Survival extrapolation - comparison of methods

NCPE

July 2023

## 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.

MLE Parameter Estimates

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

MLE Covariance Matrix

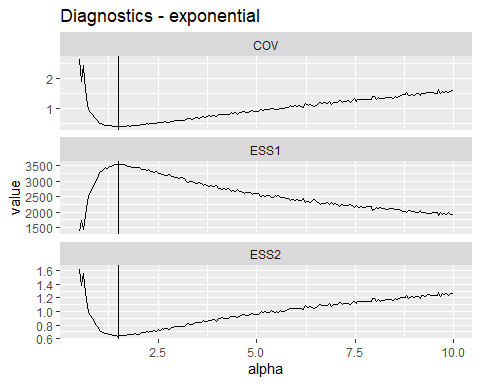
|  | rate |
| --- | --- |
| rate | 0.0169491 |

IS Parameter Estimates

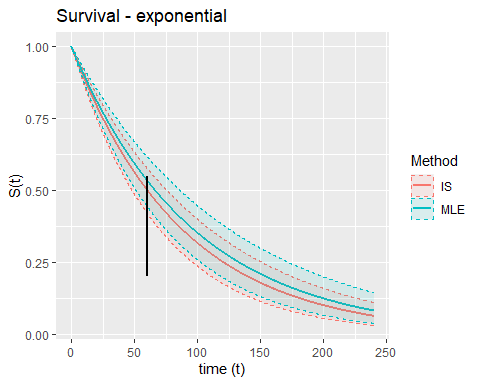
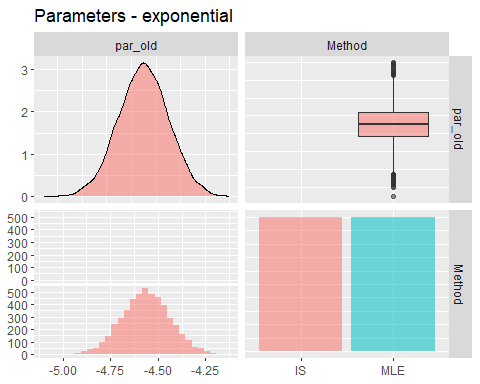
| x |
| --- |
| -4.467088 |

IS Covariance Matrix

|  |
| --- |
| 0.0138444 |



## `stat\_bin()` using `bins = 30`. Pick better value with `binwidth`.



MLE Parameter Estimates

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

MLE Covariance Matrix

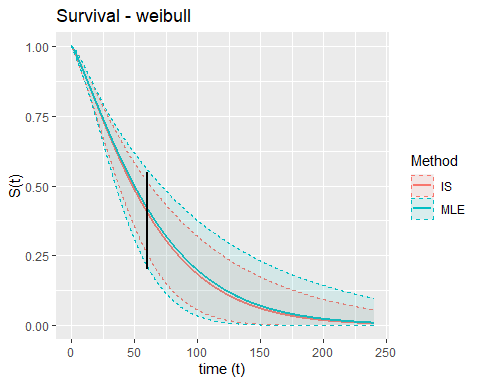
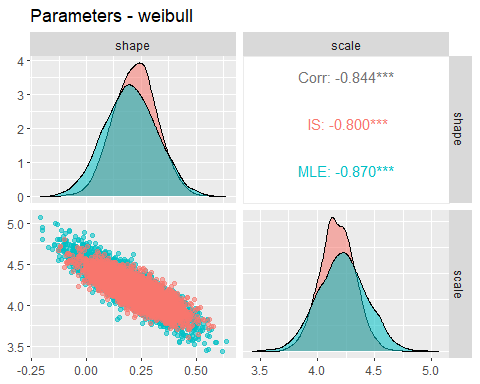
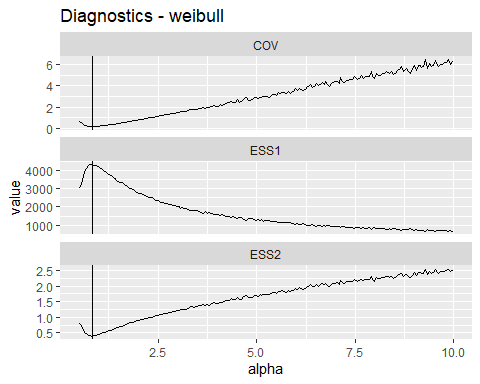
|  | shape | scale |
| --- | --- | --- |
| shape | 0.0147844 | -0.0228526 |
| scale | -0.0228526 | 0.0466213 |

IS Parameter Estimates

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

IS Covariance Matrix

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



MLE Parameter Estimates

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

MLE Covariance Matrix

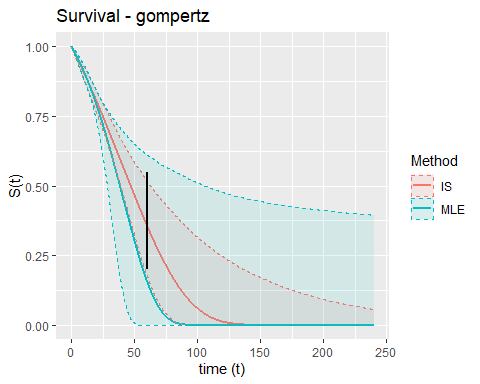
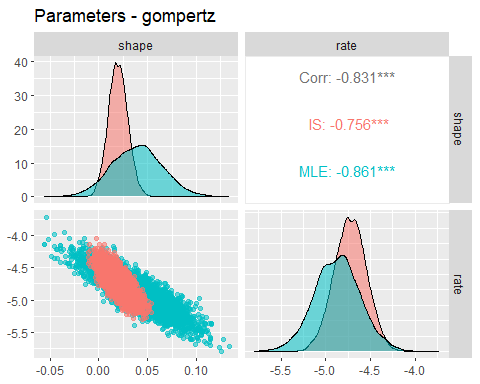
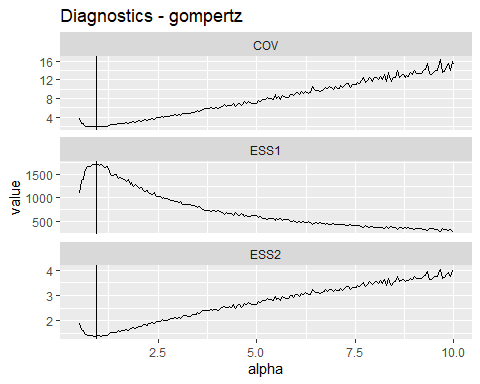
|  | shape | rate |
| --- | --- | --- |
| shape | 0.0006747 | -0.0056125 |
| rate | -0.0056125 | 0.0636359 |

IS Parameter Estimates

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

IS Covariance Matrix

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



MLE Parameter Estimates

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

MLE Covariance Matrix

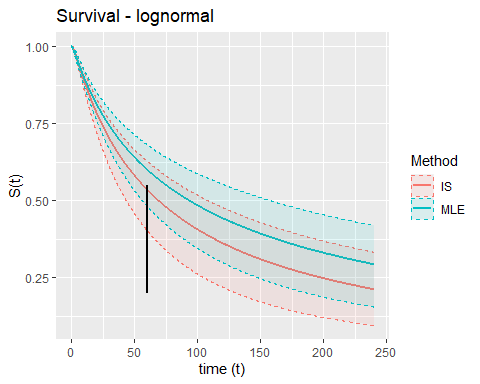
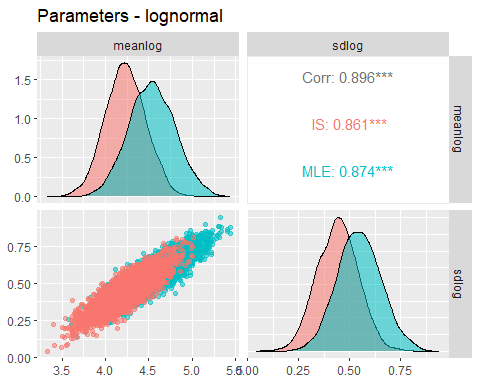
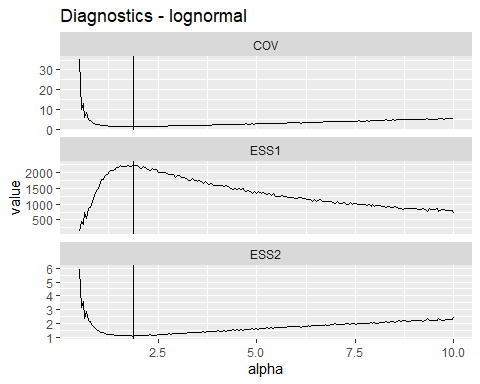
|  | meanlog | sdlog |
| --- | --- | --- |
| meanlog | 0.0696811 | 0.0247171 |
| sdlog | 0.0247171 | 0.0114622 |

IS Parameter Estimates

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

IS Covariance Matrix

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



MLE Parameter Estimates

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

MLE Covariance Matrix

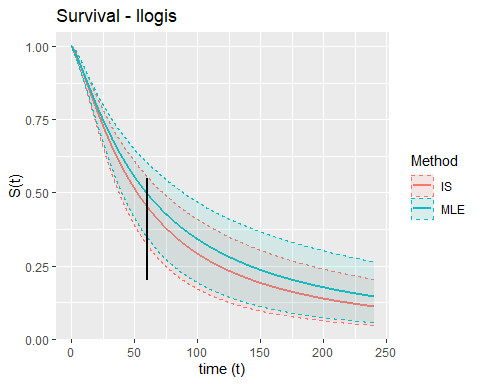
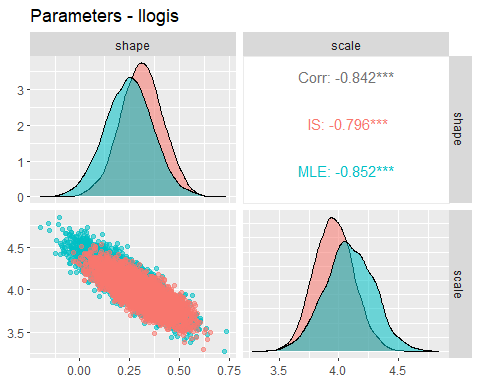
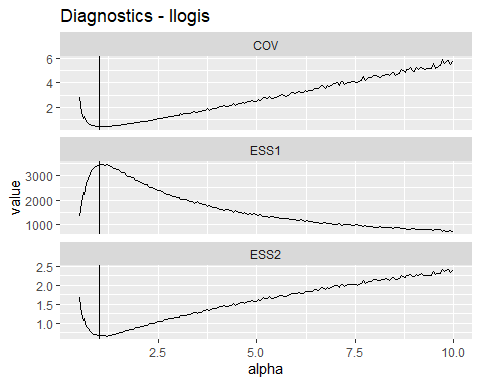
|  | shape | scale |
| --- | --- | --- |
| shape | 0.0144928 | -0.0213001 |
| scale | -0.0213001 | 0.0434079 |

IS Parameter Estimates

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

IS Covariance Matrix

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



MLE Parameter Estimates

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

MLE Covariance Matrix

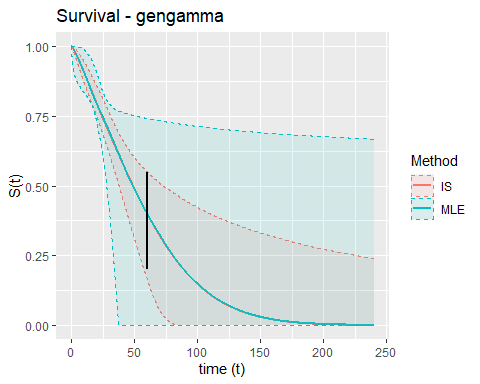
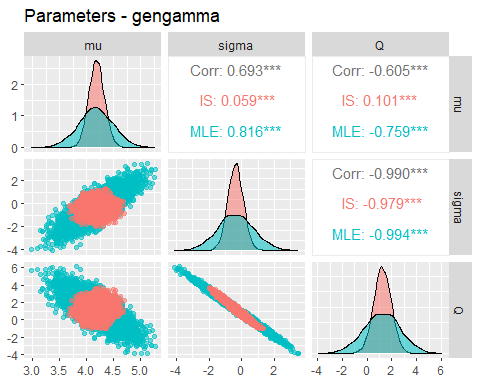
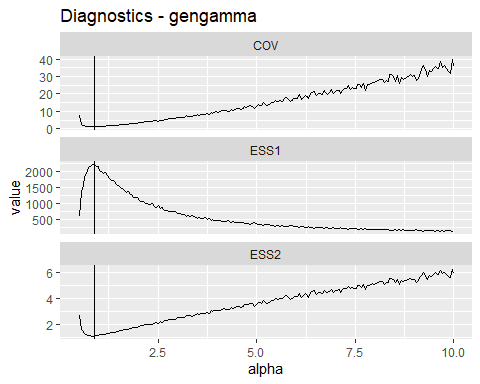
|  | mu | sigma | Q |
| --- | --- | --- | --- |
| mu | 0.1026807 | 0.2899736 | -0.3589428 |
| sigma | 0.2899736 | 1.2303463 | -1.6290913 |
| Q | -0.3589428 | -1.6290913 | 2.1837103 |

IS Parameter Estimates

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

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 |



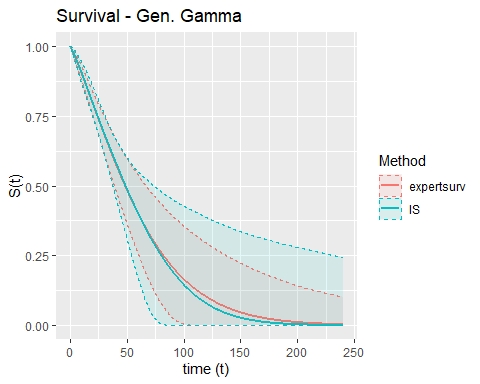
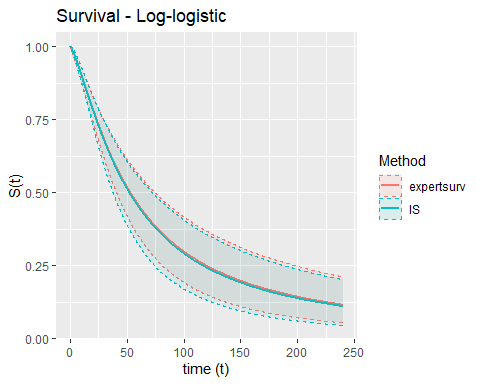
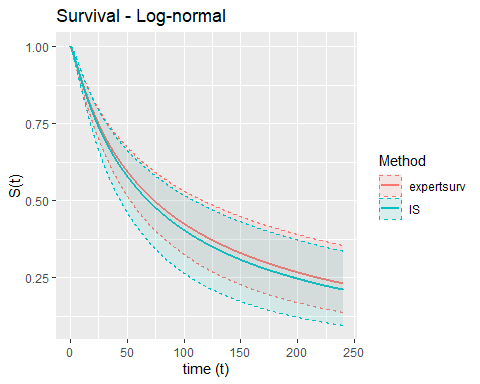
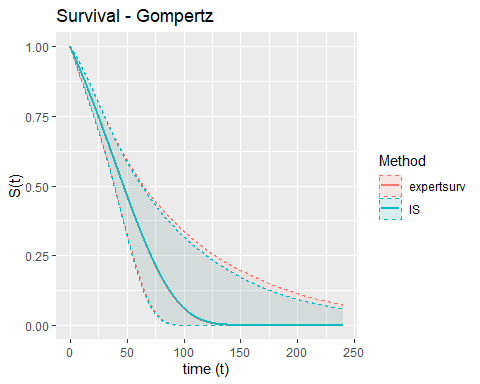
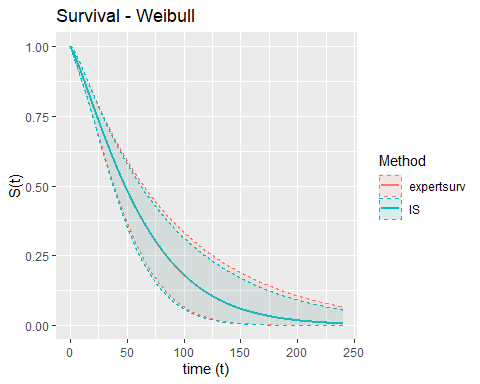
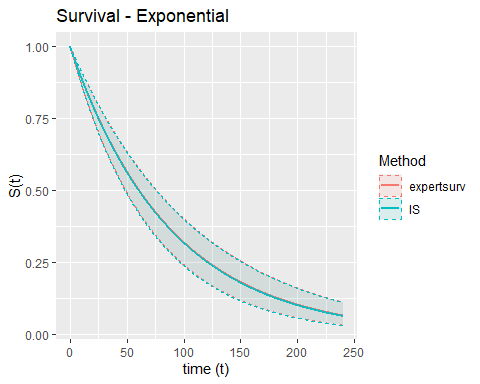
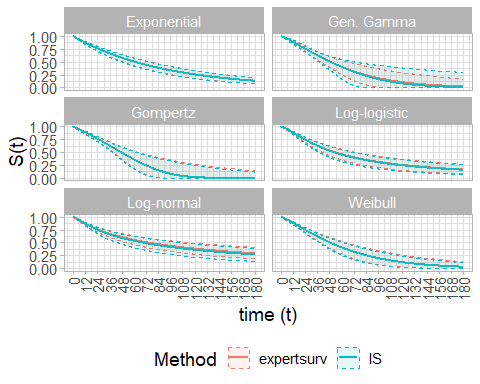
## Parameter variability

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> .

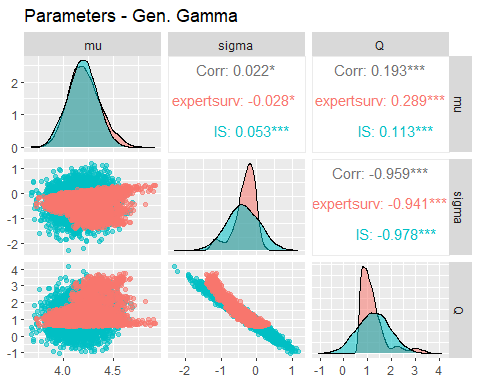
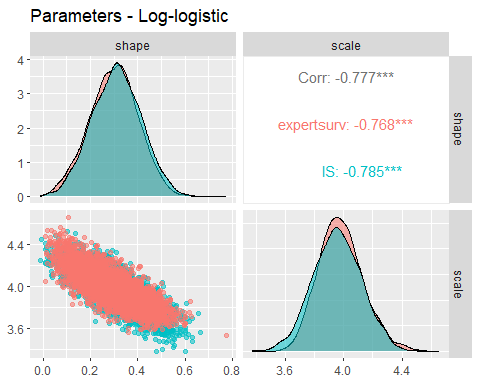
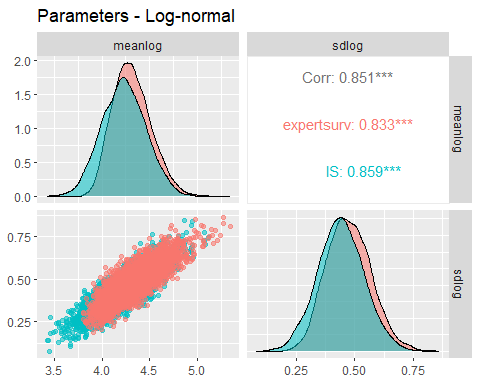
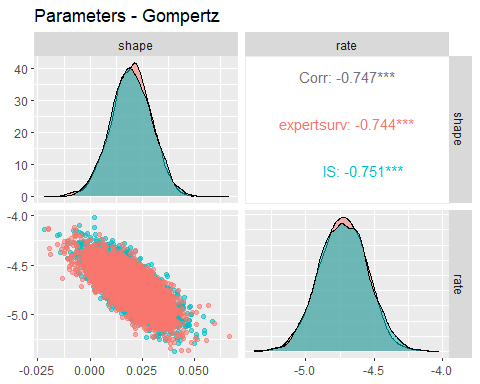
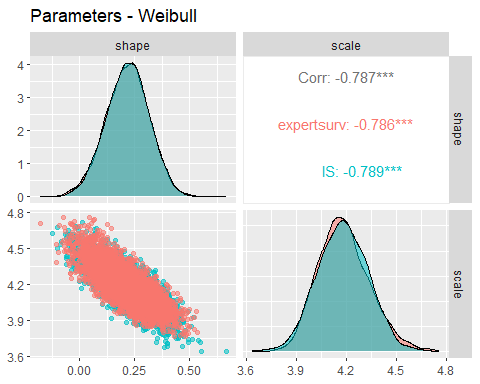
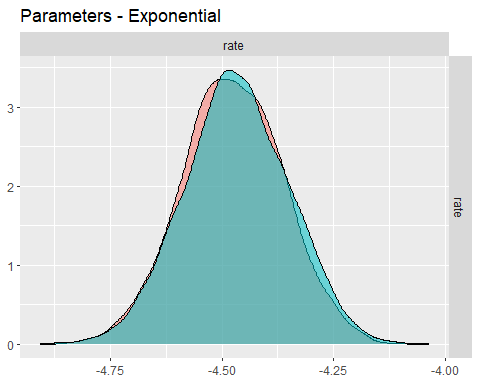
| Distribution | Distance | MLE.Variance | IS.Variance | Ratio |
| --- | --- | --- | --- | --- |
| exponential | 0.0957855 | 0.0169491 | 0.0138444 | 0.8168193 |
| weibull | 0.0413796 | 0.0001670 | 0.0000827 | 0.4948566 |
| gompertz | 0.1474564 | 0.0000114 | 0.0000013 | 0.1140791 |
| lognormal | 0.3260830 | 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



### Comparisons of parameter distributions

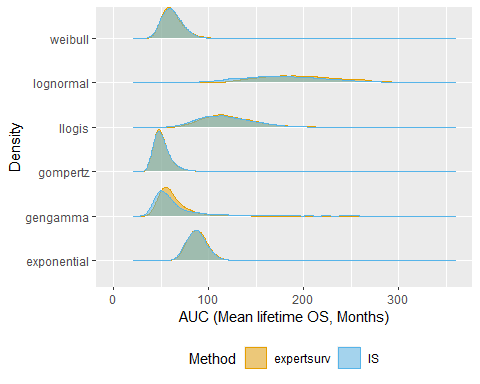


## Comparisons of AUC distributions

## `summarise()` has grouped output by 'Distribution'. You can override using the  
## `.groups` argument.

| Distribution | expertsurv | IS | Mean.Diff | Var.Ratio |
| --- | --- | --- | --- | --- |
| exponential | 88.48 (70.48, 109.73) | 87.74 (69.78, 109.28) | -0.74 | 1.06 |
| gengamma | 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 |
| llogis | 123.17 (77.65, 189.59) | 119.06 (71.11, 181.96) | -4.11 | 1.01 |
| lognormal | 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 |

## Picking joint bandwidth of 3.28



## Comparisons of 5-year OS

## `summarise()` has grouped output by 'Distribution'. You can override using the  
## `.groups` argument.

| Distribution | Output | mean | median | sd | lwr.95 | upr.95 |
| --- | --- | --- | --- | --- | --- | --- |
| Exponential | IS | 0.5015712 | 0.5028130 | 0.0403055 | 0.4232340 | 0.5775170 |
| Exponential | expertsurv | 0.5046627 | 0.5055975 | 0.0387414 | 0.4268043 | 0.5787865 |
| Gen. Gamma | IS | 0.3894131 | 0.4011250 | 0.0973911 | 0.1665180 | 0.5504477 |
| Gen. Gamma | expertsurv | 0.4008263 | 0.4002772 | 0.0711704 | 0.2544532 | 0.5387806 |
| Gompertz | IS | 0.3563374 | 0.3597580 | 0.0886875 | 0.1767547 | 0.5186724 |
| Gompertz | expertsurv | 0.3588510 | 0.3600741 | 0.0871142 | 0.1883793 | 0.5277247 |
| Log-logistic | IS | 0.4489415 | 0.4525138 | 0.0597830 | 0.3221308 | 0.5546484 |
| Log-logistic | expertsurv | 0.4587555 | 0.4594696 | 0.0537035 | 0.3519203 | 0.5629648 |
| Log-normal | IS | 0.5294063 | 0.5343886 | 0.0572427 | 0.4076783 | 0.6269207 |
| Log-normal | expertsurv | 0.5511250 | 0.5519835 | 0.0450352 | 0.4642199 | 0.6366939 |
| Weibull | IS | 0.4005433 | 0.4056199 | 0.0665464 | 0.2585982 | 0.5130380 |
| Weibull | expertsurv | 0.4032310 | 0.4040838 | 0.0652862 | 0.2763925 | 0.5268926 |

## Picking joint bandwidth of 0.0105

