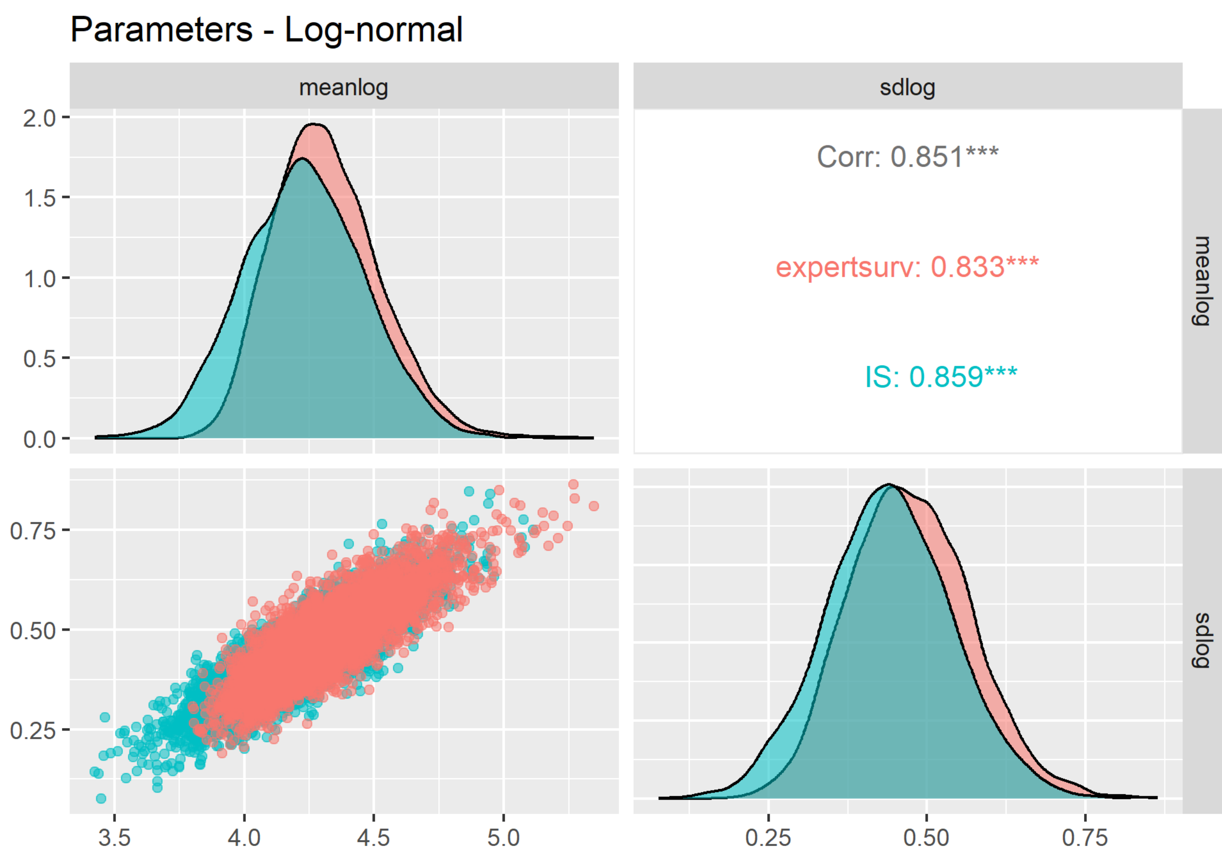


Figure 28: Survival curve parameter distributions and covariance estimates obtainedby combining trial data with external information using the importance sampling (IS) and expertsurv methods, Log-logistic distribution

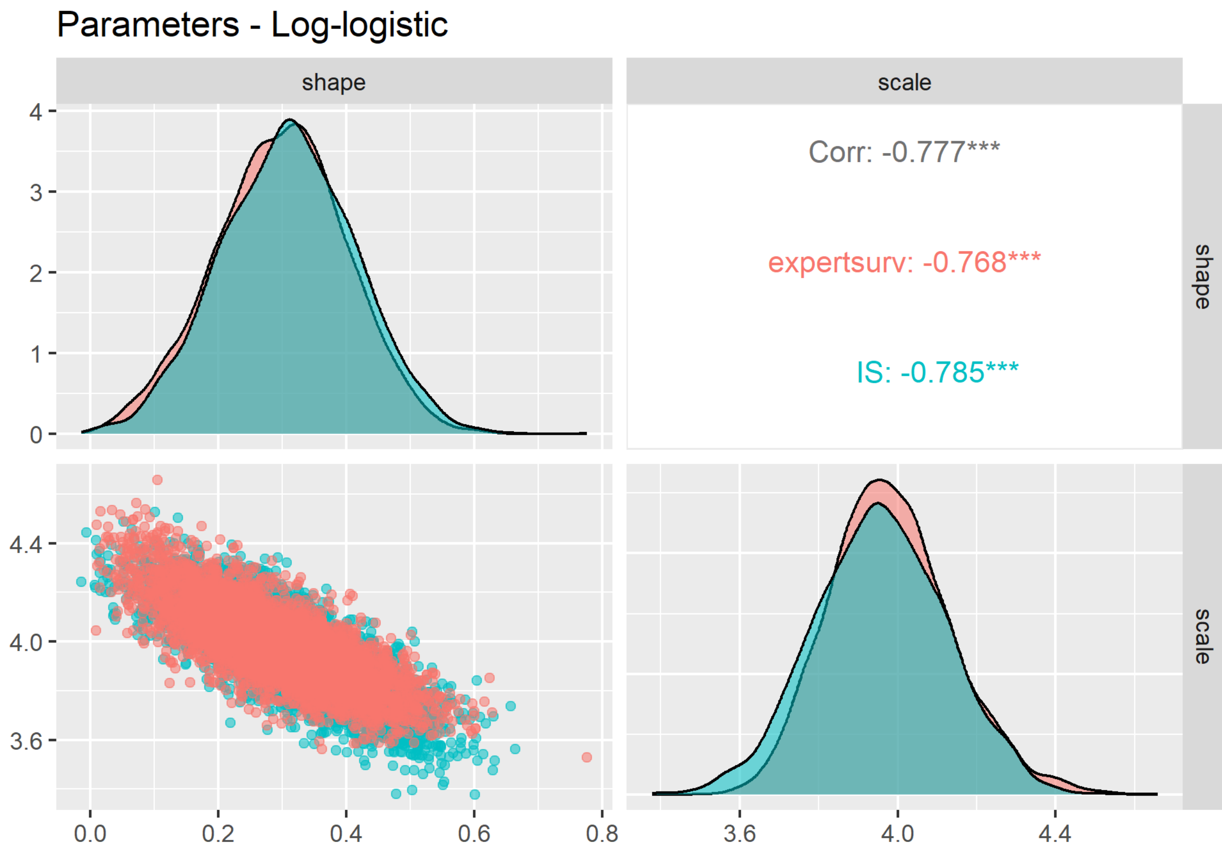


Figure 29: Survival curve parameter distributions and covariance estimates obtainedby combining trial data with external information using the importance sampling (IS) and expertsurv methods, Gompertz distribution

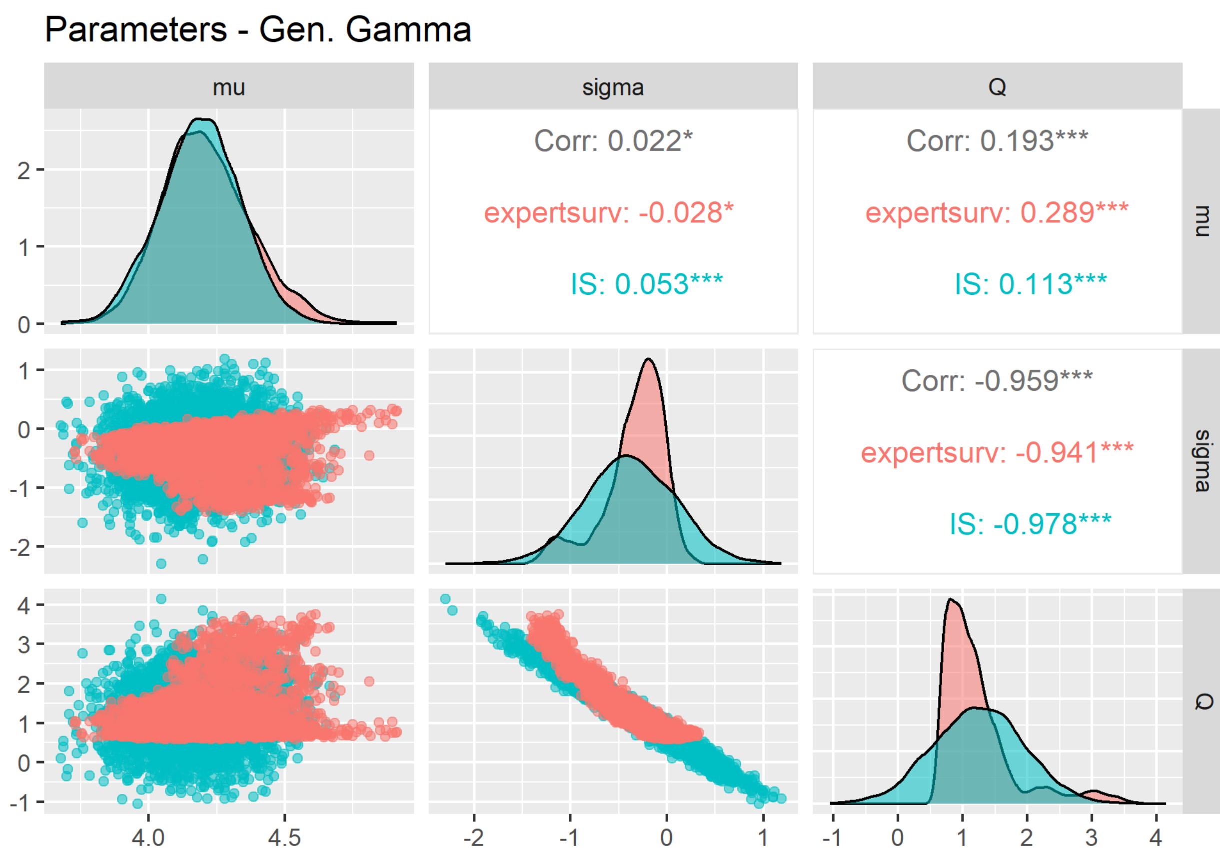


Figure 30: Survival curve parameter distributions and covariance estimates obtainedby combining trial data with external information using the importance sampling (IS) and expertsurv methods, Gen. Gamma distribution

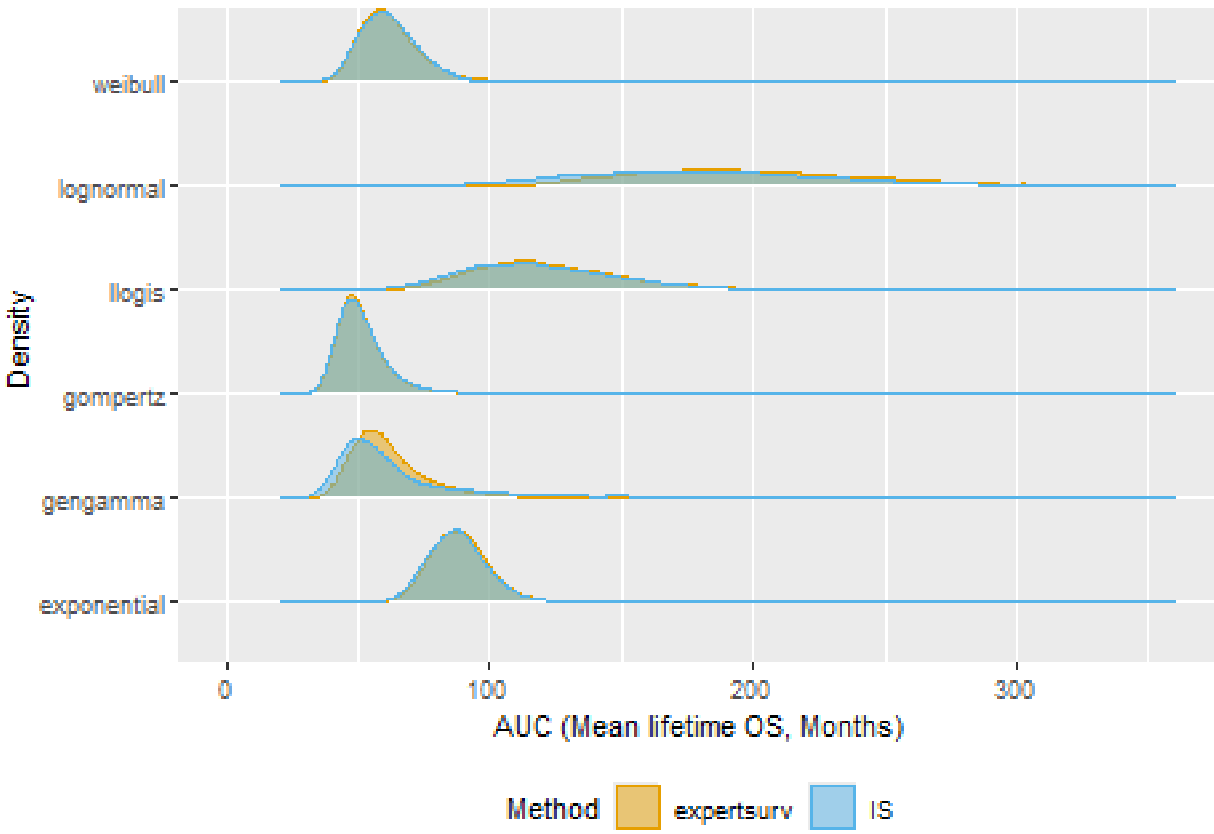


Figure 31: Density plots comparing probabilistic total area under the curve (mean OS) distributions obtained from combining trial data with external information using the importance sampling (IS) method described in the paper, with those obtained from the fully Bayesian method of Cooney & White implemented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

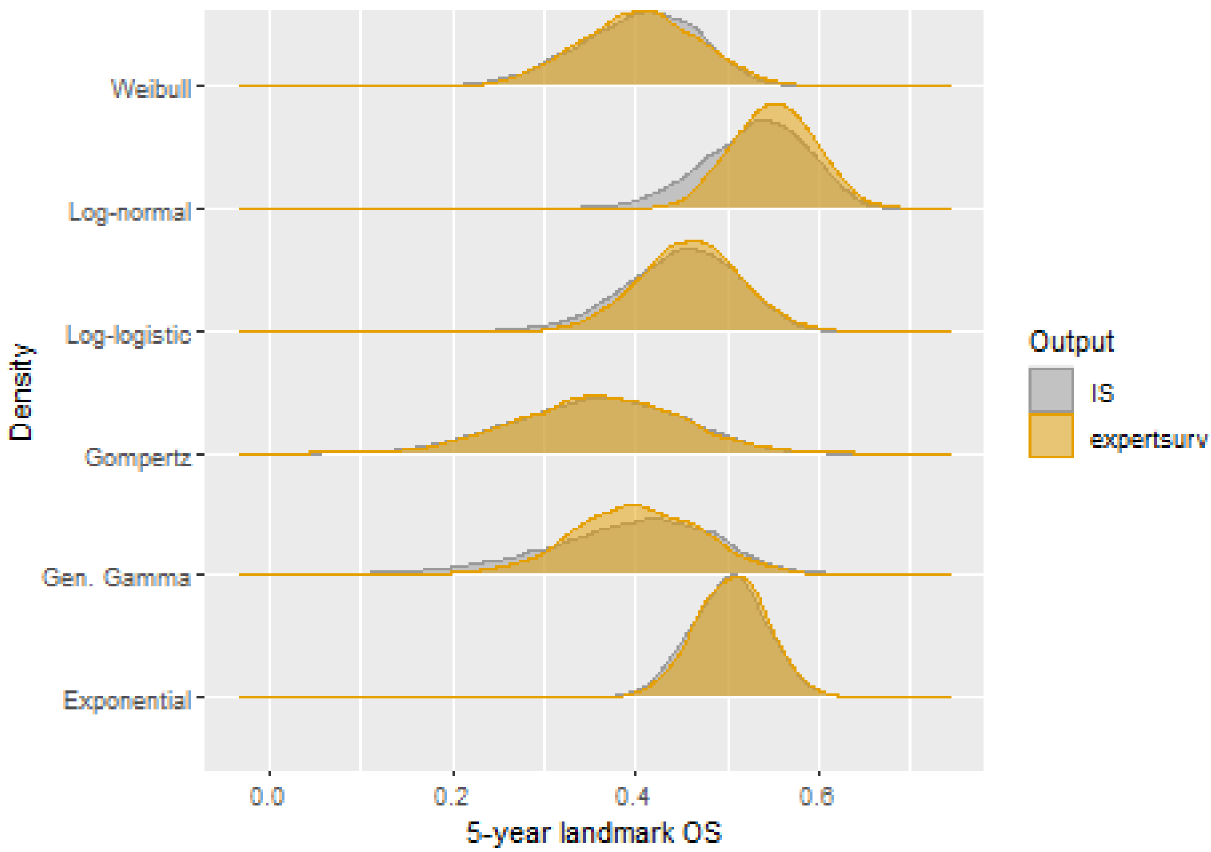


Figure 32: Density plots comparing 5-year OS estimates, obtained from combining trial data with external information using the importance sampling (IS) method described in the paper, with those obtained from the fully Bayesian method of Cooney & White implemented in the expertsurv package.