

**Parametric and semi-parametric model
strategies with applications in chemical and
microbial risk assessment**

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List of Abbreviations

AIC	Akaike Information Criteria
AST	Arcsin Transformation
BIC	Bayesian Information Criteria
CDF	Cumulative Distribution Function
ECDF	Empirical Cumulative Distribution Function
FPE	Forward Prediction Error
IQR	InterQuantile Range
L	Likelihood
LN	Log-normal
LOD	Limit of Detection
LOQ	Limit of Quantification
LOOCV	Leave-One-Out Cross Validation
MA	Model Averaging
ML	Maximum Likelihood
MSE	Mean Squared Error
OSCV	One-Sided Cross Validation
SD	Standard Deviation
SemiNP	Semi-NonParametric
Y. Enterocolitica	Yersinia Enterocolitica

Introduction

Within the framework of chemical risk assessment, the handling of concentration data reported to be below the limit of detection (LOD, left-censored) or between the limit of detection and the limit of quantification (LOQ, interval-censored) presents interesting challenges to the statistical analysis of chemical occurrence data. Parametric models for concentration data play a crucial role in probabilistic food safety exposure assessment (EFSA, 2010; Hewett and Ganser, 2007; Moy, 2013), and hence the choice of the distribution for such censored data is an important step in the analysis. We will introduce two case studies on chemical contaminants, more specifically data on Cadmium concentrations. In the first study 42% of the data are left-censored by an LOD; in the second study almost 18% is left- or interval-censored. The log-normal distribution is a very popular distribution in this field. Is it a good choice for the two case studies, or should we use another model? Moreover, can we combine information from multiple models to obtain even better information on the population underlying the case studies?

In the classical one-sample non-censored goodness-of-fit problem, we observe a random sample from a population with density function f . As the density function is unknown, we want to test the null hypothesis that f is equal to a completely specified density function f_0 . The specification of this distribution f_0 can be based on past studies, prior experience or claims by previous researchers. This problem, where f_0 is completely specified, is called a simple null hypothesis. However, in most cases the density f_0 is not completely specified and we simply want to test the null hypothesis that the density function f belongs to some family of distributions \mathcal{G}_f , such as the family of normal distributions (where the mean and variance are not specified). This is called a composite null hypothesis.

Goodness-of-fit tests for censored data have not been studied as extensively as one

might expect. Hollander and Proschan (1979) present a test for a simple null hypothesis for right-censored data. This test can be applied for left-censored data by reversing the order of the observations. The null distribution of this test however is not applicable in the situation where the parameters of the hypothesized distribution are unknown. Despite this invalidity, the Hollander-Proschan test is proposed in this setting in the antimicrobial literature (see e.g. pages 217-220 in Haas et al., 1999). Another test for right-censored data, based on the Cramér-von Mises test, is proposed by Koziol and Green (1976). Akritas (1988) proposed a test for a simple and composite null hypothesis for right-censored data. The test is based on the Pearson statistic and on partitioning the data. A generalization to interval-censored data is not straightforward. A test for interval-censored data, based on the Cramér-von Mises statistic and a leveraged bootstrap, was introduced by Ren (2003). We propose and study a (composite) goodness-of-fit test for censored data. We define an extended family of distributions with extra flexibility. If we need extra flexibility to describe the data, then we reject the hypothesis and we conclude that f does not belong to the family of distributions \mathcal{G}_f . We will use the family of semi-nonparametric models SemiNP (Fenton and Gallant, 1996; Gallant and Nychka, 1987) to describe the flexibility, and the test is based on the order-selection test of Aerts et al. (1999).

We often select the best model via a model selection criterion, and inference is then based on that model. However, it is also possible to make formal inferences based on an entire family of distributions. The conditioning is on all the models in the family instead of on one best model, and this has advantages. In model averaging (Burnham and Anderson, 2002), the members of the family of distributions are ranked from best to worst. Each member receives a weight: the better the model, the higher the weight. Based on every distribution in the family of distributions, we can estimate a parameter of interest. The model averaged parameter of interest is obtained by weighting the individual estimates. Model selection and model averaging over a family of fractional polynomials was proposed and discussed in Faes et al. (2007) and Namata et al. (2008). We will use model averaging in the context of censored data, for example to model average the distribution function for a fixed concentration for the Cadmium data and we will perform a simulation study.

In chemical risk assessment, it is also important to determine the quantiles of the distribution of the concentration data. For a continuous distribution, the p -quantile is the number η where $\eta = F^{-1}(p)$. As described above, we can select the best model from a family of distributions and estimate the quantile in this model. Another possibility is to compute a model averaged quantile. In this case, there are two ways to carry out the model averaging, as we could average over the estimates directly, or average over the distribution function first and invert afterwards. We illustrate both techniques on the Cadmium data. In a case study on Cesium concentrations, there is an extra uncertainty

because measurement errors are possible for the limit of detection. We propose a way to deal with the uncertainty. A simulation study is carried out to investigate the performance of the two approaches of model averaging.

Mathematical models defined by a system of non-linear differential equations are widely applied to describe dynamic processes in biology and other fields. For instance, the SIR model (Susceptible-Infected-Recovered) and accompanying system of differential equations is one of the basic compartmental models in infectious disease epidemiology, which is widely used and well suited to model many viral infections in childhood (see e.g. Hens et al., 2012). In the field of predictive microbiology, mathematical models defined by differential equations are developed to predict the growth rate of a microorganism population under a set of environmental conditions (see e.g. Barany and Roberts, 1995). Two case studies are introduced from these fields of infectious disease and microbial growth modelling. The first dataset concerns 15 concentration measurements of *Yersinia enterocolitica*, a bacterium causing the yersiniosis disease, a zoonotic disease in humans as well as animals. Several mathematical models for microbial growth have been proposed in literature (see e.g. López et al., 2004), but not so much attention has been given to more data-driven nonparametric and semiparametric approaches. Such flexible models might indicate local deviations from the parametric model, deviations that might indicate model misspecification or unexpected patterns that deserve some more attention. Figure 2.4 shows an unexpected decrease of concentrations in the so-called “lag phase” (the initial phase of no-growth as the cells will only start growing after a certain unknown lag time). Is it possible to relax the differential equation model so that it follows the data more closely? On the other hand, growth curves are expected to be monotone globally, and therefore it would be natural to consider more smooth models constrained to be monotone. And where and how much would a more flexible model, constrained to be monotone or not, differ from the global parametric model? Unfortunately, it is not always possible to provide closed-form solutions for the system and numerical techniques need to be used to solve the differential equations. Ramsay et al. (2007) describe a method for estimating parameters in ordinary differential equations that is robust to model misspecification. The approach is based on a modification of data smoothing methods along with a generalization of profiled estimation. We briefly describe this generalized profiling estimation procedure and extend it with an additional penalization term to incorporate shape constraints such as monotonicity.

The second dataset concerns a seroprevalence survey conducted in Belgium. It is a sample of 3075 individuals with ages up to 65, tested for Parvovirus B19 IgG antibody

activity. Figure 2.5 displays the proportion of positive samples per age class, with dots proportional to the number of samples collected. As seropositivity of an individual of age a at the time of test indicates that that individual has been infected somewhere in the past, i.e. in the interval $[0, a]$, the seroprevalence curve is expected to be monotone as a function of age. Figure 2.5 shows there is an issue of monotonicity, as the seroprevalence shows a dip around the age of 30 years. Several modeling approaches are discussed in Hens et al. (2012). Here we follow again the approach of Ramsay et al. (2007) and Hooker et al. (2011), who applied the generalized profiling methodology to parameterize state-space models for measles in Ontario. Again, as in the previous example, we focus on the issue of monotonicity.

As for all smoothing methods, the selection of the smoothing parameter plays a central role in generalized profiling. Ramsay et al. (2007) considered two rationales for choosing the amount of smoothing, corresponding to the need for robustness with respect to poor initial parameter values or model misspecification. They chose the smoothing parameter manually for their examples, and suggested some algorithms to automate these choices. Hooker et al. (2011) discussed and illustrated the use of forward cross-validation (CV) or forward prediction error as an objective way to choose the smoothing parameter. In analogy with the idea to “move forward and predict” in the forward cross-validation method, we propose and illustrate the use of one-sided cross-validation. One-sided cross-validation (OSCV) has been introduced by Hart and Yi (1998) to select the smoothing parameter in local linear and kernel regression estimation as a method that has the objectivity of CV and statistical properties comparable to those of a plug-in rule. OSCV is introduced for generalized profiling and compared to traditional leave-one-out cross-validation (LOOCV).

As mentioned by Hooker et al. (2011), an advantage of the generalized profiling method is that it provides readily accessible diagnostics for assessing model fit through visual inspection of different types of plots. There is a huge literature on model diagnostics and lack-of-fit tests in particular, for different types of regression models and based on a variety of approaches (see e.g. Hart, 1997; Aerts et al., 1999; Li, 2012). Model diagnostics and lack-of-fit tests for functions defined by ordinary differential equations (ODEs) was studied more recently in Hooker and Ellner (2015). Our approach differs from that of Hooker (2009) and Hooker and Ellner (2015) in that it focuses on the ODE solution as (conditional) mean of the observed outcomes and by the construction of the test statistic, being an empirical measure of discrepancy between the parametric and the semiparametric solution. Bootstrap methodology is proposed for inferential purposes, more precisely, for the construction of pointwise and simultaneous confidence bands, for testing lack of fit of a particular parametric model and for testing monotonicity.

In Chapter 2 we describe the data examples that we will use throughout the thesis. An overview of various parametric models that are commonly used in the handling of concentration data, is given in Chapter 3. We also introduce a family of semi-nonparametric models. In Chapter 4 we propose and study a goodness-of-fit test of parametric models for censored data. Model averaging of the distribution function is discussed in Chapter 5. Chapter 6 focuses on estimating the quantiles. We compare estimates based on a single parametric model to a model averaged estimate. The final Chapter 7 concerns generalized profiling estimation procedure for systems of differential equations.

Chapter 2

Data description

This chapter summarizes relevant background information on the data on which the methods in this dissertation are based.

2.1 Chemical contaminant data

There are a lot of regulations to ensure the safety of the food that we consume everyday. In Belgium the food producers have developed a system of self control to ensure the quality and safety of their products. Regular checks and analyses in different parts of the food chain, are conducted by the federal agency of food safety (FAVV, Federaal Agentschap voor de Veiligheid van de Voedselketen). On the European level, the European Food Safety Authority provides independent scientific advice to the decision makers who regulate food safety in Europe.

The most important risks concerning food safety can be divided into two categories: microbiological (caused by bacteria, viruses, etc.) and chemical (caused by pesticides, medication, heavy metals, etc.). In this section, we will deal with the concentration of Cadmium and Cesium in certain food stuffs.

The parameters limit of detection (LOD) and limit of quantification (LOQ) are of special importance for exposure estimations in risk assessments as they describe the lower end of the distribution of occurrence data. The LOD and LOQ are often calculated on the basis of the response of the analytical instrument. In this way, the limits are determined through a dilution series of the component in question in a suitable solvent and by evaluating the observed concentration after injection of a standard solution into the system, in a sort of controlled process. These are known as instrumental limits. The LOD represents the minimum concentration or mass of a component that can be detected with

Table 2.1: Cadmium data 1. Summary statistics on Cadmium concentration.

	Observed LOD	
n	57	42
mean	0.1265	0.0074
variance	0.2954	1.0×10^{-5}
min	0.0015	0.0010
max	4.1380	0.0100

a given confidence for a given analytical procedure. Similarly, the LOQ is the minimum concentration or mass of the component that can be quantified with acceptable accuracy and precision (Keith et al., 1983).

2.1.1 Cadmium data

The scientific report prepared by a Working Group on Left-Censored Data of the European Food Safety Authority (EFSA), uses Cadmium level data from several food categories and different countries to compare different substitution methods, nonparametric and parametric models. The Cadmium concentrations are obtained in several laboratories, and different limits of detection or quantification can apply to different laboratories.

We will consider two subsets of the sample. The first subset contains data from the food category “meat and meat products” from Country A (see Section 4.3.1. in EFSA, 2010) to compare several models. A summary of the data is provided in Table 2.1. The number of samples is 99, but only 57 report an exact concentration. The remaining 42 values represent an upper bound of the actual Cadmium level, the limit of detection. The LODs are small and lie in between 0.001 and 0.01, which is in the left tail of the distribution. This results in left-censored data in the particular area of small concentration values. As different laboratories may use different LODs, some of the exactly observed values from one lab can be smaller than the LOD used at another lab.

A visual representation of the data is given in Figure 2.1. On the left is a kernel density of the logarithm of the concentrations. As noted from Table 2.1, the LODs are concentrated in the left tail. In the right panel of Figure 2.1 is the Kaplan-Meier estimate, a frequently used estimator of the survival function in censored data (see introduction of Chapter 3). The estimator is comparable to the empirical survival function (where survival function is equal to 1 - distribution function: $S = 1 - F$), but censored values increase the jumps for concentrations that are measured below the censored values. In this example a

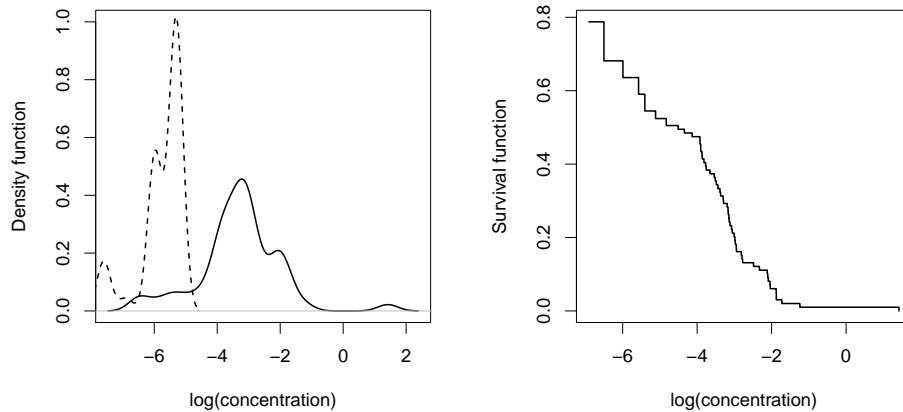


Figure 2.1: Cadmium data 1. Kernel density function (left panel: solid line represents uncensored data, dashed line represents LODs) and Kaplan-Meier estimate of survival function (right panel) of logarithm of concentrations.

small concentration measured below the LOD of another laboratory.

In Chapter 3 we will fit parametric and semi-nonparametric models to the Cadmium data 1. Their performance is measured and compared. In Chapter 4 we will perform a goodness-of-fit test for the log-normal distribution. An estimate for the distribution function of the Cadmium data 1 and model averages are computed in Chapter 5. Finally, estimates and model averages for the quantiles of this sample are computed in Chapter 6.

A second sample concerns data from the food category “coffee, tea and cacao” from Country B. Apart from the left censoring, also interval censoring is present in this data set. In total there are 114 observations, of which 94 concentrations are measured, while 3 are censored by a limit of detection and 17 are in between a limit of detection and a limit of quantification.

Data are shown in Figure 2.2, where left-censored values are replaced by $\text{LOD}/2$ and interval-censored by $(\text{LOD} + \text{LOQ})/2$.

Several models are fit to the Cadmium data 2 in Chapter 3. In Chapter 4 we test whether this sample comes from a log-normal distribution. Estimates for the distribution function are computed and are used for model averages in Chapter 5.

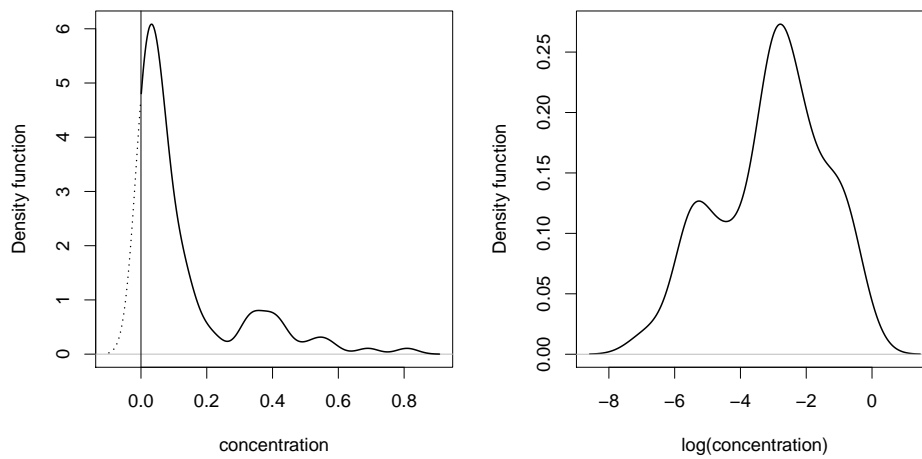


Figure 2.2: Cadmium data 2. Kernel density function of concentrations (left panel, the standard kernel density estimator does not account for concentrations to be positively valued) and logarithm of concentrations (right panel). Left-censored values have been replaced by $\text{LOD}/2$ and interval-censored by $(\text{LOD}+\text{LOQ})/2$.

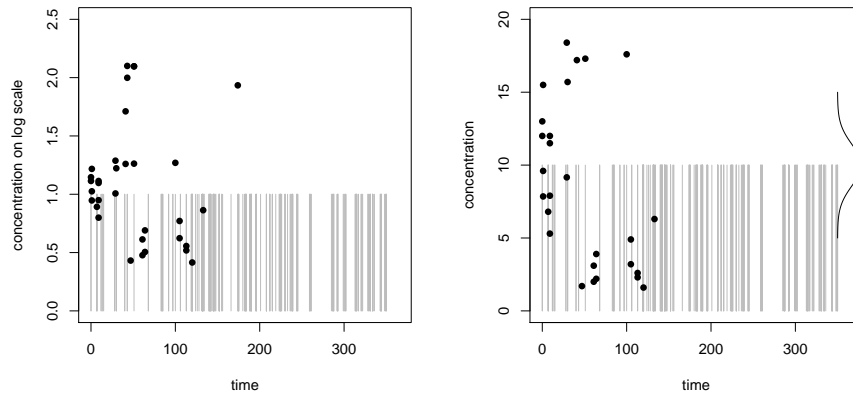


Figure 2.3: Cesium data. The censored observations are represented by a grey vertical line, representing the range in which the true unknown value is located, below the LOD value of 10; on the \log_{10} scale (left panel) and on regular scale cut off at 20 (right panel). The right panel shows on the right vertical scale a normal distribution at the value of the LOD value of 10, representing the uncertainty about the true LOD values.

2.1.2 Cesium data

Immediately after the accident at Tokyo Electric Power Company's Fukushima Daiichi Nuclear Power Plant in March 2011, the Government of Japan had taken comprehensive actions, such as establishing provisional regulatory values, monitoring of foods and materials for agricultural production, restriction of distribution of food with higher radionuclide levels than the regulatory values, and decontamination of farm land in order to ensure sufficient supply of safe foods distributed within Japan as well as for export. In April 2012, new limits were established for foods on a basis of intervention exemption level of 1 mSv/year (Sievert or Sv is a derived unit of radiation dose), equivalent to the Codex Standard and monitoring results accumulated. The data are publicly available on the website of the Japanese Ministry of Health (<http://www.mhlw.go.jp/english/topics/2011eq/index.html>).

We consider a sample of 278 $^{134}\text{Cesium}$ measurements in pork meat (excl. wild boar) at 106 unique points in time, in the prefecture Fukushima. 88% of the measurements is censored, meaning that the concentration is below a LOD. The LOD is fixed and equal to 10 across all measurements. The actual LOD values are unknown but are expected to be “about” 10. A graphical representation of the sample is given in Figure 2.3.

In Chapter 6 we estimate and model average the quantiles. In contrast to the Cadmium data, there is a time component in this sample and we explain how we can cope with this component in the analysis. We also deal with the uncertainty about the LOD.

Table 2.2: Signal Tandmobiel data. Number of observations: interval - right-censored.

	sound	decayed
Girls	778-447	663-220
Boys	647-630	687-314

2.2 Signal Tandmobiel data

A typical example of time-to-event data comes from the Signal Tandmobiel study. The study was conducted in Flanders (Belgium) from 1996 to 2001. A cohort of 4430 randomly sampled schoolchildren (2297 boys and 2133 girls) attending the first year of the primary school at the beginning of the study, was examined annually by one of 16 trained dentists. From a methodological viewpoint, this data set has already been presented in Bogaerts and Lesaffre (2004) and in Komarek and Lesaffre (2006; 2007; 2008), among others. We will restrict analysis to the emergence time distribution of the permanent upper left first premolar (tooth 24 in European dental notation). The age of emergence of the permanent tooth 24, denoted by T , can be interval-censored as well as right-censored, but is never observed exactly. As suggested in Komarek and Lesaffre (2009), since permanent teeth do not emerge before the age of 5, the origin time for all analyses is set at 5 years and $T - 5$ is taken instead of T throughout. We split the data according to gender and the status of the primary predecessor of their tooth (0 if sound and 1 if decayed, missing due to caries or filled), resulting in four subgroups. The number of observations in each group is given in Table 2.2.

In Chapter 4 we will use a newly proposed goodness-of-fit test to test whether the data are log-normally distributed.

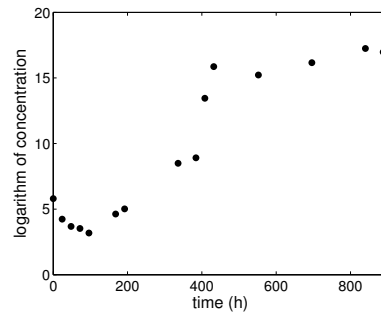


Figure 2.4: *Y. enterocolitica* data. Scatter plot of logarithm of concentration versus time.

2.3 Microbial risk data

The example concerns the concentration of a species of gram-negative coccobacillus-shaped bacterium *Yersinia enterocolitica*. The bacteria cause the yersiniosis disease, a zoonotic disease in humans as well as animals (cattle, pigs, birds). The disease usually does not require treatment, but for severe infections antibiotics might be needed.

The data are available on the ComBase website (<http://www.combase.cc>), and the sample consists of $n = 15$ measurements at a temperature of 20°C and pH equal to 7. The first measurement was done at time 0 and the next after 1, 2, 3 and 4 days. After the fourth day, the recording was no longer daily. The last concentration was measured after 37 days (888h). The data are shown in Figure 2.4, with log transformed counts of *Yersinia enterocolitica* bacteria on the y-axis.

In Chapter 7 we will use a model, characterized by differential equations, to describe the *Y. enterocolitica* data. On the one hand we will allow for deviations from the model; on the other hand we impose a monotonicity constraint.

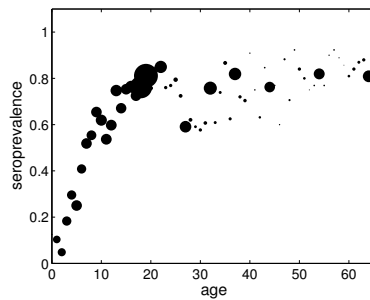


Figure 2.5: Parvovirus B19 data. Proportion of positive samples for every age, with dots proportional to sample size.

2.4 Serological data

A seroprevalence survey testing for Parvovirus B19 IgG antibody was performed on a large representative national serum bank in Belgium between November 2001 and March 2003 and in other countries. In this dissertation we only use data from Belgium. Sera of 3080 individuals with ages varying between 0 and 82 year for a total of 71 different ages (in years) were tested (more details in Hens et al., 2012). As for the highest age groups (66, 71, 78, 79 and 82) only 1 individual was tested (all being positive), these age groups were excluded from the sample, resulting in $n = 66$ different age groups. Parvovirus B19 is the infectious agent of erythema infectiosum, also known as the slapped cheek syndrome or fifth disease. The disease is usually mild in children and teenagers, but infection during pregnancy can lead to miscarriage, fetal anemia, etc. The disease is mainly transmitted through respiratory route, but other transmission rates are reported as well. The proportion of positive samples per age class is shown in Figure 2.5.

We will use the model of Farrington (1990) to describe the data in Chapter 7, but we allow for deviations from the model. We will also test whether the model is appropriate.

Chapter 3

Statistical models related to the log-normal distribution for censored data

Concentration measurements, such as in the Cadmium or Cesium data, are positively valued and, often, skewed to the right. A typical way to deal with the skewness is to use a logarithmic transform of the concentrations, leading to the log-normal distribution as a natural and convenient option for the concentration data. As family of parametric models we consider other parametric distributions which are directly related to or are extensions of the log-normal distribution: the log-skew-normal, the log-t, the log-skew-t, the Weibull and the gamma distributions. The generalized gamma distribution includes several of the previously mentioned distributions as special cases. Each of these distributions will be described briefly. We also consider a family of semi-nonparametric models, SemiNP (Fenton and Gallant, 1996; Gallant and Nychka, 1987), which will be described in Section 3.2. For both families we use maximum likelihood theory for censored data.

Instead of using parametric models or a family of semi-nonparametric models, we could also fit a nonparametric distribution to the data. The Kaplan-Meier estimator is a frequently used estimator for the survival function of right-censored data. For every event in the sample, there is a jump in the estimator. There is no jump for a censored observation, but all following events will have a larger jump. The Kaplan-Meier estimator

is defined as

$$\hat{S}_{KM}(y) = \prod_{j: y_j \leq y} \left(\frac{n-j}{n+1-j} \right)^{\delta_j}, \quad (3.1)$$

where $\delta_j = \delta_{E_j}$ (see Section 3.3), $y_j = \min\{x_j, t_j\}$, $y_1 \leq y_2 \leq \dots \leq y_n$ and in case of ties the censoring happens instantaneously after an event. Sometimes the survival function of the censored observations is used, which is defined as

$$\hat{S}_{KM,T}(y) = \prod_{j: y_j \leq y} \left(\frac{n-j}{n+1-j} \right)^{1-\delta_j}.$$

The Kaplan-Meier estimator can also be used for left-censored data, by reversing the order of the observations (Gomez et al., 1992). Another approach to obtain a non-parametric estimate of the survival curve in case of left-censored data, is given by Turnbull (1976). An advantage of this approach is that it can also be used for interval-censored data. Note that we will not focus on the fully nonparametric models such as the Kaplan-Meier estimator. This is because such models are of a different nature, and moreover they might not be applicable for our setting of interest. Indeed if the smallest value in the data is censored, which is essentially always the case for censoring caused by LOD, the Kaplan-Meier estimator is undefined in the left tail of the distribution (see e.g. Gillespie et al., 2010).

The performance of the parametric models will be compared to the performance of the semi-nonparametric family of distributions in a data example and in a simulation study.

3.1 Parametric models

We will introduce the log-normal distribution, with its link to the normal distribution. Next the log-t distribution is introduced, and a skewed log-normal and skewed log-t distribution. Then we deal with the gamma and Weibull distribution. Finally a link between the distributions is given by the generalized gamma distribution.

Log-normal distribution A log-normal distribution for concentrations Y corresponds to a normal distribution on the log-scale $X = \log Y$. The mean and variance of Y are given by $E(Y) = e^{\mu + \sigma^2/2}$ and $\text{Var}(Y) = (e^{\sigma^2} - 1)e^{2\mu + \sigma^2}$, with $\mu = E(X)$ and $\sigma^2 = \text{Var}(X)$ the mean and variance on the log-scale. The median is equal to $\text{Med}(Y) = e^\mu$, so back-transforming the mean on the log-scale to the original scale results in the median $\text{Med}(Y) = \exp(E(\log Y))$.

Log-t distribution A first extension is the log-t distribution, corresponding to the Student's t-distribution on the log-scale. A random variable Y with a log-t distribution with parameters μ , σ (location and scale on log-scale) and n (degrees of freedom), can be represented as $Y = \exp(\mu + \sigma X)$ with $X \sim t(n)$, a Student's t distribution with n degrees of freedom. If the degrees of freedom increase to infinity, the log-t distribution converges to the log-normal distribution. The mean and variance of Y are infinite (see e.g. Schmoyer et al., 1996); the median of Y is equal to $\text{Med}(Y) = e^\mu$.

Log-skew-normal and log-skew-t distribution On the log-scale, the skew-normal distribution $SN(\mu = 0, \sigma = 1, \alpha)$ has as density $f(x; \mu = 0, \sigma = 1, \alpha) = 2\phi(x)\Phi(\alpha x)$, where α is a skewness parameter, ϕ is the density and Φ the distribution function of the standard normal distribution (Azzalini, 1985; Azzalini and Dalla Valle, 1996; Azzalini and Capitanio, 2003; Azzalini et al., 2003). On the original scale Y , the location parameter μ and scale parameter σ can be introduced by setting $\log Y = \mu + \sigma X$, where X is a skew-normal $SN(\mu = 0, \sigma = 1, \alpha)$ distributed random variable. The density function of the log-skew-normal with parameters (μ, σ, α) is given by

$$f_{LSN}(y; \mu, \sigma, \alpha) = \frac{2}{\sigma y} \phi\left(\frac{\log y - \mu}{\sigma}\right) \Phi\left(\alpha \frac{\log y - \mu}{\sigma}\right), \quad y > 0.$$

If $\alpha = 0$, this distribution reduces to the log-normal distribution. Lin and Stoyanov (2009) proved that a log-skew-normal random variable Y with parameters $\mu = 0, \sigma = 1, \alpha$ has t -order moment, for any real t ,

$$E(Y^t) = 2 \exp(t^2/2) \Phi(\delta t), \quad \text{where } \delta = \frac{\alpha}{\sqrt{1 + \alpha^2}},$$

but does not have a moment generating function and is moment-indeterminate. There is to our knowledge no closed form for the mean and variance of a general log-skew-normal distributed random variable Y , nor for the median.

In the same way, the log-skew-t distribution with parameters (μ, σ, α, n) is defined as $Y = \exp(\mu + \sigma X)$ with X a skew-t distribution. Azzalini et al. (2003) used the log-skew-normal and log-skew-t distributions as models for family income data.

Gamma and Weibull distribution The gamma distribution with shape parameter k and scale parameter a ($a, k > 0$) is defined by

$$f(y; a, k) = a^{-k} y^{k-1} \exp(-y/a) / \Gamma(k), \quad y > 0,$$

with mean $\mu = ak$ and variance $\sigma^2 = ka^2$. The Weibull distribution with shape parameter b and scale parameter a ($a, b > 0$) is defined by

$$f(y; a, b) = ba^{-b} y^{b-1} \exp(-(y/a)^b), \quad y > 0,$$

with $\mu = a\Gamma(1 + 1/b)$ and $\sigma^2 = a^2\Gamma(1 + 2/b) - \mu^2$.

Generalized gamma distribution The generalized gamma distribution is a continuous probability distribution with three parameters. It is a generalization of the two-parameter gamma distribution. The gamma and Weibull distribution are special cases of the family. The probability density function can be written as

$$f(y; a, k, b) = ba^{-bk}y^{bk-1} \exp(-(y/a)^b)/\Gamma(k), \quad y > 0,$$

with parameters $a, k, b > 0$. The gamma distribution is obtained for $b = 1$ and the Weibull for $k = 1$. Other special cases are the exponential distribution ($b = k = 1$) and the chi-squared distribution with $n/2$ degrees of freedom ($a = 2, k = n/2, b = 1$). The log-normal distribution is a limiting case for $k \rightarrow \infty$. This can be proven via the reparametrization $\lambda = \frac{1}{\sqrt{k}}$, $\sigma = \frac{1}{b\sqrt{k}}$ and $\mu = \log a + \frac{1}{b} \log k$:

$$f(y; \mu, \sigma, \lambda) = \frac{\lambda}{y\sigma\Gamma(\frac{1}{\lambda^2})} \exp \left[\frac{\lambda \frac{\log y - \mu}{\sigma} + \log(\frac{1}{\lambda^2}) - \exp \left\{ \lambda \frac{\log y - \mu}{\sigma} \right\}}{\lambda^2} \right],$$

with Stirling's formula and a Taylor expansion.

3.2 A semi-nonparametric family of distributions

A convenient way to extend a distribution is by use of the SemiNP model (Fenton and Gallant, 1996; Gallant and Nychka, 1987). The SemiNP representation of a density is given by

$$f_r(y) = P_r^2(y)f(y). \quad (3.2)$$

In this formulation $P_r(y) = a_0 + a_1y + \dots + a_r y^r$ is a polynomial of degree r with $(a_0, \dots, a_r)^T$ such that $\int f_r(y)dy = 1$. Furthermore $P_0 \equiv a_0 = 1$, such that $f_0(y)$ corresponds to the base density. Values $r > 0$ control the extent of departure from the base density and the larger the order r the more flexible the density f_r . It is assumed that the true unknown density lies in a broad class whose elements may be approximated by the SemiNP density estimator, tailored to provide an excellent approximation to virtually any plausible density. Zhang and Davidian (2008) proposed a general framework for regression analysis of time-to-event data subject to arbitrary patterns of censoring based on the SemiNP representation and showed that this formulation allows popular models, such as the proportional hazards, proportional odds, and accelerated failure time models, to be placed in a common framework.

Zhang and Davidian (2008) present an algorithm to determine the coefficients \mathbf{a} . The estimation consists of first applying a matrix decomposition and spherical transformation to uniquely define the coefficients a_0, \dots, a_r that determine the extended density function. The transformed parameters are denoted by ϕ_1, \dots, ϕ_r . We will go through these steps for $r = 3$, where we assume that the null distribution f_0 is the density function of the standard normal distribution.

Firstly, we note that

$$\begin{aligned} \int f_3(y)dy &= \int (a_0 + a_1y + a_2y^2 + a_3y^3)^2 f_0(y)dy, \\ &= \mathbf{a}^T \mathbf{A} \mathbf{a}, \\ &= 1, \end{aligned} \tag{3.3}$$

where $\mathbf{a} = (a_0, a_1, a_2, a_3)$ is the vector of coefficients, $\mathbf{A} = E(\mathbf{W}\mathbf{W}^T)$ represents the moments and $\mathbf{W} = (1, Y, Y^2, Y^3)^T$ is a stochastic vector. As the moments of the standard normal distribution are not hard to calculate, it is easy to construct the matrix \mathbf{A} :

$$\mathbf{A} = E \begin{pmatrix} 1 & Y & Y^2 & Y^3 \\ Y & Y^2 & Y^3 & Y^4 \\ Y^2 & Y^3 & Y^4 & Y^5 \\ Y^3 & Y^4 & Y^5 & Y^6 \end{pmatrix} = \begin{pmatrix} 1 & 0 & 1 & 0 \\ 0 & 1 & 0 & 3 \\ 1 & 0 & 3 & 0 \\ 0 & 3 & 0 & 15 \end{pmatrix}. \tag{3.4}$$

Secondly, we want to express the matrix of moments \mathbf{A} as the product of $\mathbf{B}^T \mathbf{B}$. The matrix \mathbf{B} can be obtained by the Cholesky decomposition which results in an upper triangle matrix. Basic matrix-calculation can be used to find the Cholesky decomposition and these calculations are programmed in many mathematical programs (e.g. Maple):

$$\mathbf{B} = \begin{pmatrix} 1 & 0 & 1 & 0 \\ 0 & 1 & 0 & 3 \\ 0 & 0 & \sqrt{2} & 0 \\ 0 & 0 & 0 & \sqrt{6} \end{pmatrix}.$$

By using the decomposition in (3.3) and replacing $\mathbf{B}\mathbf{a}$ by \mathbf{c} , we get

$$\begin{aligned} 1 &= \mathbf{a}^T \mathbf{B}^T \mathbf{B} \mathbf{a} \\ &= \mathbf{c}^T \mathbf{c}. \end{aligned} \tag{3.5}$$

Thirdly, equation (3.5) implies that $\mathbf{c} = (c_0, \dots, c_3)$ lies on the unit sphere, suggesting

the spherical transformation

$$\begin{aligned} c_0 &= \sin(\phi_1), \\ c_1 &= \cos(\phi_1) \sin(\phi_2), \\ c_2 &= \cos(\phi_1) \cos(\phi_2) \sin(\phi_3), \\ c_3 &= \cos(\phi_1) \cos(\phi_2) \cos(\phi_3). \end{aligned}$$

Fourthly, we will estimate the parameters (ϕ_1, \dots, ϕ_3) and as such obtain estimates for \mathbf{c} . As $\mathbf{a} = \mathbf{B}^{-1}\mathbf{c}$, it is only a matter of matrix multiplication to get estimates for \mathbf{a} . Note that \mathbf{A} and \mathbf{B} are positive definite matrices, such that \mathbf{B}^{-1} exists.

We are interested in the SemiNP representation as a framework to model distributions of data such as the cadmium data, where data are positive. A popular distribution is the log-normal distribution, that is directly linked to the well known normal distribution. By a simple transformation $Z = \frac{\log Y - \mu}{\sigma}$, the density f_0 of the log-normal distribution can be written as

$$f_0(y) = (y\sigma)^{-1} \phi\left(\frac{\log y - \mu}{\sigma}\right).$$

In the same way, we define the density of the extension of the log-normal distribution as

$$f_r(y) = (y\sigma)^{-1} P_r^2\left(\frac{\log y - \mu}{\sigma}\right) \phi\left(\frac{\log y - \mu}{\sigma}\right).$$

As we will mention in the next section, we also need the survival function in order to compute the likelihood for censored data. Once the density is known, it is straightforward to obtain the survival function:

$$S_r(y) = \int_{\frac{\log y - \mu}{\sigma}}^{\infty} P_r^2(z) \phi(z) dz.$$

Some examples of the density function for $r = 1$ are provided in Figure 3.1. One additional parameter ϕ_1 defines the coefficients a_0 and a_1 of the polynomial P_r . The left panel shows the density with $\mu = 0$ and $\sigma = 1$, while $\mu = 0$ and $\sigma = 0.5$ in the right panel. The log-normal distribution corresponds to $\phi_1 = \pi/2$ ($a_0 = 1$, $a_1 = 0$, solid line), while other values of ϕ_1 result in other densities: $\phi_1 = \pi/4$ ($a_0 = \sqrt{2}/2$, $a_1 = \sqrt{2}/2$, dashed line), $\phi_1 = 3\pi/4$ ($a_0 = \sqrt{2}/2$, $a_1 = -\sqrt{2}/2$, dotted line) and $\phi_1 = \pi$ ($a_0 = 0$, $a_1 = 1$, dash-dotted line).

Zhang and Davidian (2008) propose a recursive way to determine the extension of the survival and density function in terms of the SemiNP representation. Since $P_r(y)$ is a polynomial, partial integration can be used to simplify the integral. Hence the distribution

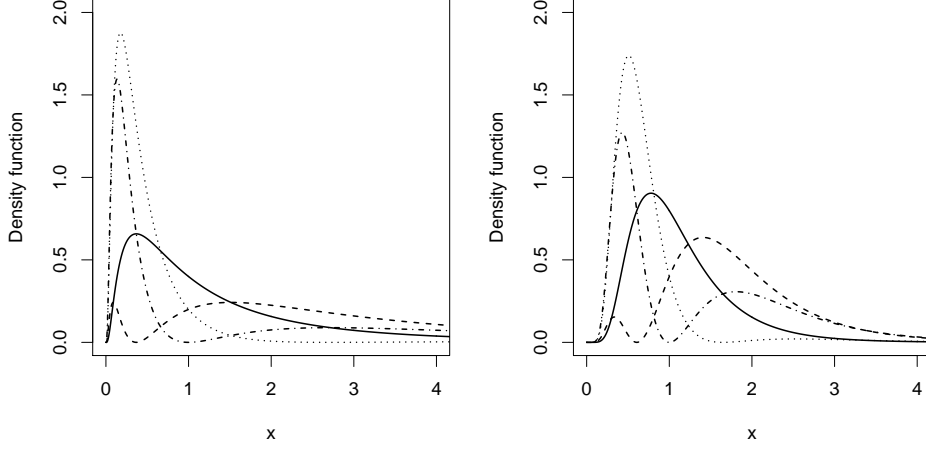


Figure 3.1: SemiNP models. Examples of density function f_1 , with $\mu = 0$ and $\sigma = 1$ (left panel) or $\sigma = 0.5$ (right panel). Additional parameter ϕ_1 is set to $\pi/4$ ($a_0 = \sqrt{2}/2$, $a_1 = \sqrt{2}/2$, dashed line), $\pi/2$ ($a_0 = 1$, $a_1 = 0$, solid line, log-normal distribution), $3\pi/4$ ($a_0 = \sqrt{2}/2$, $a_1 = -\sqrt{2}/2$, dotted line) and π ($a_0 = 0$, $a_1 = 1$, dash-dotted line).

function can be expressed as a linear combination of the density and the cumulative distribution function of the standard normal. Zhang and Davidian (2008) introduce the integral $I(k, c) = \int_c^\infty z^k \varphi(z) dz$. The survival function $S_r(y)$ can be expressed as the sum of several of these integrals:

$$\begin{aligned} S_r(y) &= \int_{(\log y - \mu)/\sigma}^{\infty} P_r^2(z) \phi(z) dz \\ &= a_0^2 I\left(0, \frac{\log y - \mu}{\sigma}\right) + a_0 a_1 I\left(1, \frac{\log y - \mu}{\sigma}\right) + (a_1^2 + a_0 a_2) I\left(2, \frac{\log y - \mu}{\sigma}\right) \\ &\quad + \dots + a_r^2 I\left(r^2, \frac{\log y - \mu}{\sigma}\right). \end{aligned}$$

Furthermore, the integrals $I(k, c)$ define a recursive relation, i.e.

$$\begin{aligned} I(0, c) &= 1 - \Phi(c), \\ I(1, c) &= \varphi(c), \\ I(k, c) &= c^{k-1} \varphi(c) + (k-1) I(k-2, c), \quad k \geq 2. \end{aligned}$$

Whereas Fenton and Gallant (1996) and Zhang and Davidian (2008) argue that f_r with $r \leq 4$ can well approximate a diverse range of true densities, our experience is that

larger values of r might be needed. For practical and computational feasibility we limit ourselves to $r \leq 7$.

For each fixed r , the set of parameters $\mu, \sigma, a_0, \dots, a_r$ can be estimated by maximizing the likelihood function (3.6) for censored data, with now f and S replaced by f_r and S_r . The order r can be selected adaptively by inspection of an information criterion. For a given dataset, \hat{r} denotes that value of r that optimizes Akaike's information criterion (see Section 3.3), resulting in the final SemiNP model $f_{\hat{r}}$.

The likelihood is maximized by taking starting values for ϕ over a grid. For example, for $r = 1$, we use the estimates $\hat{\mu}$ and $\hat{\sigma}$ from the null model and let ϕ_1 start at 0 and increase in steps of $\pi/16$. For the other degrees of extension, we use the estimated parameters from the lower degree and let the *new* ϕ_r vary in the same range as above. By following this procedure, we obtain a set of local maxima for each r and the maximum likelihood is then chosen to be the largest from this set.

General expressions can be derived for the moments and the median for any value of r . However the expressions become quite unattractive. For instance, for $r = 1$, the mean equals $\exp(\mu + \sigma^2/2)(1 + 2\sigma a_0 a_1 + \sigma^2 a_1^2)$ and the variance $\exp(2\mu + 2\sigma^2)(1 + 4\sigma a_0 a_1 + 4\sigma^2 a_1^2) - \exp(2\mu + \sigma^2)(1 + 2\sigma a_0 a_1 + \sigma^2 a_1^2)^2$.

3.3 Terminology for censored data

Suppose X has a distribution function F and x_1, \dots, x_n is a sample from this distribution. These observations can be left- or right-censored by a value t_i or interval-censored by two values t_{L_i} and t_{R_i} . Indicator functions for the different types of censoring on the i -th observation can be defined as follows

$$\begin{aligned}\delta_{R_i} &= 1 \text{ if right-censoring at } t_i < x_i, 0 \text{ otherwise;} \\ \delta_{L_i} &= 1 \text{ if left-censoring at } t_i > x_i, 0 \text{ otherwise;} \\ \delta_{I_i} &= 1 \text{ if interval-censoring at } t_{L_i} < x_i \leq t_{R_i}, 0 \text{ otherwise;} \\ \delta_{E_i} &= 1 \text{ if the event is observed exactly at } t_i = x_i, 0 \text{ otherwise.}\end{aligned}$$

It holds that $\delta_{E_i} + \delta_{R_i} + \delta_{L_i} + \delta_{I_i} = 1$.

An observation is right-censored $\delta_{R_i} = 1$ at t_i when the true value x_i is not observed before t_i and is known to exceed t_i . The observed value is given by $y_i = \min(x_i, t_i)$. For example, the true event is time-to-death which cannot be observed because censoring happens at the end of the study.

An observation is left-censored $\delta_{L_i} = 1$ when the value x_i is known to be smaller than t_i , e.g. limit of detection (LOD). In this case, the observed value is $y_i = \max(x_i, t_i)$.

An observation is interval-censored $\delta_{I_i} = 1$ when x_i is known to be larger than a value t_{L_i} , but smaller than t_{R_i} , e.g. between the limit of detection (LOD) and the limit of quantification (LOQ). Left and right censoring are special cases of interval censoring.

All observations can be represented by $(t_{L_i}, t_{R_i}, \delta_{R_i}, \delta_{L_i}, \delta_{I_i})$. For left censoring we have $t_{L_i} = -\infty$ (or $t_{L_i} = 0$ if all observations are assumed to be non-negative, e.g. in survival analysis) and $t_{R_i} = t_i$. In case of right censoring we have $t_i = t_{L_i}$ and $t_{R_i} = \infty$. If the observation is not censored, then $t_{L_i} = t_{R_i} = t_i = x_i$.

Let the density function of the true values X be represented by $f(\cdot)$, the cumulative distribution function by $F(\cdot)$ and the survival function by $S(\cdot)$. Typically these functions depend on some parameters θ . If we assume that censoring of the observations occurs independently, then the likelihood function for the sample of n observations is

$$L(\theta) = \prod_{i=1}^n \left\{ f(t_i)^{\delta_{E_i}} [1 - S(t_i)]^{\delta_{L_i}} [S(t_i)]^{\delta_{R_i}} [S(t_{L_i}) - S(t_{R_i})]^{\delta_{I_i}} \right\}. \quad (3.6)$$

When there is no censoring, the likelihood function reduces to the simple likelihood $\prod f(t_i)$.

All parametric models can be fitted to censored data by maximizing the likelihood $L(\theta)$ as defined in (3.6). Akaike's information criterion (AIC, Akaike, 1973) is a commonly used measure to compare the fit of several candidate models. It is defined as $AIC = -2 \log L(\theta) + 2K$, where K represents the number of parameters in the model. The lower the AIC value, the better the model succeeds in fitting to the data while accounting for complexity. Claeskens and Carroll (2007) used AIC for model selection in general semi-nonparametric problems. AIC has also been studied for selection of the smoothing parameter in nonparametric models, see e.g. Hurvich et al. (1998).

Other model selection criteria can be used (e.g. Bayesian information criterion, BIC, Schwarz (1978)), each having pros and cons, but to our knowledge their behavior has not been studied in a comparative study for censored data and a detailed and full comparison of the performance characteristics of AIC with other criteria in our particular setting is beyond the scope of this research.

3.4 Application to data example

In the previous chapter, we have proposed several models that are related to the log-normal distribution. The AIC of each model, fitted to the Cadmium data, is given in Table 3.1.

It appears that from a computational point of view, the fit on the log-scale is often easier and a more global minimum is achieved. Therefore, in Table 3.1, AIC of these models is chosen to be the smallest of AIC on regular and (transposed) AIC on log-scale.

Table 3.1: Cadmium data 1 and 2. AIC of parametric and SemiNP models.

Distribution	Nr Par	Cadmium 1 Cadmium 2	
		AIC	AIC
GenGam	3	-64.918	-67.311
Gamma	2	-47.238	-68.086
Weibull	2	-65.741	-69.278
Log-skew-t	4	-72.846	-65.407
Log-t	3	-62.616	-57.669
Log-skew-n	3	-66.642	-67.744
Log-normal	2	-64.734	-59.863
SemiNP1	2+1	-65.783	-61.600
SemiNP2	2+2	-69.484	-60.781
SemiNP3	2+3	-78.382	-59.352
SemiNP4	2+4	-77.952	-57.690
SemiNP5	2+5	-76.637	-55.914
SemiNP6	2+6	-75.556	-54.073
SemiNP7	2+7	-74.215	-69.302

In these examples, only SemiNP7 for the Cadmium data 2 achieved a better fit on the log scale. We could improve the fit on the original scale by using the (transformed) estimates on the log scale (and vice versa) if it results in a better fit. This can be considered as an additional step or as an alternative to the use of different starting values for the parameter estimates.

For Cadmium 1, the gamma distribution has the largest AIC and is therefore the worst model. The AIC of the log-normal distribution, log-skew-normal, Weibull and generalized-gamma distribution are close. From the class of parametric models, the log-skew-t distribution performs best. Within the class of the SemiNP models, three extra parameters added to the log-normal distribution results in the best fit and the AIC value of this model is smaller than that of any parametric model. The non-parametric estimate and the estimated distribution functions of the log-normal and the log-skew-t distribution are depicted in the left panel of Figure 3.2, together with the adaptive SemiNP model.

The best parametric fit for Cadmium 2 is given by the Weibull distribution, with AIC equal to -69.278 . In the family of SemiNP models, the model with 7 extra parameters has the best global fit, with AIC = -69.302 . The fitted distributions are shown in the right panel of Figure 3.2, together with the non-parametric estimate.

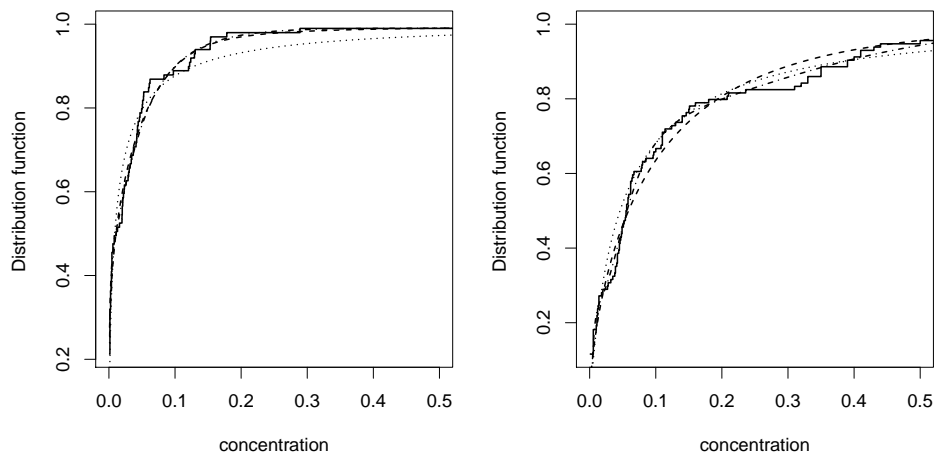


Figure 3.2: Cadmium data 1 (left) and 2 (right). Distribution function of concentration. Non-parametric estimate (solid line); fit of parametric models: log-normal (dots) and best fitting (dashed line, log-skew-t and Weibull respectively); and best SemiNP (dash-dotted line, $r = 3$ and $r = 7$ respectively).

3.5 Simulation study

In this section we describe a simulation study, which we will use for the goodness-of-fit test in Chapter 4 and model averaging in Chapters 5 and 6.

We focus on the setting of chemical risk assessment and testing for log-normality. In the first section we describe the generation of uncensored data under the null hypothesis and under two types of alternative hypotheses: i) a mixture of log-normal distributions with one component being the null distribution, and a second component located to the right of the first component (representing a local deviation from the null distribution), ii) a gamma distribution (representing a global deviation from the null distribution). In the second section the censoring mechanism is introduced. In Section 3.5.3 we elaborate on the computational issues that occurred when fitting the semiNP models. The models are compared with respect to AIC in Section 3.5.4. More results will follow in the next chapters.

3.5.1 Data sampling

The null model is defined as the log-normal distribution with mean 1 and standard deviation 2. This null model is then mixed with a second log-normal distribution with mean 2.818 and standard deviation 0.771, with a mixing proportion varying from 5% (as a contiguous alternative), 10% (less contiguous) to 25% (non-contiguous). We will refer to these distributions as the 95%, 90% and 75% mixture distributions. The left panel of Figure 3.3 shows that these mixture distributions deviate locally in the right tail from the null distribution. As another alternative model which deviates more globally from the null model, we consider the gamma distribution with the same mean 1 and standard deviation 2 as the log-normal null distribution (right panel of Figure 3.3). Sample sizes $n = 100, 200, 500$ were used, and for each setting 500 simulation runs.

3.5.2 Censoring scheme

As for the Cadmium data, we again assume that the data originate from several laboratories. Assume that there are five different limits of detection (LODs) and each LOD is associated with a laboratory. Each laboratory contributes the same amount of data. The LODs in the simulations correspond to theoretical percentiles of the aforementioned log-normal distribution. For example, the (1, 5, 10, 20, 25)-percentiles correspond to LODs 0.023, 0.055, 0.088, 0.154, 0.190 resulting in on average 12% censoring for a sample from the log-normal distribution. Figure 3.3 shows the location of the LODs (\blacktriangle) graphically. By taking the (25, 50, 75)-percentiles for the LODs, on average 50% is censored. They

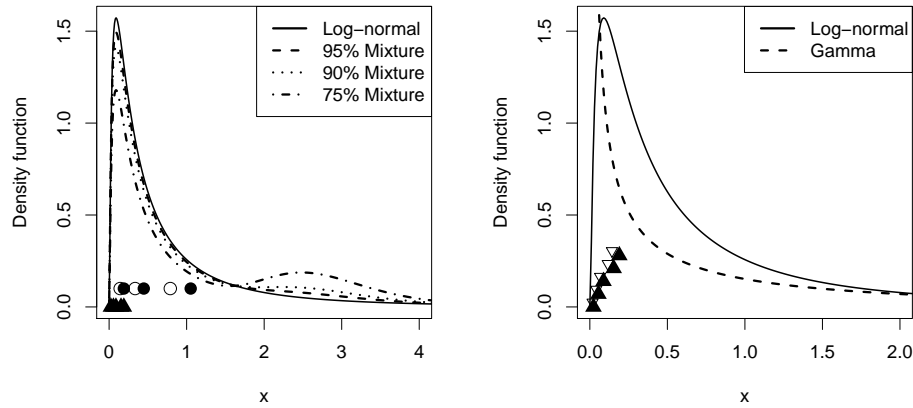


Figure 3.3: Simulation study. Left panel: sampling distributions are log-normal and mixture distributions; left censoring based on 5 LODs (▲) and 3 LODs (●); left and interval censoring based on LODs (▲) and LOQs (omitted) or 3 LODs (○) and LOQs (●). Right panel: log-normal and gamma distribution; left censoring for gamma based on 5 LODs (▲); left and interval censoring based on 5 LODs (▼) and LOQs (▲).

are represented by ● in Figure 3.3.

Additionally interval-censored data are sampled. A limit of quantification is set equal to a constant times the limit of detection. Data below LOD are left-censored and data in between LOD and LOQ are interval-censored. Only above LOQ, data can be exactly measured.

In the simulations of the log-normal and mixture distributions with 5 LODs, the LOQ is equal to 1.5 times the LOD. For this kind of interval censoring, more data are censored compared to the left-censored data. As LOD and LOQ are close together and not distinguishable in the graph, we omit the LOQs in the left panel of Figure 3.3. In case we have 3 LODs, we set LOQ equal to the (25, 50, 75)-percentiles and LOD (○) equal to 0.75 times LOQ (●). The simulations of the gamma distribution use the (1, 5, 10, 20, 25)-percentiles as 5 LODs, resulting in 42% left censoring (▲ in right panel of Figure 3.3). The interval censoring in this case is determined by $\text{LOD} = \frac{3}{4}\text{LOQ}$ and LOQ equal to the (1, 5, 10, 20, 25)-percentiles. The right panel of Figure 3.3 shows the location of these five LODs (▼) and LOQs (▲) in the gamma distribution, along a sloping line to make them visible.

To get more insights in how the left censoring occurs and what influence it has on the density function, some kernel density functions are calculated. Figure 3.4 shows a sample drawn from the log-normal distribution with sample sizes 200 and 500, of which 12% or

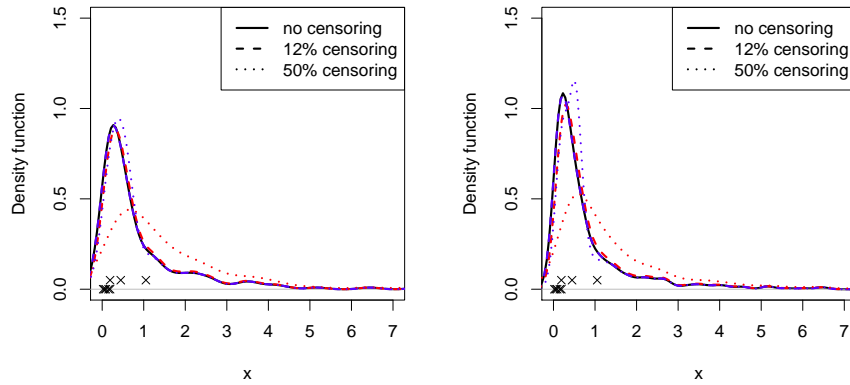
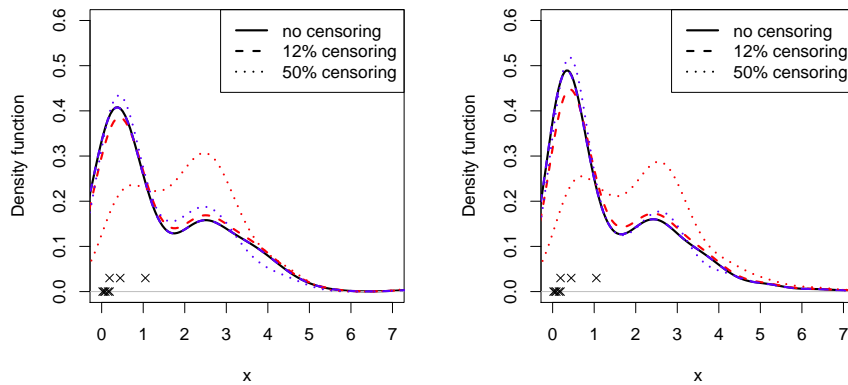


Figure 3.4: Simulations. Influence of censoring in log-normal distribution. Sample size 200 (left) and 500 (right). Censoring varies from none (full line) to 12% (dashed lines) and 50% (dotted lines). Kernel density function based only on uncensored observations in red; based on sample where censored values are replaced by $\text{LOD}/2$ in blue. Crosses represent location of LODs.

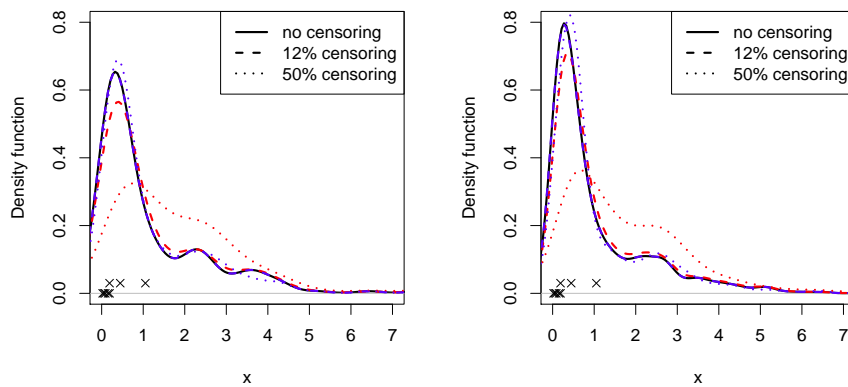
50% is censored. For each sample size, different curves are drawn: the solid line represents all data of which no point is censored, the dashed line represents 12% censoring and the dotted line 50%. For the censored case, the red line uses only the uncensored observations and is thereby based on less data. The blue line uses all data, but the (left-)censored data are replaced by the half of their limit of detection ($\text{LOD}/2$). The LODs are indicated by a cross on the x -axis for 12% censoring and above the axis for 50% censoring.

The censoring occurs on the left of the distribution. The influence of the 12% censoring is minor, but for 50% censoring there is a big difference in density functions.

The same patterns appear when samples are drawn from the mixture of two log-normal distributions. In Figure 3.5(a) the kernel density function of a sample from the 90% mixture distribution is drawn, causing the second bump in the density function. The means of the two distributions are quite distant. However, only 10% of the observations come from this second (log-normal) distribution. In Figure 3.5(b) we draw the kernel density function of a sample from the 75% mixture distribution. These data are quite far away from the null hypothesis. The more data ($< 50\%$) come from the right distribution, the more they differ from the null hypothesis.



(a) 90% mixture distribution



(b) 75% mixture distribution

Figure 3.5: Simulations. Influence of censoring in mixture of two log-normal distributions. Sample size 200 (left) and 500 (right). Censoring varies from none (full line) to 12% (dashed lines) and 50% (dotted lines). Kernel density function based only on uncensored observations in red; based on sample where censored values are replaced by $\text{LOD}/2$ in blue. Crosses represent location of LODs.

3.5.3 Computational issues

For the parametric models, especially for the generalized-gamma distribution, it appears necessary to provide a series of several starting values to solve the convergence issues. As the fitting of the SemiNP models is very time consuming and computer intensive, we cannot provide multiple starting values for all fits. The SemiNP extensions are nested, so we use the estimates for the log-normal distribution as starting values for the first extensions with 16 different values for the extra parameter. These estimates are in turn used as starting values for the second extensions with again 16 values for the extra parameter, and so on. Nevertheless there are major problems. Eventually there are no error messages for the calculation of the estimates, but standard errors cannot always be computed (the final Hessian matrix is of full rank but with at least one negative eigenvalue). Only estimates of the models of which the hessian has no negative eigenvalue, are included in the tables. For the uncensored data, at least one extended model of the SemiNP family has no converging issues. For the samples with censoring, drawn from the log-normal distribution with sample size 100, 200 and 500 respectively, there are 121, 179 and 210 samples where none of the extended models converge. For the 75% mixture, every sample has at least one extension, for the 90% mixture there are 10, 9 and 6 samples (for the respective sample sizes) where none of the extended models converge, while for the 95% mixture 28, 38 and 70 samples have no converging extended model. For the data sampled from the gamma distribution there are 104, 74 and 42 samples for which none of the extended model converge. The lower values in the mixed samples can be expected since the SemiNP models can more easily detect local deviations from the base distribution compared to global. If none of the extended models converge, then the family of SemiNP models for this sample reduces to only one member, the log-normal distribution. Although there are major problems in the simulation study, these problems can be avoided in an individual analysis by carefully selecting the starting values.

3.5.4 Results

The models are ordered according to AIC, where order 1 corresponds to the best model and order 14 to the worst. Based on the orders of the 500 samples, we can make a boxplot for each fitted model. The results for a sample of size 500 from the log-normal distribution are given in Figure 3.6. Since the sample is taken from the log-normal distribution, we expect that the log-normal model fits the data best. This can be seen in the graph. The skewed distributions do not fit better than the original. The reason is that AIC penalizes for the number of parameters. Since data are sampled from the log-normal distribution, there is no skewness and the parameter accounting for skewness is redundant. The gamma

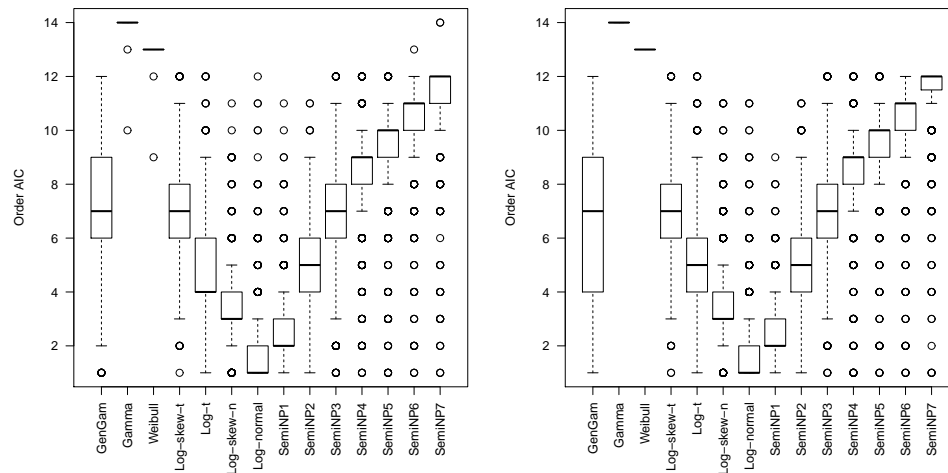


Figure 3.6: Simulation study. AIC order of every fitted model for sample from log-normal distribution with sample size 500. Left panel: no censoring, right panel: left censoring based on 5 LODs.

and the Weibull distributions provide no good fit on the simulated data. Furthermore we observe that the SemiNP models fit better with less parameters, which agrees with the penalization for extra parameters. Similar results are obtained for data with and without censoring.

As expected, when sampling from the gamma distribution, the best model according to AIC is the gamma distribution (see Figure 3.7). The log-skew-t distribution is often the second best model, while the log-t and the log-normal distribution provide no good fit. However we observe that the SemiNP model fits better when more parameters are used. This coincides with the expectation that any model can be well approximated with a member of the SemiNP family of distributions. If part of the data is censored (in this case almost 50% is censored), there is less information in the data. Therefore it is obvious that the benefit of extra parameters in the SemiNP distribution is limited. In this simulation we see that the best extension of the log-normal is given by 3 extra parameters.

For the other settings, we provide a summary plot in Figure 3.8 and 3.9 by only looking at the median order of AIC. For the samples from the pure distributions (log-normal or gamma) it is clear that it is harder to have enough information in the data such that the SemiNP distribution fits well. The decrease in AIC order stops at about 3 or 4 extra parameters when sampling from the gamma distribution. Also in the case of censoring, the minimum order for the SemiNP fits, is shifted to the right when compared to sample size 500. For the mixture distributions, the same pattern can be observed for both uncensored

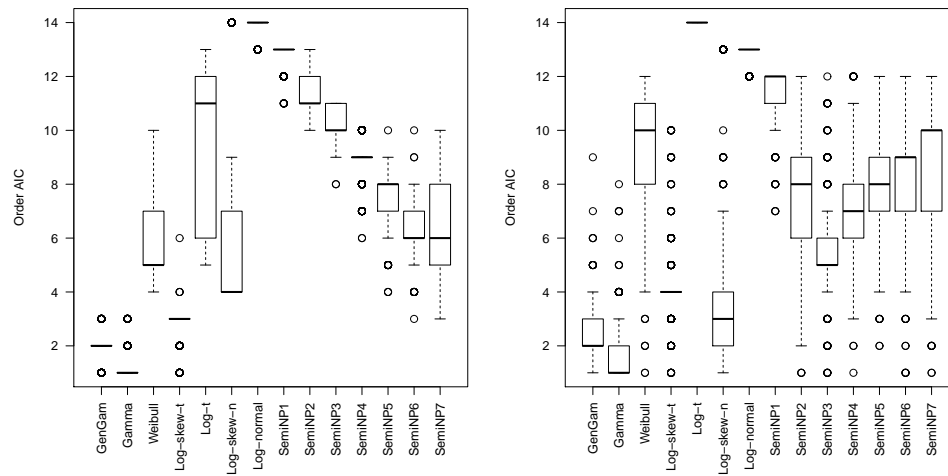


Figure 3.7: Simulation study. AIC order of every fitted model for sample from gamma distribution with sample size 500. Left panel: no censoring, right panel: left censoring based on 5 LODs.

and censored samples. The SemiNP distribution performs better than the log-normal. As the data are more mixed, the log-normal performs worse, but the SemiNP performs better. There is a dip around 3 to 5 parameters.

A disadvantage of the description of the results by means of the order of the model is that it does not show how much the fitted models differ from each other with regard to AIC. In other words, we do not know how large the difference is between the AIC of the fitted models.

3.6 Conclusion

In this chapter, we have discussed various statistical models that are related to the log-normal distribution. We started the discussion with parametric models and continued with a semi-nonparametric family of distributions. Maximum likelihood theory, with an adapted likelihood, was used to fit the models to censored data. All models were fit to the Cadmium data and were compared. Although the fit of the log-normal distribution was not bad, we found both parametric and SemiNP models that performed better with regard to AIC. For Cadmium data 1, the log-skew-t distribution and SemiNP3 models performed best. Different parametric and SemiNP models were chosen for Cadmium data 2: Weibull and SemiNP7.

The performance of the models was examined in a simulation study, by comparing their global fit to the data. Different scenarios for the simulated distribution and percentage

of censoring were considered. When sampling from the log-normal distribution, the best fitting distribution is often the log-normal itself, but also the log-skew-normal and SemiNP perform good. When sampling from a distribution other than the log-normal, the SemiNP models perform better than the log-normal, but also some of the parametric models are plausible depending on the situation. We will use the same simulation study in the next chapters to study the performance of a goodness-of-fit test for censored data and model averaging.

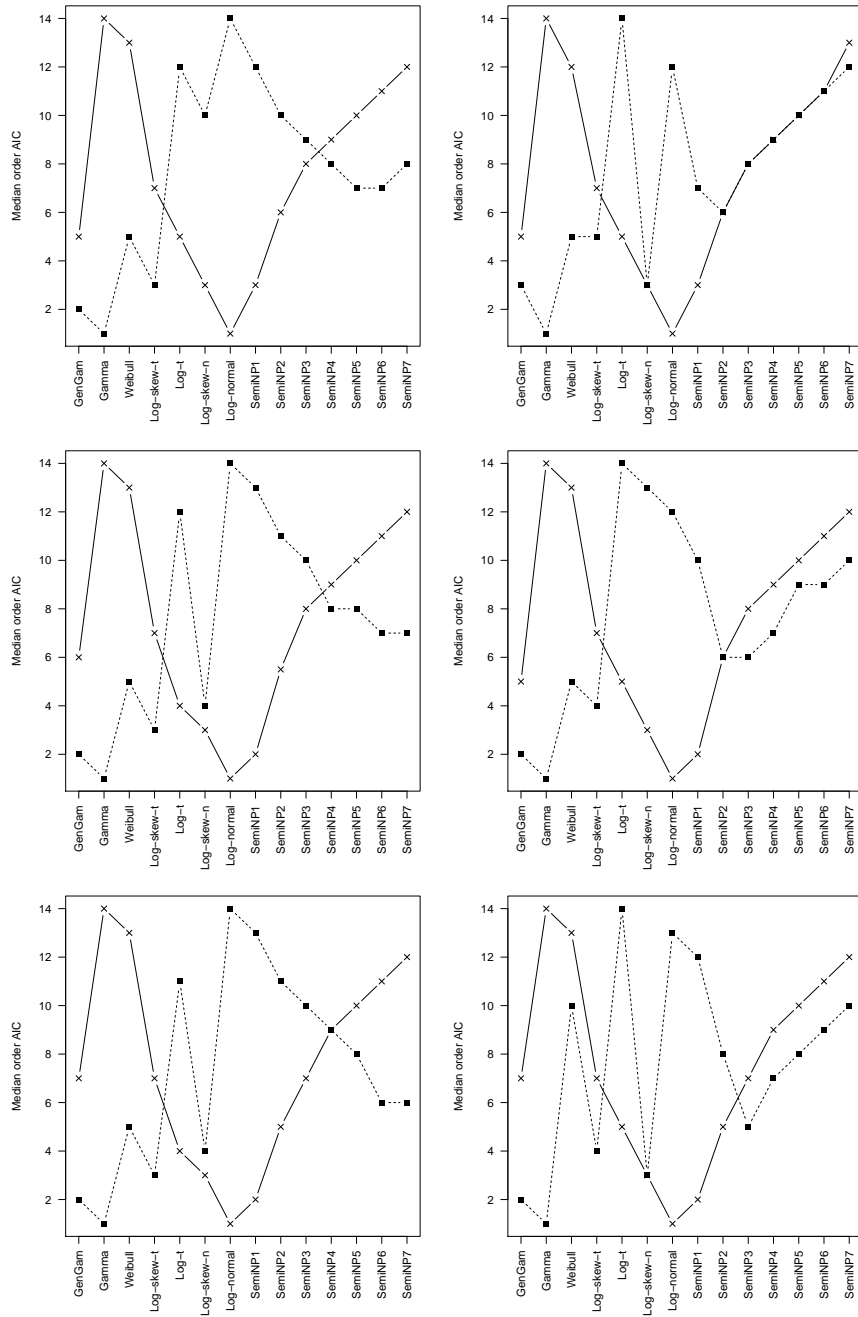


Figure 3.8: Simulation study. Median order AIC of samples from log-normal (\times) and gamma (\blacksquare) distribution with sample sizes 100 (upper), 200 (middle) and 500 (lower). Left panels: no censoring, right panel: left censoring based on 5 LODs.

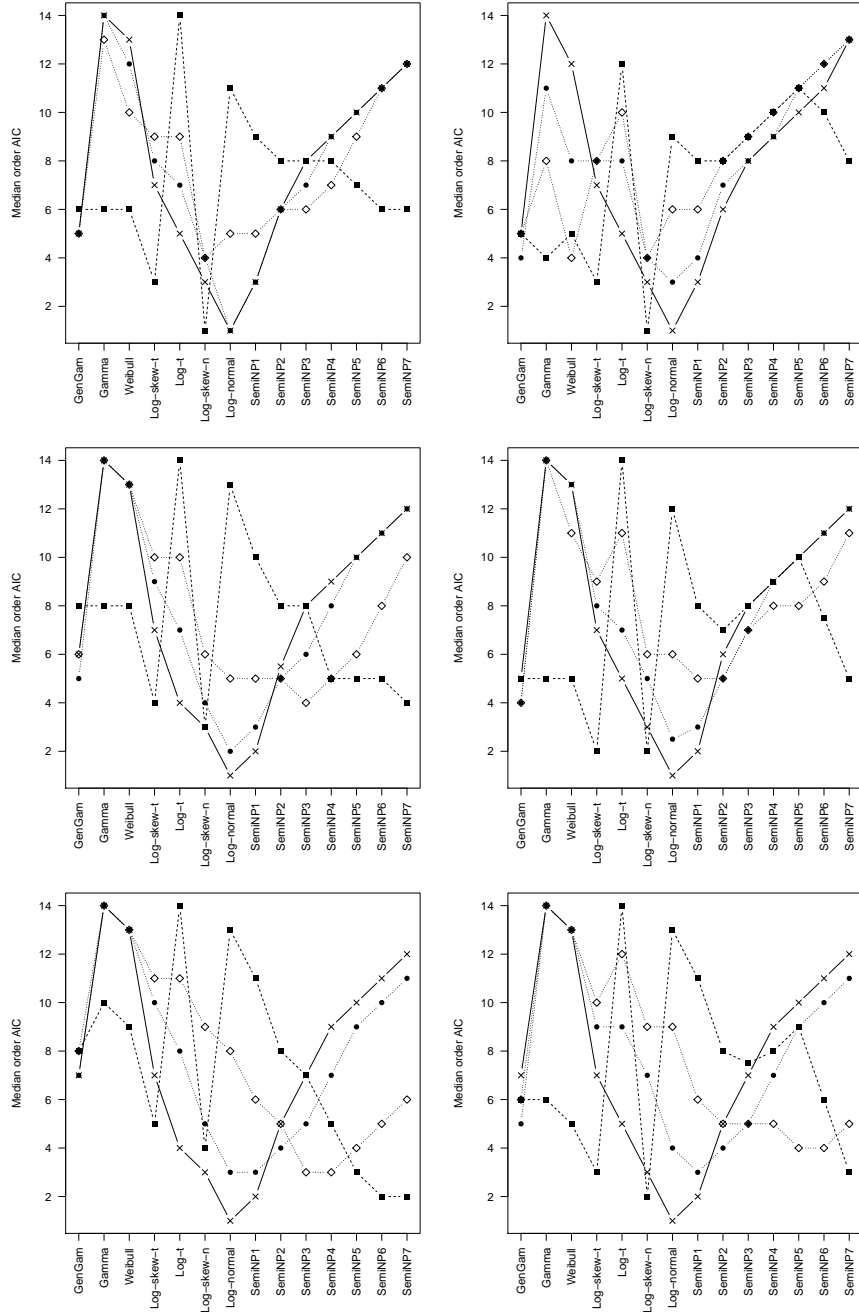


Figure 3.9: Simulation study. Median order AIC of samples from log-normal (\times), 95% (\bullet), 90% (\diamond) and 75% (\blacksquare) mixture distributions with sample sizes 100 (upper), 200 (middle) and 500 (lower). Left panel: no censoring, right panel: left censoring based on 5 LODs.

Chapter 4

Goodness-of-fit

In this chapter we propose and study a new goodness-of-fit test for left-, right- and interval-censored data, assuming random censorship. The test is based on the order selection test as described by Aerts et al. (1999), which requires a series of nested alternative models extending the null model. For censored data, such a family of densities is described by the SemiNP (Semi-NonParametric) representation (Fenton and Gallant, 1996; Gallant and Nychka, 1987; Zhang and Davidian, 2008) (see Chapter 3). The combination of the order selection test and the SemiNP representation results in the goodness-of-fit test for censored data proposed in this chapter. The material in this chapter was summarized in Nysen et al. (2012).

In goodness-of-fit testing, a distinction is made between a simple and a composite hypothesis. In a simple hypothesis, interest is only in the specific parameters of the distribution. For example, testing whether the data come from a normal distribution with mean zero and variance one. With a composite null hypothesis, we are interested in the shape of the underlying distribution. For example, testing whether the data follow a normal distribution, without specifying the parameters.

To test whether the true data come from a distribution with completely specified distribution function $F_0(y)$ (and survival function $S_0(y)$), the simple null-hypothesis equals

$$H_0 : F(y) = F_0(y) \quad \forall y. \quad (4.1)$$

The null hypothesis of the composite null hypothesis can be stated as follows:

$$H_0 : f \in \mathcal{G}_f, \quad (4.2)$$

where \mathcal{G}_f is some parametric family of density functions, like the family of log-normal distributions.

If the data are not censored, multiple tests exist for the composite null hypothesis. For example, the tests of Kolmogorov-Smirnov, Anderson-Darling and Cramér-von Mises (see e.g. D'Agostino and Stephens, 1986, for more details) are based on the empirical distribution function and are implemented in most statistical software.

The Kolmogorov-Smirnov statistic is defined as $\mathcal{D} = \sup_y |F_n(y) - F(y)|$. It is computed as the maximum of \mathcal{D}^+ and \mathcal{D}^- , where \mathcal{D}^+ is the largest vertical distance between the ECDF and the distribution function when the ECDF is greater than the distribution function, and \mathcal{D}^- is the largest vertical distance when the ECDF is less than the distribution function.

The Anderson-Darling and the Cramér-von Mises statistic belong to the quadratic class of ECDF statistics. This class of statistics is based on the squared difference of the ECDF and the distribution function. In general, quadratic statistics have the form $\mathcal{Q} = n \int_{-\infty}^{\infty} (F_n(y) - F(y))^2 \psi(y) dF(y)$. The function $\psi(y)$ weights the squared difference. The Anderson-Darling statistic is defined as $\mathcal{A}^2 = n \int_{-\infty}^{\infty} (F_n(y) - F(y))^2 [F(y)(1 - F(y))]^{-1} dF(y)$. By introducing the transformation $U_{(i)} = F(Y_{(i)})$, where (i) denotes the i -th ordered value, the statistic is computed as

$$\mathcal{A}^2 = -n - \frac{1}{n} \sum_{i=1}^n [(2i - 1) \log U_{(i)} + (2n + 1 - 2i) \log(1 - U_{(i)})].$$

The Cramér-von Mises statistic is defined as $\mathcal{W}^2 = n \int_{-\infty}^{\infty} (F_n(y) - F(y))^2 dF(y)$ and can be computed as

$$\mathcal{W}^2 = \sum_{i=1}^n \left(U_{(i)} - \frac{2i - 1}{2n} \right)^2 + \frac{1}{12n}.$$

Thus, compared with the Cramér-von Mises statistic, the Anderson-Darling statistic places more weight on observations in the tails of the distribution.

First we present some tests that are capable of dealing with censored data. Then we will review the order selection test and the SemiNP representation to develop a hypothesis test for censored data.

4.1 Goodness-of-fit test

We give a non-comprehensive overview of goodness-of-fit tests that can be used for censored data. Next we discuss the order selection test and explain how we have adapted the test to be suitable for censored data.

4.1.1 Existing tests for censored data

Hollander and Proschan (1979) present a test of a simple null hypothesis for right-censored data. Suppose data can only be observed or right-censored and let $y_{(1)}, y_{(2)}, \dots, y_{(n)}$ represent the ordered values. The Hollander-Proschan test is based on the test statistic

$$C = - \int S_0(y) d\hat{S}_{KM}(y),$$

where \hat{S}_{KM} is the Kaplan-Meier estimator (3.1) of the survival function S . Normalizing this expression results in $C^* = \sqrt{n} \frac{C - \frac{1}{2}}{\hat{\sigma}}$, where the asymptotic variance of C is estimated by

$$\hat{\sigma}^2 = \frac{1}{16} \sum_{i=1}^n \frac{n}{n-i+1} \left([S_0(y_{(i-1)})]^4 - [S_0(y_{(i)})]^4 \right),$$

and $y_{(0)} = -\infty$. Under the null hypothesis, C^* converges in probability to the standard normal distribution.

To compute C^* , there is a simplified version of C given by

$$C = \sum_{\delta_{E(i)}=1} S_0(y_{(i)}) \hat{f}_{KM}(y_{(i)}),$$

where $\hat{f}_{KM}(y_{(i)})$ is the jump of the Kaplan-Meier estimator at $y_{(i)}$, i.e. $\hat{f}_{KM}(y_{(i)}) = \hat{S}_{KM}(y_{(i)}) - \hat{S}_{KM}(y_{(i-1)})$.

This test can be extended for left-censored data by reversing the order of the observations. In practice it means that the survival function is replaced by the cumulative distribution function and the jump of the Kaplan-Meier estimator is calculated as follows. Note that by subtracting every observation from the largest observation, we obtain again a right-censored data set y_1^*, \dots, y_n^* , where $y_i^* = y_{(n)} - y_{(i)}$. Let S_{Y^*} represent the survival function of Y^* and $\hat{f}_{KM,Y^*}(y_i^*)$ the jump of the Kaplan-Meier estimator of the survival function in y_i^* ,

$$\begin{aligned} \hat{f}_{KM,Y^*}(Y_i^*) &= \hat{f}_{KM,Y}(y_{(n)} - y_{(i)}) \\ &= \hat{S}_{KM,Y^*}(y_{(n)} - y_{(i)}) - \hat{S}_{KM,Y^*}(y_{(n)} - y_{(i-1)}) \end{aligned}$$

and $y_{(0)} = -\infty$. The simplified expression of C for left-censored data is given by

$$C = \sum_{\delta_{E(i)}=1} F_0(y_{(i)}) \hat{f}_{KM,Y^*}(y_{(n)} - y_{(i)}).$$

The asymptotic variance of C is now estimated by

$$\hat{\sigma}^2 = \frac{1}{16} \sum_{i=1}^n \frac{n}{n-i+1} \left([F_0(y_{(i-1)})]^4 - [F_0(y_{(i)})]^4 \right).$$

A drawback of the Hollander-Proschan test is that it is only available for a simple null hypothesis. In this dissertation we are interested in testing a composite null hypothesis, e.g. do the data come from a log-normal distribution? By first estimating the parameters of the distribution and substituting them into the null model, an estimated null model can be obtained. Next, the model S_0 can be replaced by the estimated null model \hat{S}_0 to obtain a test for a composite null hypothesis. However, the performance of this test is bad, as we illustrate in a small simulation study in Section 4.3.1.

Another test for right-censored data is proposed by Koziol and Green (1976). Let x_1, \dots, x_n be a sample that may be right-censored by t_1, \dots, t_n . The available data are given by the pairs (y_i, δ_{R_i}) , where $y_i = \min(x_i, t_i)$ and $\delta_{R_i} = 1$ as $y_j = x_j$. Koziol and Green (1976) use the integral-probability transformation to form new pairs (V_i, δ_{R_i}) , where $V_i = \min(F_0(X_i), F_0(T_i))$. If F_0 is the true distribution function of X_i , then the null hypothesis reduces to testing whether $U = F_0(X_i)$ is uniformly distributed on $(0, 1)$. The Koziol-Green statistic is given by

$$\psi^2 = n \int_0^1 (\hat{F}_{KM}(y) - y)^2 dy, \quad (4.3)$$

where \hat{F}_{KM} is the Kaplan-Meier estimator of the distribution of U . Properties about the asymptotic distribution are known for a special form of censoring distribution where the distribution function G of the censoring variable is related to the true distribution F_0 via

$$1 - G(y) = (1 - F_0(y))^\beta,$$

for some β , $0 < \beta < 2$. Asymptotic critical points of the test statistic ψ^2 in (4.3) for some values of β are available.

Ren (2003) proposes a test statistic for interval-censored data by introducing the leveraged bootstrap procedure to obtain a test statistic similar to the Cramér-von Mises statistic

$$T_n = n \int_0^\infty (F_n(y) - F_0(y))^2 dF_0(y)$$

where F_n is the empirical distribution of X_1, \dots, X_n . For the Cramér-von Mises statistic, it is known that under H_0

$$T_n \xrightarrow{D} W, \quad \text{as } n \rightarrow \infty, \quad (4.4)$$

where W has a distribution function given in Shorack and Wellner (1986, p147). The statistic cannot be used as such by replacing the empirical distribution function with an estimator \hat{F}_n using censored data, because the convergence rate of \hat{F}_n is slower than \sqrt{n} . The leveraged bootstrap procedure consists of three main steps.

- (LB1) Compute the non-parametric maximum likelihood estimator \hat{F}_n using the observed data $(t_{L_i}, t_{R_i}, \delta_{I_i}), i = 1, \dots, n$.
- (LB2) For an integer m satisfying $m \rightarrow \infty$, as $n \rightarrow \infty$, obtain an independently and identically distributed leveraged bootstrap sample $X_{n1}^*, \dots, X_{nm}^*$, which is drawn from \hat{F}_n .
- (LB3) For the statistic of interest $H_n(X_1, \dots, X_n)$ formulated for a complete i.i.d. sample, compute $H_m^*(X_{n1}^*, \dots, X_{nm}^*)$ and draw inference.

The test statistic for the null hypothesis, using the leveraged bootstrap is given by

$$T_m^* = m \int_0^{\infty} (F_{nm}^*(x) - F_0(x))^2 dF_0(x),$$

where F_{nm}^* is the empirical distribution function of a leveraged bootstrap sample $X_{n1}^*, \dots, X_{nm}^*$ from \hat{F}_n . The following result holds for this statistic.

Assume

$$n^\gamma(\hat{F}_n - F) = O_p(1), \quad \text{for some } \gamma > 0,$$

and let $m = o(n^{2\gamma})$ satisfy $m \rightarrow \infty$, as $n \rightarrow \infty$. Then, under H_0 ,

$$\lim_{n \rightarrow \infty} \sup_{0 < x < \infty} |P(T_m^* \leq x | \mathcal{O}^n) - P(W \leq x)| = 0,$$

in probability, where $\mathcal{O}^n = \{(t_{L_i}, t_{R_i}, \delta_{I_i}) | 1 \leq i \leq n\}$ and W is as in (4.4).

Two possible decision rules are proposed. The first rule uses only one leveraged bootstrap sample and rejects H_0 at significance level α if $T_m^* \geq C_\alpha$, where $P(W \geq C_\alpha) = \alpha$.

By obtaining N different leveraged bootstrap samples, one can define

$$\bar{W} = \frac{1}{N} \sum_{k=1}^N I(T_{km}^* \geq C_\alpha),$$

$$p_n = P_n(T_{km}^* \geq C_\alpha),$$

where P_n denotes the conditional probability given \hat{F}_n . The statistic $N\bar{W}$ follows a binomial distribution with parameters p_n and N and is asymptotically normal for large N . Denote by z_α the $(1 - \alpha)$ 100-th percentile of the standard normal distribution. For some ρ such that $0 < \rho < \alpha < 1$, we choose

$$N = \max \left\{ 1, \frac{p_n(1 - p_n)}{\left[\frac{\alpha - p_n}{z_{\alpha - \rho} - z_\alpha} \right]^2} \right\}.$$

The null hypothesis is rejected at significance level α if $\bar{W} \geq \alpha + z_{\alpha-\rho} \sqrt{\frac{\alpha(1-\alpha)}{N}}$. This is the second decision rule and it is called the LB-goodness-of-fit test (LB-GOF test).

In D'Agostino and Stephens (1986) modifications for some types of left- and right-censored data, of the Kolmogorov-Smirnov and the Cramér-von Mises statistics are proposed. The modifications are valid for testing a simple null hypothesis. Modifications for testing a composite null hypothesis for censored data, are available for some continuous (normal, exponential, ...) distributions, but not for the log-normal distribution. No modifications for interval-censoring are presented. Other goodness-of-fit tests based on the Kolmogorov-Smirnov statistic are introduced by Koziol (1980), Castro-Kuriss et al. (2009) and Grané (2012).

Akritas (1988) proposed a test for a simple and composite null hypothesis for right-censored data. The test is based on the Pearson statistic and on partitioning the data. A generalization to interval-censored data is not straightforward. Some other goodness-of-fit tests were presented by Hyde (1977) and Gray and Pierce (1985).

Bayesian tests were proposed by Yin (2009), Cao et al. (2010) and Calle and Gómez (2008, Chap. 21).

4.1.2 Order selection test

Let y_1, \dots, y_n be a sample having unknown density $f(y)$, and we want to test the composite hypothesis (4.2). Aerts et al. (1999) proposed a general method for testing the fit of a parametric function. The underlying idea is to "accept" the prescribed parametric model if and only if it is chosen by a model selection criterion. Their test also has a connection with nonparametric smoothing since they employ orthogonal series estimators to detect departures from a parametric model. Aerts et al. (1999) illustrate the applicability of their method in a wide variety of settings, including goodness-of-fit tests. In their Example 1 they represent f as $f(y) = C_\gamma \exp(\gamma(y))$ such that hypothesis (4.2) can be restated as

$$H_0 : \gamma \in \mathcal{G}$$

for some parametric family of functions \mathcal{G} , and let

$$\mathcal{G} = \{\gamma(y; \theta_1, \dots, \theta_p) : (\theta_1, \dots, \theta_p) \in \Theta\}.$$

The null model is extended by an approximator to $\gamma(y)$ of the form

$$\gamma_r(y; \theta_1, \dots, \theta_{p+r}) = \gamma(y; \theta_1, \dots, \theta_p) + \sum_{j=1}^r \theta_{p+j} u_j(y), r = 1, 2, \dots \quad (4.5)$$

where u_1, u_2, \dots are known functions that span some 'large' space of functions (such as (orthogonal) polynomials, trigonometric functions, ...).

The log-likelihood of the approximator equals

$$L_r(\theta_1, \dots, \theta_{p+r}) = \sum_{i=1}^n \gamma(Y_i; \theta_1, \dots, \theta_p) + \sum_{i=1}^n \sum_{j=1}^r \theta_{p+j} u_j(Y_i) + n \log C_{\gamma_r(\cdot; \theta_1, \dots, \theta_{p+r})}.$$

Note that $L_0(\theta_1, \dots, \theta_p)$ corresponds to the log-likelihood of the null model. The supremum over all parameters will be denoted by $\mathcal{L}_r = \sup_{\theta_1, \dots, \theta_{p+r}} L_r(\theta_1, \dots, \theta_{p+r})$.

Aerts et al. (1999) defined the modified AIC by

$$\text{MAIC}(r; C_n) = 2(\mathcal{L}_r - \mathcal{L}_0) - C_n r, \quad r = 0, 1, \dots, \quad (4.6)$$

where C_n is some constant larger than 1, and let \hat{r}_{C_n} be the maximizer of $\text{MAIC}(r; C_n)$. By appropriate choice of C_n , the asymptotic type I error probability of the test

$$\text{“reject } H_0 \text{ when } \hat{r}_{C_n} > 0\text{”}, \quad (4.7)$$

can be any number between 0 and 1. For example, a test of asymptotic significance level 0.05 is obtained by using $C_n = 4.18$ (See Hart, 1997, p. 178 for values of C_n leading to other test levels). In practice we limit the possible values of r to $\{1, \dots, R_n\}$, depending on the application and the functions u_1, u_2, \dots defining the space of functions. Rejection rule (4.7) can be reformulated as “reject H_0 when $\hat{r}_{C_n} \in \{1, \dots, R_n\}$ ”.

The test described above, rejects H_0 if and only if $\text{MAIC}(r; C_n)$ is larger than 0 for some r in $\{1, \dots, R_n\}$, because $\hat{r}_{C_n} = 0$ corresponds to $\text{MAIC}(\hat{r}_{C_n}; C_n) = 0$ and $\hat{r}_{C_n} > 0$ corresponds to a strictly positive MAIC. The test is also equivalent to rejecting H_0 when $T_n \geq C_n$, with $T_n = \max_{1 \leq r \leq R_n} \{2(\mathcal{L}_r - \mathcal{L}_0)/r\}$. The asymptotic distribution of $T_n = \max_{1 \leq r \leq R_n} \{2(\mathcal{L}_r - \mathcal{L}_0)/r\}$ is given by

$$P(T \leq t) = \exp \left[- \sum_{s=1}^{\infty} \frac{P(\chi_s^2 > st)}{s} \right],$$

where χ_s^2 has the chi-square distribution with s degrees of freedom. Hence, in addition to playing the role of penalty constant, C_n is a critical value of the statistic T_n . Using this version of the test one may approximate the P -value corresponding to an observed T_n by using either a large-sample distribution or the bootstrap.

In the next section we explain how the order selection test is combined with the SemiNP representation to develop a goodness-of-fit test for the log-normal distribution.

4.1.3 Test for a log-normal distribution

Here, we make the link between the SemiNP representation and the order selection test, and as such, we propose a goodness-of-fit test for the log-normal distribution.

In the notation of Aerts et al. (1999), we have the density $f(y; \theta_1, \dots, \theta_p) = C_\gamma \exp(\gamma(y; \theta_1, \dots, \theta_p))$, the approximator

$$\begin{aligned} f_r(y; \theta_1, \dots, \theta_{p+r}) &= C_{\gamma_r} \exp(\gamma_r(\theta_1, \dots, \theta_{p+r})) \\ &= P_r^2(y; \theta_{p+1}, \dots, \theta_{p+r}) f(y; \theta_1, \dots, \theta_p), \end{aligned}$$

and additional parameters $(\theta_{p+1}, \dots, \theta_{p+r}) = (a_1, \dots, a_r)$ such that the log-likelihood (for uncensored data) becomes

$$L_r(\theta_1, \dots, \theta_{p+r}) = \sum_{i=1}^n \log f(Y_i; \theta_1, \dots, \theta_p) + \sum_{i=1}^n \log P_r^2(Y_i; \theta_{p+1}, \dots, \theta_{p+r}).$$

When testing log-normality, we define a random variable Y by $\log(Y) = \mu + \sigma X$, $\sigma > 0$. The variable Y has a log-normal distribution when r is set to zero and the number of parameters p of the null distribution is 2. The density function of the log-normal distribution is given by $f(y; \mu, \sigma) = (y\sigma)^{-1} \phi\left(\frac{\log(y) - \mu}{\sigma}\right)$, where $\phi(\cdot)$ is the density function of the standard normal distribution. The extended distributions are from the SemiNP family of distributions, as explained in Section 3.2. Note that the polynomial P_r is constructed such that $f_r(y) = P_r^2(y)f(y)$ is a density function, thus eliminating the parameter C_{γ_r} .

In Section 3.2, we described a recursive way to determine the extension of the survival and density function in terms of the SemiNP representation. These functions can be imputed in the (log-)likelihood function (3.6) for censored or uncensored observations. Next the MAIC-value (4.6) can be computed to determine $\hat{r}_{C_n} > 0$ for the test in (4.7).

One starts by calculating \mathcal{L}_0 , the log-likelihood under the null hypothesis ($r = 0$). Next the log-likelihood \mathcal{L}_r for $r > 0$ is determined and compared to \mathcal{L}_0 . In our calculations, the maximal value of r is set to 7. To simplify the calculations, it is possible to interrupt the calculations as soon as a positive value of MAIC is obtained.

In general, when the density function is represented by $f(y; \theta_1, \dots, \theta_{p+r}) = C_{\gamma_r} \exp(\gamma_r(y; \theta_1, \dots, \theta_{p+r}))$, with γ_r as in (4.5), the distribution function $F(y; \theta_1, \dots, \theta_{p+r}) = \int_{-\infty}^y f(t; \theta_1, \dots, \theta_{p+r}) dt$ cannot be easily obtained.

Likelihood ratio test Suppose the maximal value of r is equal to 1. In this case, the statistic T_n equals $2(\mathcal{L}_r - \mathcal{L}_0)/r$ which is the likelihood ratio test statistic, where the alternative model has one or more parameters than the model under the null hypothesis. The 5% critical value for a likelihood ratio test (χ^2 -distribution with one degree of freedom) equals 3.84, which is smaller than $C_n = 4.18$. Hence, the likelihood ratio test rejects sooner.

Table 4.1: Cadmium data 1 and 2. Results of the proposed test: MAIC and value of test statistic T_n (maximum of column $2(\mathcal{L}_r - \mathcal{L}_0)/r$).

Distribution	r	Cadmium 1		Cadmium 2	
		$2\frac{\mathcal{L}_r - \mathcal{L}_0}{r}$	MAIC	$2\frac{\mathcal{L}_r - \mathcal{L}_0}{r}$	MAIC
SemiNP1	1	3.049	-1.131	3.738	-0.442
SemiNP2	2	4.375	0.390	2.459	-3.442
SemiNP3	3	6.549	7.108	1.830	-7.050
SemiNP4	4	5.305	4.498	1.457	-10.892
SemiNP5	5	4.380	1.002	1.210	-14.849
SemiNP6	6	3.804	-2.258	1.035	-18.869
SemiNP7	7	3.354	-5.779	3.349	-5.820

4.2 Application to data examples

In this section we show the results of the proposed test for both samples concerning cadmium concentrations. We also apply the test to the Signal Tandmobiel data as introduced in Section 2.2.

4.2.1 Cadmium data

As mentioned before, we could use Hollander-Proschan to test for a log-normal distribution on the Cadmium data. The value of the test statistic is $c^* = -0.664$ with a p-value equal to 0.506, indicating that the null hypothesis cannot be rejected. However, as this is a composite null hypothesis, the asymptotic theory fails and the test result is non-reliable.

The results of the proposed test are summarized in Table 4.1. To test the null hypothesis of log-normal distribution, the maximum value of the log-likelihood in each extension of the null model is compared to the maximum log-likelihood in the null model. The difference is used to compute the modified AIC value (4.6) or T_n . The maximum MAIC for Cadmium data 1, is attained at $r = 3$ and is strictly positive, such that $\hat{r}_{C_n} = 3$ is not zero. This is equivalent to computing the value of T_n as the maximum of $2(\mathcal{L}_r - \mathcal{L}_0)/r$, which is in this example 6.549. This value exceeds the critical value 4.18. The null hypothesis of a log-normal distribution is rejected at 5% significance level. The model that best describes the data, is the log-normal distribution extended with 3 parameters.

The left panel of Figure 3.2 already showed that the fitted distribution function of the log-normal distribution deviates from the Kaplan-Meier estimate, while the extended distribution is closer to the Kaplan-Meier estimate.

In the second Cadmium example, the value of the test statistic is 3.738 and the null hypothesis of the log-normal distribution cannot be rejected at significance level 5%.

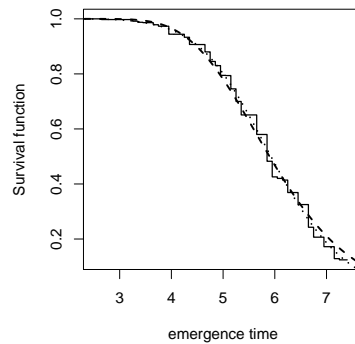


Figure 4.1: Signal Tandmobiel data: boys with sound primary predecessors. Survival function of emergence time. Non-parametric estimate (solid), log-normal (dashed) fit and fit of the best SemiNP distribution ($r = 2$, dotted).

4.2.2 Signal Tandmobiel data

All four subgroups of the Signal Tandmobiel data have been analyzed. All tests reject the null hypothesis at 5% significance level (critical value 4.18). The group of boys with sound primary predecessors reaches a maximum of 8.635 at the extension with two parameters (see Figure 4.1), while a maximum of 8.294 is achieved at one extra parameter for the boys in the group 'decayed, missing due to caries or filled'. Both groups of girls reach a maximum value at one extra parameter, with values 7.465 and 6.233 respectively. So we conclude that none of the groups originates from a log-normal distribution. A better description of the data is given by the extension with one (first group) or two extra parameters.

4.3 Simulation study

In the first section we investigate the test of Hollander-Proschan in case of a simple and a composite null hypothesis. We expect that the test will not perform good in case of a composite null hypothesis, because it does not account for the estimation of the parameters. The second section presents the results of the simulations of the proposed test. The test is compared to some standard goodness-of-fit tests in case of no censoring. As no tests for censored data were available in the software and it is not straightforward to implement the tests for left- and interval-censoring, we do not make a comparison with other tests when data are censored.

Table 4.2: Simulation study Hollander-Proschan. Simple null hypothesis. Percentage of rejected null hypotheses based on 1000 replicates for null hypothesis of exponential distribution.

$\alpha \setminus \theta$		1	0.8	0.6	0.4	1	0.8	0.6	0.4
		33.33% censoring				50% censoring			
Sample size 20	0.01	0.010	0.065	0.306	0.793	0.017	0.069	0.303	0.769
	0.05	0.047	0.154	0.531	0.904	0.062	0.162	0.490	0.884
	0.10	0.087	0.240	0.634	0.936	0.111	0.242	0.597	0.927
Sample size 50	0.01	0.011	0.138	0.676	0.995	0.016	0.121	0.630	0.993
	0.05	0.048	0.274	0.841	0.998	0.059	0.247	0.807	0.998
	0.10	0.106	0.373	0.896	0.998	0.102	0.347	0.872	0.999

4.3.1 Hollander-Proschan

Two cases are considered, the simple null hypothesis and the composite null hypothesis. In the simple null hypothesis, it is assumed that the data come from a specified distribution and the corresponding parameters are tested. For example, we suppose that data come from an exponential distribution and the null hypothesis states that the parameter equals one: $H_0 : X \sim \text{Exp}(1)$. Table 1(b) in Hollander and Proschan (1979) is reproduced concerning the C-statistic. Data are simulated from the exponential distribution with parameter θ . The censoring process occurs according to the survival function $R_H(x) = R_F(x)^\beta$, where β is equal to 1/2 and 1, corresponding to a percentage c of 33.33 and 50.00 respectively. The significance level α is set to 1%, 5% and 10%. For each setting, 1000 samples are drawn.

Table 4.2 shows that under the null hypothesis ($\theta = 1$), the correct amount of hypotheses is rejected. When the alternative hypothesis is true ($\theta \neq 1$), the rejection rate grows as the true parameter lies further away from 1. Power also increases as sample sizes grow. In most cases, the rejection rate is smaller when more censoring is present.

The method collapses when a composite null hypothesis is considered, such as a test for the log-normal distribution. Figure 4.2 shows the cumulative density functions of the standard normal distribution (solid line) and of C_n^* , the Hollander-Proschan statistic. The dashed line is obtained by first estimating the parameters of the log-normal distribution and then using these estimates to calculate C_n^* . The dotted line is obtained by using the true parameters from the distribution to calculate C_n^* .

100 simulations were run, each with sample size between 500 and 550. Data are sampled from a log-normal distribution with parameters -0.8047 and 1.2686 . The data in Figure 4.2(a) are not censored, the data in Figure 4.2(b) contain 10% (left-)censoring.

From both figures, we conclude that the statistic C^* has too little variation and

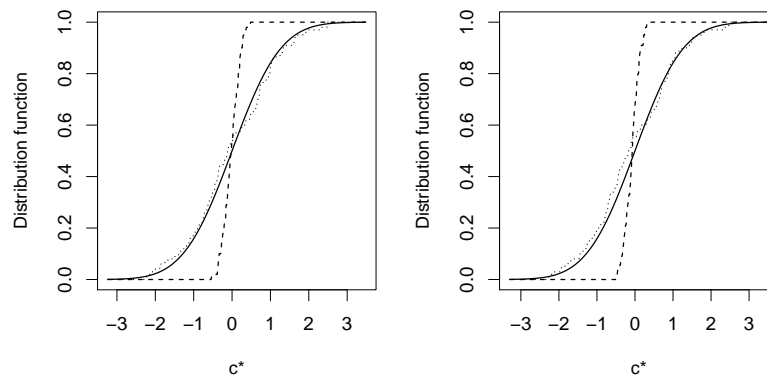


Figure 4.2: Simulation study Hollander-Proschan. Distribution of statistic C^* : theoretical (normal distribution, solid line) and simulation-based with true (dotted line) or estimated parameters (dashed line), based on 100 replicates for null hypothesis of log-normal distribution. No censoring (left panel) versus 10% censoring (right panel).

therefore has no standard normal distribution. In conclusion, the asymptotic variance used to obtain the standardized version of the statistic, is incorrect when the parameters of the distribution need to be estimated first.

4.3.2 Order selection test

We will compare the performance of the proposed test to some standard goodness-of-fit tests in case of no censoring. Although modifications of these standard tests for censored data are proposed in literature, they are not available in software. In case of censoring we therefore only study the performance of the order selection test, without implementing the modifications of the standard goodness-of-fit tests.

In case of no censoring

If the data are not censored, then we can rely on standard tests, like Kolmogorov-Smirnov, Anderson-Darling and Cramér-von Mises. In this section we compare the performance of the proposed order selection test to the performance of these standard tests.

Table 4.3 shows that the proposed order selection test seems to be especially good for local deflections from the null distribution, like in the mixture case with 95% of the observations coming from the left log-normal distribution. The percentage of rejected null hypotheses of all tests is fairly good in this setting, though the proposed test seems to be a bit conservative, especially for small samples. It seems that the convergence is

Table 4.3: Simulation study without censoring. Percentage of rejected null hypotheses based on 500 replicates for null hypothesis of log-normal distribution. Null hypothesis of the log-normal distribution, with data sampled from the log-normal distribution, a mixture of two log-normal distributions or a gamma distribution.

	Significance level	Sample size 100		Sample size 200		Sample size 500	
		10%	5%	10%	5%	10%	5%
Log-normal	Order selection	0.054	0.034	0.060	0.032	0.094	0.050
	Kolmogorov-Smirnov	0.114	0.052	0.094	0.050	0.096	0.044
	Cramér-von Mises	0.090	0.048	0.090	0.048	0.084	0.050
	Anderson-Darling	0.080	0.048	0.096	0.056	0.092	0.050
95% mixture	Order selection	0.166	0.068	0.236	0.096	0.418	0.282
	Kolmogorov-Smirnov	0.210	0.112	0.194	0.102	0.354	0.202
	Cramér-von Mises	0.202	0.116	0.208	0.114	0.332	0.210
	Anderson-Darling	0.246	0.156	0.306	0.182	0.512	0.328
90% mixture	Order selection	0.316	0.168	0.576	0.326	0.882	0.776
	Kolmogorov-Smirnov	0.464	0.286	0.616	0.424	0.950	0.888
	Cramér-von Mises	0.452	0.300	0.630	0.418	0.936	0.862
	Anderson-Darling	0.598	0.424	0.802	0.622	0.988	0.966
75% mixture	Order selection	0.928	0.670	0.998	0.990	1.000	1.000
	Kolmogorov-Smirnov	0.998	0.996	1.000	1.000	1.000	1.000
	Cramér-von Mises	1.000	1.000	1.000	1.000	1.000	1.000
	Anderson-Darling	1.000	1.000	1.000	1.000	1.000	1.000
Gamma	Order selection	0.998	0.998	1.000	1.000	1.000	1.000
	Kolmogorov-Smirnov	0.998	0.990	1.000	1.000	1.000	1.000
	Cramér-von Mises	1.000	1.000	1.000	1.000	1.000	1.000
	Anderson-Darling	1.000	1.000	1.000	1.000	1.000	1.000

slower as compared to the other tests. Because the level is too small, the power will be smaller.

For global deviations from the null distribution, the other tests have better performance. For the gamma distribution and the 75% mixture, it is difficult to compare the tests as all hypotheses are rejected.

We now turn to the next stage, where part of the data is censored. The standard tests can no longer be used, but we will investigate the performance of the proposed test.

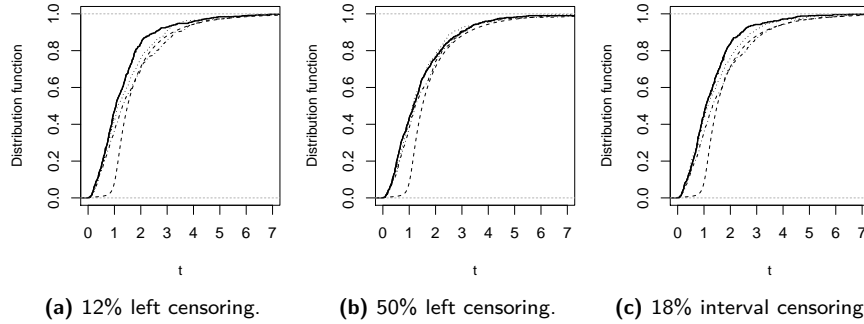


Figure 4.3: Simulations. Distribution of statistic T : theoretical (χ^2 distribution, dashed line) and simulation-based, based on 500 replicates. Null hypothesis of the log-normal distribution, with data sampled from the log-normal distribution. Sample size 100 (solid), 200 (dotted), 500 (dash-dot).

In case of censoring

As mentioned before, the asymptotic distribution of $T_n = \max_{1 \leq r \leq R_n} \{2(\mathcal{L}_r - \mathcal{L}_0)/r\}$ is given by

$$P(T \leq x) = \exp \left[- \sum_{s=1}^{\infty} \frac{P(\chi_s^2 > sx)}{s} \right],$$

where χ_s^2 has the chi-square distribution with s degrees of freedom.

For each sample size, 500 samples are drawn from the log-normal distribution. The empirical distribution function of the resulting values of the test statistic T_n is shown in Figure 4.3.

Compared to the theoretical distribution, the empirical distribution function is located too much to the left. By using the theoretical critical values, the rejection rate will be too small. For large sample size, the empirical distribution function is a better approximation for the theoretical distribution function, at least for large values of the statistic. Especially those large values are important for the test of a null hypothesis. Because only few large values are available, a large number of samples should be used to conduct the simulation study.

The most upper part of Table 4.4, showing rejection percentages when data are generated under the null hypothesis, shows that the test seems to be somewhat over-conservative, especially for small samples. This even holds in case of no censoring. As sample sizes grow to 500, the rejection percentages converge to the nominal level, indicating the asymptotic distribution is indeed valid, even in case the data are interval-censored

Table 4.4: Simulations. Percentage of rejected null hypotheses based on 500 replicates. Null hypothesis of the log-normal distribution, with data sampled from the log-normal distribution, a mixture of two log-normal distributions or a gamma distribution. c is the percentage of censoring.

		c	Sample size 100		Sample size 200		Sample size 500	
Significance level			10%	5%	10%	5%	10%	5%
Left censoring	Log-normal	0%	0.054	0.034	0.060	0.032	0.094	0.050
		12%	0.062	0.038	0.060	0.034	0.116	0.050
		50%	0.080	0.036	0.068	0.038	0.094	0.042
	95% mixture	0%	0.166	0.068	0.236	0.096	0.418	0.282
		12%	0.158	0.074	0.234	0.096	0.484	0.306
		48%	0.168	0.084	0.246	0.118	0.464	0.298
	90% mixture	0%	0.316	0.168	0.576	0.326	0.882	0.776
		11%	0.276	0.140	0.560	0.338	0.926	0.836
		45%	0.736	0.638	1.000	1.000	1.000	1.000
	75% mixture	0%	0.928	0.670	0.998	0.990	1.000	1.000
		9%	0.876	0.542	0.998	0.980	1.000	1.000
		38%	0.736	0.638	0.994	0.950	1.000	1.000
Gamma	0%	0.998	0.998	1.000	1.000	1.000	1.000	
	42%	0.766	0.696	0.992	0.930	1.000	1.000	
Interval censoring	Log-normal	0%	0.054	0.034	0.060	0.032	0.094	0.050
		18%	0.050	0.026	0.068	0.032	0.106	0.052
		50%	0.074	0.048	0.060	0.028	0.096	0.042
	95% mixture	0%	0.166	0.068	0.236	0.096	0.418	0.282
		18%	0.150	0.070	0.244	0.110	0.492	0.308
		48%	0.120	0.062	0.174	0.084	0.472	0.292
	90% mixture	0%	0.316	0.168	0.576	0.326	0.882	0.776
		17%	0.260	0.134	0.568	0.326	0.932	0.832
		45%	0.236	0.148	0.478	0.230	0.938	0.818
	75% mixture	0%	0.928	0.670	0.998	0.990	1.000	1.000
		14%	0.880	0.514	0.996	0.992	1.000	1.000
		38%	0.658	0.498	0.992	0.930	1.000	1.000
Gamma	0%	0.998	0.998	1.000	1.000	1.000	1.000	
	42%	0.764	0.690	1.000	0.960	1.000	1.000	

and 50% is censored.

For the most contiguous alternative model, the 95% mixture model, rejection percentages grow to about 7% and 16% (at level 0.05 and 0.10 respectively) for samples of size 100, to about 10% and 24% for samples of size 200 and about 30% and 47% for size 500. The rejection percentages are mostly quite similar despite very different percentages of the data that are censored. The same similarity holds whether it concerns left-censoring only or left- and interval-censoring.

As expected, the power increases as the alternative model deviates more substantially

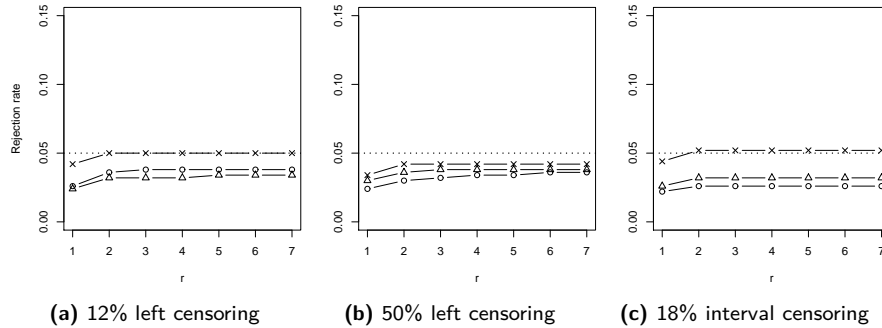


Figure 4.4: Simulations. Percentage of rejected null hypotheses versus degree of extension (r). Null hypothesis of the log-normal distribution, with data sampled from log-normal distribution. Sample sizes 100 (circle), 200 (triangle) and 500 (cross).

from the null model, as in the 90% and 75% mixture models. Although the deviation is represented by a local bump at the right (as shown in Figure 3.3), the percentage rejected increases to about 80% for samples of size 100, up to 100% for samples of size 500.

Finally for the gamma distribution, representing a global deviation from the null model, the rejection percentages are already about 70% for samples of size 100 and quickly grow to about 95% for samples of size 200.

A more visual representation of the results, only showing the percentages of rejected null hypotheses based on the theoretical critical values, is given in Figures 4.4 and 4.5. In the former we expect the lines to approach the nominal values of 5%, while in the latter the percentage should grow as high as possible (representing the power of the test).

A final representation of the results is the calculation of simulation-based critical values (Table 4.5). The empirical values are smaller than the corresponding theoretical values (3.22 and 4.18). However, as the sample size n increases, they approach the theoretical values.

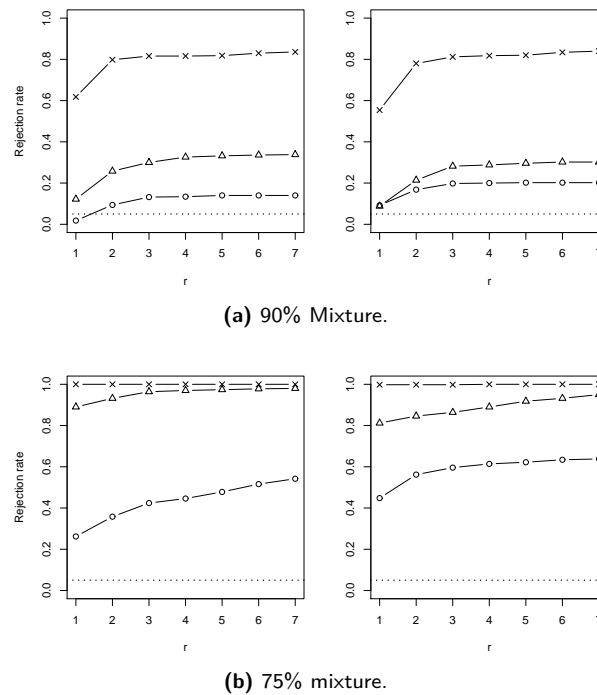


Figure 4.5: Simulations. Percentage of rejected null hypotheses versus degree of extension (r). Null hypothesis of the log-normal distribution, with data sampled from mixture of log-normal distributions. 9% censoring in the left panel and 37% (39%) in the right panel. Sample sizes 100 (circle), 200 (triangle) and 500 (cross).

Table 4.5: Simulations. Simulation-based critical points. Null hypothesis of the log-normal distribution, with data sampled from the log-normal distribution. c is the percentage of left (upper part) and interval (lower part) censoring.

	c	Sample size 100		Sample size 200		Sample size 500	
Significance level		10%	5%	10%	5%	10%	5%
Log-normal	12%	2.554	3.803	2.959	3.487	3.306	4.133
	50%	2.941	3.653	2.639	3.746	3.011	3.791
Log-normal	18%	2.426	3.223	2.825	3.556	3.342	4.190
	50%	2.628	3.937	2.635	3.381	3.206	3.985

4.4 Bootstrap

From the simulation study it becomes clear that the asymptotic significance level does not correspond to reality. In other words, the rejection rate is too low, when decision is based on the theoretical distribution. In this section, we describe some bootstrap methods in order to give an alternative to the theoretical critical values.

Suppose a data set is given and some of the observations are censored $(t_{L_i}, t_{R_i}, \delta_{R_i}, \delta_{L_i}, \delta_{I_i})$, $i = 1, \dots, n$. We denote the test statistic by T and from the original sample we obtain a value t_{obs} . For each bootstrap sample $b = 1, \dots, B$, Efron and Tibshirani (1993) compute the test statistic t_b and the observed value of the test statistic is compared to the bootstrap values. The approximate bootstrap significance level is defined as

$$\widehat{ASL}_{boot} = \# \{t_b \geq t_{obs}\} / B.$$

Some methods to obtain bootstrap samples with censored values are listed in the next sections.

Non-parametric bootstraps were proposed for right-censored data (Efron and Tibshirani, 1986; Davison and Hinkley, 1997) and interval-censored data (Lawless and Babineau, 2006; Ren, 2003). In the context of hypothesis testing, we are more interested in a parametric bootstrap. In the latter, the data are simulated with respect to the null hypothesis.

Hjort (1992) focusses on aspects of maximum likelihood estimation applied to parametric survival data models, only for right-censored data. The parametric bootstrap simulates pseudo-data $(Y_1^*, \delta_1^*), \dots, (Y_n^*, \delta_n^*)$ from the parametrically estimated model. More specifically, X_i^* is simulated from the distribution with hazard rate $\alpha(\cdot, \hat{\theta})$ and t_i^* from \hat{G} , independently, such that $Y_i^* = \min(X_i^*, t_i^*)$ and $\delta_{R_i}^* = I\{X_i^* \geq t_i^*\}$ define the bootstrap sample. For the nonparametric bootstrap, the nonparametric Kaplan-Meier estimate \hat{F} is used instead of the hazard rate. Both bootstraps are used to approximate the limiting distribution of the MLE.

Beran (1988) focusses on the bootstrap of a hypothesis test that postulates that θ is a member of Θ_0 , a specified subset of the parameter space Θ . This formulation is equivalent to the simple null hypothesis in equation (4.1). Let $c_n(\alpha)$ denote the largest $(1 - \alpha)$ th quantile of the null distribution of the test statistic T_n . Then the test

$$\phi_n = \begin{cases} 1 & \text{if } T_n > c_n(\alpha), \\ 0 & \text{otherwise,} \end{cases}$$

has level α . To obtain asymptotically valid critical values for the test ϕ_n , the following bootstrap method can be used. Suppose that $\hat{\theta}_n = \hat{\theta}_n(x_1, \dots, x_n)$ is an estimate of θ ,

based on the sample x_1, \dots, x_n , that is consistent under the null hypothesis and takes its values in Θ_0 . Given the original sample x_1, \dots, x_n , let x_1^*, \dots, x_n^* be an artificial sample of size n drawn from the fitted null hypothesis model $F_{\hat{\theta}_n}$. Let $T_n^* = T_n(x_1^*, \dots, x_n^*)$ denote the value of the test statistic, recalculated from the bootstrap sample x_1^*, \dots, x_n^* . The conditional distribution of T_n^* , given x_1, \dots, x_n , is the bootstrap estimate for the null distribution of T_n . The largest $(1 - \alpha)$ th quantile of the bootstrap null distribution is the bootstrap critical value $c_n(\alpha)$ for the test ϕ_n .

4.4.1 Four approaches

We describe four approaches to obtain a bootstrap sample. While the first approach is rather naive (no censoring), there is a different mechanism of censoring in the other approaches. To facilitate the explanation of the approaches, we assume that data are left-censored by a limit of detection. The results are shown in Paragraph 4.4.2.

Approach 1

In a first approach, the bootstrap samples are drawn from the null distribution, i.e. log-normal. While censoring occurs in the original data, no censoring is introduced in the bootstrap sample.

Approach 2

The second approach is an attempt to let the bootstrap sample resemble the original data. How to draw a sample that resembles the true data well? Suppose only left censoring occurs in the original data set. In the first step, we draw an uncensored sample. As we assume that data come from the distribution under the null hypothesis, we fit the parameters of the distribution on the given data set and sample from the distribution with the estimated parameters. In the second step, censoring is introduced. Remember that simulations were based on data coming from 5 laboratories, each with a different limit of detection. Denote these limits of detection by $L_1 < L_2 < \dots < L_5$. As all data below L_1 cannot be truly observed by any of the laboratories, all values in the bootstrap samples below L_1 are censored by L_1 . Next, calculate the probability of being censored in the interval $[0, L_2]$ and censor with probability such that the probability in the bootstrap sample of being unobserved in the same interval is the same as in the original data.

For example, suppose in the original data 6 observations are censored by L_1 , one is observed in $(L_1, L_2]$ and 4 are censored by L_2 . In the bootstrap sample 5 observations are already censored by L_1 in the first step and 9 are remaining for the second step. Based on the cumulative probabilities, $\frac{6+4}{6+1+4} = 90.9\%$ of the observations should be censored.

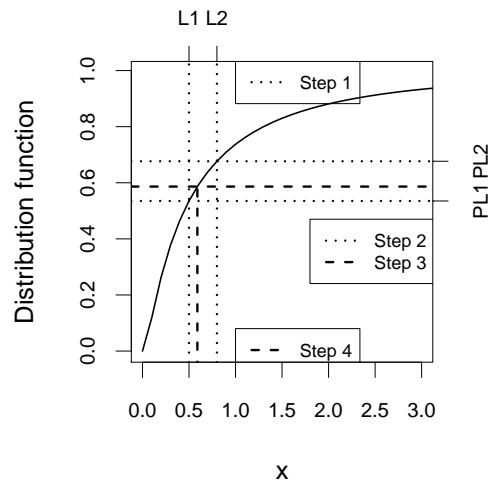


Figure 4.6: Simulations. Bootstrap approach 3. Illustration of generating uncensored value. Determine interval to which sampled value belongs (step 1) and use \hat{F} to compute probabilities PL_1 and PL_2 (step 2). Next generate number between PL_1 and PL_2 (Step 3). Bootstrap value is the corresponding quantile (step 4).

In the bootstrap there are already 5 values censored by L_1 and 9 remaining. We want to censor a fraction p of the remaining 9 values:

$$\frac{6 + 4}{6 + 1 + 4} = \frac{5 + 9p}{5 + 9} \rightarrow p = \frac{1}{9} \left(\frac{10}{11} \times 14 - 5 \right) = 85.9\%.$$

If too many observations are censored by the smallest LOD, then this is corrected for by the cumulative probabilities.

Approach 3

This approach is based on the idea of Efron and Tibshirani (1986). Assign an equal weight $1/n$ to each observation (Y_i, δ_{L_i}) and draw with replacement from this sample. If the sampled value $(Y_i^{0*}, \delta_{L_i}^*)$ has censoring indicator $\delta_{L_i}^* = 1$ (i.e. is censored), then the bootstrap value equals the sampled value: $(Y_i^*, \delta_{L_i}^*) = (Y_i^{0*}, \delta_{L_i}^*)$. However, if the sampled value was truly observed ($\delta_{L_i}^* = 0$), then a new value Y_i^* is drawn from the estimated distribution \hat{F} under the condition that the new value falls in between the same LODs as the original value. The process is illustrated in Figure 4.6. For example, suppose the sampled value Y_i^{0*} is in between L_1 and L_2 (Step 1). Based on the estimated distribution function \hat{F} , the probabilities $PL_1 = \hat{F}(Y < L_1)$ and $PL_2 = \hat{F}(Y < L_2)$ can be computed (Step 2). Next a number p^* is generated from the uniform distribution

between PL_1 and PL_2 (Step 3). The quantile corresponding to this number is the new bootstrap value $Y_i^* = \hat{F}^{-1}(p^*)$ (Step 4).

Approach 4

The bootstrap in this paragraph is probably the most intuitive approach and is based on the method of Hjort (1992). We translate the method to left-censored data. The parametric bootstrap simulates pseudo-data $(Y_1^*, \delta_1^*), \dots, (Y_n^*, \delta_n^*)$ from the parametrically estimated model. More specifically, X_i^* is simulated from the distribution with distribution function $F(\cdot, \hat{\theta})$ and t_i^* from \hat{G} , where \hat{G} is the empirical distribution function of the LODs or equivalently a table distribution with a fixed probability for each LOD (resampling from LODs). Finally $Y_i^* = \max(X_i^*, t_i^*)$ and $\delta_{L_i}^* = I\{X_i^* \leq t_i^*\}$ define the bootstrap sample.

This approach can be easily extended to interval-censored data. Each censored value can be represented by a couple (t_L, t_R) , which in case of interval censoring is (LOD, LOQ) and (0, LOD) in case of left censoring. The couples are resampled such that $\delta_{E_i}^* = I\{X_i^* \geq t_{R_i}^*\}$, $\delta_{L_i}^* = I\{X_i^* < t_{L_i}^*\}$ and $\delta_{I_i}^* = I\{t_{L_i}^* < X_i^* \leq t_{R_i}^*\}$. There is no right censoring in the original, nor in the bootstrap sample.

4.4.2 Results

The results of the bootstraps for the simulation study and the data examples (both cadmium samples and the Signal Tandmobiel data) are given below.

Simulation study

As the bootstrap approaches are very computer intensive and preliminary exploratory results seem to indicate comparable results, we limited the bootstrap analysis to the log-normal distribution and the 75% mixture, for the setting with five laboratories and sample size 100. The results from approach 1 are disappointing: the p-values are systematically lower than the theoretical p-values and even more hypotheses are rejected. For each original sample, 200 bootstrap samples were generated with left censoring as in approach 2 and 3. The rejection percentages are shown in Table 4.6.

For approach 4, the results are based on 500 bootstrap samples and we show the rejection percentage for both left and interval censoring. Although the number of bootstrap replicates is still rather low (due to computational intensity), Table 4.7 confirms the conservative behaviour of the test procedure under the null (at least in case of a relatively small size of 100). For the mixture distribution, rejection percentages are roughly similar. This limited simulation study indicates that all bootstrap procedures perform similar and asymptotical theory is reliable.

Table 4.6: Simulation study. Bootstrap approach 2 and 3. Percentage of rejected null hypotheses based on 200 bootstrap samples.

Censoring	Method	Significance level		
		10%	5%	
Left	Log-normal	Bootstrap approach 2	0.065	0.030
		Bootstrap approach 3	0.060	0.025
		Asymptotic theory	0.070	0.030
	75% mixture	Bootstrap approach 2	0.850	0.630
		Bootstrap approach 3	0.795	0.630
		Asymptotic theory	0.855	0.525

Table 4.7: Simulation study. Bootstrap approach 4. Percentage of rejected null hypotheses based on 500 replicates for 200 samples of size 100, compared to theoretical results.

Censoring	Method	Significance level		
		10%	5%	
Left	Log-normal	Bootstrap approach 4	0.095	0.045
		Asymptotic theory	0.070	0.030
	75% mixture	Bootstrap approach 4	0.970	0.765
Asymptotic theory		0.855	0.525	
Interval	Log-normal	Bootstrap approach 4	0.095	0.055
		Asymptotic theory	0.065	0.025
	75% mixture	Bootstrap approach 4	0.955	0.825
		Asymptotic theory	0.840	0.485

Cadmium data 1

Using the bootstrap algorithm in approach 2 and based on 500 bootstrap samples from the Cadmium data 1, the estimated critical points are 20.456 (at 5%) and 16.186 (at 10%). The bootstrap in approach 3 leads to the estimated critical points 7.245 (at 5%) and 5.692 (at 10%) and the bootstrap in approach 4 to 3.562 and 2.568. For this particular example, there seems to be some discrepancy between both bootstrap approaches, as well as with the asymptotic null distribution: the value 6.549 of the test statistic on the original data exceeded 4.18, the critical point at 5% based on the asymptotic distribution. The same conclusion was made based on bootstrap approach 4. However the test does not reject at 10% using the first bootstrap procedure, and it does reject at 10% but not at 5% for the second bootstrap procedure.

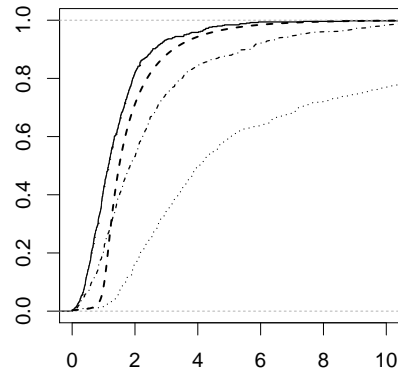


Figure 4.7: Cadmium data 1. Bootstrap. Theoretical (dashed line) and empirical distribution function of proposed test, based on 500 bootstrap samples. Approach 2 (dotted), approach 3 (dash-dot) and approach 4 (solid).

Cadmium data 2

These data are left- and interval-censored and therefore the extended approach was used to generate bootstrap samples. In 15 out of 500 samples, the test statistic of the bootstrap sample exceeded the original value 3.738. The critical points of the bootstrap distribution are 3.073 (at 5% significance level) and 2.341 (at 10%). Although the asymptotical theory did not reject the null hypothesis at 5%, the bootstrap does. However both decisions are borderline.

Signal Tandmobiell data

The structure of the data is different from the Cadmium data. Data collection is based on check-ups by the dentist and no exact measurements were recorded. Original data are of the form (t_L, t_R) or (t_L, ∞) and all data are by definition censored and with t_L strictly positive. Therefore the bootstrap sample will have the same structure, with $\delta_{L_i}^* = I\{x_i^{0*} < t_{L_i}^*\}$; if $t_{R_i}^* = \infty$ then $\delta_{R_i}^* = I\{x_i^{0*} > t_{L_i}^*\}$ or if $t_{R_i}^* \neq \infty$ then $\delta_{R_i}^* = I\{t_{L_i}^* < x_i^{0*} < t_{R_i}^*\}$ and $\delta_{R_i}^* = I\{x_i^{0*} > t_{R_i}^*\}$. Note that the bootstrap sample can contain left-, interval- and right-censored data, while the original sample does not contain left-censored data. From the 500 bootstrap samples, respectively 1, 5, 2 and 5 samples have a test statistics exceeding the statistic in the original sample of 8.635 (girls with sound primary predecessors), 8.294 (girls, decayed), 7.465 (boys, sound) and 6.233 (boys, decayed). The critical points at 5% significance level according to the bootstrap are 4.118, 3.980, 4.010 and 3.966 respectively for the girls with sound and decayed primary predecessors, and the boys with sound and decayed primary predecessors. Therefore,

for every group of children the null hypothesis of the lognormal distribution is strongly rejected at 5% significance level, based on the bootstrap.

4.5 Conclusion

We have proposed a general omnibus test for goodness-of-fit of parametric models for arbitrary censored data, using the order selection test in combination with the SemiNP representation. The method is straightforward to implement using standard optimization software, but the estimation is dependent on the choice of appropriate starting values. No formal proof is provided for the asymptotic behavior of the test, but simulation studies show that the test performs well. The results of the data examples and the simulation study indicate that the bootstrap approach offers a worthwhile alternative to the asymptotic approach. In fact, the results show that the nominal level is reached more accurately and that the power behavior is better for the bootstrap approach.

Although we focused on testing log-normality, the approach is generally applicable for competing distributions such as the loglogistic, gamma etc. This is the topic of further research, in combination with extensions to models with covariates (regression models) and to models with fixed and random effects, for instance to represent heterogeneity from different food categories (as illustrated in EFSA (2010)). It should be possible to adapt the approach also to other applications and settings such as to problems involving both censoring and truncation (because the SemiNP representation is in “parametric” form, the likelihood function is straightforward under the usual assumption that censoring and truncation are independent of event time).

Chapter 5

Model averaging distribution functions

The determination of an appropriate distribution for concentration data is of major importance in chemical risk assessment. The selection and the estimation of an appropriate distribution is hindered by observations below the limit-of-detection and the limit-of-quantification, leading to left-censored and interval-censored data. The log-normal distribution is a typical choice, owing its popularity from the use of the log transform in daily laboratory practice, in combination with the nice mathematical and computational properties of the normal distribution. But the log-normal should not be the only choice and other distributions need to be considered as well. Here we focus on several families of distributions that are related to the log-normal distribution in some direct or indirect way, and that are parametric or semi-nonparametric extensions of the log-normal distribution (see Chapter 3): the log-skew-normal, the log-t, the log-skew-t, the Weibull, the gamma, the generalized-gamma, and the semi-nonparametric estimator of Zhang and Davidian (2008). Whereas in Chapter 4 we developed methodology to test the goodness-of-fit of a particular hypothesized distribution, our interest here goes to model selection and model averaging, using all parametric models only or in addition the series of extensions of the log-normal distribution underlying the semi-nonparametric estimator. The models and methods of selection and averaging are illustrated on data of cadmium concentration in food products (Section 5.2) and further investigated through simulations (Section 5.3). The material in this chapter was published in Nysen et al. (2015).

5.1 Model averaging

By selecting one final best model and subsequently using it for inference, the preceding step of model selection and model uncertainty is fully ignored. Standard inference on such a final best model is “conditional” on that model. Model averaging offers a possibility to include model uncertainty and to provide multi-model inference or unconditional inference.

Model averaging (Burnham and Anderson, 2002) starts from a rich set of plausible candidate models and combines all fitted models such that better models have higher influence than moderate and poor models. Let \mathcal{M} be the family of candidate models, as defined in the previous section, with M_i ($i = 1 \dots, K$) the individual candidate models from family \mathcal{M} , and F_i the corresponding cumulative distribution function. The natural parameters θ_i are estimated by maximum likelihood and their covariance matrix is denoted by $\text{Cov}(\hat{\theta}_i)$.

In model averaging, a good model is defined by a small AIC. The weight that each model receives, is based on the difference of its AIC with the smallest AIC of all candidate models. The sum of the weights is equal to one:

$$w_i = \frac{\exp\left(-\frac{1}{2}\Delta_i\right)}{\sum_{j=1}^K \exp\left(-\frac{1}{2}\Delta_j\right)}$$

with

$$\Delta_i = \text{AIC}_i - \text{AIC}_{\min}.$$

Suppose we are interested in a parameter *eta* of the distribution, such as the mean, median or the value of the density function in a specified location. For every candidate model M_i , we can obtain an estimate $\hat{\eta}_i$. The model averaged value of parameter η is given by the weighted average of the estimates from all candidate models:

$$\hat{\eta}_{MA} = \sum_{i=1}^K w_i \hat{\eta}_i,$$

with estimated variance

$$\widehat{\text{Var}}(\hat{\eta}) = \left[\sum_{i=1}^K w_i \sqrt{\widehat{\text{var}}(\hat{\eta}_i) + (\hat{\eta}_i - \hat{\eta}_{MA})^2} \right]^2.$$

The variance estimator is the sum of two components. The first component is the conditional variance, given model M_i . The second component reflects the variation in the estimates across the K models.

For each model M_i , a parameter η can be estimated and the standard error can be obtained with the delta method. If the natural parameters θ_i of a distribution are estimated and their variance-covariance matrix $\text{Var}(\hat{\theta}_i)$ is known, then the delta method states that

$$\text{Var}(\hat{\eta}) \approx \nabla h(\theta_i)^T \text{Var}(\hat{\theta}_i) \nabla h(\theta_i), \quad (5.1)$$

where the parameter η can be written in terms of the natural parameters: $\eta = h(\theta_i)$. In formula (5.1) the gradient $\nabla h(\theta_i)$ can be estimated by $\nabla h(\hat{\theta}_i)$.

A central question in model averaging is the choice of the family \mathcal{M} of candidate models. A general guideline for selection and averaging in case of parametric models is that the family needs to be rich enough (so that it contains at least one good approximating model), and that it should only contain “sensible” models. Sensible models refer to all models $M \in \mathcal{M}$ that should really be serious “candidates” within the context of the application, and should obey possible constraints such as known shape restrictions (for more discussion on this issue, see e.g. Burnham and Anderson, 1998). For our area of interest (distribution of concentration data), the family of parametric models listed and described in Section 3.1 seems to comply with this general guideline. This family of parametric models will be denoted by \mathcal{M}_P . However, there is no guarantee that this family \mathcal{M}_P includes a good approximating model as a family member, and consequently, in case none of the family members fit well to the data, neither the best model selected within this family nor the averaged estimate will fit well.

This latter observation is the main motivation to consider our very rich family of models, being the series of SemiNP models $f_r, r \geq 0$ of Section 3.2. The family is so rich that it can approximate in principle any distribution, under very general conditions. The family of SemiNP models will be denoted as \mathcal{M}_S . The family is similar to the family of orthogonal series estimators or a family of nonparametric smoothers indexed over the smoothing parameter (kernel smoothers, splines). The order r acts as a smoothing parameter similar to e.g. the bandwidth for kernel or local polynomial smoother (see e.g. Hart, 1997). The family can also be compared to a family of fractional polynomials indexed over a fine grid of fractional powers. Model selection and model averaging over a family of fractional polynomials was proposed and discussed in Faes et al. (2007) and Namata et al. (2008).

We will apply the family \mathcal{M}_S in two ways: i) as a whole family of indexed models, ii) represented by a single model, being the model $f_{\hat{r}}$ adaptively selected with AIC as best within \mathcal{M}_S , or, in other words, the model with data-driven smoothing parameter. This model will be denoted as \hat{M}_S . So next to \mathcal{M}_P , we will consider the extended families $\mathcal{M}_P \cup \{\hat{M}_S\}$ and $\mathcal{M}_P \cup \mathcal{M}_S$ as families over which model selection and model averaging

can be performed. It is important to note that the composition of the extended family $\mathcal{M}_P \cup \{\hat{M}_S\}$ depends on the data. It is a data-driven family, because the particular member \hat{M}_S varies across samples in its selected order \hat{r} . Moreover, in case $\hat{r} = 0$ indicates the best model, no extra member will be added and $\mathcal{M}_P = \mathcal{M}_P \cup \{\hat{M}_S\}$. To our knowledge such extensions or combinations have not been considered and studied yet.

It is also possible to consider only the SemiNP models. However in the simulation study, we have encountered a lot of numerical issues, especially for the models in the family of SemiNP models. Therefore we decided not to consider the family \mathcal{M}_S as a separate family of candidate models. But it does seem an interesting option. Of course, in principle the family \mathcal{M}_S or \hat{M}_S should suffice as the SemiNP estimator can approximate essentially any distribution, but this might be at the cost of many parameters (r or \hat{r} large), whereas a parametric model with only a few parameters might also be a good approximation, and therefore to be preferred or at least to be considered.

In this chapter, we will apply model averaging to the density function and the cumulative distribution function, both evaluated in a real number y . For each candidate model, the natural parameters are estimated by maximum likelihood theory. These estimates are implemented in the density and cumulative distribution function and the delta method is used to estimate the variance of the function value. In the next chapter we will focus on model averaging of quantiles.

5.2 Application to data examples

We are interested in the estimation of the cumulative distribution function $F(y)$ and the density function $f(y)$, in some selected points y in the left tail of the distribution, ranging from the 5% quantile up to the average of the LODs. We report on the estimation of $\eta = F(y)$ and $\eta = f(y)$, for a fixed value y .

The three columns to the right in Table 5.1 show the weights on which the model averaged estimates for the different families are based. Throughout all weighting schemes, it is clear that the gamma distribution performs worst, getting weights very close to 0 and thus will not contribute at all to the model averaged estimate. For the \mathcal{M}_P family, the log-skew-t outperforms all other parametric models with weight 0.89611. Interestingly, when extending the family \mathcal{M}_P with one additional, albeit data adaptive model to the family $\mathcal{M}_P \cup \{\hat{M}_S\}$, the SemiNP model with $\hat{r} = 3$ fully takes over with weight 0.93454. The weight of the log-skew-t model reduces to 0.05866 and all other models get approximately a weight zero. The weight of all parametric models reduces even further when extending the family further to the larger family $\mathcal{M}_P \cup \mathcal{M}_S$. In the latter case, the weight of the SemiNP model with $\hat{r} = 3$ is spread over the SemiNP models with r ranging essentially

Table 5.1: Cadmium data 1. AIC and model averaging weights based on parametric models (\mathcal{M}_P) and based on parametric models together with best estimate of SemiNP ($\mathcal{M}_P \cup \{\hat{M}_S\}$) or all 7 SemiNP models ($\mathcal{M}_P \cup \mathcal{M}_S$).

Distribution	Nr par	AIC	$w(\mathcal{M}_P)$	$w(\mathcal{M}_P \cup \{\hat{M}_S\})$	$w(\mathcal{M}_P \cup \mathcal{M}_S)$
GenGam	3	-64.92	0.01701	0.00111	0.00045
Gamma	2	-47.24	2.46E-06	1.61E-07	6.45E-08
Weibull	2	-65.74	0.02568	0.00168	0.00067
Log-skew-t	4	-72.85	0.89611	0.05866	0.02346
Log-t	3	-62.62	0.00538	0.00035	0.00014
Log-skew-n	3	-66.64	0.04029	0.00264	0.00105
Log-normal	2	-64.73	0.01552	0.00102	0.00041
SemiNP1	2+1	-65.78			0.00069
SemiNP2	2+2	-69.48			0.00437
SemiNP3	2+3	-78.38		0.93454	0.37374
SemiNP4	2+4	-77.95			0.30144
SemiNP5	2+5	-76.64			0.15612
SemiNP6	2+6	-75.56			0.09094
SemiNP7	2+7	-74.22			0.04653

from 3 to 5.

In Table 5.2, the estimates $\hat{\eta} = \hat{F}(y)$ are computed for $y = q_{LN,0.05}$, $\min(\text{LOD})$, $q_{LN,0.25}$ and $\overline{\text{LOD}}$, where $q_{LN,\alpha}$ represents the α -th quantile of the log-normal distribution with parameters fitted to the data. The last rows correspond to the model averaged value, based on the three families of candidate models, without and with the SemiNP representation.

We can clearly see that different models lead to widely varying estimates of $F(y)$, especially when y is small. While selection of the best parametric model is standard, it is seen that the addition of the more flexible SemiNP model can have an important impact on the estimates. For each value of $F(y)$ (each column) one can clearly observe the effect of the weights: the \mathcal{M}_P -average is close to the estimate of the log-skew-t, the $\mathcal{M}_P \cup \{\hat{M}_S\}$ -average is close to the SemiNP3 estimate, and the $\mathcal{M}_P \cup \mathcal{M}_S$ -average follows the trend in the estimates when going further from the SemiNP3- to the SemiNP5-estimates. The estimated standard error of the averaged estimates is equal or slightly higher as the estimate of the best single model.

When comparing the columns from left to right, corresponding to the estimation of $F(y)$ with y growing from $y = 0.00028$ to $y = 0.00738$, the model averaged estimates over the families $\mathcal{M}_P \cup \{\hat{M}_S\}$ and $\mathcal{M}_P \cup \mathcal{M}_S$ turn from being smaller than the \mathcal{M}_P -

Table 5.2: Cadmium data 1. Estimates $\hat{F}(y)$ of parametric models and model averaged value (standard errors between brackets). Model averaging based on parametric models only (\mathcal{M}_P), on parametric models and best SemiNP ($\mathcal{M}_P \cup \{\hat{M}_S\}$), or on all fitted models ($\mathcal{M}_P \cup \mathcal{M}_S$). Corresponding weights are given in Table 5.1.

Distribution	$\hat{F}(q_{LN,0.05})$ $\hat{F}(2.77E - 04)$	$\hat{F}(\min(\text{LOD}))$ $\hat{F}(1.00E - 03)$	$\hat{F}(q_{LN,0.25})$ $\hat{F}(2.13E - 03)$	$\hat{F}(\overline{\text{LOD}})$ $\hat{F}(7.38E - 03)$
GenGam	0.098(0.055)	0.195(0.101)	0.281(0.136)	0.466(0.190)
Gamma	0.244(0.063)	0.320(0.070)	0.374(0.073)	0.484(0.075)
Weibull	0.145(0.033)	0.239(0.041)	0.315(0.045)	0.477(0.046)
Log-skew-t	0.212(0.066)	0.276(0.061)	0.329(0.057)	0.452(0.049)
Log-t	0.050(0.024)	0.149(0.042)	0.247(0.049)	0.465(0.048)
Log-skew-n	0.115(0.046)	0.213(0.054)	0.294(0.054)	0.466(0.047)
Log-normal	0.050(0.024)	0.150(0.042)	0.250(0.049)	0.467(0.047)
SemiNP1	0.034(0.016)	0.223(0.047)	0.389(0.050)	0.481(0.049)
SemiNP2	0.072(0.058)	0.253(0.072)	0.355(0.060)	0.466(0.050)
SemiNP3	0.061(0.045)	0.240(0.070)	0.353(0.060)	0.468(0.050)
SemiNP4	0.039(0.030)	0.215(0.067)	0.349(0.060)	0.472(0.050)
SemiNP5	0.020(0.022)	0.188(0.071)	0.348(0.061)	0.475(0.051)
SemiNP6	0.006(0.008)	0.140(0.069)	0.335(0.064)	0.479(0.051)
SemiNP7	0.008(0.010)	0.150(0.068)	0.338(0.062)	0.479(0.051)
\mathcal{M}_P	0.201(0.071)	0.269(0.064)	0.325(0.059)	0.454(0.052)
$\mathcal{M}_P \cup \{\hat{M}_S\}$	0.070(0.053)	0.242(0.070)	0.351(0.060)	0.467(0.050)
$\mathcal{M}_P \cup \mathcal{M}_S$	0.044(0.043)	0.212(0.076)	0.348(0.061)	0.471(0.051)

Table 5.3: Cadmium data 2. AIC and model averaging weights based on parametric models (\mathcal{M}_P) and based on parametric models together with best estimate of SemiNP ($\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$) or all 7 SemiNP models ($\mathcal{M}_P \cup \mathcal{M}_S$).

Distribution	Nr par	AIC	$w(\mathcal{M}_P)$	$w(\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\})$	$w(\mathcal{M}_P \cup \mathcal{M}_S)$
GenGam	3	-67.311	0.14691	0.10511	0.10373
Gamma	2	-68.086	0.21643	0.15486	0.15281
Weibull	2	-69.278	0.39276	0.28102	0.27731
Log-skew-t	4	-65.407	0.05671	0.04058	0.04004
Log-t	3	-57.669	0.00118	0.00085	0.00084
Log-skew-n	3	-67.744	0.18245	0.13055	0.12882
Log-normal	2	-59.863	0.00355	0.00254	0.00250
SemiNP1	2+1	-61.600			0.00597
SemiNP2	2+2	-60.781			0.00396
SemiNP3	2+3	-59.352			0.00194
SemiNP4	2+4	-57.690			0.00084
SemiNP5	2+5	-55.914			0.00035
SemiNP6	2+6	-54.073			0.00014
SemiNP7	2+7	-69.302		0.28450	0.28074

estimate to being larger. The difference between the estimates over $\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$ and $\mathcal{M}_P \cup \mathcal{M}_S$ gets smaller for growing y .

When we consider the family of parametric models for Cadmium data 2, the Weibull distribution fits the data best with regard to AIC and thus receives the highest weight (Table 5.3). When adding one or all members from the SemiNP family of distributions, the largest model (SemiNP7) also receives a substantial part of the weight. This is reflected in the estimates for the distribution function (Table 5.4).

Table 5.4: Cadmium data 2. Estimates $\hat{F}(y)$ of parametric models and model averaged value (standard errors between brackets). Model averaging based on parametric models only (\mathcal{M}_P), on parametric models and best SemiNP ($\mathcal{M}_P \cup \{\hat{M}_S\}$), or on all fitted models ($\mathcal{M}_P \cup \mathcal{M}_S$). Corresponding weights are given in Table 5.3.

Distribution	$\hat{F}(q_{LN,0.05})$ $\hat{F}(0.002)$	$\hat{F}(\min(\text{LOD}))$ $\hat{F}(0.003)$	$\hat{F}(q_{LN,0.25})$ $\hat{F}(0.004)$	$\hat{F}(\overline{\text{LOD}})$ $\hat{F}(0.015)$
GenGam	0.059 (0.021)	0.080 (0.023)	0.102 (0.025)	0.233 (0.033)
Gamma	0.072 (0.019)	0.092 (0.022)	0.114 (0.025)	0.232 (0.033)
Weibull	0.062 (0.015)	0.082 (0.019)	0.105 (0.022)	0.233 (0.033)
Log-skew-t	0.059 (0.021)	0.082 (0.025)	0.106 (0.027)	0.242 (0.033)
Log-t	0.029 (0.011)	0.050 (0.016)	0.076 (0.021)	0.247 (0.035)
Log-skew-n	0.057 (0.020)	0.080 (0.024)	0.105 (0.026)	0.243 (0.033)
Log-normal	0.029 (0.011)	0.050 (0.016)	0.076 (0.021)	0.250 (0.035)
SemiNP1	0.033 (0.012)	0.054 (0.017)	0.080 (0.021)	0.247 (0.035)
SemiNP2	0.034 (0.012)	0.056 (0.017)	0.081 (0.021)	0.246 (0.035)
SemiNP3	0.035 (0.013)	0.056 (0.017)	0.082 (0.021)	0.245 (0.035)
SemiNP4	0.035 (0.013)	0.057 (0.017)	0.083 (0.021)	0.245 (0.034)
SemiNP5	0.036 (0.013)	0.057 (0.017)	0.083 (0.021)	0.244 (0.034)
SemiNP6	0.036 (0.013)	0.058 (0.017)	0.083 (0.021)	0.244 (0.034)
SemiNP7	0.019 (0.014)	0.054 (0.026)	0.102 (0.033)	0.255 (0.041)
\mathcal{M}_P	0.063 (0.019)	0.083 (0.022)	0.106 (0.024)	0.235 (0.033)
$\mathcal{M}_P \cup \{\hat{M}_S\}$	0.050 (0.026)	0.075 (0.026)	0.105 (0.027)	0.241 (0.037)
$\mathcal{M}_P \cup \mathcal{M}_S$	0.050 (0.026)	0.075 (0.026)	0.105 (0.027)	0.241 (0.037)

5.3 Simulation study

Data are simulated according to the simulation scheme in Section 3.5. Three scenarios are considered: scenario 1 assumes that data come from a log-normal distribution, scenario 2 assumes that data are gamma distributed and scenario 3 is the setting where data come from a mixture distribution. In this section we only focus on left censoring. The parameters η of interest are particular values of the cumulative distribution function F and the density function f . In this section we only summarize and discuss the results for $F(y_1)$ (resp. $F(y_2)$), with F the generating distribution, and $y_1 = 0.0555$ (resp. $y_2 = 0.1901$) the 5% (resp. 25%) quantile of the log-normal ($\mu=-0.8047; \sigma=1.2686$) distribution. We will discuss the results for some sample sizes and generating distributions in detail in this section. The results for the other sample sizes and generating distributions are presented in Appendix A, as are the results for estimating the density function.

As we are looking at the 5% and 25% quantile of the log-normal distribution, we are interested in estimating the value of the distribution function in the left tail of the distribution, in a region where most of the data are left-censored, and more towards the center, where most of the data are uncensored. In the log-normal case y_1 is located as extreme in the left tail of the distribution as the smallest point at which the cumulative distribution function is estimated in the analysis of the Cadmium data. The values for η being $F(y_1)$ and $F(y_2)$ are (obviously) 0.05 and 0.25 respectively for the first scenario, 0.3776 and 0.5103 for the second scenario. For the last scenario, $\eta = F(y_1)$ equals 0.0375, 0.045 and 0.0475 corresponding to the 75%, 90% and 95% mixtures respectively; and $\eta = F(y_2)$ equals 0.1875, 0.225 and 0.2375 respectively.

The performance of the estimator is measured by the mean squared error (MSE), decomposed in a squared bias and a variance term. Let $\hat{\eta}^{(r)}$ denote the estimate based on the r -th generated dataset, for $r = 1, \dots, R$. With $\bar{\hat{\eta}}$ the average of the $\hat{\eta}^{(r)}$'s, the MSE is approximated as $(\bar{\hat{\eta}} - \eta)^2 + \sum_r (\hat{\eta}^{(r)} - \bar{\hat{\eta}})^2 / (R - 1)$, with the first term approximating the squared bias, and the second term the variance. To evaluate the performance for the estimator for the standard error of $\hat{\eta}$, the average squared estimated standard error is compared to the approximate variance $\sum_r (\hat{\eta}^{(r)} - \bar{\hat{\eta}})^2 / (R - 1)$. The number of simulations is set to 500 ($R = 500$).

In total, we compare 12 different estimators $\hat{\eta}$: seven estimators based on the seven fully parametric models, the best parametric model according to AIC, the best model from the SemiNP family according to AIC, the model average based on the parametric models only (\mathcal{M}_P), based on the parametric models supplemented with only the best model from the SemiNP family ($\mathcal{M}_P \cup \{\hat{M}_S\}$), and finally based on the parametric models supplemented with all SemiNP extensions ($\mathcal{M}_P \cup \mathcal{M}_S$). Note that, as mentioned before,

Table 5.5: Simulation study. Sample from log-normal distribution of size 100 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse ^(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse ^(rank)	$\overline{\text{var}}$
GenGam	0.347 (+)	2.243	2.589 (6)	3.186	1.482 (+)	3.592	5.074 (8)	5.125
Gamma	20.625 (+)	3.662	24.286 (11)	5.351	41.595 (+)	6.749	48.344 (11)	7.660
Weibull	30.418 (+)	3.878	34.297 (12)	4.680	44.392 (+)	5.506	49.898 (12)	5.861
Log-skew-t	0.016 (-)	2.662	2.679 (9)	3.405	0.184 (+)	5.624	5.808 (10)	6.448
Log-t	0.012 (-)	2.096	2.108 (1)	2.387	0.000 (+)	2.593	2.593 (1)	3.044
Log-skew-n	0.008 (-)	2.817	2.825 (10)	2.955	0.121 (-)	4.153	4.274 (4)	4.004
Log-normal	0.008 (-)	2.295	2.303 (2)	2.458	0.004 (-)	2.801	2.805 (2)	3.032
Best Parametric	0.015 (-)	2.527	2.543 (4)	2.528	0.060 (+)	5.732	5.792 (9)	3.389
Best SemiNP	0.028 (-)	2.627	2.655 (7)	2.496	0.000 (-)	4.124	4.124 (3)	4.859
\mathcal{M}_P	0.000 (+)	2.453	2.453 (3)	2.943	0.161 (+)	4.413	4.574 (5)	5.082
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.002 (-)	2.543	2.545 (5)	2.953	0.156 (+)	4.764	4.920 (7)	5.764
$\mathcal{M}_P \cup \mathcal{M}_S$	0.011 (-)	2.658	2.669 (8)	2.977	0.120 (+)	4.752	4.873 (6)	6.836

the first and third model average is based on a fixed set of candidate models, whereas the second model average has one data-selected member in the family of candidate models.

We select four tables in order to summarize and discuss our main findings: two under the scenario of the log-normal distribution, and one for both other scenarios (mixture and gamma distribution). The other results are presented in Appendix A. As the simulation settings are the same as in Section 3.5, we encountered the same computational as mentioned in that section. The four leftmost columns of the table show the results without censoring. The results for the same samples but now censored according to the LOD values as described above, are shown in the right columns. The first of these columns shows the (simulated) squared bias and the sign of the bias (“+” in case of overestimation, and “-” otherwise); the second shows the (simulated) variance, both combined in the third column in the Mean Squared Error (MSE). In between brackets is the rank of the models according to MSE (1=best, 12=worst). Finally, the fourth column (labeled $\overline{\text{var}}$) provides insights in the performance of the estimates for the standard error of the estimates. Indeed, comparing the variance result in column 2 with the average of the squared estimate for the standard errors over all runs in column 4 allows us to assess the bias of the se-estimate.

Scenario 1: generating from a log-normal distribution Table 5.5 and Table 5.6 summarize the results for sample size 100. Focusing on the left columns (no censoring) of

Table 5.6: Simulation study. Sample from log-normal distribution of size 100 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse ^(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse ^(rank)	$\overline{\text{var}}$
GenGam	0.713 (-)	11.714	12.427 ⁽³⁾	12.286	0.045 (-)	13.225	13.270 ⁽²⁾	13.752
Gamma	1.899 (-)	6.751	8.650 ⁽¹⁾	11.645	1.022 (+)	10.341	11.363 ⁽¹⁾	14.049
Weibull	0.965 (+)	8.933	9.898 ⁽²⁾	12.258	6.610 (+)	11.406	18.016 ⁽¹²⁾	13.724
Log-skew-t	0.478 (-)	14.217	14.695 ⁽¹²⁾	13.641	0.300 (-)	14.963	15.263 ⁽⁸⁾	14.405
Log-t	0.388 (-)	13.851	14.239 ⁽¹¹⁾	12.999	0.329 (-)	15.037	15.365 ⁽¹⁰⁾	15.401
Log-skew-n	0.114 (-)	13.786	13.899 ⁽⁷⁾	12.813	0.027 (-)	15.647	15.674 ⁽¹¹⁾	13.980
Log-normal	0.036 (-)	13.556	13.592 ⁽⁴⁾	12.220	0.034 (-)	14.747	14.780 ⁽⁴⁾	13.728
Best Parametric	0.083 (-)	13.950	14.033 ⁽⁹⁾	12.417	0.043 (-)	15.055	15.098 ⁽⁷⁾	13.835
Best SemiNP	0.019 (-)	14.125	14.143 ⁽¹⁰⁾	12.527	0.056 (-)	15.233	15.289 ⁽⁹⁾	15.510
\mathcal{M}_P	0.218 (-)	13.446	13.663 ⁽⁵⁾	12.889	0.062 (-)	14.620	14.681 ⁽³⁾	14.315
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.157 (-)	13.707	13.865 ⁽⁶⁾	13.111	0.061 (-)	14.771	14.831 ⁽⁵⁾	14.952
$\mathcal{M}_P \cup \mathcal{M}_S$	0.078 (-)	13.825	13.904 ⁽⁸⁾	13.494	0.061 (-)	14.779	14.841 ⁽⁶⁾	17.806

the first table ($\eta = F(y_1)$), we observe that the log-t, log-normal, log-skew-t, and the log-skew-normal perform best, in that order, with very small negative bias. Bias is very large and positive (overestimation) for the gamma and Weibull distribution, due to the location of y_1 in the very left tail of the distributions. Their extension to the generalized-gamma distribution performs as one of the better ones. In a simulation setting we know the true generating model, but of course in practice we don't. So interest mainly goes to the data-selected and averaged models. Here we can conclude that performance of all (five) approaches are essentially the same, but there is a small increase in MSE when the family of distributions for model averaging is larger. Comparing data-selected and averaged models with the oracle model (the generating model), we can conclude that performances are quite close. Regarding the bias of the se-estimate, the main conclusions are: i) slight overestimation for the parametric models, ii) essentially zero for the data-selected models, iii) some overestimation for the averaged models.

Switching to the right columns (with censoring) of Table 5.5, many of the above findings remain valid. As expected, bias, variance and MSE values are now higher, because y_1 is located in the left tail of the distribution where the censoring is imposed. The impact of censoring is very limited for the log-t and the log-normal model, but for most other models, including the data-selected and averaged model, the MSE values double in value, more or less. We can also see that censoring has an impact on the magnitude of the standard errors. Again the data-selected and averaged models perform quite similar, with

Table 5.7: Simulation study. Sample from gamma distribution of size 200 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse ^(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse ^(rank)	$\overline{\text{var}}$
GenGam	0.099 (-)	7.581	7.680 (2)	7.280	0.004 (-)	12.621	12.625 (3)	12.831
Gamma	0.115 (-)	6.935	7.050 (1)	6.806	0.034 (-)	12.066	12.101 (1)	12.017
Weibull	6.571 (+)	11.246	17.818 (8)	8.140	12.260 (-)	12.284	24.544 (10)	10.994
Log-skew-t	0.704 (+)	9.415	10.119 (7)	9.243	0.052 (-)	12.439	12.491 (2)	12.929
Log-t	0.695 (-)	24.614	25.309 (9)	14.509	23.084 (-)	14.246	37.331 (12)	12.073
Log-skew-n	39.619 (+)	11.788	51.408 (11)	5.819	8.404 (-)	11.092	19.497 (9)	12.388
Log-normal	126.980 (+)	8.693	135.674 (12)	7.953	21.952 (-)	14.240	36.192 (11)	12.090
Best Parametric	0.001 (-)	8.224	8.224 (6)	6.912	0.055 (-)	12.915	12.970 (7)	11.999
Best SemiNP	4.648 (+)	32.432	37.079 (10)	9.094	2.173 (-)	17.317	19.490 (8)	20.471
\mathcal{M}_P	0.008 (+)	7.834	7.842 (3)	8.057	0.121 (-)	12.601	12.722 (4)	12.804
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.005 (+)	7.896	7.900 (4)	8.126	0.102 (-)	12.738	12.840 (5)	13.363
$\mathcal{M}_P \cup \mathcal{M}_S$	0.003 (+)	7.919	7.922 (5)	8.144	0.102 (-)	12.761	12.862 (6)	13.429

some advantage for the best SemiNP model.

The results in Table 5.6 for the parameter $\eta = F(y_2)$ are very much the same, albeit with some remarkable and important differences. For the true model, the log-normal, MSE increases. Being the poorest models for $\eta = F(y_1)$, the gamma and Weibull model outperform all other models, especially in the absence of censoring. The next best parametric model is the generating log-normal model. Conclusion is that the estimation of local features of a distribution is not necessarily predestinated for the “true” model. Not directly deducible from this table is the fact that AIC most often selected the log-normal model as best model, and not the gamma model. Indirectly this is confirmed by the results for the best parametric (data-selected) model whose results are close to that of the log-normal. AIC is of course a model selection criterion that assesses the global fit of a model to the data, whereas focus is here on a local characteristic of the distribution. Another remarkable observation is that the loss of precision when censoring is introduced is quite limited. Of course, censoring is concentrated in the left tail of the distribution, and even to the left of y_2 .

Scenario 2: generating from a gamma distribution In the second part of the study, samples are drawn from the gamma distribution. The results for samples of size 200 estimating the cumulative distribution function in y_1 , are provided in Table 5.7. In all simulations from the gamma distribution, the mean squared error is the smallest when

fitting the gamma model. For this correctly specified distribution, i.e. gamma, MSE increases if the data are censored. The MSE for the gamma model is much smaller than for the other models and only the generalized gamma model is of about the same magnitude. It is clear that the SemiNP models are not the best way to describe these data. However, the performance is better in Scenario 3 below, where data are simulated from a distribution with a local deviation from the log-normal distribution instead of a global deviation. We can also observe that for some fitted distributions, MSE is smaller in the censored case. This is the case when using the log-skew-normal and the log-normal, and the best SemiNP. This is mainly located in the bias component. The use of the log-skew-normal and the log-normal result in estimates for the cumulative distribution function of the gamma (at y_1) that are extremely highly biased upwards. Introducing censoring (42%) in the data reduces that bias considerably. This peculiar effect when using a misspecified model for the estimation of the cumulative distribution function based on censored data seems contradictory, but the use of a misspecified model can lead to 'unpredictable' effects when censoring is introduced.

Regarding the bias of the se-estimates, the conclusions are: i) slight underestimation for the parametric models, except for the oracle model where there is almost no bias, ii) underestimation for the data-selected models, iii) slight overestimation for the averaged models. Because the AIC of the gamma model is the smallest (not deducible from this table), the MSE and mean variance for the model averages are close to the corresponding values of the gamma model.

Scenario 3: generating from a mixture of log-normal distributions The last part of the simulation study contains data sampled from the 75%, 90% or 95% mixture distributions. All results are in Appendix A, but we show here only the results for the 75% mixture with sample size 500, when estimating $F(y_2)$ in Table 5.8. The data-selected model based on the parametric distributions and the model average in the \mathcal{M}_P family, are biased and the standard errors are overestimated. The data-selected model based on the SemiNP models is only little biased, but the standard error is underestimated. The model averages based on $\mathcal{M}_P \cup \{\hat{M}_S\}$ and $\mathcal{M}_P \cup \mathcal{M}_S$ show also little bias. The standard errors are still underestimated, but closer to the variance in the second column. For the censored data, the standard error in both the data-selected models and model-averages is overestimated, but the bias is much smaller for the model averages. In Table 5.8, we can also observe an 'improved' behavior in case of censoring. But here all models are misspecified, except for the SemiNP model which is known to be able to capture local departures. For that SemiNP model the MSE increases when introducing censoring, as one would expect.

Table 5.8: Simulation study. Sample from 75% mixture distribution of size 500 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse ^(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse ^(rank)	$\overline{\text{var}}$
GenGam	8.852 (-)	1.096	9.949 (12)	1.752	2.187 (-)	1.666	3.853 (9)	2.193
Gamma	7.189 (-)	0.944	8.133 (10)	1.772	1.470 (-)	1.422	2.892 (7)	2.128
Weibull	5.600 (-)	1.179	6.778 (8)	1.698	2.100 (-)	1.453	3.554 (8)	1.906
Log-skew-t	5.281 (-)	1.012	6.293 (4)	1.803	0.724 (-)	1.499	2.223 (1)	2.243
Log-t	6.391 (-)	1.757	8.148 (11)	1.816	6.896 (-)	1.868	8.764 (12)	1.984
Log-skew-n	5.331 (-)	1.032	6.363 (7)	1.786	1.032 (-)	1.514	2.546 (6)	2.191
Log-normal	5.864 (-)	1.768	7.632 (9)	1.797	6.528 (-)	1.884	8.412 (11)	1.982
Best Parametric	5.316 (-)	1.031	6.347 (6)	1.789	0.829 (-)	1.546	2.375 (5)	2.217
Best SemiNP	0.077 (+)	4.105	4.182 (3)	2.502	1.027 (-)	4.058	5.085 (10)	6.089
\mathcal{M}_P	5.314 (-)	1.027	6.340 (5)	1.793	0.826 (-)	1.527	2.353 (2)	2.227
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.024 (-)	3.928	3.952 (2)	2.676	0.106 (-)	2.257	2.363 (4)	5.104
$\mathcal{M}_P \cup \mathcal{M}_S$	0.007 (-)	3.885	3.892 (1)	2.701	0.102 (-)	2.260	2.362 (3)	5.395

Of course it does not make sense to recommend the use of a misspecified model in case of censoring, but it stresses the importance of careful selecting candidate models (possibly based on prior or expert knowledge) and of considering model averaging. In Table 5.8 where all models are misspecified, the model averaged estimates perform very good, especially the extended versions (last two lines).

The tables in Appendix A show that for the less contaminated samples (95% and 90% mixture), the family with all members of the SemiNP model has smaller MSE than the family with only the best member. When simulating from the 75% mixture, it depends on the sample size and censoring which family of candidate models gives the smallest MSE.

Similar results are obtained for the estimate of the density function in a fixed value. The tables are available in Appendix A. Data from the log-normal distribution are least biased by the log-normal model. An exception is the Weibull model for uncensored data and the generalized gamma model for censored data while estimating the density in the 5% quantile. While AIC of the Weibull model was the second worst for uncensored, log-normally distributed data, the bias is the smallest. The bias in the SemiNP models is close to the bias of the true (log-normal) model. The variance is clearly larger than the square of the bias and therefore has more influence on the mean squared error. MSE of the Weibull model is the smallest for the estimate of the density in the 5% quantile, but the log-normal performs well, as expected. The MSE of the SemiNP models is close to the log-normal model. For the censored samples, the MSE of the log-normal model is the

smallest, closely followed by the SemiNP model with one extra parameter. In the case of the 25% quantile, the least biased models are the SemiNP. MSE of these models is close to MSE of the log-normal, but the Weibull (uncensored) and generalized gamma (censored) have a MSE that is slightly smaller. For data simulated from the gamma distribution, the gamma model has the smallest mean squared error. The bias is clearly smallest for the true gamma model, but the variance is smaller for some other models. The best SemiNP model has one extra parameter compared to the log-normal model for uncensored data and the maximum number of 7 extra parameters for censored data. The same conclusions hold for sample size 200, except for the censored case and 25% quantile, where the SemiNP model with three parameters performs slightly better than the model with seven parameters.

5.4 Conclusion

In this chapter we focused on different model strategies for the estimation of the distribution function of chemical contaminant data, which are typically left-censored. It is shown that it is highly important to select an appropriate and rich enough family of candidate models. The use of the SemiNP model is recommended when working with real data. Its semi-parametric nature offers more flexibility to the standard parametric models. As the fitting of the SemiNP model needs some specialized code, and turns out to be quite computer intensive and highly sensitive to starting values, this might hinder its use in daily statistical practice. But, while these computational issues were a major problem in our simulation study, this is less the case for fitting a single data example. Our experience learned that convergence could be reached in all cases after trying out a few different sets of starting values.

The techniques described in this article, are based on maximum likelihood estimation. As the likelihood is defined for any type of censoring (left-, right- or interval-censoring), we do expect the methods to be applicable to other censoring schemes and to other data structures such as hierarchical and longitudinal data. Throughout this thesis AIC has been used as the information criterion to select and to average different models, but other choices can be made. While the AIC is asymptotically efficient, BIC is an asymptotically consistent model selection criterion (Burnham et al., 2011). The comparison of both criteria for model selection and averaging in case of censored data is another interesting topic for future research. In some instances we are also only interested in some local property of the distribution and using AIC or BIC might not be the best option (as they compare models globally). Focused information criteria as introduced and studied in Claeskens and Hjort (2003) offer an appealing way to go in that case.

Chapter 6

Model averaging quantiles

Whereas in Chapter 5 we focused on the model averaging of the distribution function, our interest here goes to model averaging of quantiles. As a quantile is the inverse of the distribution function, there are two approaches to model average quantiles. One approach consists of estimating the quantile in every model, followed by averaging over the estimates. In the other approach we first construct a model averaged distribution function and then take the inverse to obtain an estimate for the quantile. Both approaches are illustrated on Cadmium and Cesium data (Section 6.4). The study of the Cesium data is further complicated by the presence of a time effect and by the uncertainty of the limit of detection. A way to deal with these complications is discussed in Section 6.3. The performance of both model averaging approaches is compared in a simulation study in Section 6.2. The material in this chapter was published in Nysen et al. (2016b).

6.1 Two approaches of model averaging quantiles

The quantile ξ_p of a distribution is the point where the cumulative distribution function achieves the level p . It can be computed by inverting the cumulative distribution function. To compute a model averaged quantile, there are two natural approaches. In the first approach we estimate the quantile in each model and compute the average over all estimated quantiles. In the second approach, we model average the cumulative distribution function and invert the model averaged function to estimate the quantile. A prior comparison of the approaches is given in the last subsection.

6.1.1 Direct method of model averaging

In this first approach, the quantile ξ_p is estimated for each candidate model M_i ($i = 1, \dots, K$) and the model averaged estimate is a weighted average of the K estimates. Based on model M_i , the ML-estimate for ξ_p is given by $\hat{\xi}_{p,i} = F_i^{-1}(p; \hat{\theta}_i)$, with variance (as approximated by the delta method)

$$\text{Var}(\hat{\xi}_{p,i}) \approx \nabla F_i^{-1}(p; \theta_i)^T \text{Cov}(\hat{\theta}_i) \nabla F_i^{-1}(p; \theta_i). \quad (6.1)$$

The gradient $\nabla F_i^{-1}(p; \theta_i)$ with respect to θ_i can be estimated by $\nabla F_i^{-1}(p; \hat{\theta}_i)$.

The model averaged estimate is defined as the weighted average

$$\hat{\xi}_{p,MA_1} = \sum_{i=1}^K w_i \hat{\xi}_{p,i}, \quad (6.2)$$

with weights w_i defined as (Burnham and Anderson, 2002)

$$w_i = \frac{\exp(-\frac{1}{2}\Delta_i)}{\sum_{j=1}^K \exp(-\frac{1}{2}\Delta_j)}, \quad (6.3)$$

where $\Delta_i = \text{AIC}_i - \text{AIC}_{\min}$. The variance estimator

$$\widehat{\text{Var}}(\hat{\xi}_{p,MA_1}) = \left[\sum_{i=1}^K w_i \sqrt{\widehat{\text{Var}}(\hat{\xi}_{p,i}) + (\hat{\xi}_{p,i} - \hat{\xi}_{p,MA_1})^2} \right]^2,$$

is the sum of two components, the conditional variance, given model M_i , and the second component reflects the variation in the estimates across the K models. For a general discussion on the construction of the AIC-based weights, its motivation in the frequentist approach, the use and comparison with other weights as well as with Bayesian averaging, we refer to Burnham and Anderson (2002). It is of course important to include sufficiently good approximating models in the set of candidate models. This could be assured through knowledge about the setting, or by making the family of candidate models rich enough (excluding however models that make no sense for a particular application of interest).

6.1.2 Indirect method of model averaging

A second approach follows the opposite order: instead of inverting all model specific CDFs F_i and next averaging the obtained quantiles, first average the model specific CDFs F_i , and next invert the obtained average. As inverting a CDF is nonlinear, the approaches are not identical. See next section for some more comparative considerations.

Let y be a real number in the domain of the candidate distribution function. The averaged distribution function is given by

$$F_{MA}(y; \hat{\theta}) = \sum_{i=1}^K w_i F_i(y; \hat{\theta}_i),$$

with the same weights (6.3) and with $\hat{\theta}$ the stacked vector of all estimated natural parameters $\hat{\theta}_i$ of all candidate models $M_i, i = 1, \dots, K$.

The estimated variance of $F_{MA}(y; \hat{\theta})$ is then given by

$$\widehat{\text{Var}}(F_{MA}(y; \hat{\theta})) = \left[\sum_{i=1}^K w_i \sqrt{\widehat{\text{Var}}(F_i(y; \hat{\theta}_i)) + (F_i(y; \hat{\theta}_i) - F_{MA}(y; \hat{\theta}))^2} \right]^2. \quad (6.4)$$

Note that $F_{MA}(y; \hat{\theta})$ is indeed a valid cumulative distribution function of a positive continuous random variable. The performance of the estimator $F_{MA}(y; \hat{\theta})$ has been studied in Nysen et al. (2015). They illustrated the importance of choosing a good model and how selecting an incorrect model can bias the results. Model averaging reduces the bias and therefore offers a worthwhile solution. It is interesting to compare their results on the CDF scale to our results on the inverted quantile scale. Indeed, we define the indirect averaged estimate for the p -quantile ξ_p as

$$\hat{\xi}_{p, MA_2} = F_{MA}^{-1}(p; \hat{\theta}). \quad (6.5)$$

In practice $\hat{\xi}_{p, MA_2}$ is computed by numerically solving the equation $F_{MA}(y; \hat{\theta}) = p$. Based on the implicit function theorem, the variance of $\hat{\xi}_{p, MA_2}$ can be approximately estimated by

$$\widehat{\text{Var}}(\hat{\xi}_{p, MA_2}) = \frac{\widehat{\text{Var}}(F_{MA}(\hat{\xi}_{p, MA_2}; \hat{\theta}))}{f_{MA}^2(\hat{\xi}_{p, MA_2}; \hat{\theta})},$$

using expression (6.4) and with averaged density $f_{MA}(y; \hat{\theta}) = (\partial/\partial y)F_{MA}(y; \hat{\theta})$.

The direct estimate $\hat{\xi}_{p, MA_1}$ and the indirect estimate $\hat{\xi}_{p, MA_2}$ will be not the same, but are expected to be not too far apart. Figure 6.4 illustrates the two different approaches for the estimation of the 25% quantile of the cadmium distribution. The figure shows that the model specific estimates $\hat{\xi}_{0.25, i}$ vary substantially. A poor model choice may thus result into a poor estimate. The model averaged estimates $\hat{\xi}_{0.25, MA_1}$ and $\hat{\xi}_{0.25, MA_2}$ are close in this case. The estimate resulting from the log-skew-t model, selected by AIC as best model (see Section 6.4.1) and contributing most to $\hat{\xi}_{0.25, MA_1}$, is slightly smaller (as indicated by the dashed black vertical line). In the following section we go into some prior considerations on the difference between both estimates $\hat{\xi}_{p, MA_1}$ and $\hat{\xi}_{p, MA_2}$.

6.1.3 Prior comparison of direct and indirect estimator

A quite similar, though different situation appears in the construction of model-averaged benchmark dose (BMD) estimation. The BMD is defined as the dose corresponding to a very small increase in risk over background, a ‘‘safe level’’ of exposure, and such a BMD

is estimated from dose-response models, e.g. through developmental toxicity studies designed to assess the potential adverse effect of a chemical exposure on developing fetuses. Faes et al. (2007) proposed the use of the flexible family of fractional polynomials (FP, Royston and Altman, 1994) to estimate the BMD and proposed to average the FP-specific BMD-estimates directly (similar to our “direct” approach). In the same setting, Wheeler and Bailer (2007, 2009) pointed at some shortcomings of this direct method, and proposed to first average the dose-response models and to define a BMD estimate from there. This latter approach is the translation of our “indirect” approach to this BMD setting. Wheeler and Bailer (2007) recommend the latter method, but as other issues of implementation were involved, and as the setting is not identical (no censored data but binary response variable in a regression context), their conclusions cannot be straightforwardly extended to our setting.

Although a theoretical study of both approaches along the lines and with methodology as introduced in Claeskens and Hjort (2008) is beyond the scope of this dissertation, some first order approximations might lead to some further insights in how the estimates $\hat{\xi}_{p,MA_1}$ and $\hat{\xi}_{p,MA_2}$ differ. Based on a first order Taylor expansion applied to $F_i(y, \hat{\theta}_i)$ around ξ_p , it follows that for each model M_i (i, \dots, K), we have that, for a particular fixed value of $0 < p < 1$,

$$p - F_i(\xi_p, \hat{\theta}_i) = f_i(\xi_p, \hat{\theta}_i)(\hat{\xi}_{p,i} - \xi_p) + O_P((\hat{\xi}_{p,i} - \xi_p)^2),$$

with $f_i(y; \hat{\theta}_i) = (\partial/\partial y)F_i(y; \hat{\theta}_i)$, and consequently, with weights w_i as in (6.3) summing to 1,

$$p - F_{MA}(\xi_p, \hat{\theta}) = \sum_{i=1}^K w_i f_i(\xi_p, \hat{\theta}_i)(\hat{\xi}_{p,i} - \xi_p) + \sum_{i=1}^K w_i O_P((\hat{\xi}_{p,i} - \xi_p)^2). \quad (6.6)$$

A similar first order Taylor expansion applied to $F_{MA}(y, \hat{\theta})$ around ξ_p yields

$$p - F_{MA}(\xi_p, \hat{\theta}) = f_{MA}(\xi_p, \hat{\theta})(\hat{\xi}_{p,MA_2} - \xi_p) + O_P((\hat{\xi}_{p,MA_2} - \xi_p)^2)$$

such that, ignoring the remainder O_P -terms

$$(\hat{\xi}_{p,MA_2} - \xi_p) \approx \sum_{i=1}^K w_i \frac{f_i(\xi_p, \hat{\theta}_i)}{f_{MA}(\xi_p, \hat{\theta})} (\hat{\xi}_{p,i} - \xi_p) \neq (\hat{\xi}_{p,MA_1} - \xi_p).$$

This relationship expresses the difference between both model-averaged estimators, in terms of the differences between the model specific density estimates $f_i(\xi_p, \hat{\theta}_i)$ and the model averaged density estimate $f_{MA}(\xi_p, \hat{\theta})$. A sufficient (but not necessary) condition for $(\hat{\xi}_{p,MA_2} - \xi_p) \approx (\hat{\xi}_{p,MA_1} - \xi_p)$ is that

$$\frac{f_i(\xi_p, \hat{\theta}_i)}{f_{MA}(\xi_p, \hat{\theta})} \approx 1, \text{ for all } i = 1, \dots, K.$$

It is very unlikely that this sufficient condition is fulfilled for all models, but it might be reasonable to assume that it holds for those model M_i having the highest weights w_i and contributing most to the averaged estimate.

As these considerations do not reveal sufficient insights in how both approaches perform for small and varying sample sizes and with varying percentages of left-censoring, simulations were set up and results thereof are reported in the next section.

6.2 Simulation study

The settings and scenarios of the simulation study are similar to those in Chapter 5, where the performance of the individual candidate models is compared to the performance of the best model and the model average, for estimating the distribution function $F(y)$ at some predefined y . The simulation study in Nysen et al. (2015) did indicate that results and conclusions thereof are quite scenario dependent. However, in this chapter we focus on quantile estimation and the results are not a priori the same as for the estimation of the distribution function. Indeed, a distribution function $F(y)$ is, as an average of indicators $I(Y \leq y)$, a linear combination of random variables and is restricted to a value between 0 and 1, whilst a quantile is a non-linear functional and is only restricted to be positive in our setting.

The objective of this simulation study is to compare the performance and accuracy of different approaches to estimate the quantiles in terms of i) mean squared error of the estimates, decomposed in squared bias and variance, ii) bias of the estimated standard errors of the estimates. In this comparison we consider the following different estimates, based on: i) each of the individual parametric models, as members of the family \mathcal{M} , ii) that member of \mathcal{M} , selected as best by AIC and iii) the model average over \mathcal{M} according to the direct and indirect method.

Two censoring schemes are used. The first is explained in Section 3.5.2.

The second censoring scheme is based on the first data example. For the Cadmium 1 data, 5 different limits of detection are used, representing 42% of all data. The LODs correspond to the 15%, 24%, 39%, 46% and 52% percentiles of the fitted log-normal distribution, with frequencies 4, 1, 12, 2 and 23 (the other 57 are not censored). If we assume that the LODs in the sample occur with the same probability as in reality, it means that the distribution of the 15%, 24%, 39%, 46% and 52% percentiles is equal to 9% ($=4/42$), 2% ($=1/42$), 29% ($=12/42$), 5% ($=2/42$) and 55% ($=23/42$). For the simulation study we use the same percentiles of the log-normal distribution, with the same discrete distribution. This results in 44% censoring for the samples from the log-normal distribution, 41%, 39% and 32% for the mixture distributions and 59.6% for the gamma

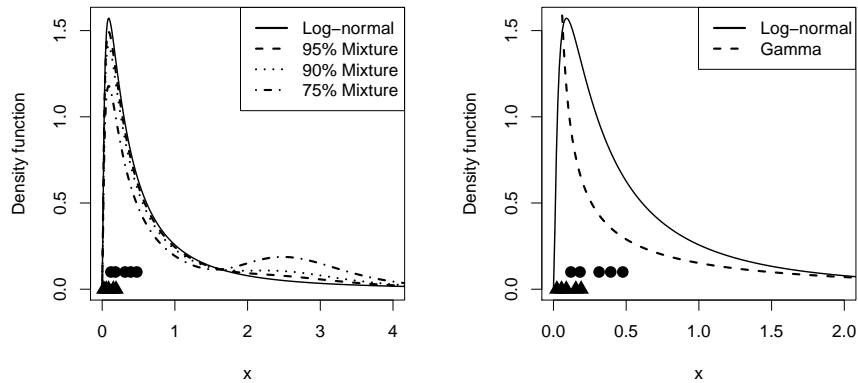


Figure 6.1: Simulation study. Left panel: sampling distributions log-normal and mixture distributions. Right panel: sampling distributions log-normal and gamma distribution. Left censoring based on censoring scheme 1 (▲) and censoring scheme 2 (●).

distribution. The LODs are shown by the circles on the horizontal axis in Figure 6.1.

We selected three tables in order to summarize and discuss our main findings. The upper part of these tables summarize the performance of the individual members of the parametric family \mathcal{M} , followed by the best data-driven representative of this family (selected by AIC), and the averaged models over this family (according to the two methods of averaging: direct indicated by * and indirect by **). The four leftmost columns show the results without censoring. The results for the same samples but now censored according to the LOD values as described above, are shown in the middle (first censoring scheme) and right (second censoring scheme) columns. So, from left to right, the percentage of censored data increases. Every first column shows the (simulated) squared bias and the sign of the bias (“+” in case of overestimation, and “-” otherwise); the second shows the (simulated) variance, both combined in the third column with the Mean Squared Error (MSE). In between brackets is the rank of the models according to MSE (1=best, 9=worst). Finally, the fourth column (labeled $\overline{\text{var}}$) provides insights in the performance of the estimates for the standard error of the estimates. Indeed, comparing the variance result in column 2 with the average of the squared estimate for the standard errors over all runs in column 4 allows us to assess the bias of the standard error-estimate (s.e.-estimate).

Scenario 1: generating from a log-normal distribution. Table 6.1 summarizes the results for sample size 100 while estimating the 5% quantile (0.0555) of the data. A first overall observation is that the MSE increases for all models when increasing the degree

Table 6.1: Simulation study. Sample from log-normal distribution of size 100 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No censoring				Censoring 1				Censoring 2			
	bias ²	var	mse ^(rank)	$\sqrt{\text{var}}$	bias ²	var	mse ^(rank)	$\sqrt{\text{var}}$	bias ²	var	mse ^(rank)	$\sqrt{\text{var}}$
Gamma	9.163 ⁽⁻⁾	0.833	9.995 ⁽⁸⁾	1.064	13.581 ⁽⁻⁾	0.800	14.382 ⁽⁹⁾	0.831	23.098 ⁽⁻⁾	0.484	23.582 ⁽⁹⁾	0.441
Weibull	10.820 ⁽⁻⁾	0.517	11.337 ⁽⁹⁾	0.569	13.162 ⁽⁻⁾	0.500	13.662 ⁽⁸⁾	0.495	18.736 ⁽⁻⁾	0.438	19.174 ⁽⁷⁾	0.388
Log-skew-t	0.079 ⁽⁺⁾	1.689	1.767 ⁽⁷⁾	1.930	0.005 ⁽⁻⁾	3.066	3.071 ⁽⁷⁾	3.254	0.029 ⁽⁻⁾	20.920	20.949 ⁽⁸⁾	19.412
Log-t	0.075 ⁽⁺⁾	1.300	1.376 ⁽²⁾	1.328	0.041 ⁽⁺⁾	1.506	1.548 ⁽¹⁾	1.609	0.214 ⁽⁺⁾	2.807	3.021 ⁽¹⁾	3.130
Log-skew-n	0.060 ⁽⁺⁾	1.638	1.698 ⁽⁶⁾	1.534	0.238 ⁽⁺⁾	2.355	2.593 ⁽⁵⁾	2.038	5.121 ⁽⁺⁾	13.078	18.199 ⁽⁶⁾	9.129
Log-normal	0.065 ⁽⁺⁾	1.294	1.359 ⁽¹⁾	1.246	0.069 ⁽⁺⁾	1.510	1.579 ⁽²⁾	1.490	0.197 ⁽⁺⁾	2.891	3.087 ⁽²⁾	3.022
AIC-selected	0.076 ⁽⁺⁾	1.467	1.542 ⁽⁵⁾	1.307	0.005 ⁽⁺⁾	2.762	2.766 ⁽⁶⁾	1.568	1.334 ⁽⁺⁾	13.283	14.617 ⁽⁵⁾	4.887
$\mathcal{M}_P^{(1)}$	0.051 ⁽⁺⁾	1.453	1.505 ⁽³⁾	1.526	0.001 ⁽⁺⁾	2.273	2.274 ⁽³⁾	2.311	0.108 ⁽⁻⁾	4.943	5.051 ⁽³⁾	13.322
$\mathcal{M}_P^{(2)}$	0.052 ⁽⁺⁾	1.458	1.510 ⁽⁴⁾	1.159	0.000 ⁽⁺⁾	2.356	2.356 ⁽⁴⁾	2.046	2.292 ⁽⁻⁾	3.494	5.785 ⁽⁴⁾	18.811

⁽¹⁾ direct method of model averaging (MA₁)

⁽²⁾ indirect method of model averaging (MA₂)

of censoring (from left to right), as to be expected. For the log-normal (the true model), the log-t, the direct and the indirect model average, this increase stays quite limited but for some methods the increase is dramatic (log-skew-t, log-skew-normal, the AIC-selected model). For the second censoring scheme several models and methods get into problem, in one or another way.

Focusing first on the individual parametric models, the estimators based on the log-t and the true log-normal distribution outperform all other estimators and provide the best fits (as to be expected in this scenario). Both their MSE values are actually very close, with the smallest value for the true log-normal distribution in case of no censoring, and the reverse in case of moderate or highly censored data. But the log-t and the true log-normal estimators are closely followed by the direct and indirect model average. Both methods of model averaging behave very similar; in case of no or moderate censoring, the variance of the direct method is slightly smaller, and the reverse for the higher censoring scheme 2. For the gamma and Weibull model the increase in the MSE is mainly located in the squared bias component, for the log-skew-t it is rather the variance component, and for the log-skew-normal and the AIC-selected model it happens in both components.

The estimates for the standard errors perform well for the log-t and the log-normal model, regardless of the degree of censoring. But for the others, the performance of the estimates for the standard errors is also affected by the degree of censoring: from overestimation to underestimation for the gamma, Weibull, log-skew-t, and to an extreme extent for the AIC-selected model. For the log-skew-normal the se-estimates always underestimate the variability in the estimates but bias increases with the degree of censoring. For no and moderate censoring, the estimates for the standard errors perform well for the direct and indirect model average. However, for censoring scheme 2, the se-estimates

Table 6.2: Simulation study. Sample from log-normal distribution (upper panel), gamma distribution (lower left panel) or mixture of 2 log-normal distributions (lower right panel). Average AIC rank of models within \mathcal{M}_p .

Scenario 1						
Log-normal distribution						
Sample size 100						
Censoring	No	Censoring 1	Censoring 2			
Gamma	5.90	5.66	4.82			
Weibull	4.91	4.49	3.39			
Log-skew-t	3.85	3.98	4.50			
Log-t	3.03	3.21	3.74			
Log-skew-n	2.02	2.26	2.87			
Log-normal	1.29	1.40	1.68			

Scenario 2				Scenario 3		
Gamma distribution				75% Mixture distribution		
Sample size 200				Sample size 500		
Censoring	No	Censoring 1	Censoring 2	No	Censoring 1	Censoring 2
Gamma	1.18	1.26	1.30	4.19	3.69	2.43
Weibull	3.71	2.98	2.24	3.18	3.38	3.13
Log-skew-t	2.05	2.60	2.67	1.95	1.73	1.02
Log-t	4.98	6.00	5.95	5.84	5.97	5.99
Log-skew-n	3.13	3.77	4.96	1.05	1.27	4.17
Log-normal	5.96	4.40	3.88	4.79	4.96	4.26

seem to highly overestimate the true variability. A further investigation in the distributional properties of the se-estimates in these particular cases indicates a very right-skewed distribution, explaining the high value of the average of the variance estimates.

The averaged AIC ranks of the individual parametric models (Table 6.2) show that the log-normal distribution leads to the best quantile estimators, but that its dominance decreases slightly with the degree of censoring. The two worst performers (gamma and Weibull) seem to perform relatively somewhat better when more censoring is present. It is not unexpected that the higher the level of censoring the worse the performance of any method and the more alike the different methods perform; although there is a clear winner for this scenario.

The above findings generalize to the other sample sizes and different quantiles (results not shown here), except how both model averaged estimators compare with each other. The first model averaging approach is usually the best for small quantiles, while for larger

Table 6.3: Simulation study. Sample from (a) gamma distribution of size 200 - estimate of 25% quantile ($\times 10^{-4}$) and (b) 75% mixture distribution of size 500 - estimate of 1% quantile (Results $\times 10^{-4}$).

(a)												
Censoring	No censoring				Censoring 1				Censoring 2			
	bias ²	var	mse ^(rank)	$\overline{\text{var}}$	bias ²	var	mse ^(rank)	$\overline{\text{var}}$	bias ²	var	mse ^(rank)	$\overline{\text{var}}$
Gamma	0.018 ⁽⁺⁾	0.220	0.238 ⁽⁵⁾	0.224	0.026 ⁽⁺⁾	0.405	0.430 ⁽¹⁾	0.436	0.083 ⁽⁺⁾	0.878	0.961 ⁽¹⁾	0.851
Weibull	0.023 ⁽⁺⁾	0.222	0.246 ⁽⁶⁾	0.158	1.935 ⁽⁺⁾	0.699	2.635 ⁽⁶⁾	0.665	7.080 ⁽⁺⁾	1.880	8.960 ⁽³⁾	1.804
Log-skew-t	0.003 ⁽⁺⁾	0.218	0.222 ⁽³⁾	0.227	0.111 ⁽⁺⁾	0.481	0.592 ⁽³⁾	0.755	0.485 ⁽⁺⁾	1.573	2.058 ⁽²⁾	3.303
Log-t	1.116 ⁽⁺⁾	1.080	2.195 ⁽⁹⁾	0.623	5.088 ⁽⁺⁾	0.774	5.862 ⁽⁹⁾	0.693	36.221 ⁽⁺⁾	3.421	39.642 ⁽⁹⁾	3.439
Log-skew-n	0.225 ⁽⁻⁾	0.085	0.311 ⁽⁷⁾	0.048	2.223 ⁽⁺⁾	0.782	3.005 ⁽⁷⁾	0.621	35.282 ⁽⁺⁾	3.494	38.776 ⁽⁸⁾	3.396
Log-normal	0.385 ⁽⁻⁾	0.050	0.435 ⁽⁸⁾	0.021	4.979 ⁽⁺⁾	0.762	5.741 ⁽⁸⁾	0.683	35.185 ⁽⁺⁾	3.450	38.635 ⁽⁷⁾	3.393
AIC-selected	0.011 ⁽⁺⁾	0.219	0.231 ⁽⁴⁾	0.215	0.060 ⁽⁺⁾	0.526	0.586 ⁽²⁾	0.447	33.050 ⁽⁺⁾	4.134	37.183 ⁽⁶⁾	3.305
$\mathcal{M}_P^{(1)}$	0.008 ⁽⁺⁾	0.211	0.219 ⁽²⁾	0.225	0.108 ⁽⁺⁾	0.503	0.611 ⁽⁴⁾	0.572	29.062 ⁽⁺⁾	3.602	32.665 ⁽⁴⁾	4.339
$\mathcal{M}_P^{(2)}$	0.007 ⁽⁺⁾	0.210	0.216 ⁽¹⁾	0.240	0.105 ⁽⁺⁾	0.510	0.615 ⁽⁵⁾	0.492	29.304 ⁽⁺⁾	3.668	32.973 ⁽⁵⁾	3.632

(b)												
Censoring	No censoring				Censoring 1				Censoring 2			
	bias ²	var	mse ^(rank)	$\overline{\text{var}}$	bias ²	var	mse ^(rank)	$\overline{\text{var}}$	bias ²	var	mse ^(rank)	$\overline{\text{var}}$
Gamma	4.197 ⁽⁻⁾	0.020	4.217 ⁽⁹⁾	0.031	4.962 ⁽⁻⁾	0.017	4.978 ⁽⁹⁾	0.021	6.012 ⁽⁻⁾	0.009	6.021 ⁽⁸⁾	0.011
Weibull	3.881 ⁽⁻⁾	0.019	3.899 ⁽⁸⁾	0.022	4.305 ⁽⁻⁾	0.017	4.322 ⁽⁸⁾	0.019	4.883 ⁽⁻⁾	0.015	4.898 ⁽⁴⁾	0.016
Log-skew-t	2.091 ⁽⁻⁾	0.048	2.139 ⁽⁷⁾	0.087	3.693 ⁽⁻⁾	0.095	3.788 ⁽⁷⁾	0.144	7.127 ⁽⁻⁾	0.005	7.132 ⁽⁹⁾	0.073
Log-t	0.141 ⁽⁺⁾	0.131	0.272 ⁽¹⁾	0.133	0.160 ⁽⁺⁾	0.146	0.305 ⁽¹⁾	0.157	0.907 ⁽⁺⁾	0.226	1.133 ⁽¹⁾	0.315
Log-skew-n	1.714 ⁽⁻⁾	0.044	1.758 ⁽³⁾	0.072	2.421 ⁽⁻⁾	0.044	2.465 ⁽³⁾	0.061	0.052 ⁽⁺⁾	1.880	1.932 ⁽³⁾	0.243
Log-normal	0.182 ⁽⁺⁾	0.132	0.314 ⁽²⁾	0.131	0.222 ⁽⁺⁾	0.147	0.369 ⁽²⁾	0.155	1.110 ⁽⁺⁾	0.232	1.342 ⁽²⁾	0.317
AIC-selected	1.786 ⁽⁻⁾	0.056	1.842 ⁽⁴⁾	0.074	3.082 ⁽⁻⁾	0.147	3.229 ⁽⁴⁾	0.072	4.917 ⁽⁻⁾	0.017	4.934 ⁽⁵⁾	0.017
$\mathcal{M}_P^{(1)}$	1.840 ⁽⁻⁾	0.049	1.889 ⁽⁵⁾	0.082	3.140 ⁽⁻⁾	0.102	3.242 ⁽⁵⁾	0.110	4.910 ⁽⁻⁾	0.024	4.935 ⁽⁶⁾	0.030
$\mathcal{M}_P^{(2)}$	1.846 ⁽⁻⁾	0.049	1.895 ⁽⁶⁾	0.051	3.199 ⁽⁻⁾	0.108	3.307 ⁽⁶⁾	0.131	5.015 ⁽⁻⁾	0.020	5.035 ⁽⁷⁾	0.061

⁽¹⁾ direct method of model averaging (MA_1)

⁽²⁾ indirect method of model averaging (MA_2)

quantiles the second approach results in a smaller mean squared error. So there is no clear model averaged winner, but both perform well, mostly taking rank 3-5 across all 9 estimators.

We can conclude that for this setting the true log-normal and the log-t perform globally best. The direct and indirect model average also perform well in case of no or moderate censoring, but they collapse in the second censoring scheme in the variance estimation.

Scenario 2: generating from a gamma distribution. The results of estimating the 25% quantile (0.0106) from a sample of size 200, generated from the gamma distribution, are given in part (a) of Table 6.3. This scenario differs from the first one in several ways: another distribution, a less extreme quantile, a higher percentage censored data, and a larger sample size.

Globally, the mean squared errors are again larger in case of censored data, and there are no pronounced differences in the MSE characteristics between both methods of aver-

aging. In many cases, the bias squared term dominates the MSE, and this holds especially for censoring scheme 2. Only the true gamma model, followed by the log-skew-t and, to a lesser extent, the Weibull model are performing well across all censoring schemes.

Most individual parametric models perform very similar in case of no censoring. When introducing censoring, the gamma distribution outperforms the rest, most closely followed by the log-skew-t. The AIC-selected and averaged models perform quite well, with some loss in performance with increasing degree of censoring, especially for AIC-selected model. The table also shows varying performance of the se-estimates: in some cases more or less underestimation, in other situations some overestimation. Performance is best for the true gamma model. But overall bias seems to be the larger problem when estimating this particular quantile. Table 6.2, showing the average AIC-ranks across the simulation runs, confirms the (expected) outstanding performance of the gamma model.

For smaller quantiles (not shown here), the variance and mean squared error of the indirect approach are smaller than those of the direct approach; the estimated standard errors are smallest for the direct approach. However, the differences are small. The results for the 25% quantile in the small and large sample, are similar to the discussion above. For the largest quantile that we considered (50%), the mean squared error of the direct and indirect approach are close together, but there is no winner. The estimated standard errors are smaller for the indirect approach.

We can conclude that for this second scenario the gamma and the log-skew-t perform best, followed by the averaged models and the AIC-selected model, but following at a larger distance with increasing degree of censoring (due to inflating squared bias).

Scenario 3: generating from a mixture of log-normal distributions. Part (b) of Table 6.3 shows the results of estimating the 1% quantile (0.0269) in a sample of size 500 from the 75% mixture distribution. This scenario is again quite different: a bimodal distribution with a relatively small second bump in the right tail of the distribution, a different percentage censoring and even larger sample size, and a quantile in the extreme left tail of the distribution. In this setting all candidate models are wrong, and a related point of interest here is how, when estimating an extreme quantile in the extreme left tail, this second component to the right of the mixture model disturbs the performance of the individual models (especially of the log-normal model) as well as the performance of the model selection and the model averaging methods.

As before MSE values get larger with increasing degree of censoring, and as in the first scenario, the log-t and log-normal distribution are performing best, now closely followed by the log-skew-normal. The log-skew-normal distribution acts better than in the first scenario, as it tries to deal with the skewness (on the log scale) introduced by the second

component of the mixture model. The next group of comparably performing estimates consists of the AIC-selected model and both model averages, taking the next three positions. Only in the second censoring scheme the AIC-selected model has to leave its fourth position to the Weibull. Similar to scenario 1, the gamma, Weibull and log-skew-t take the last positions in the MSE ranking.

Compared to the log-t, log-normal and log-skew-normal, the AIC-selected, direct and indirect model averages show a more growing squared bias component as the degree of censoring increases. This indicates that AIC not only selects one of the two or three best models, but also one of the less performing models (also suffering from bias problems). And indeed, the three right columns of Table 6.2 show that surprisingly neither the log-t nor the log-normal get the lower averaged ranks, but the log-skew-normal and the log-skew-t do, and especially this latter distribution has bias problems. As a global measure of fit, AIC selects the models allowing the accommodation of the additional skewness (on log scale) introduced by the second mixture component, rather than selecting the models that perform best in the left tail of the distribution. In general the se-estimates are slightly to moderately overestimating the variability of the estimates, and both model averages perform essentially equally well.

We can conclude that there is some effect of the introduction of the second component in the log-normal mixture, but the global findings of scenario 1 hold in this case as well. Although the quantile estimates and their se-estimates in this third scenario seem to suffer less from aberrations induced by the second censoring scheme as compared to the first scenario. The explanation for this is the lower 32% censoring as compared to the 44% in the first scenario. The same LODs were used but the second component shifts probability area from the left tail to the right tail of the distribution.

Across all scenarios. Figure 6.2 summarizes the performance of all 9 different quantile estimators (6 parametric models, the AIC-selected model and 2 model averages) across all 60 settings (5 distributions: log-normal, gamma, three mixtures; 3 sample sizes; 4 quantiles). The performance of each estimator for a particular setting is summarized by its MSE rank for that setting: the smaller the MSE value, the lower the rank and the darker the bar in the bar chart in Figure 6.2. The upper and lower bar chart fully at the left show the result for the uncensored data, the middle panels for censoring scheme 1 and the two right panels for censoring scheme 2. Although these bar charts obviously only summarize the global performance across the particular settings included in the simulation study, they shed some light on the performance of a particular estimator at a higher, more global level.

The estimators based on the log-normal and gamma distribution take the extreme

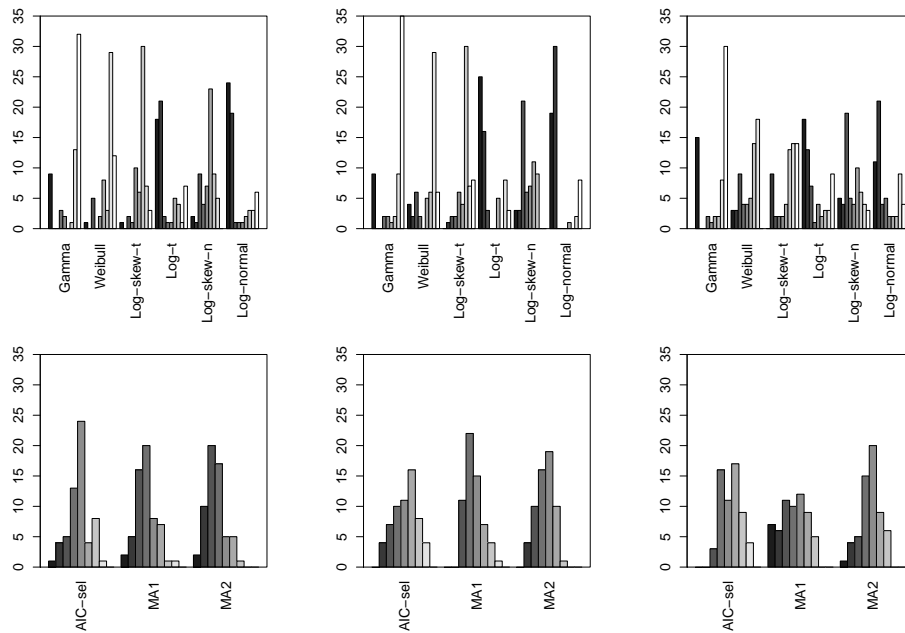


Figure 6.2: Simulation study. Bar chart of the MSE rank (black=rank 1; white=rank 9): bar height represents the number of settings that selected a model with the given rank. Left panels: no censoring; middle panels: censoring 1; right panels: censoring 2.

lowest and highest rank positions more often than any other estimator, which is not surprising as they perform best in case the data are generated according to the log-normal and gamma distribution. The log-normal and log-t are performing best in terms of having highest frequencies for the best ranks 1 and 2. But they do appear to be also the worst performing estimator for the setting where data are generated from a gamma distribution.

The AIC-selected model and the model averages $\mathcal{M}^{(1)}$ and $\mathcal{M}^{(2)}$ have rarely the highest or lowest MSE, but often a position at the better side in the middle, indicating that they are not often performing as best and mostly not as worst estimator but quite often as good performing estimators. So, in case one has no prior knowledge about the true distribution, the AIC-selected model and the model averaged estimators are certainly a worthwhile option. When the degree of censoring increases, comparing the panels from left to right, the rank distribution flattens out, especially for the direct averaging method. Comparing the AIC-selected model, and the direct and indirect method of model averaging, there is no clear winner.

6.3 Extensions

In the next section we will apply both approaches of model averaging to the Cadmium and $^{134}\text{Cesium}$ data. Before we show the results, we discuss some interesting extensions. A first extension is the use of the family \mathcal{M}_S of semiNP models, which we illustrate on the Cadmium data. Limiting yourself to the set of typical parametric models, and selecting your final model from that set or averaging over those models, will still end in a poor estimate in case all parametric candidate models fit poorly. It is therefore important to include a good approximating model in the set of candidate models. This could be assured through knowledge about the setting. Another way is to make the family of candidate models rich enough. One way to do this is to include the best member or the whole nested series of \mathcal{M}_S as part of the family of candidate models.

The second extension is the inclusion of covariates, more precisely a time effect. Finally we propose a method to account for the uncertainty about the true LOD-values. The last two extensions are illustrated on the $^{134}\text{Cesium}$ data. These extensions were not included in the simulation study as we encountered too many computational problems (non-convergence related to the choice of starting values, the large number of parameters and the existence of local maxima).

6.3.1 Covariates

In practice the natural parameters are expressed as a function of the logarithmic mean and variance and as such plugged into the likelihood function. To our knowledge there is no closed form expression of the logarithmic mean and variance of the log-skew-t distribution. We assume that the logarithmic mean includes the parameter μ in a linear way as it holds for the log-skew-normal distribution.

Models can be extended to incorporate the effect of covariates. Typically the mean of the distribution is modelled as a (linear) function of the covariate, e.g. $\mu = \beta_0 + \beta_1 t$. These parameters can be plugged into the density and distribution function to obtain an extended likelihood:

$$L(\beta_0, \beta_1, \theta | y, \delta) = \prod_{i=1}^n \{ f(y_i; \mu = \beta_0 + \beta_1 t)^{1-\delta_{L_i}} [F(y_i; \mu = \beta_0 + \beta_1 t)]^{\delta_{L_i}} \}, \quad (6.7)$$

where θ represents all final parameters to be estimated (with parameter μ replaced by β_0 and β_1). As consequence of including time-dependent parameters, the quantile of interest $\xi_p(t)$ and its estimators now also depend on the covariate t .

In the $^{134}\text{Cesium}$ data we are interested in the effect of time on the estimation of the quantiles of the distribution of $^{134}\text{Cesium}$ concentrations. We will model the logarithmic

Table 6.4: Overview of distributions and the corresponding logarithmic mean and variance.

Distribution	$E(\log Y)$	$\text{Var}(\log Y)$	Remarks
Gamma (shape k , scale a)	$\Psi(k) + \log(a)$	$\Psi'(k)$	Ψ is digamma function
Weibull (shape b , scale a)	$(b \log a - \gamma)/b$	$\pi^2/(6b^2)$	γ is Euler's constant
Log-skew-t	/	/	
Log-t (df n)	μ (if $n > 1$)	$\sigma^2 n/(n-2)$ (if $n > 2$)	
Log-skew-n (skewness α)	$\mu + \sigma \delta \sqrt{2/\pi}$	$\sigma^2(1 - 2\delta^2/\pi)$	$\delta = \alpha/\sqrt{1 + \alpha^2}$
Log-normal	μ	σ^2	

mean $E(\log Y)$ as a function of time. Table 6.4 provides an overview of the parametric models with the corresponding logarithmic mean and variance.

6.3.2 Measurement error on limit of detection

Reconsider the likelihood expression (3.6) assuming the LOD values to be known (in our case all equal to 10). Similar to random effects models, we now consider this likelihood as the likelihood, given the LOD value. Next, we assign a distribution $f_U(u; LOD_i)$ to the “random” LOD, with mean LOD_i , and maximize the marginal likelihood

$$L(\theta|y, \delta) = \prod_{i=1}^n \left\{ f(y_i; \theta)^{1-\delta_{L_i}} \left[\int F(u; \theta) f_U(u; LOD_i) du \right]^{\delta_{L_i}} \right\}, \quad (6.8)$$

where, as before, δ_{L_i} is equal to 1 for a left-censored observation and 0 otherwise, and f and F are the density and distribution function of the data, respectively. This likelihood can be extended in the same way as in (6.7) to include covariate effects.

Note that $G(LOD_i; \theta) = \int F(u; \theta) f_U(u; LOD_i) du$ is again a cumulative distribution function (under some mild regularity conditions). The likelihood expression (6.8) equals expression (3.6) with CDF $F(LOD_i; \theta)$ replaced by CDF $G(LOD_i; \theta)$.

6.4 Application to data examples

The Cadmium and ¹³⁴Cesium data are used to illustrate both approaches of model averaging. For the Cadmium data, we compare estimates based on the parametric models to estimates based on models from the SemiNP family of distributions. Three families of candidate models are used for the model averages. For the ¹³⁴Cesium data we have information on the time of measurement and we consider this as a covariate. Further, the limit of detection is unknown and we deal with the uncertainty.

Table 6.5: Cadmium data 1. For each parametric and semiNP model, according to different families: AIC, weights, and quantile estimates (standard error estimates). The first line shows the empirical estimates. (Estimate and standard error $\times 10^{-2}$)

Distribution	AIC	$w(\mathcal{M}_P)$	$w(\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\})$	$w(\mathcal{M}_P \cup \mathcal{M}_S)$	$\hat{\xi}_{0.05}$	$\hat{\xi}_{0.25}$
					0.145	0.500
Gamma	-47.24	0.000	0.000	0.000	0.000(0.000)	0.031(0.038)
Weibull	-65.74	0.026	0.002	0.001	0.002(0.002)	0.113(0.051)
Log-skew-t	-72.85	0.912	0.059	0.023	0.000(0.000)	0.063(0.076)
Log-t	-62.62	0.005	0.000	0.000	0.028(0.014)	0.217(0.070)
Log-skew-n	-66.64	0.041	0.003	0.001	0.006(0.006)	0.144(0.073)
Log-normal	-64.73	0.016	0.001	0.000	0.028(0.014)	0.213(0.069)
$\mathcal{M}_P^{(1)}$					0.001(0.002)	0.071(0.079)
$\mathcal{M}_P^{(2)}$					0.000(0.003)	0.072(0.081)
SemiNP1	-65.78			0.001	0.034(0.008)	0.113(0.024)
SemiNP2	-69.48			0.004	0.022(0.013)	0.098(0.045)
SemiNP3	-78.38		0.936	0.374	0.024(0.013)	0.106(0.045)
SemiNP4	-77.95			0.302	0.032(0.013)	0.120(0.043)
SemiNP5	-76.64			0.156	0.043(0.018)	0.133(0.042)
SemiNP6	-75.56			0.091	0.059(0.021)	0.153(0.041)
SemiNP7	-74.22			0.047	0.056(0.020)	0.150(0.041)
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}^{(1)}$					0.023(0.013)	0.104(0.048)
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}^{(2)}$					0.021(0.014)	0.105(0.046)
$\mathcal{M}_P \cup \mathcal{M}_S^{(1)}$					0.033(0.018)	0.120(0.047)
$\mathcal{M}_P \cup \mathcal{M}_S^{(2)}$					0.030(0.018)	0.123(0.047)

⁽¹⁾ direct method of model averaging (MA₁)

⁽²⁾ indirect method of model averaging (MA₂)

6.4.1 Cadmium data

The parametric and semiNP models were fit to the Cadmium data. The estimated distribution functions are shown in Figure 6.3, showing that the (log-)normal distribution is a reasonable fit, but other distributions fit better. Especially the log-skew-t and the SemiNP distribution describe the data quite well, as indicated by AIC in Table 6.5. The model averaging weights are computed as in (6.3) and are also listed in Table 6.5. The best parametric fit is convincingly the log-skew-t distribution and consequently it has a major impact on the model average over the family \mathcal{M} . The estimates for the 5% and 25% quantiles are shown in Table 6.5. The naive estimates (substituting the censored values by LOD/2) are shown on the first line. The results for other quantiles (e.g. 1% and 50%) are similar and are available in Appendix B.

As already shown in the simulations under different scenarios, the direct and indirect estimates are similar for the family \mathcal{M} of candidate models. Both approaches are illus-

trated in Figure 6.4 for the 25% quantile. On the one hand the quantiles of the individual distributions are projected on the horizontal axis, and the model average is represented by the cross (direct approach). On the other hand the model averaged distribution is shown (squares) together with its quantile (indirect approach).

Within the family of semi-nonparametric models, the SemiNP3 model (extending the log-normal with three additional parameters) is the best model based on AIC and therefore $\hat{r} = 3$ and $\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\} = \mathcal{M}_P \cup \{\hat{f}_3\}$, i.e. extending the family of parametric models with the SemiNP3 model. Moreover AIC of the parametric models is larger, resulting in a high weight for the SemiNP3 model and a higher estimate for the quantiles. When turning to the family $\mathcal{M}_P \cup \mathcal{M}_S$, the SemiNP3 and SemiNP4 model take over the leading role and result in considerably higher estimates for both quantiles. The model averaged estimates combining the parametric and the SemiNP estimates are mainly determined by the higher weights given to the SemiNP3, SemiNP4 and even SemiNP5 model.

In this particular application the SemiNP models seem to outperform the parametric models. This is also confirmed graphically by comparing all models with the fully non-parametric Kaplan-Meier estimate, at least for concentrations larger than the smallest LOD. Indeed the SemiNP models in the right panels of Figure 6.3 seem to follow the Kaplan-Meier estimate much closer. The Kaplan-Meier estimate however has a major disadvantage, as it is undefined below the smallest LOD and therefore does not allow to estimate small quantiles below this point.

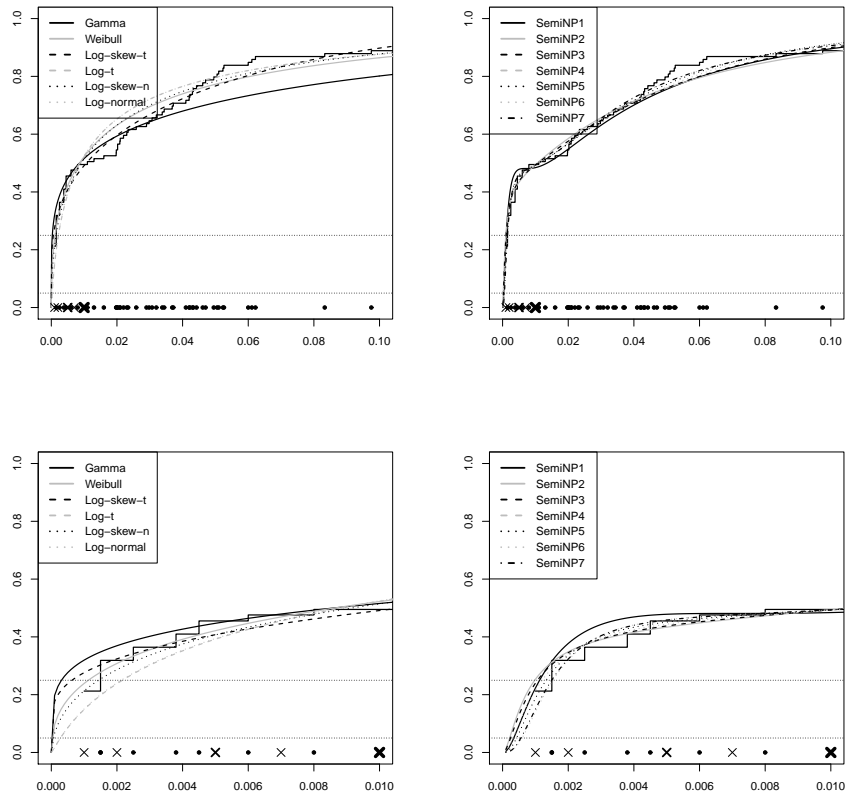


Figure 6.3: Cadmium data 1. Cumulative distribution function of the concentrations. Parametric fitted distributions (left) and SemiNP fitted distributions (right). The censored data are represented by crosses, where the thickness represents the number of censored data. The dots represent the uncensored data. The thin black line represents the Kaplan-Meier estimate. The fit of the log-normal and log-t distribution cannot be distinguished. The lower panels zoom in on the left tail (up to the largest observed LOD) of the corresponding upper panels.

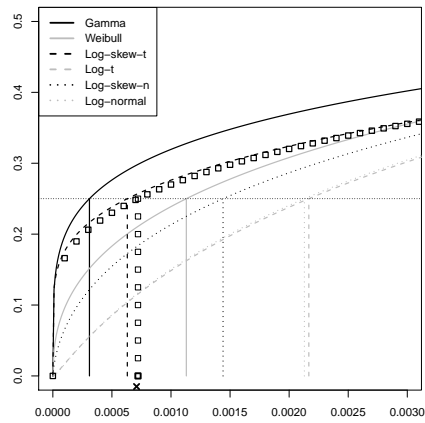


Figure 6.4: Cadmium data 1. Illustration of direct and indirect approach, based on the cumulative distribution functions. The squares represent the model averaged distribution function. The vertical lines indicate the location of the model-specific 25% quantile estimates $\hat{\xi}_{0.25,i}$ and the indirect estimate $\hat{\xi}_{0.25,MA_2}$ (vertical line of squares). The cross on the horizontal line represents the model averaged quantile $\hat{\xi}_{0.25,MA_1}$ from the direct approach.

Table 6.6: Cesium data: AIC and model averaging weights. A constant value 10 is assumed for the LODs.

Distribution	$\hat{\beta}_0(s.e.)$	$\hat{\beta}_1(s.e.)$	AIC	weight
Gamma	0.4180(0.7680)	-0.0128(0.0023)	363.5246	0.0000
Weibull	1.2859(0.3950)	-0.0155(0.0032)	343.4477	0.0000
Log-skew-t		-0.0127(0.0023)	308.2874	0.4975
Log-t	2.1817(0.1256)	-0.0120(0.0020)	308.3320	0.4865
Log-skew-n	2.4391(0.2115)	-0.0142(0.0029)	315.1819	0.0158
Log-normal	2.1675(0.2458)	-0.0142(0.0030)	324.7135	0.0001

6.4.2 Cesium data

As mentioned in Section 2.1.2, an extra difficulty occurs for the Cesium data, because the LODs are not exactly known. They are only known to vary about an average value of 10. We handle this problem in two different manners. The first is by replacing the unknown LODs by the average value 10, the second is by assuming a distribution for the LOD. We will assume here that the LODs are normally distributed with mean 10 and variance 2 as well as a triangular distribution centered around 10, with base from 0 to 20 (as a sensitivity analysis about the unknown distribution of LODs). In case more precise information is available, e.g. about the laboratory techniques and corresponding LODs, this could be incorporated in the distribution.

In what follows we limit ourselves to the parametric models. Extending the SemiNP models with both extensions was not feasible within the scope of this study.

6.4.2.1 Assuming the LOD to be known and equal to 10

Table 6.6 shows some goodness-of-fit statistics (AIC) for every parametric model and the corresponding weights for model averaging. Based on AIC, the log-t and log-skew-t distribution provide the best fit. Therefore the weights of these distributions are highest.

Figure 6.5 shows the parametrically estimated 5% and 25% quantiles as a function of time t . The fitted quantile function of the Weibull and gamma distribution is quite different from the other quantiles of the other distributions. The AIC of these distributions is relatively high and therefore they do not contribute to the model averaged quantile. The model averaged quantiles are in between the log-t and log-skew-t distribution, as expected, since these distributions receive almost all the weight. We can hardly observe a difference between the direct and indirect method.

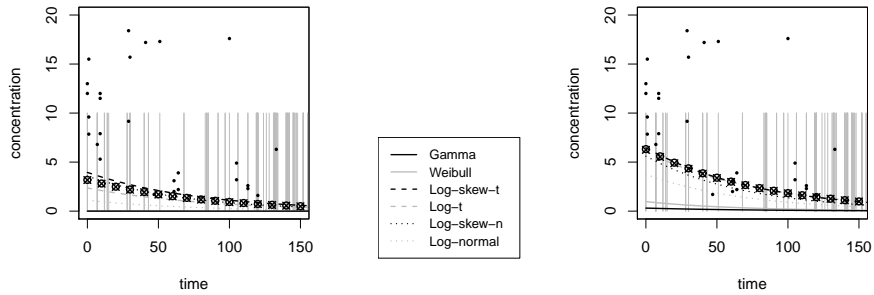


Figure 6.5: Cesium data. Quantiles (left: 5% - right: 25%) based on parametric estimates. The model averaged quantiles are represented by bold squares (direct method) and crosses (indirect method). A constant value 10 is assumed for the LODs.

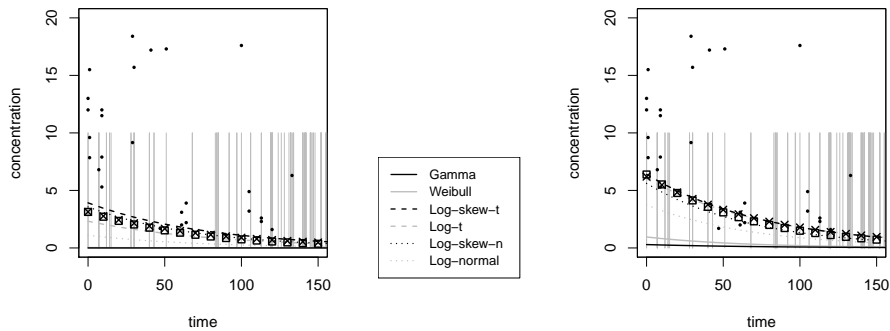


Figure 6.6: Cesium data. Quantiles (left: 5% - right: 25%) based on parametric estimates. The model averaged quantiles are represented by bold squares (direct method) and crosses (indirect method). A normal distribution (mean 10, variance 2) is assumed for the LODs.

6.4.2.2 Using an uncertainty distribution for the LOD, centered at 10

Normal distribution for LOD. Next, we assume that the LODs are not exactly equal to 10, but have a value close to 10. Therefore we assume a normal distribution with mean 10 and variance 2 (right panel of Figure 2.3). 99% of the LODs are then in the interval $[6.36, 13.64]$ and for computational ease we limit the region over which we integrate to $[0, 20]$. The results as shown in part (a) of Table 6.7 and Figure 6.6 are close to those with fixed $\text{LOD}=10$. This result indicates that the choice of an LOD equal to 10 would be sufficient.

Triangular distribution for LOD. Finally we assume a triangular distribution with center 10 and base $[0, 20]$. Now the results in part (b) of Table 6.7 differ a bit more from

Table 6.7: Cesium data: AIC and model averaging weights. (a) A normal distribution (mean 10, variance 2) and (b) a triangular distribution is assumed for the LODs.

(a)				
Distribution	$\hat{\beta}_0(s.e.)$	$\hat{\beta}_1(s.e.)$	AIC	weight
Gamma	0.3791(0.7815)	-0.0129(0.0023)	364.1902	0.0000
Weibull	1.2761(0.3975)	-0.0156(0.0033)	343.9874	0.0000
Log-skew-t		-0.0127(0.0022)	309.3092	0.4971
Log-t	2.1809(0.1291)	-0.0121(0.0021)	309.3565	0.4854
Log-skew-n	2.4405(0.2112)	-0.0144(0.0029)	316.0206	0.0173
Log-normal	2.1659(0.2471)	-0.0144(0.0030)	325.4342	0.0002

(b)				
Distribution	$\hat{\beta}_0(s.e.)$	$\hat{\beta}_1(s.e.)$	AIC	weight
Gamma	-0.0340(0.9027)	-0.0140(0.0024)	370.7506	0.0000
Weibull	1.2034(0.4259)	-0.0175(0.0035)	349.5870	0.0000
Log-skew-t		-0.0149(0.0027)	319.3412	0.4582
Log-t	2.2235(0.1410)	-0.0140(0.0021)	319.1392	0.5069
Log-skew-n	2.5143(0.2269)	-0.0167(0.0031)	324.5242	0.0343
Log-normal	2.1826(0.2716)	-0.0168(0.0032)	332.9782	0.0005

those in Table 6.6 and the log-t takes over from the log-skew-t as the best model, with a slightly higher slope. The final fits (Figure 6.7) are however close again. This shows that the sensitivity to the choice of the distribution for the LOD is negligible in this setting.

6.5 Conclusion

In this chapter we studied the estimation of quantiles of distributions as they appear for concentration data in chemical risk assessment. This estimation is complicated by the presence of left-censored data. Also the model selection and model averaging is hampered by this form of incomplete data.

Next to the performance of the quantile estimators based on the individual candidate models and on the AIC-selected model, two different model averaged quantile estimators are defined and compared: averaging the quantile estimators, each derived from the estimated distributions (direct method) and vice versa, inverting the averaged estimator of the distribution function to derive the quantile estimator (indirect method).

Main conclusions. The main conclusions from the obtained insights are i) the true model or a good approximating model performs best; ii) AIC-selected model or averaged models are in general not performing best, but do achieve acceptable performance char-

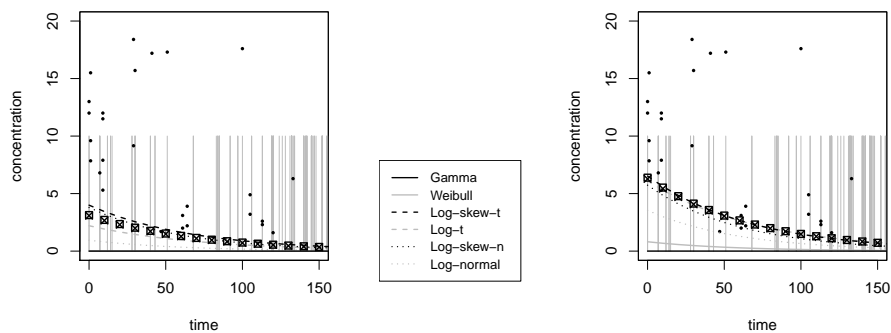


Figure 6.7: Cesium data. Quantiles (left: 5% - right: 25%) based on parametric estimates. The model averaged quantiles are represented by bold squares (direct method) and crosses (indirect method). A triangular distribution is assumed for the LODs.

acteristics in case one has no prior knowledge of the true distribution (as in most cases); iii) there is no favorite method of averaging; in some cases the direct method performs somewhat better, and reversed in other cases, without a clear pattern; iv) only the true or closely approximating model can deal with extremely high percentages of censoring (40% or more) and model selected or model averaged estimates might turn into highly variable estimates and their se-estimates might inflate dramatically; v) the family of candidate models, the model selection and model averaging can be extended with the SemiNP family of models, as illustrated in the Cadmium data; and can be extended with covariates and measurement error on the LODs as illustrated in the $^{134}\text{Cesium}$ data; vi) Including the SemiNP family of models is an appealing option to ensure that the family of candidate models is rich enough. It needs however some careful selection of starting values (due to the large number of parameters and the existence of local maxima); vii) when estimating local characteristics such as quantiles in the left tail, model selection and model averaging based on global measures of fit are sensitive to deviations located at the right tail of the distribution.

Global and local measures. Regarding point vii) of the main conclusions, the use of a focused information criterion (see e.g. Claeskens and Hjort, 2008) for model selection and model averaging in this particular setting and for quantile regression (Behl et al., 2014) is a promising avenue of further research. Determining the maximum percentage of censoring or the minimum sample size to estimate extreme percentiles of the distribution might be another goal of future research. It depends on several factors including the particular distribution of the LOD values and of course on the true underlying distribution of the data.

Bayesian approach. Bayesian model averaging (see e.g. Hoeting et al., 1999) offers

an attractive alternative computational and inferential paradigm for estimating quantiles in the presence of censoring. It has been successfully applied in other fields such as in dose-response modelling (see e.g. Morales and Ryan, 2006). A Bayesian implementation of model averaging might also circumvent some of the computational problems as we encountered with the SemiNP models.

Several software packages such as the R package BMS (<http://bms.zeugner.eu>) and BMA (<http://www.research.att.com/volinsky/bma.html>) exist to perform Bayesian model averaging. A study comparing the direct and indirect method of model averaging for the estimation of quantiles based on censored data from a Bayesian point of view would be very welcome in the field of chemical risk assessment. Such a study and comparison with the frequentist approach is beyond the scope of this work but is an interesting avenue for further research.

Chapter 7

Generalized profiling

Statistical parametric models describing changes over time (or other dimensions) as defined by differential equations occur in several fields of applied statistics. For such models, Ramsay et al. (2007) introduced a generalized smoothing estimation approach that is robust to model misspecification. As illustrated by two examples from bacterial growth and infectious disease transmission, a monotonicity constraint can appear as a very natural limitation of any candidate model, or one might want to test for monotonicity in order to check the validity of the assumed model. In this chapter we extend the generalized profiling approach with an additional penalty term in order to guarantee a monotone solution. As an alternative to the forward prediction error and cross-validation for selecting a data-driven smoothing parameter, the method of one-sided cross-validation of Hart and Yi (1998) is proposed and shown to be useful in this setting. Finally bootstrap pointwise and simultaneous confidence intervals, a bootstrap omnibus lack-of-fit test of the proposed parametric model and a bootstrap test for monotonicity are introduced and applied to both examples.

The material in this chapter is proposed in Nysen et al. (2016a).

7.1 Differential equation models for the *Y. enterocolitica* and Parvovirus B19 data

This section briefly describes differential equation models for the two data examples.

7.1.1 The *Y. enterocolitica* data

The first example concerns the concentration of a species of gram-negative coccobacillus-shaped bacterium *Yersinia enterocolitica* (see Section 2.3).

The microbial growth process is typically described by three or four phases. The first phase is called the *lag* phase, because the growth of the cells will only start after a certain lag time. During the *exponential* phase the cells will grow. Finally the growth is inhibited and a *stationary* phase is attained. The fourth phase is the *death* phase, where the cells die, but this phase is often omitted. A popular growth model reflecting the three first phases has been introduced by Baranyi and Roberts (1994). Denoting $\mu(t)$ the mean of the log of the cell concentration of a bacterial batch culture, the Baranyi and Roberts' BR-model is defined by the differential equation

$$\frac{d\mu(t)}{dt} = \kappa\alpha(t)u(\mu(t)), \quad (7.1)$$

with the initial value $\mu(0) = \mu_0$, with the "inhibition" function (ensuring the transition of the growth curve to the stationary phase)

$$u(\mu(t)) = \left(1 - e^{(\mu(t) - \mu_{\max})}\right),$$

and with the "adjustment" function (describing the adjustment of the culture to the new environment)

$$\alpha(t) = \frac{1}{1 + e^{-Q(t)}},$$

where $Q(t) = \ln q(t)$, $q(t)$ characterizing the physiological state of the cells, satisfying

$$\frac{dQ(t)}{dt} = \kappa, \quad (7.2)$$

with initial condition $Q(0) = \log q_0$. The BR-model extends pure exponential (Malthus) growth with $\alpha(t) \equiv 1$, $u(y(t)) \equiv 1$ and logistic growth (Verhulst, 1838; Pearl and Reed, 1920) with $\alpha(t) \equiv 1$.

The set of differential equations (7.1) and (7.2) can be solved analytically with solution given by

$$\mu(t) = \mu_{\max} - \ln \left(1 + \frac{1}{C(1 + q(t))}\right), \quad (7.3)$$

with $q(t) = q_0 e^{\kappa t}$ and

$$C = \frac{e^{\mu_0}}{(e^{\mu_{\max}} - e^{\mu_0})(1 + q_0)}.$$

See e.g. López et al. (2004) for an evaluation of the BR- and other mathematical models for microbial growth. The above mathematical model does however not reflect any random variation in the observed concentrations but it rather describes how the mean log concentrations depend on time. Denote z_j , for $j = 1, \dots, n$, the j -th observed concentration at time t_j and assume z_j has a log-normal distribution with geometric mean $\mu(t_j) = E(z_j|t_j)$ depending on t_j in a non-linear way as described by the BR-model of differential equations (7.1) and (7.2) and with a constant geometric variance $\sigma^2 = \text{Var}(z_j|t_j)$. So, the parameters of the log-normal distribution (typically defined on log-scale) are $\ln(\mu(t_j))$ and $\ln(\sigma^2)$. The use of geometric mean and variance are very common in the field of microbial risk assessment.

Using the data $(t_j, y_j = \ln(z_j))$ ordinary least squares (OLS) provides parameter estimates $\widehat{\log(\mu_{\max})} = 16.45$, $\widehat{\kappa} = 0.08$, $\widehat{\log(\mu_0)} = 4.30$, $\widehat{\log(q_0)} = -24.11$ and $\widehat{\sigma} = 1.01$ for the BR-model, resulting in the fitted curve shown by the dotted line in Figure 2.4.

The fitted curve seems to describe the growth pattern in the data fairly well. But one could consider a more flexible, semiparametric alternative such as an approach based on penalized splines. A more data-driven approach is however likely to follow the decreasing trend of the first five measurements and hence violating the natural assumption of monotonicity for growth curves. The method proposed here allows to consider more flexible models but penalized i) in the “direction” of the parametric BR-model and ii) to be monotone. A bootstrap approach provides confidence intervals and hypothesis tests for lack of fit and for monotonicity.

7.1.2 The Parvovirus B19 data

The second example concerns the Parvovirus B19 data (see Section 2.4).

The SIR transmission model consists of three compartments: susceptible (S), infected (I) and recovered (R) and the flow in and out each of the three compartments can be described by a system of three differential equations in age and time. Under endemic equilibrium (steady state), there is no time dependence. Assuming that the disease is irreversible, meaning that immunity is lifelong and that mortality caused by infection is negligible, and turning to the so-called prevalence, the fraction of non-susceptible individuals (infected or immune) $\pi(a)$, the system simplifies to one single differential equation

$$\frac{d\pi(a)}{da} = \lambda(a)(1 - \pi(a)), \quad (7.4)$$

with $\lambda(a)$ the so-called force of infection (FOI, see e.g. Hens et al., 2012). Having an estimator for the age-dependent prevalence $\pi(a)$, equation (7.4) can be easily applied to get an estimate for the FOI $\lambda(a)$. It is also important to mention that the prevalence $\pi(a)$

is non-decreasing as a function of the age a and that the estimator should be as well. Indeed the seroprevalence $\pi(a)$ reflects the probability to have been infected somewhere in past at the time of the test, for an individual of age a , and hence can only increase with age. Although not exactly equal, the prevalence $\pi(a)$ is commonly replaced by the so-called 'seroprevalence', i.e., the proportion of subjects of age a who test positive on a serological test, as the data we have at hand (Bollaerts et al., 2012).

The solution of (7.4) for a constant force of infection $\lambda(a) \equiv \lambda$ is given by

$$\pi(a) = 1 - Ce^{-\lambda a}, \quad (7.5)$$

and C the initial probability to be susceptible. Given an SIR model, the constant C equals 1. A constant FOI does not hold for most infections including Parvovirus B19. A flexible parametric age-dependent model for the force of infection was proposed by Farrington (1990)

$$\lambda(a) = (\alpha a - \gamma)e^{-\beta a} + \gamma. \quad (7.6)$$

Farrington's model assumes that the force of infection increases to a peak in a linear fashion followed by an exponential decrease. The parameter γ is called the long term residual value of the force of infection, as a tends to ∞ , $\lambda(a)$ tends to γ . In order to ensure that the monotonicity of $\pi(a)$ or equivalently that the force of infection satisfies $\lambda(a) \geq 0$, Farrington (1990) constrained the parameter space to be nonnegative.

The solution is given by

$$\pi(a) = 1 - C^* \exp\left(e^{-\beta a} \left(\frac{\alpha}{\beta} a + \frac{\alpha}{\beta^2} - \frac{\gamma}{\beta}\right) - \gamma a\right).$$

with C^* related to the initial probability $1 - \pi_0 = 1 - \pi(0)$ to be susceptible at birth.

In Section 7.2.1 we will use a (weighted) least-squares approach to find a solution for the differential equations. Therefore we transform the observed proportions p_j for j -th age group a_j by the arcsin transformation (given by $y_j = \text{asin}\sqrt{p_j}$), leading to approximately normal observations with mean $\text{asin}\sqrt{\pi_j}$ and variance $1/4n_j$ (Johnson and Kotz, 1969), where n_j is the number of individuals in the j -th age group. It has also been recommended (Bartlett, 1947) to replace a proportion of 0 by $1/4n_j$ and a proportion of 1 by $1 - 1/4n_j$. In the sample of $n = 66$ age groups that we consider, none of the proportions was equal to 0 or 1.

Using the age-grouped data $(a_j, y_j = \text{asin}\sqrt{p_j})$, weighted least squares (WLS) was used to estimate the approximate mean $\text{asin}\sqrt{\pi(a_j)}$ with $\pi(a)$ the parametric non-linear model of Farrington and with weights $w_j = n_j$, leading to estimates $\hat{\alpha} = 0.065$, $\hat{\beta} = 0.219$, $\hat{\gamma} = 0.005$, $\hat{\pi}_0 = 0.031$. The fitted curve is shown by the dotted line in Figure 2.5.

Non-negative values were obtained for the parameters α , β and γ by the reparameterisation $\alpha = \exp(\alpha_h)$, $\beta = \exp(\beta_h)$ and $\gamma = \exp(\gamma_h)$.

Two important observations from the data and the fitted model as shown in Figure 2.5. Farrington's model is not able to fit the data well at ages around 30. The observed proportions of seropositive around the age of 30 seem to deviate unexpectedly from the natural monotone trend of a growing probability to have been ever infected when getting older. This might indicate that an assumption might be violated, such as the steady state assumption or life-long immunity or another assumption of the SIR model. A formal test for monotonicity can provide scientific evidence that assumptions need to be reconsidered or the model has to be modified or extended.

7.2 Generalized profiling with monotonicity constraints

A first section describes briefly the generalized estimation procedure, as introduced in Ramsay et al. (2007) and using largely their notation. Next we extend the estimation procedure to include shape restrictions, with focus on monotonicity constraints.

7.2.1 Generalized profiling

Following the notation of Ramsay et al. (2007), \mathbf{x} is a d -dimensional vector, depending on a variable t . A system of d non-linear differential equations is defined as

$$\dot{\mathbf{x}}(t) = \frac{d\mathbf{x}}{dt} = \mathbf{f}(\mathbf{x}, t|\boldsymbol{\theta}), \quad t \in [0, T], \quad (7.7)$$

with parameter $\boldsymbol{\theta}$. Initial or boundary values $\mathbf{x}_0 = \mathbf{x}(0)$ may be considered as parameters that must be included in the (augmented) parameter vector $\boldsymbol{\theta}$. For the *Y. enterocolitica* example, $d = 2$, $\mathbf{x}(t) = (\mu(t), Q(t))'$, \mathbf{f} is defined by (7.1) and (7.2), and $\boldsymbol{\theta} = (\mu_{\max}, \kappa, \mu_0, Q_0)'$. For the Parvovirus B19 example, $d = 1$, $t = a$, $x(a) = a \sin \sqrt{\pi(a)}$, f is defined by (7.4), and $\boldsymbol{\theta} = (\alpha, \beta, \gamma, \pi_0)'$.

Following the collocation method, each component x_i ($i = 1, \dots, d$) of \mathbf{x} is approximated in terms of a basis function expansion \tilde{x}_i

$$\tilde{x}_i(t) = \sum_{k=1}^{K_i} c_{ik} \phi_{ik}(t) = \mathbf{c}'_i \boldsymbol{\phi}_i(t), \quad i = 1, \dots, d, \quad (7.8)$$

or in short, $\tilde{\mathbf{x}} = \boldsymbol{\Phi} \mathbf{c}$, where the number K_i of basis functions in vector $\boldsymbol{\phi}_i$ is chosen to ensure enough flexibility to capture the variation in the approximated function x_i and its derivatives. A spline basis is a typical and popular choice. For the *Y. enterocolitica* example, $K_1 = K_2 = 91$ (from 0 to 900 in steps of 10), and in the Parvovirus B19 example $K = 66$ (from 0 to 65 in steps of 1).

Using a sample $(\mathbf{t}_j, \mathbf{y}_j), j = 1, \dots, n$, with $\mathbf{t}_j = (t_{1j}, \dots, t_{ij}, \dots, t_{dj})'$ and corresponding (independent) observations $\mathbf{y}_j = (y_{1j}, \dots, y_{ij}, \dots, y_{dj})'$ with mean $E(\mathbf{y}_j | \mathbf{t}_j) = \mathbf{x}(\mathbf{t}_j)$ and variance $\boldsymbol{\sigma}^2 = (\sigma_1^2, \dots, \sigma_i^2, \dots, \sigma_d^2)'$, the (weighted) least squares estimation procedure to estimate the unknown parameter $\boldsymbol{\theta}$ of the model \mathbf{x} satisfying (7.7) and the coefficients \mathbf{c} of the corresponding basis function approximation $\tilde{\mathbf{x}}$ consists of two steps: i) estimation of the coefficients \mathbf{c} for a given value of $\boldsymbol{\theta}$ and a particular value of the smoothing parameter $\boldsymbol{\lambda}$ (inner loop), and ii) estimating $\boldsymbol{\theta}$ (outer loop).

Estimating $\hat{\mathbf{c}}(\boldsymbol{\theta}, \boldsymbol{\lambda})$ (inner optimization) In the first step, the parameters \mathbf{c} are updated by minimizing the weighted least squares criterion

$$J(\mathbf{c} | \boldsymbol{\theta}, \boldsymbol{\lambda}) = \sum_{i \in \mathcal{D}^o} \sum_{j=1}^n w_{ij} (y_{ij} - \tilde{x}_i(t_{ij}))^2 + \text{PEN}(\tilde{\mathbf{x}} | \boldsymbol{\lambda}), \quad (7.9)$$

with weights w_{ij} to deal with e.g. heteroscedasticity and/or post-stratification, \mathcal{D}^o the subset of *observed* variables (those i for which data y_{ij} are available), and penalty PEN representing the extent to which an actual function \tilde{x}_i satisfies the ODE system. Note that for simplicity formula (7.9) assumes that the sample size n is the same for each $i \in \mathcal{D}^o$. In the first Y. enterocolitica example, $w_{ij} \equiv 1$ and $\mathcal{D}^o = \{1\}$ as only data are available on the first equation for $\mu(t)$ and not on the second for $Q(t)$. Also in the second Parvovirus B19 example $\mathcal{D}^o = \{1\}$ as $d = 1$. Here age-specific weights $w_{1j} = n_j$ reflect different sample sizes and hence different variances for the observed proportions per age group a_j .

Re-expressing equation (7.7) as the differential operator equation

$$L_{i,\boldsymbol{\theta}}(x_i) = \dot{x}_i - f_i(\mathbf{x}, t | \boldsymbol{\theta}) = 0,$$

the extent to which the approximation $\tilde{\mathbf{x}}$ satisfies the system of differential equations, can be measured by

$$\text{PEN}_i(\tilde{\mathbf{x}}) = \int L_{i,\boldsymbol{\theta}}(\tilde{x}_i(t))^2 dt,$$

resulting in a total penalization measure as given by

$$\text{PEN}(\tilde{\mathbf{x}} | \boldsymbol{\lambda}) = \sum_{i=1}^d \lambda_i \text{PEN}_i(\tilde{\mathbf{x}}),$$

where the smoothing parameter $\boldsymbol{\lambda} = (\lambda_1, \dots, \lambda_d)$ controls the size of the extent that $\tilde{\mathbf{x}}$ fails to satisfy the differential equation exactly. In most cases the integral in the penalization measure $\text{PEN}_i(\tilde{\mathbf{x}})$ will be approximated numerically (see Ramsay et al., 2007).

Estimating $\theta(\lambda)$ (outer optimization) In the second step $\hat{\theta}$ is updated by optimizing $H(\theta|\lambda)$ with respect to θ alone, with

$$H(\theta|\lambda) = \sum_{i \in D^o} \sum_{j=1}^n w_{ij} (y_{ij} - \tilde{x}_i(t_{ij}))^2.$$

The “smoothing” penalty λ is fixed in both inner and outer optimization steps. In its simplest form it can be adjusted manually by visual inspection (if data available), but preferably one uses automated, data-driven selection procedures. Ramsay et al. (2007) discuss two rationales for choosing λ , corresponding to the need for robustness with respect to poor initial parameter values or model misspecification. Hooker et al. (2011) apply forward cross-validation to model for infectious disease dynamics for measles in Ontario. For more details on generalized profiling, see Ramsay et al. (2007) and Hooker et al. (2011).

7.2.2 Monotonicity constraints

In models for microbial growth, we assume that the number of bacteria or the concentration increases with time. When applying generalized profiling as explained in previous section, there is no guarantee that the approximation is monotone. Therefore we introduce a second penalization term, which penalizes local deviations from this assumption. We use a well-known technique, that was also used by Bollaerts et al. (2006a,b) among others. Using a B-spline basis, the solution \tilde{x}_i is guaranteed to be non-decreasing if successive coefficients c_{ik} are non-decreasing. Define the additional penalization term for monotonicity of \tilde{x}_i as

$$\text{PEN}_{M,i}(\tilde{\mathbf{x}}) = \sum_{k=2}^{K_i} I\{(-1)^{p_i}(c_{ik} - c_{i,k-1}) < 0\}(c_{ik} - c_{i,k-1})^2,$$

with indicator $I\{(-1)^{p_i}(c_{ik} - c_{i,k-1}) < 0\}$ equal to 1 if the first order difference $(-1)^{p_i}(c_{ik} - c_{i,k-1}) < 0$ and 0 otherwise. Here $p_i = 1$ if the fit should be monotone non-increasing and $p_i = 2$ if the fit should be monotone non-decreasing. With \mathcal{M} the subset of components i for which monotonicity is required, the total penalization term equals, with additional regulation parameter $\kappa = \{\kappa_i\}_{i \in \mathcal{M}}$,

$$\text{PEN}_M(\tilde{\mathbf{x}}|\kappa) = \sum_{i \in \mathcal{M}} \kappa_i \text{PEN}_{M,i}(\tilde{\mathbf{x}}),$$

leading to the extended expression $J(\mathbf{c}|\theta, \lambda, \kappa)$ in the first step of the estimation procedure:

$$J(\mathbf{c}|\theta, \lambda, \kappa) = \sum_{i \in D^o} \sum_{j=1}^n w_{ij} (y_{ij} - \tilde{x}_i(t_{ij}))^2 + \text{PEN}(\tilde{\mathbf{x}}|\lambda) + \text{PEN}_M(\tilde{\mathbf{x}}|\kappa).$$

In both applications $\mathcal{M} = \{1\}$ and $p_1 = 1$.

7.2.3 Parametric and semiparametric estimators

To simplify notation, presentation is limited to the case where only one variable is observed ($\mathcal{D}^o = \{1\}$), as in both data examples. Interest goes to estimators for the mean $x(t) = E(y|t)$ as a function of t . First of all there is the “fully parametric” estimator, denoted by $\hat{x}^{\text{PAR}}(t)$, resulting from fitting the parameter θ to the data by least squares, and equivalent to the result of generalized profiling with $\lambda = \infty$ (very large) and $\kappa = 0$. Next to the fully parametric estimator, the model $\tilde{x}(t) = \sum_{k=1}^K c_k(\theta, \lambda, \kappa) \phi_k(t)$ fitted by generalized profiling for different choices of λ and κ provides “semiparametric” estimators, being spline estimators penalized “in the direction” of the fully parametric model. The first option is the semiparametric solution $\hat{x}^{\text{GP}}(t; \hat{\lambda}_{\text{opt}})$ corresponding to a data-driven optimal choice $\lambda = \hat{\lambda}_{\text{opt}}$ and $\kappa = 0$. Next, assuming the underlying model is monotone, the generalized profiling with monotonicity constraint results in another penalized semiparametric solution $\hat{x}^{\text{MGP}}(t; \hat{\lambda}_{\text{opt}})$ corresponding to a data-driven optimal choice $\lambda = \hat{\lambda}_{\text{opt}}$ and $\kappa = \infty$ (very large). So, main interest does not go to the estimators for the parameter θ corresponding to different choices for λ and κ , but rather to the estimated curves $\hat{x}(t) = \sum_{k=1}^K \hat{c}_k(\hat{\theta}, \hat{\lambda}, \kappa) \phi_k(t)$.

7.3 Selection of penalty parameters

Several techniques to obtain an appropriate data-driven value for the penalty parameter λ are briefly described, and one-sided cross-validation is proposed as an additional method for generalized profiling. In general the value for λ is first selected without any monotonicity constraints ($\kappa = 0$). If that fit is monotone increasing (or similarly decreasing), no additional penalization is necessary and by definition $\text{PEN}_M(\tilde{x}|\kappa) = 0$. If the fit is not monotone, κ is set to an arbitrary but sufficiently high value (such as 10^4) to guarantee the desired monotonicities. In what follows, focus is on methods to select the smoothing parameter λ and, for ease of notation, it is assumed that there is only one *observed* variable ($\mathcal{D}^o = \{1\}$) as is the case for the *Y. enterocolitica* and the Parvovirus B19 data.

Hooker et al. (2011) described a forward cross validation method, being a forward prediction error (FPE) when predicting future responses based on the parametric model with the estimated parameters. The terms in FPE are the (squared) errors made in predicting the observation at time t_j by starting from the estimated trajectory at time $t_j - h$, and solving the differential equation model from time $t_j - h$ to time t .

Our interest however lies less in the parametric solution of the differential equation (with θ based on generalized profiling), but rather in the semiparametric estimators, and

therefore we do not consider this option further. We will use leave-one-out and one-sided CV methods based on the semiparametric estimators, as discussed in the following paragraphs.

Leave-one-out cross-validation Another computer-intensive method, which is feasible in case of a small data set, is leave-one-out CV. In this case the j -th observation (in turn for $j = 1, \dots, n$) is dropped from the data and the differential equation is solved with the profiling method with solution $\tilde{x}^{[-j]}(t, \hat{\theta}_\lambda^{[-j]})$, where the superscript $[-j]$ indicates the deletion of the j -th observation, and the dependence on the *estimated* parameters θ is also explicitly included. The dropped observation y_j is compared to the predicted value of this observation, based on the profiling without that observation:

$$LOOCV(\lambda) = \sum_{j=1}^n w_j \left(y_j - \tilde{x}^{[-j]}(t_j, \hat{\theta}_\lambda^{[-j]}) \right)^2.$$

That value of λ minimizing the criterion $LOOCV(\lambda)$ over a grid of values is selected to be the optimal choice.

One-sided cross-validation Hart and Yi (1998) introduced the one-sided CV. It has the objectivity of LOOCV but statistical properties comparable to those of a plug-in rule (less variable and more stable). Moreover it resembles, similar to FPE, that there is a natural time- or age-order in the sequence of the data (being ordered in that sense). For the left one-sided cross-validation, the observations 1 to $j - 1$ are used to obtain a prediction ($\tilde{x}^{[1, j-1]}$) for the j -th observation. This procedure is repeated for $j = (k+1), \dots, n$, with k some small number (guaranteeing sufficient data for prediction when j is small). The reverse holds for the right one-sided cross validation, where the observation $j + 1$ to n are used to obtain a prediction ($\tilde{x}^{[j+1, n]}$) for the j -th observation, leading to the criteria

$$OSCV_L(\lambda) = \sum_{j=k+1}^n w_j \left(y_j - \tilde{x}^{[1, j-1]}(t_j, \hat{\theta}_\lambda^{[1, j-1]}) \right)^2,$$

$$OSCV_R(\lambda) = \sum_{j=1}^k w_j \left(y_j - \tilde{x}^{[j+1, n]}(t_j, \hat{\theta}_\lambda^{[j+1, n]}) \right)^2.$$

For the Y. enterocolitica data we took $k = 8$ (left) and $k = 10$ (right); for the Parvo B19 data $k = 20$ (left) and $k = 50$ (right).

In the next sections the CV criteria are applied to our two data examples. Remember that the original Y. enterocolitica data are of the form $(t_j, \ln z_j)$, with $j = 1, \dots, 15$ and the Parvovirus B19 data are of the form $(a_j, \text{asin}\sqrt{p_j})$, with $j = 1, \dots, 66$.

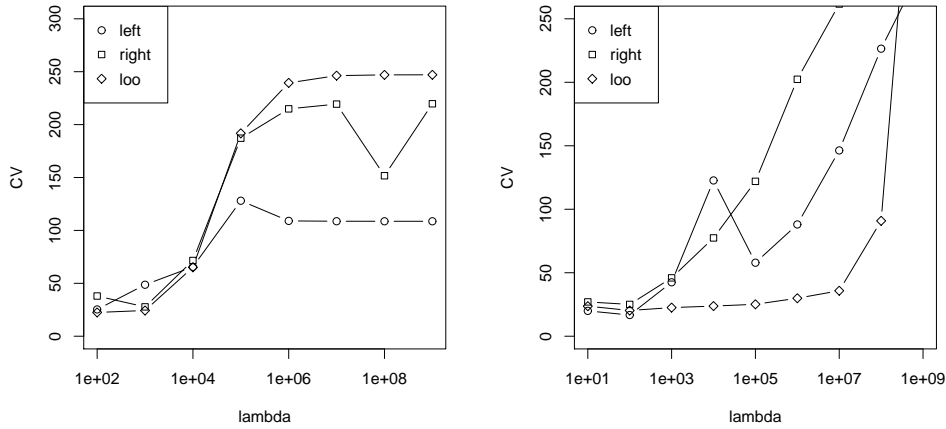


Figure 7.1: *Y. enterocolitica* (left panel) and Parvovirus B19 (right panel) data. Selection of optimal penalty term λ . Graphs of $LOOCV(\lambda)$ (\diamond), $OSCV_L(\lambda)$ (\circ), and $OSCV_R(\lambda)$ (\square) as of function of λ over a grid $10^2, \dots, 10^9$ (left) and $10^1, \dots, 10^9$ (right).

7.3.1 The *Y. enterocolitica* data

In order to find a good value for λ , a grid search was performed over powers of 10 ($10^2, 10^3, \dots$). The curves in the left panel of Figure 7.1 show no clear minimum within the chosen grid but they do show a clear upward trend, for all CV criteria $LOOCV(\lambda)$, $OSCV_L(\lambda)$, and $OSCV_R(\lambda)$, for λ between 10^4 and 10^5 . For small values of λ in the chosen grid, the corresponding fit is primarily data-driven and goes almost perfectly through nearly all observations. For large values of λ , the profile is closer to the OLS fit, with local deviations. As the sample size is quite small the CV criteria are less accurate and more variable and one might not really obtain a useful minimum, so that one in this case typically does not select the value of λ that minimizes the CV criteria, but rather the point where a substantial increase or a jump appears in the CV pattern. Here, the jump in the CV criteria between 10^4 and 10^5 corresponds to the transition between the two extremes. As we are interested in a compromise between a data-driven and a fully parametric solution, we believe that the optimal value of λ is in between 10^4 and 10^5 . When further searching for the best value in the range $1 \cdot 10^4, 2 \cdot 10^4, \dots, 10 \cdot 10^4$, we notice that the three criteria do not fully agree. While we would choose $\lambda = 2 \cdot 10^4$ based on the left one-sided and leave-one-out cross-validation, a choice $\lambda = 6 \cdot 10^4$ is more appropriate for the right one-sided cross-validation. In general a smoother solution (large penalty) is preferred over a more “wiggly” solution (small penalty) and therefore we opted for $\hat{\lambda}_{\text{opt}} = 6 \cdot 10^4$.

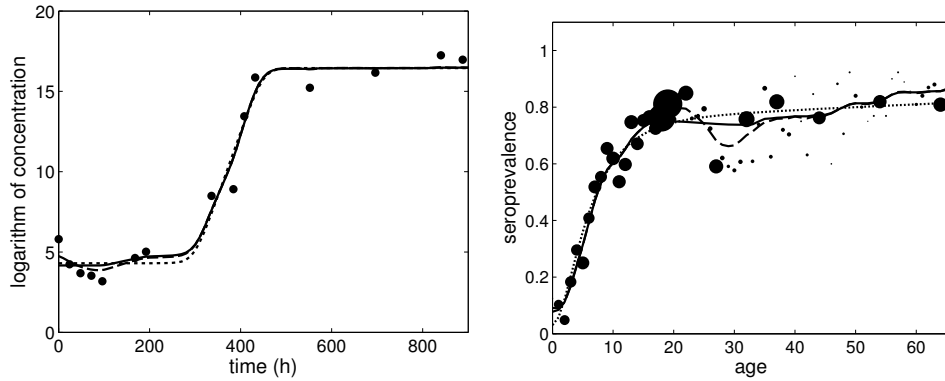


Figure 7.2: *Y. enterocolitica* (left panel) and Parvovirus B19 (right panel) data. Parametric fit (dotted line), data-modified semiparametric (dashed line) and data-modified semiparametric with monotonicity constraint (solid line).

The parameter values that result from the generalized profiling, based on $\lambda = 6 \cdot 10^4$ are $\widehat{\log(\mu_{\max})} = 16.455$, $\widehat{\kappa} = 0.079$, $\widehat{\log(\mu_0)} = 4.742$ and $\widehat{\log(q_0)} = -23.641$. These estimates are different when the restriction for monotonicity is imposed ($\kappa = 10^4$): $\widehat{\log(\mu_{\max})} = 16.444$, $\widehat{\kappa} = 0.079$, $\widehat{\log(\mu_0)} = 4.166$ and $\widehat{\log(q_0)} = -23.886$. The resulting fitted curves are shown in the left panel of Figure 7.2.

The data-modified semiparametric solution (dashed line) in the left panel of Figure 7.2 shows a decrease in the lag phase following the observed concentrations, but expected to be not inherent to the underlying model. The fit beyond the lag phase is close to the OLS fit. By introducing the monotonicity constraint (solid line), the decrease in the lag phase is no longer present and consequently the fit gets overall close to the OLS fit.

7.3.2 The Parvovirus B19 data

Again a grid search was applied to select an appropriate value for the penalty parameter λ . The situation here is quite different from the previous example, as much more data are available and consequently the CV curves might show more clearly a minimum. A rough search with λ a power of 10 ($10, 10^2, 10^3, \dots$) tells us that the optimal value is somewhere between 10 and 1000 (see right panel of Figure 7.1), and a finer search was set up. Again the three criteria do not fully agree: the right one-sided would select $\lambda = 30$, while the leave-one-out would select $\lambda = 80$ and the left one-sided $\lambda = 100$. Again preferring the larger value, the final choice for λ is $\hat{\lambda}_{\text{opt}} = 100$, corresponding to parameter values $\hat{\alpha} = 0.023$, $\hat{\beta} = 0.127$, $\hat{\gamma} = 0.037$ and an initial seroprevalence of $\hat{\pi}_0 = 0.091$. If the monotonicity restriction is applied, the parameter values change as follows: $\hat{\alpha} = 0.033$,

$\hat{\beta} = 0.101$ and $\hat{\gamma} = 0.020$, $\hat{\pi}_0 = 0.078$. The resulting fits are shown in the right panel of Figure 7.2.

In the next section the use of the bootstrap is proposed for the construction of confidence intervals and testing lack of fit.

7.4 Bootstrap confidence regions and lack-of-fit tests

To not complicate notation, it is assumed again that there is only one observed variable ($\mathcal{D}^o = \{1\}$) as in both data examples. In a first section bootstrap methodology is introduced to construct pointwise and simultaneous confidence bounds for $\hat{x}^{\text{GP}}(t; \hat{\lambda}_{\text{opt}})$ and $\hat{x}^{\text{MGP}}(t; \hat{\lambda}_{\text{opt}})$. In a next section focus is on a bootstrap lack-of-fit test, i.e. for testing the null hypothesis that the underlying model (e.g. Baranyi-Roberts or Farrington model) holds. A second bootstrap test investigates whether there is evidence in the data against the monotonicity assumption, i.e. testing the null hypothesis that the underlying model is monotone.

7.4.1 Weighted residual bootstrap

Both applications are based on a weighted residual bootstrap, using standardized residuals. More precisely, the structure

$$y_j = \tilde{x}(t_j) + \text{se}(y_j|t_j) \times \varepsilon_j, \quad (7.10)$$

with $\tilde{x}(t_j)$ approximating the mean $E(y_j|t_j)$, $\text{se}(y_j|t_j) = \sqrt{\text{var}(y_j|t_j)}$ and normalized error terms

$$\varepsilon_i = \frac{y_j - \tilde{x}(t_j)}{\text{se}(y_j|t_j)}, \quad (7.11)$$

suggests bootstrap data to be generated as

$$y_j^* = \hat{x}_M(t_j) + \widehat{\text{se}}(y_j|t_j) \times \varepsilon_j^*, \quad (7.12)$$

with $\varepsilon_j^*, j = 1, \dots, n$, sampled with replacement from the n standardized residuals

$$\left\{ \frac{y_j - \hat{x}_R(t_j)}{\widehat{\text{se}}(y_j|t_j)}; j = 1, \dots, n \right\}, \quad (7.13)$$

and using two estimators $\hat{x}_M(t_j)$ and $\hat{x}_R(t_j)$ for the (approximate) mean $\tilde{x}(t_j)$, not necessarily identical, and an estimate or known expression $\widehat{\text{se}}(y_j|t_j)$ for the heteroscedastic part of the standard error. We recommend to always use $\hat{x}_R(t_j) = \hat{x}^{\text{GP}}(t_j; \hat{\lambda}_{\text{opt}})$ such that the residuals are not based on any constrained type of model (constrained to be fully parametric or to be monotone).

In this way B bootstrap samples $\{(t_j, y_{(b),j}^*)\}_{j=1}^n$, $b = 1, \dots, B$, can be constructed, being different in the resampled standardized residuals $\{\varepsilon_{(b),j}^*\}_{j=1}^n$. For each of these B bootstrap samples all estimates can be recalculated, in this way providing information on the sampling distribution of the estimators. The larger the number of bootstrap samples B , the more accurately characteristics of the sampling distribution such as percentiles can be estimated. As the generalized profiling method is very computer intensive on its own, the number of bootstrap runs was taken as $B = 1000$ for both applications. In principle, for each bootstrap sample the optimal data driven smoothing parameter $\hat{\lambda}_{\text{opt}}$ could be recalculated, but this appeared to be computationally not feasible in our data examples and the value of $\hat{\lambda}_{\text{opt}}$ was fixed across the bootstrap samples, being the optimal choice as determined on the original sample. For more details on the residual bootstrap, see e.g. Davison and Hinkley (1997).

For the *Y. enterocolitica* example it is assumed that the $\text{se}(y_j|t_j)$ do not depend on j (homoscedasticity) and hence they can be dropped (or put equal to 1 without loss of generality) in (7.12)-(7.13) and ordinary residuals $\{y_j - \hat{x}(t_j)\}_{j=1}^n$ can be resampled. For the Parvovirus B19 example, the standard errors $\text{se}(y_j|t_j) = 1/(2\sqrt{n_j})$ are known and do not need to be estimated and hence the weighted residuals $\{2\sqrt{n_j}(y_j - \hat{x}(t_j))\}_{j=1}^n$ (or dropping the 2) need to be resampled. Depending on the application, confidence bounds or hypotheses testing, different estimators for the structural part of the model $\hat{x}_M(t_j)$, $j = 1, \dots, n$ need to be chosen.

7.4.2 Bootstrap confidence bounds

Here, the estimator $\hat{x}^{\text{GP}}(t_j; \hat{\lambda}_{\text{opt}})$ (or alternatively the monotone version $\hat{x}^{\text{MGP}}(t_j, \hat{\lambda}_{\text{opt}})$) is used as the estimator $\hat{x}_M(t_j)$ in the construction (7.12)-(7.13) of B bootstrap samples.

The notation $\hat{x}^{*(M)\text{GP}}(t_j; \hat{\lambda}_{\text{opt}})$ in the sequel indicates with (M) the two alternative estimators. For each bootstrap sample ($b = 1, \dots, B$), the generalized profiling estimates can be recalculated at any value t of interest, leading to the bootstrap replicates or $\hat{x}_{(b)}^{*(M)\text{GP}}(t; \hat{\lambda}_{\text{opt}})$, $b = 1, \dots, B$. Pointwise bootstrap percentile intervals (see e.g. Davison and Hinkley, 1997) and simultaneous bootstrap confidence intervals are constructed, the latter as follows. Suppose that B bootstrap samples are drawn. Consider a predefined finite set of grid points of interest $\{t_1, \dots, t_g, \dots, t_G\}$. For each grid point t_g , the bootstrap replicates $\{\hat{x}_{(b)}^{*(M)\text{GP}}(t_g; \hat{\lambda}_{\text{opt}}); b = 1, \dots, B\}$ are ordered and their corresponding ranks are denoted by $\{r_g^{(b)}; b = 1, \dots, B\}$. The b -th ordered replicate is denoted by $\hat{x}_{[b]}^{*(M)\text{GP}}(t_g; \hat{\lambda}_{\text{opt}})$ for $b = 1, \dots, B$.

Define b_k as the k -th order statistic of

$$\left[\max \left\{ \max_{1 \leq g \leq G} (r_g^{(b)}); B + 1 - \min_{1 \leq g \leq G} (r_g^{(b)}) \right\}; b = 1, \dots, B \right].$$

By construction, the intervals over the grid points

$$\left\{ \left[\hat{x}_{[B+1-b_k]}^{*(M)GP}(t_g; \hat{\lambda}_{\text{opt}}); \hat{x}_{[b_k]}^{*(M)GP}(t_g; \hat{\lambda}_{\text{opt}}) \right]; g = 1, \dots, G \right\}$$

have a global confidence level of at least $100 \frac{k}{B} \%$. This method has also been applied by Claeskens and Aerts (2000), see also Besag et al. (1995).

7.4.3 Omnibus bootstrap lack-of-fit test

The generalized profiling approach offers an interesting framework for testing the lack of fit of a parametric model, as defined by differential equations and estimated by $\hat{x}^{\text{PAR}}(t)$. Tuned by a data adaptive smoothing parameter the final (monotone) semiparametric estimator $\hat{x}^{(M)GP}(t; \hat{\lambda}_{\text{opt}})$ might deviate more or less from the parametric estimator $\hat{x}^{\text{PAR}}(t)$. Larger deviations indicate evidence against the parametric model. So, interest goes to testing the null hypothesis of goodness of fit of the parametric model

$$H_0^{\text{GoF}} : \dot{\mathbf{x}}(t) = \mathbf{f}(\mathbf{x}, t | \boldsymbol{\theta}),$$

against the alternative hypothesis of lack of fit. The proposed test is not designed to detect specific types of departures from the prescribed null model, but is expected to be consistent ('omnibus') against virtually any departure from the hypothesized parametric model. Hooker (2009) proposed estimating lack of fit in terms of *empirical forcing functions*, being nonparametric functions $\mathbf{g}(t)$ which modify (7.7) to $\dot{\mathbf{x}}(t) = \mathbf{f}(\mathbf{x}, t | \boldsymbol{\theta}) + \mathbf{g}(t)$ and represent both random disturbances to the system and deterministic lack of fit of \mathbf{f} . Recently Hooker and Ellner (2015) took a more general way that includes the possibility of parameter values changing over time, producing a system $\dot{\mathbf{x}}(t) = \mathbf{f}(\mathbf{x}, \mathbf{g}(t) | \boldsymbol{\theta})$ in which $\mathbf{g}(t)$ can modify \mathbf{f} more generally than by additive forcing. Our approach differs from that of Hooker (2009) and Hooker and Ellner (2015) in that it focuses on the ODE (approximate) solution $\mathbf{x}(t)$ as (conditional) mean of the observed outcomes \mathbf{y} and by the construction of the test statistic, being an empirical measure of discrepancy between the parametric and semiparametric solution estimating the weighted integrated absolute difference $\int | \hat{x}^{\text{PAR}}(t) - \hat{x}^{(M)GP}(t; \hat{\lambda}_{\text{opt}}) | f(t) dt$ (with $f(t)$ the design density behind the observed t_1, \dots, t_n) and defined as

$$t_n^{\text{GoF}} = \sum_{j=1}^n \frac{n_j}{N} | \hat{x}^{\text{PAR}}(t_j) - \hat{x}^{(M)GP}(t_j; \hat{\lambda}_{\text{opt}}) |. \quad (7.14)$$

As interest goes in generating the null distribution of T_n^{GoF} , B bootstrap samples are generated as defined by (7.12)-(7.13) with $\hat{x}_m(t_j) = \hat{x}^{\text{PAR}}(t_j)$. These choices make sure that the generated data are reflecting the hypothesized mean structure, while the

residuals are obtained from the original data and a semiparametric model estimate. For each bootstrap sample the test statistic is recalculated in the same way as for the original sample, leading to B bootstrap test statistic replicates (omitting the GoF superscript) $\{t_n^{(b)}; b = 1, \dots, B\}$. The bootstrap estimate for the p-value is then defined as the proportion of bootstrap test values exceeding the original value, or more precisely $(\sum_{b=1}^B I\{t_n^{(b)} \geq t_n\} + 1)/(B + 1)$.

7.4.4 Testing monotonicity

Here interest goes to testing whether the underlying semiparametric model is monotone, or testing

$$H_0^M : \mathbf{x}(t) \text{ is a monotone function of } t.$$

Following the same ideas as in the previous section, the test statistic is now measuring the distance between the unconstrained and monotone semiparametric fit, defined as

$$t_n^M = \sum_{j=1}^n \frac{n_j}{N} | \hat{x}^{\text{MGP}}(t_j; \hat{\lambda}_{\text{opt}}) - \hat{x}^{\text{GP}}(t_j; \hat{\lambda}_{\text{opt}}) |, \quad (7.15)$$

and B bootstrap samples are generated as defined by (7.12)-(7.13) with $\hat{x}_M(t_j) = \hat{x}^{\text{MGP}}(t_j; \hat{\lambda}_{\text{opt}})$ and $\hat{x}_R(t_j) = \hat{x}^{\text{GP}}(t_j; \hat{\lambda}_{\text{opt}})$. Again, for each bootstrap sample the test statistic is recalculated in the same way as for the original sample, leading to B bootstrap test statistic replicates and resulting in a bootstrap estimate for the p-value.

7.5 Application to *Y. enterocolitica* and Parvovirus B19 data

The application of the bootstrap (simultaneous) confidence intervals and bootstrap tests are presented in this section. Based on the plots of the fitted curves $\hat{x}^{\text{PAR}}(t)$, $\hat{x}^{\text{GP}}(t; \hat{\lambda}_{\text{opt}})$ and $\hat{x}^{\text{MGP}}(t; \hat{\lambda}_{\text{opt}})$ in Figure 7.2 and taking into account the sample size, one might expect to not have enough evidence against both the null hypotheses H_0^{GoF} and H_0^M for the *Y. enterocolitica* data, but that both hypotheses might be rejected at 5% level for the Parvovirus B19 data.

7.5.1 The *Y. enterocolitica* data

Figure 7.3 shows the confidence bounds for the *Y. enterocolitica* data, pointwise (left panels) and simultaneous bounds (right panels) using the semiparametric estimator $\hat{x}^{\text{GP}}(t; \hat{\lambda}_{\text{opt}})$ (top panels) and its monotone alternative $\hat{x}^{\text{MGP}}(t; \hat{\lambda}_{\text{opt}})$ (lower panels), and based on a grid from 0 to 900 in steps of 10. As compared to the pointwise bounds, the simultaneous

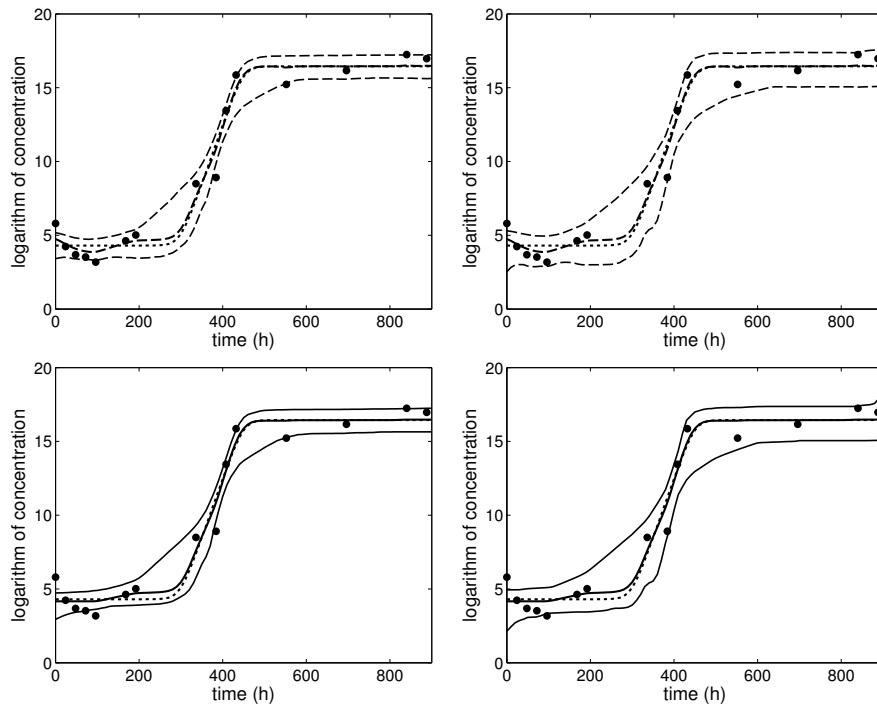


Figure 7.3: *Y. enterocolitica* data. Parametric fit (dotted line), bootstrapped pointwise (left) and simultaneous (right) confidence intervals, with $\lambda = 6 \times 10^4$, while $\kappa = 0$ (upper) or $\kappa = 10^4$ (lower).

bounds are wider as expected. The difference between the unconstrained and monotone versions are rather quite small.

The null hypothesis H_0^{GoF} that the BR-model holds cannot be rejected, with p-value 0.137 (using t_n^{GoF} with $\hat{x}^{\text{GP}}(t_j; \hat{\lambda}_{\text{opt}})$) and 0.175 (using t_n^{GoF} with $\hat{x}^{\text{MGP}}(t_j; \hat{\lambda}_{\text{opt}})$). For testing the monotonicity hypothesis H_0^{M} , the left panel of Figure 7.4 shows the bootstrap generated null distribution of the test statistic t_n^{M} and its value (0.116) for the original dataset as a bullet on the horizontal axis. The p-value is estimated as 0.116 and consequently there is insufficient evidence by the local decrease of the concentration data in the lag phase to reject monotonicity.

7.5.2 The Parvovirus B19 data

Figure 7.5 depicts the bootstrapped confidence bounds for the Parvovirus B19 data, again unconstrained (monotone) in the upper (lower) panels and pointwise (simultaneous) in the left (right) panels. To improve interpretability the bounds are shown on the $[0, 1]$ proba-

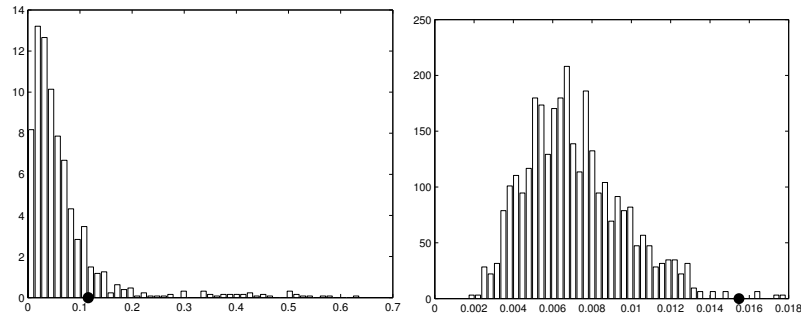


Figure 7.4: *Y. enterocolitica* (left panel) and Parvovirus B19 (right panel) data. Distribution of test statistic when testing the monotonicity of the fit.

bility scale, obtained by first computing the confidence bounds on the arcsin-transformed scale and then transforming to the $[0, 1]$ scale. Monotonizing the semiparametric estimator has, not unexpectedly, quite an effect on the bounds around the age of 30.

The null hypothesis H_0^{GoF} that Farrington's model holds can be rejected with p-value 0.002 using t_n^{GoF} with $\hat{x}^{\text{GP}}(t_j; \hat{\lambda}_{\text{opt}})$ and with p-value 0.006 when using t_n^{GoF} with $\hat{x}^{\text{MGP}}(t_j; \hat{\lambda}_{\text{opt}})$. Monotonizing forces the semiparametric estimator to be more similar to Farrington's model, thus explaining the second version of the test having a slightly higher p-value.

For testing the monotonicity hypothesis H_0^{M} , the right panel of Figure 7.4 shows the bootstrap generated null distribution of the test statistic t_n^{M} and its value (0.016) for the original dataset. H_0^{M} is clearly rejected with a p-value 0.005. Main conclusion is that the flexible but parametric and monotone model of Farrington is not appropriate or that another process is causing the decrease or plateau between the ages of 20 and 40. Goeyvaerts et al. (2011) investigated whether this phenomenon is induced by waning antibodies for Parvovirus B19 and, if this is the case, whether secondary infections are plausible, or whether boosting may occur. They tested several immunological scenarios by fitting different compartmental dynamic transmission models to serological data using data on social contact patterns.

7.6 Conclusions

In this chapter generalized profiling has been extended with an additional penalization, constraining the semiparametric solution to be monotone. The bootstrap is applied for the construction of simultaneous confidence bands and for formal tests of goodness/lack-of-fit and monotonicity. The methodology is applied to two motivating examples. For the *Y. enterocolitica* data, the Baranyi and Roberts model was not rejected; neither was

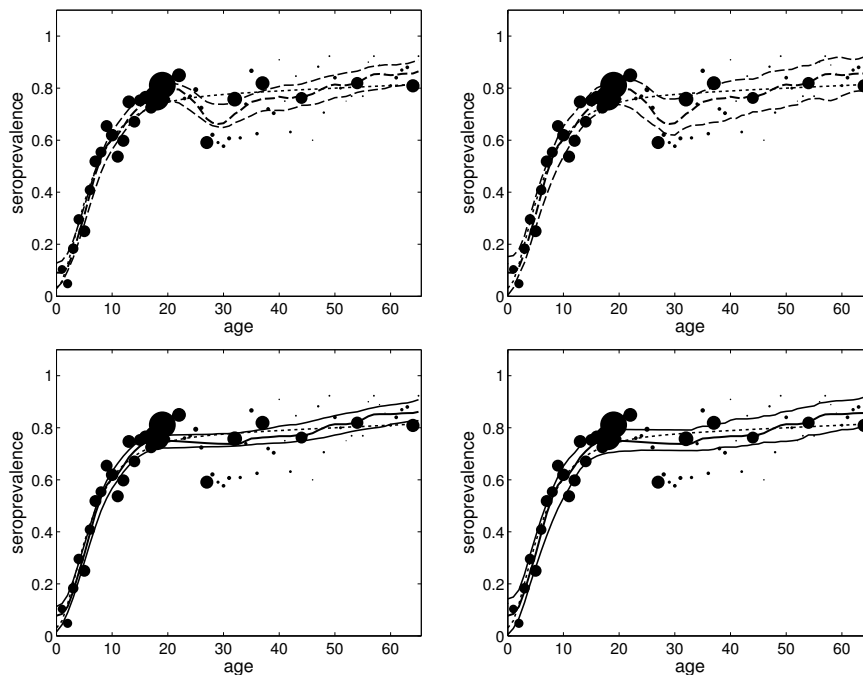


Figure 7.5: Parvovirus B19 data. Parametric fit (dotted line), bootstrapped pointwise (left) and simultaneous (right) confidence intervals, with $\lambda = 100$, while $\kappa = 0$ (upper) or $\kappa = 10^4$ (lower).

monotonicity. Both hypotheses, that the Farrington model holds, and that the solution is monotone, were rejected however for the Parvovirus B19 data.

Other applications might imply other natural shape restrictions such as single-peaked or U-shaped patterns. As proposed by Bollaerts et al. (2006b), asymmetric discrete penalties can be used to enforce different types of shape constraints. Such other penalties could be used as well within the generalized profiling approach.

Generalized profiling is computer-intensive and sensitive to appropriate starting values, even within the least squares estimation framework. Conceptually it is rather straightforward to extend generalized profiling to non-normal data and general maximum likelihood (ML) estimation and inference. Here we applied least squares and normal approximation for both motivating examples. The inherent nature of the *Y. enterocolitica* data is however count data, and the non-aggregated Parvovirus B19 data are binary. The use of Poisson or Bernoulli based maximum likelihood estimation and inference makes the method even more computer-intensive and more sensitive to starting values and more unstable. Therefore a genuine ML based implementation of generalized profiling is an interesting avenue of further research but is considered beyond the scope of this research.

Chapter 8

General discussion and conclusion

In this thesis we discuss several ways to deal with censored data. Different statistical models are used to describe the data, but all models are related to the log-normal distribution. Parametric models are used, but also a family of semi-nonparametric models is applied. We introduce a test to check the goodness of fit of a model and we use model averaging to obtain an estimate for a parameter of interest. In the final chapter of the thesis we extend the generalized profiling technique with an additional constraint to monotonize the solution, and we apply the bootstrap for the construction of confidence bands and for hypothesis testing.

In Chapter 4 we propose a goodness-of-fit test of parametric models for censored data. The test is based on the order selection test (Aerts et al., 1999), in combination with the SemiNP family of distributions (Fenton and Gallant, 1996; Gallant and Nychka, 1987; Zhang and Davidian, 2008). Although we do not provide a formal proof for the behaviour of the test, simulation studies show that the test performs well across several scenarios. A bootstrap approach is suggested as an alternative to the asymptotic approach, and the data examples and simulation study show similar results. In this research we focus on a test for the log-normal distribution. However, the approach is applicable for other distributions, such as the gamma, Weibull, etc. and this is an interesting avenue for further research. Extensions to models with covariates or random effects is also subject of further research.

Chapter 5 describes different strategies for the estimation of the distribution function for censored data. As the true underlying model is mostly unknown, it is important to

select a good model to draw inference on the whole sample or make a statement on the concentration below LOD and LOQ. We compare the estimates of parametric and the more flexible semiNP models, but also investigate model averaging. As model averaging (Burnham and Anderson, 1998) takes into account the uncertainty of the model, it is a worthwhile alternative to model selection. Still, the choice of an appropriate and rich enough family of candidate models is highly important. In Chapter 6 we continue with model averaging, but now we focus on quantiles. We propose two methods: averaging the quantile estimators, each derived from the estimated distributions (direct approach) or inverting the averaged estimator of the distribution function (indirect approach). The simulation study does not reveal a preference for one approach. In order to select a good model and as such obtain an estimate based on this model, we use AIC, which is a global measure of fit. Such a global measure of fit is sensitive to deviations in the right tail of the distribution. As we are mostly interested in characteristics in the left tail of the distribution, the use of other measures like a focused information criterion (see e.g. Claeskens and Hjort, 2008) is a valuable option and is a topic of further research. We are also hindered by the numerical instability of the semiNP models. A Bayesian approach to model averaging (see e.g. Hoeting et al., 1999) might offer an attractive alternative and is also subject of further research.

In Chapter 7 we study generalized profiling (Ramsay et al., 2007), a generalized smoothing estimation approach that is robust to model misspecification, as a way to numerically solve systems of differential equations through a semi-parametric solution. In some situations, the solution is assumed to be monotone and we recommend to use an additional penalty constraining the semi-parametric solution. We apply the bootstrap to obtain confidence bands for the solution, but also to perform hypothesis tests. We test two hypotheses, where the first deals with the goodness-of-fit of the proposed system of differential equations, and the second concerns the monotonicity of the solution. The methodology is illustrated on two examples. In the first example we use the Baranyi-Roberts model (Baranyi and Roberts, 1994) to describe *Y. enterocolitica* data. In the second example, Parvovirus B19 data are described by the Farrington model (Farrington, 1990).

Bibliography

- Aerts, M., Claeskens, G., and Hart, J. D. (1999). Testing the fit of a parametric function. *Journal of the American Statistical Association*, 94(447):869–879.
- Akaike, H. (1973). Information theory and an extension of the maximum likelihood principle. In Petrov, B. N. and Csaki, F., editors, *2nd International Symposium on Information Theory*, pages 267–281, Akademiai Kiado, Budapest (Reproduced in *Breakthroughs in Statistics*, Volume 1 (eds. S. Kotz and N. L. Johnson), Springer Verlag, New York (1992)).
- Akritis, M. G. (1988). Pearson-type goodness-of-fit tests: The univariate case. *Journal of the American Statistical Association*, 83(401):222–230.
- Azzalini, A. (1985). A class of distributions which includes the normal ones. *Scandinavian Journal of Statistics. Theory and Applications*, 12:171–178.
- Azzalini, A. and Capitanio, A. (2003). Distributions generated by perturbation of symmetry with emphasis on a multivariate skew t -distribution. *Journal of the Royal Statistical Society. Series B. Statistical Methodology*, 65(2):367–389.
- Azzalini, A., Dal Cappello, T., and Kotz, S. (2003). Log-skew-normal and log-skew- t distributions as model for family income data. *Journal of Income Distribution*, 11:12–20.
- Azzalini, A. and Dalla Valle, A. (1996). The multivariate skew-normal distribution. *Biometrika*, 83(4):715–726.
- Barany, J. and Roberts, T. A. (1995). Mathematics of predictive food microbiology. *International Journal of Food Microbiology*, 26:199–218.

- Baranyi, J. and Roberts, T. A. (1994). A dynamic approach to predicting bacterial growth in food. *International Journal of Food Microbiology*, 23(3–4):277–294.
- Bartlett, M. (1947). The use of transformations. *Biometrics*, 3(1):39–52.
- Behl, P., Claeskens, G., and Dette, H. (2014). Focused model selection in quantile regression. *Statistica Sinica*, 24(2):601–624.
- Beran, R. (1988). Prepivoting test statistics: A bootstrap view of asymptotic refinements. *Journal of the American Statistical Association*, 83(403):687–697.
- Besag, J., Green, P., Higdon, D., and Mengersen, K. (1995). Bayesian computation and stochastic systems (with discussion). *Statistical Science*, 10(1):1–66.
- Bogaerts, K. and Lesaffre, E. (2004). A new, fast algorithm to find the regions of possible support for bivariate interval-censored data. *Journal of Computational and Graphical Statistics*, 13(2):330–340.
- Bollaerts, K., Aerts, M., Shkedy, Z., Faes, C., Van der Stede, Y., Beutels, P., and Hens, N. (2012). Estimating the population prevalence and force of infection directly from antibody titres. *Statistical Modelling*, 12(5):441–462.
- Bollaerts, K., Eilers, P. H. C., and Aerts, M. (2006a). Quantile regression with monotonicity restrictions using p-splines and the l1-norm. *Statistical Modelling*, 6(3):189–207.
- Bollaerts, K., Eilers, P. H. C., and van Mechelen, I. (2006b). Simple and multiple p-splines regression with shape constraints. *British Journal of Mathematical and Statistical Psychology*, 59:451–469.
- Burnham, K., Anderson, D., and Huyvaert, K. (2011). AIC model selection and multi-model inference in behavioral ecology: some background, observations, and comparisons. *Behavioral Ecology and Sociobiology*, 65:23–35.
- Burnham, K. P. and Anderson, D. R. (1998). *Model Selection and Inference: A Practical Information-Theoretical Approach*. Springer-Verlag, New York.
- Burnham, K. P. and Anderson, D. R. (2002). *Model Selection and Inference: A Practical Information-Theoretical Approach*. Springer-Verlag, New York.
- Calle, M. L. and Gómez, G. (2008). *Statistical models and methods for biomedical and technical systems*, chapter A Sampling-Based Chi-Squared Test for Interval-Censored Data, pages 295–306. Statistics for Industry and Technology. Birkhäuser Boston.

- Cao, J., Moosman, A., and Johnson, V. E. (2010). A bayesian chi-squared goodness-of-fit test for censored data models. *Biometrics*, 66:426–434.
- Castro-Kuriss, C., Kelmansky, D., Leiva, V., and Martinez, E. (2009). A new goodness-of-fit test for censored data with an application in monitoring processes. *Communications in Statistics: Simulation and Computation*, 38(6):1161–1177(17).
- Claeskens, G. and Aerts, M. (2000). Bootstrapping local polynomial estimators in likelihood-based models. *Journal of Statistical Planning and Inference*, 86(1):63–80.
- Claeskens, G. and Carroll, R. (2007). An asymptotic theory for model selection inference in general semiparametric problems. *Biometrika*, 94:249–265.
- Claeskens, G. and Hjort, N. (2008). *Model Selection and Model Averaging*. Cambridge University Press, Cambridge.
- Claeskens, G. and Hjort, N. L. (2003). The focused information criterion. *Journal of the American Statistical Association*, 98(464):900–916.
- D’Agostino, R. B. and Stephens, M. A., editors (1986). *Goodness-of-fit techniques*, volume 68. Marcel Dekker, Inc., New York, NY, USA.
- Davison, A. C. and Hinkley, D. V. (1997). *Bootstrap Methods and their Application*, volume 1 of *Cambridge Series in Statistical and Probabilistic Mathematics*. Cambridge University Press, Cambridge.
- Efron, B. and Tibshirani, R. (1986). Bootstrap methods for standard errors, confidence intervals, and other measures of statistical accuracy. *Statistical Science. A Review Journal of the Institute of Mathematical Statistics*, 1(1):54–77.
- Efron, B. and Tibshirani, R. J. (1993). *An introduction to the Bootstrap*, volume 57 of *Monographs on Statistics and Applied Probability*. Chapman and Hall.
- EFSA (2010). Management of left-censored data in dietary exposure assessment of chemical substances. *EFSA Journal*, 8(3):96.
- Faes, C., Aerts, M., Geys, H., and Molenberghs, G. (2007). Model averaging using fractional polynomials to estimate a safe level of exposure. *Risk Analysis*, 27(1):111–123.
- Farrington, C. P. (1990). Modelling forces of infection for measles, mumps and rubella. *Statistics in Medicine*, 9(8):953–967.

- Fenton, V. and Gallant, A. R. (1996). Qualitative and asymptotic performance of snp density estimators. *Journal of Econometrics*, 74:77–118.
- Gallant, A. R. and Nychka, D. W. (1987). Semi-nonparametric maximum likelihood estimation. *Econometrica*, 55(2):363–390.
- Gillespie, B. W., Chen, Q., Reichert, H., Franzblau, A., Hedgeman, E., Lepkowski, J., Adriaens, P., Demond, A., Luksemburg, W., and Garabrant, D. H. (2010). Estimating population distributions when some data are below a limit of detection by using a reverse kaplan-meier estimator. *Epidemiology*, 21(4):S64–S70.
- Goeyvaerts, N., Hens, N., Aerts, M., and Beutels, P. (2011). Model structure analysis to estimate basic immunological processes and maternal risk for parvovirus b19. *Biostatistics*, 12(2):283–302.
- Gomez, G., Julia, O., and Utzet, F. (1992). *Survival Analysis: State of the Art*, chapter Survival Analysis for Left Censored Data, pages 269–288. Kluwer Academic Publishers.
- Grané, A. (2012). Exact goodness-of-fit tests for censored data. *Annals of the Institute of Statistical Mathematics*, 64(6):1187–1203.
- Gray, R. J. and Pierce, D. A. (1985). Goodness-of-fit tests for censored survival data. *The Annals of Statistics*, 13(2):552–563.
- Haas, C., Rose, J., and Gerba, C. (1999). *Quantitative Microbial Risk Assessment*. Wiley, New York.
- Hart, J. D. (1997). *Nonparametric smoothing and lack-of-fit tests*. Springer Series in Statistics. Springer-Verlag, New York.
- Hart, J. D. and Yi, S. (1998). One-sided cross-validation. *Journal of the American Statistical Association*, 93(442):620–631.
- Hens, N., Shkedy, Z., Aerts, M., Faes, C., Damme, P. V., and Beutels, P. (2012). *Modeling Infectious Disease Parameters Based on Serological and Social Contact Data*, volume 63 of *Statistics for Biology and Health*. Springer New York.
- Hewett, P. and Ganser, G. H. (2007). A comparison of several methods for analyzing censored data. *Annals of Occupational Hygiene*, 51(7):611–632.
- Hjort, N. L. (1992). On inference in parametric survival data models. *International Statistical Review*, 60(3):355–387.

- Hoeting, J. A., Madigan, D., Raftery, A. E., and Volinsky, C. T. (1999). Bayesian model averaging: A tutorial. *Statistical Science*, 14(4):382–417.
- Hollander, M. and Proschan, F. (1979). Testing to determine the underlying distribution using randomly censored data. *Biometrics*, 35(2):393–401.
- Hooker, G. (2009). Forcing function diagnostics for nonlinear dynamics. *Biometrics*, 65:928–936.
- Hooker, G. and Ellner, S. (2015). Goodness of fit in nonlinear dynamics: misspecified rates or misspecified states? *The Annals of Applied Statistics*, 9(2):754–776.
- Hooker, G., Ellner, S. P., Roditi, L. D. V., and Earn, D. J. D. (2011). Parameterizing state-space models for infectious disease dynamics by generalized profiling: measles in ontario. *Journal of the Royal Society Interface*, 8(60):961–974.
- Hurvich, C., Simonoff, J., and Tsai, C.-L. (1998). Smoothing parameter selection in nonparametric regression using an improved akaike information criterion. *Journal of the Royal Statistical Society B*, 60:271–293.
- Hyde, J. (1977). Testing survival under right censoring and left truncation. *Biometrika*, 64(2):225–230.
- Johnson, N. and Kotz, S. (1969). *Discrete distributions*. Distributions in statistics. Houghton Mifflin.
- Keith, L. H., Crummett, W., Jr., J. D., Libby, R. A., Taylor, J. K., and Wentler, G. (1983). Principles of environmental analysis. *Analytical Chemistry*, 55(14):2210–2218.
- Komarek, A. and Lesaffre, E. (2006). Bayesian semi-parametric accelerated failure time model for paired doubly-interval-censored data. *Statistical Modelling*, 6(1):3–22.
- Komarek, A. and Lesaffre, E. (2007). Bayesian accelerated failure time model for correlated censored data with a normal mixture as an error distribution. *Statistica Sinica*, 17:549–569.
- Komarek, A. and Lesaffre, E. (2008). Bayesian accelerated failure time model with multivariate doubly interval-censored data and flexible distributional assumptions. *Journal of the American Statistical Association*, 103(482):523–533.
- Komarek, A. and Lesaffre, E. (2009). The regression analysis of correlated interval-censored data: illustration using accelerated failure time models with flexible distributional assumptions. *Statistical Modelling*, 9(4):299–319.

- Koziol, J. A. (1980). Goodness-of-fit tests for randomly censored data. *Biometrika*, 67(3):693–696.
- Koziol, J. A. and Green, S. B. (1976). A cramér-von mises statistic for randomly censored data. *Biometrika*, 63(3):465–474.
- Lawless, J. F. and Babineau, D. (2006). Models for interval censoring and simulation-based inference for lifetime distributions. *Biometrika*, 93(3):671–686.
- Li, C.-S. (2012.). Lack-of-fit tests for generalized linear models via splines. *Communications in Statistics: Theory and Methods*, 41(23):4240–4250.
- Lin, G. D. and Stoyanov, J. (2009). The logarithmic skew-normal distributions are moment-indeterminate. *Journal of Applied Probability*, 46:909–916.
- López, S., Prieto, M., Dijkstra, J., Dhanoa, M., and France, J. (2004). Statistical evaluation of mathematical models for microbial growth. *International Journal of Food Microbiology*, 96(3):289–300.
- Morales, K.H., I. J. C. C.-J. and Ryan, L. (2006). Model averaging with applications to benchmark dose estimation for arsenic in drinking water. *Journal of the American Statistical Association*, 101:9–17.
- Moy, G. G. (2013). *Total Diet Studies*. Springer-Verlag, New York.
- Namata, H., Aerts, M., Faes, C., and Teunis, P. (2008). Model averaging in microbial risk assessment using fractional polynomials. *Risk Analysis*, 28(4):891–905.
- Nysen, R., Aerts, M., and Faes, C. (2012). Testing goodness of fit of parametric models for censored data. *Statistics in Medicine*, 31:2374–2385.
- Nysen, R., Faes, C., and Aerts, M. (2016a). Generalized profiling with monotonicity constraints. Submitted for publication.
- Nysen, R., Faes, C., Ferrari, P., Verger, P., and Aerts, M. (2015). Parametric and semi-nonparametric model strategies for the estimation of distributions of chemical contaminant data. *Environmental and Ecological Statistics*, 22(2):423–444.
- Nysen, R., Faes, C., Ferrari, P., Verger, P., and Aerts, M. (2016b). Model averaging quantiles from data censored by a limit of detection. *Biometrical Journal*, 58(2):331–356. Special Issue.

- Pearl, R. and Reed, Lowell, J. (1920). On the rate of growth of the population of the united states since 1790 and its mathematical representation. *Proceedings of the National Academy of Sciences*, 6(6):275–288.
- Ramsay, J. O., Hooker, G., Campbell, D., and Cao, J. (2007). Parameter estimation for differential equations: a generalized smoothing approach. *Journal of the Royal Statistical Society B*, 69:741–796.
- Ren, J.-J. (2003). Goodness of fit tests with interval censored data. *Scandinavian Journal of Statistics. Theory and Applications*, 30(1):211–226.
- Royston, P. and Altman, D. G. (1994). Regression using fractional polynomials of continuous covariates: Parsimonious parametric modelling. *Applied Statistics*, 43(3):429–467.
- Schmoyer, R., Beauchamp, J., Brandt, C., and Hoffman, F. (1996). Difficulties with the lognormal model in mean estimation and testing. *Environmental and Ecological Statistics*, 3:81–97.
- Schwarz, G. (1978). Estimating the dimension of a model. *The Annals of Statistics*, 6(2):461–464.
- Shorack, G. R. and Wellner, J. A. (1986). *Empirical processes with applications to statistics*. Wiley Series in Probability and Mathematical Statistics: Probability and Mathematical Statistics. John Wiley & Sons Inc., New York.
- Turnbull, B. W. (1976). The empirical distribution function with arbitrarily grouped, censored and truncated data. *Journal of the Royal Statistical Society. Series B (Methodological)*, 38(3):290–295.
- Verhulst, P.-F. (1838). Notice sur la loi que la population poursuit dans son accroissement. *Correspondance mathématique et physique*, 10:113–121.
- Wheeler, M. W. and Bailer, A. J. (2007). Properties of model-averaged bmdls: a study of model averaging in dichotomous response risk estimation. *Risk Analysis*, 27(3):659–670.
- Wheeler, M. W. and Bailer, A. J. (2009). Comparing model averaging with other model selection strategies for benchmark dose estimation. *Environmental and Ecological Statistics*, 16(1):37–51.
- Yin, G. (2009). Bayesian goodness-of-fit test for censored data. *Journal of Statistical Planning and Inference*, 139(4):1474–1483.

- Zhang, M. and Davidian, M. (2008). "Smooth" semiparametric regression analysis for arbitrarily censored time-to-event data. *Biometrics*, 64(2):567–669.

Appendix

Appendix **A**

Model averaging distribution functions

In Chapter 5 we showed the estimates of the distribution function for Cadmium data 1 and Cadmium data 2. We compared estimates based on the parametric models to estimates based on the semiNP models and to the model averages. The results for estimating the density function are presented here in Tables A.1 and A.2.

Tables A.3-A.32 give the results of the simulation study as described in Chapter 5 for estimating the value of the distribution function, while tables A.33-A.62 give the results of the simulation study for estimating the value of the density function.

Table A.1: Cadmium data 1. Estimates $\hat{f}(y)$ of parametric models and model averaged value. Model averaging based on parametric models only (\mathcal{M}_P), on parametric models and best SemiNP ($\mathcal{M}_P \cup \{\hat{M}_S\}$), or on all fitted models ($\mathcal{M}_P \cup \mathcal{M}_S$). Corresponding weights are given in Table 5.1.

Distribution	$\hat{f}(q_{LN,0.05})$ 2.77E-04	$\hat{f}(\min(LOD))$ 1.00E-03	$\hat{f}(q_{LN,0.25})$ 2.13E-03	$\hat{f}(\overline{LOD})$ 7.38E-03
GenGam	201.614(106.07)	98.297(45.20)	59.817(23.79)	22.556(5.39)
Gamma	184.542(10.73)	66.865(3.06)	36.684(1.96)	13.528(1.07)
Weibull	208.840(26.42)	89.814(7.11)	52.636(3.32)	19.853(1.43)
Log-skew-t	146.705(28.83)	61.151(13.22)	37.160(8.13)	16.559(3.29)
Log-t	172.870(52.66)	109.888(14.28)	70.905(5.74)	25.859(2.62)
Log-skew-n	214.583(34.45)	94.958(7.60)	55.767(5.27)	21.167(2.73)
Log-normal	177.009(52.86)	111.278(13.59)	71.085(5.59)	25.653(2.53)
SemiNP1	236.645(80.05)	223.457(22.26)	88.180(13.11)	0.066(0.16)
SemiNP2	360.827(151.12)	154.418(51.81)	52.569(21.85)	11.787(4.58)
SemiNP3	323.138(142.56)	165.576(38.23)	59.522(21.59)	10.654(3.98)
SemiNP4	253.960(134.37)	187.886(31.93)	71.389(22.59)	9.255(3.75)
SemiNP5	168.923(136.86)	214.446(38.18)	85.608(29.92)	7.655(3.82)
SemiNP6	70.131(82.31)	228.179(44.88)	111.873(37.79)	5.903(3.60)
SemiNP7	87.179(90.96)	226.676(41.10)	106.682(34.92)	6.128(3.58)
\mathcal{M}_P	152.581(34.01)	64.921(16.19)	39.401(9.81)	17.123(3.59)
$\mathcal{M}_P \cup \{\hat{M}_S\}$	311.973(144.30)	158.987(42.48)	58.205(21.61)	11.078(4.19)
$\mathcal{M}_P \cup \mathcal{M}_S$	239.863(155.28)	185.822(45.05)	73.589(29.71)	9.289(4.27)

Table A.2: Cadmium data 2. Estimates $\hat{f}(y)$ of parametric models and model averaged value. Model averaging based on parametric models only (\mathcal{M}_P), on parametric models and best SemiNP ($\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$), or on all fitted models ($\mathcal{M}_P \cup \mathcal{M}_S$). Corresponding weights are given in Table 5.3.

Distribution	$\hat{f}(q_{LN,0.05})$ $\hat{F}(0.002)$	$\hat{f}(\min(\text{LOD}))$ $\hat{F}(0.003)$	$\hat{f}(q_{LN,0.25})$ $\hat{F}(0.004)$	$\hat{f}(\overline{\text{LOD}})$ $\hat{F}(0.015)$
GenGam	21.043 (3.790)	18.350 (2.833)	16.213 (2.287)	9.701 (1.178)
Gamma	21.138 (3.346)	17.706 (2.368)	15.191 (1.731)	8.627 (0.553)
Weibull	21.157 (3.658)	18.301 (2.751)	16.076 (2.109)	9.525 (0.687)
Log-skew-t	23.481 (4.460)	20.317 (3.005)	17.668 (2.168)	9.590 (1.195)
Log-t	19.610 (5.344)	20.164 (4.289)	19.697 (3.310)	12.709 (0.951)
Log-skew-n	23.701 (4.479)	20.622 (3.006)	17.981 (2.137)	9.744 (1.071)
Log-normal	19.961 (5.408)	20.572 (4.252)	20.069 (3.220)	12.760 (0.931)
SemiNP1	20.596 (5.211)	20.523 (4.025)	19.621 (3.034)	12.272 (0.875)
SemiNP2	20.769 (5.118)	20.446 (3.933)	19.408 (2.963)	12.083 (0.854)
SemiNP3	20.844 (5.064)	20.390 (3.883)	19.284 (2.925)	11.981 (0.844)
SemiNP4	20.884 (5.029)	20.349 (3.851)	19.202 (2.901)	11.917 (0.837)
SemiNP5	20.909 (5.004)	20.319 (3.829)	19.143 (2.884)	11.872 (0.833)
SemiNP6	20.925 (4.986)	20.295 (3.813)	19.099 (2.872)	11.839 (0.829)
SemiNP7	27.072 (13.875)	37.428 (9.616)	35.888 (7.240)	4.668 (1.519)
\mathcal{M}_P	21.726 (3.947)	18.728 (2.934)	16.361 (2.281)	9.415 (0.949)
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	23.247 (7.143)	24.048 (9.003)	21.916 (8.734)	8.065 (2.201)
$\mathcal{M}_P \cup \mathcal{M}_S$	23.214 (7.118)	24.001 (8.936)	21.884 (8.656)	8.119 (2.209)

Table A.3: Simulation study. Sample from log-normal distribution of size 100 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	0.347 (+)	2.243	2.589 (6)	3.186	1.482 (+)	3.592	5.074 (8)	5.125
Gamma	20.625 (+)	3.662	24.286 (11)	5.351	41.595 (+)	6.749	48.344 (11)	7.660
Weibull	30.418 (+)	3.878	34.297 (12)	4.680	44.392 (+)	5.506	49.898 (12)	5.861
Log-skew-t	0.016 (-)	2.662	2.679 (9)	3.405	0.184 (+)	5.624	5.808 (10)	6.448
Log-t	0.012 (-)	2.096	2.108 (1)	2.387	0.000 (+)	2.593	2.593 (1)	3.044
Log-skew-n	0.008 (-)	2.817	2.825 (10)	2.955	0.121 (-)	4.153	4.274 (4)	4.004
Log-normal	0.008 (-)	2.295	2.303 (2)	2.458	0.004 (-)	2.801	2.805 (2)	3.032
Best Parametric	0.015 (-)	2.527	2.543 (4)	2.528	0.060 (+)	5.732	5.792 (3)	3.389
Best SemiNP	0.028 (-)	2.627	2.655 (7)	2.496	0.000 (-)	4.124	4.124 (3)	4.859
\mathcal{M}_P	0.000 (+)	2.453	2.453 (3)	2.943	0.161 (+)	4.413	4.574 (5)	5.082
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.002 (-)	2.543	2.545 (5)	2.953	0.156 (+)	4.764	4.920 (7)	5.764
$\mathcal{M}_P \cup \mathcal{M}_S$	0.011 (-)	2.658	2.669 (8)	2.977	0.120 (+)	4.752	4.873 (6)	6.836

Table A.4: Simulation study. Sample from log-normal distribution of size 100 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	0.713 (-)	11.714	12.427 (3)	12.286	0.045 (-)	13.225	13.270 (2)	13.752
Gamma	1.899 (-)	6.751	8.650 (1)	11.645	1.022 (+)	10.341	11.363 (1)	14.049
Weibull	0.965 (+)	8.933	9.898 (2)	12.258	6.610 (+)	11.406	18.016 (12)	13.724
Log-skew-t	0.478 (-)	14.217	14.695 (12)	13.641	0.300 (-)	14.963	15.263 (8)	14.405
Log-t	0.388 (-)	13.851	14.239 (11)	12.999	0.329 (-)	15.037	15.365 (10)	15.401
Log-skew-n	0.114 (-)	13.786	13.899 (7)	12.813	0.027 (-)	15.647	15.674 (11)	13.980
Log-normal	0.036 (-)	13.556	13.592 (4)	12.220	0.034 (-)	14.747	14.780 (4)	13.728
Best Parametric	0.083 (-)	13.950	14.033 (9)	12.417	0.043 (-)	15.055	15.098 (7)	13.835
Best SemiNP	0.019 (-)	14.125	14.143 (10)	12.527	0.056 (-)	15.233	15.289 (9)	15.510
\mathcal{M}_P	0.218 (-)	13.446	13.663 (5)	12.889	0.062 (-)	14.620	14.681 (3)	14.315
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.157 (-)	13.707	13.865 (6)	13.111	0.061 (-)	14.771	14.831 (5)	14.952
$\mathcal{M}_P \cup \mathcal{M}_S$	0.078 (-)	13.825	13.904 (8)	13.494	0.061 (-)	14.779	14.841 (6)	17.806

Table A.5: Simulation study. Sample from log-normal distribution of size 200 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	0.314 (+)	1.111	1.426 (10)	1.660	1.135 (+)	1.616	2.751 (9)	3.119
Gamma	22.309 (+)	1.937	24.246 (11)	2.737	44.354 (+)	3.378	47.732 (11)	3.904
Weibull	32.859 (+)	2.092	34.951 (12)	2.382	47.423 (+)	2.793	50.216 (12)	2.972
Log-skew-t	0.010 (-)	1.315	1.325 (5)	1.565	0.131 (+)	2.624	2.755 (10)	3.024
Log-t	0.007 (-)	1.036	1.043 (1)	1.195	0.001 (+)	1.250	1.250 (1)	1.479
Log-skew-n	0.004 (-)	1.382	1.386 (9)	1.478	0.026 (-)	1.819	1.845 (4)	2.068
Log-normal	0.005 (-)	1.128	1.133 (2)	1.232	0.002 (-)	1.288	1.290 (2)	1.506
Best Parametric	0.013 (-)	1.320	1.333 (7)	1.262	0.004 (+)	2.165	2.169 (8)	1.749
Best SemiNP	0.012 (-)	1.351	1.363 (8)	1.272	0.000 (+)	1.748	1.748 (3)	2.388
\mathcal{M}_P	0.001 (-)	1.209	1.210 (3)	1.424	0.036 (+)	1.893	1.930 (5)	2.332
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.003 (-)	1.278	1.281 (4)	1.434	0.030 (+)	1.953	1.983 (7)	2.637
$\mathcal{M}_P \cup \mathcal{M}_S$	0.006 (-)	1.321	1.327 (6)	1.470	0.028 (+)	1.937	1.965 (6)	3.017

Table A.6: Simulation study. Sample from log-normal distribution of size 200 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	√var	bias ² (sign)	var	mse(rank)	√var
GenGam	0.463 (-)	5.712	6.175 (3)	6.151	0.015 (-)	6.257	6.272 (2)	6.913
Gamma	1.573 (-)	3.200	4.773 (1)	5.858	1.385 (+)	4.858	6.243 (1)	7.071
Weibull	1.489 (+)	4.471	5.960 (2)	6.157	7.963 (+)	5.508	13.471 (12)	6.892
Log-skew-t	0.314 (-)	6.537	6.851 (12)	6.674	0.208 (-)	6.841	7.049 (10)	7.161
Log-t	0.250 (-)	6.385	6.635 (10)	6.511	0.162 (-)	7.026	7.188 (11)	7.273
Log-skew-n	0.062 (-)	6.436	6.498 (7)	6.397	0.015 (-)	6.950	6.965 (8)	6.977
Log-normal	0.016 (-)	6.402	6.418 (4)	6.150	0.011 (-)	6.815	6.826 (3)	6.913
Best Parametric	0.044 (-)	6.444	6.487 (6)	6.247	0.032 (-)	6.957	6.990 (9)	6.961
Best SemiNP	0.003 (-)	6.838	6.841 (11)	6.326	0.024 (-)	6.809	6.833 (5)	8.030
\mathcal{M}_P	0.114 (-)	6.339	6.453 (5)	6.449	0.047 (-)	6.824	6.871 (7)	7.094
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.068 (-)	6.501	6.569 (8)	6.593	0.049 (-)	6.798	6.847 (6)	7.391
$\mathcal{M}_P \cup \mathcal{M}_S$	0.025 (-)	6.558	6.583 (9)	6.790	0.046 (-)	6.783	6.829 (4)	8.300

Table A.7: Simulation study. Sample from log-normal distribution of size 500 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	√var	bias ² (sign)	var	mse(rank)	√var
GenGam	0.258 (+)	0.471	0.729 (10)	0.606	0.860 (+)	0.715	1.575 (10)	0.855
Gamma	22.919 (+)	0.818	23.737 (11)	1.104	45.135 (+)	1.484	46.619 (11)	1.570
Weibull	33.886 (+)	0.878	34.765 (12)	0.959	48.557 (+)	1.199	49.756 (12)	1.193
Log-skew-t	0.004 (-)	0.545	0.549 (6)	0.622	0.073 (+)	1.046	1.118 (9)	1.215
Log-t	0.005 (-)	0.459	0.464 (1)	0.482	0.000 (+)	0.556	0.556 (1)	0.589
Log-skew-n	0.000 (-)	0.562	0.562 (8)	0.576	0.032 (-)	0.788	0.820 (7)	0.797
Log-normal	0.004 (-)	0.485	0.489 (2)	0.493	0.003 (-)	0.581	0.583 (2)	0.598
Best Parametric	0.003 (-)	0.524	0.527 (4)	0.509	0.000 (+)	0.884	0.884 (8)	0.669
Best SemiNP	0.004 (-)	0.561	0.565 (9)	0.516	0.000 (-)	0.658	0.658 (3)	1.145
\mathcal{M}_P	0.000 (-)	0.511	0.511 (3)	0.562	0.006 (+)	0.757	0.762 (6)	0.869
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.001 (-)	0.530	0.531 (5)	0.568	0.004 (+)	0.738	0.742 (4)	1.011
$\mathcal{M}_P \cup \mathcal{M}_S$	0.001 (-)	0.548	0.550 (7)	0.589	0.005 (+)	0.738	0.742 (5)	1.116

Table A.8: Simulation study. Sample from log-normal distribution of size 500 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	√var	bias ² (sign)	var	mse(rank)	√var
GenGam	0.414 (-)	2.204	2.619 (5)	2.450	0.018 (-)	2.604	2.622 (1)	2.765
Gamma	1.437 (-)	1.226	2.663 (6)	2.350	1.511 (+)	1.991	3.501 (11)	2.835
Weibull	1.778 (+)	1.747	3.525 (12)	2.467	8.559 (+)	2.224	10.783 (12)	2.759
Log-skew-t	0.180 (-)	2.590	2.770 (11)	2.665	0.132 (-)	2.780	2.912 (9)	2.846
Log-t	0.131 (-)	2.592	2.723 (10)	2.595	0.084 (-)	2.889	2.973 (10)	2.906
Log-skew-n	0.034 (-)	2.521	2.555 (2)	2.548	0.011 (-)	2.832	2.843 (8)	2.777
Log-normal	0.007 (-)	2.478	2.485 (1)	2.470	0.006 (-)	2.796	2.802 (2)	2.773
Best Parametric	0.025 (-)	2.582	2.607 (4)	2.496	0.018 (-)	2.806	2.823 (5)	2.784
Best SemiNP	0.000 (-)	2.719	2.719 (9)	2.539	0.010 (-)	2.795	2.805 (3)	3.928
\mathcal{M}_P	0.062 (-)	2.501	2.562 (3)	2.580	0.030 (-)	2.794	2.824 (6)	2.827
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.031 (-)	2.649	2.680 (7)	2.646	0.031 (-)	2.795	2.826 (7)	3.091
$\mathcal{M}_P \cup \mathcal{M}_S$	0.011 (-)	2.675	2.685 (8)	2.726	0.028 (-)	2.790	2.817 (4)	3.386

Table A.9: Simulation study. Sample from gamma distribution of size 100 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	var	bias ² (sign)	var	mse(rank)	var
GenGam	0.765 (-)	30.332	31.096 (7)	14.625	0.000 (+)	24.860	24.860 (4)	25.551
Gamma	0.188 (-)	12.987	13.175 (1)	13.564	0.077 (-)	23.117	23.194 (1)	23.926
Weibull	5.926 (+)	20.662	26.588 (4)	16.206	12.705 (-)	23.565	36.270 (10)	21.885
Log-skew-t	0.573 (+)	18.311	18.884 (2)	18.264	0.031 (-)	24.514	24.545 (3)	26.066
Log-t	0.496 (-)	51.201	51.698 (10)	28.185	23.606 (-)	27.600	51.206 (12)	24.526
Log-skew-n	75.618 (+)	20.132	95.750 (11)	13.403	0.214 (-)	24.961	25.174 (8)	25.293
Log-normal	122.501 (+)	16.727	139.229 (12)	15.935	22.429 (-)	27.594	50.022 (11)	24.008
Best Parametric	0.445 (-)	31.836	32.281 (8)	13.966	0.124 (-)	24.258	24.381 (2)	23.763
Best SemiNP	0.824 (+)	36.494	37.319 (9)	18.507	1.116 (-)	34.716	35.832 (9)	35.027
\mathcal{M}_P	0.149 (-)	26.352	26.501 (3)	17.251	0.293 (-)	24.606	24.898 (5)	25.410
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.263 (-)	26.637	26.900 (5)	17.703	0.173 (-)	24.896	25.070 (6)	26.419
$\mathcal{M}_P \cup \mathcal{M}_S$	0.301 (-)	26.861	27.163 (6)	17.899	0.148 (-)	25.003	25.151 (7)	26.999

Table A.10: Simulation study. Sample from gamma distribution of size 100 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	var	bias ² (sign)	var	mse(rank)	var
GenGam	1.030 (-)	46.272	47.302 (9)	16.598	0.027 (-)	19.672	19.698 (2)	20.369
Gamma	0.085 (-)	12.534	12.619 (1)	13.063	0.037 (-)	19.855	19.892 (3)	20.204
Weibull	20.042 (+)	17.231	37.273 (4)	15.899	0.002 (-)	22.872	22.874 (9)	20.631
Log-skew-t	0.529 (+)	17.380	17.909 (2)	17.220	0.000 (+)	20.067	20.067 (6)	21.799
Log-t	5.210 (+)	39.952	45.162 (8)	24.952	5.145 (+)	22.346	27.490 (11)	20.043
Log-skew-n	64.726 (+)	15.731	80.458 (11)	12.361	0.180 (+)	19.011	19.190 (1)	19.380
Log-normal	99.533 (+)	9.472	109.005 (12)	15.354	5.626 (+)	22.080	27.707 (12)	19.526
Best Parametric	0.576 (-)	46.758	47.334 (10)	13.471	0.008 (-)	19.973	19.980 (5)	20.121
Best SemiNP	6.458 (+)	33.942	40.400 (7)	18.151	0.217 (-)	24.907	25.124 (10)	25.953
\mathcal{M}_P	0.175 (-)	36.782	36.956 (3)	18.804	0.000 (+)	19.938	19.938 (4)	20.347
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.198 (-)	37.244	37.442 (5)	19.138	0.022 (-)	20.163	20.186 (7)	21.069
$\mathcal{M}_P \cup \mathcal{M}_S$	0.197 (-)	37.537	37.734 (6)	19.311	0.036 (-)	20.338	20.374 (8)	21.328

Table A.11: Simulation study. Sample from gamma distribution of size 200 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	var	bias ² (sign)	var	mse(rank)	var
GenGam	0.099 (-)	7.581	7.680 (2)	7.280	0.004 (-)	12.621	12.625 (3)	12.831
Gamma	0.115 (-)	6.935	7.050 (1)	6.806	0.034 (-)	12.066	12.101 (1)	12.017
Weibull	6.571 (+)	11.246	17.818 (8)	8.140	12.260 (-)	12.284	24.544 (10)	10.994
Log-skew-t	0.704 (+)	9.415	10.119 (7)	9.243	0.052 (-)	12.439	12.491 (2)	12.929
Log-t	0.695 (-)	24.614	25.309 (9)	14.509	23.084 (-)	14.246	37.331 (12)	12.073
Log-skew-n	39.619 (+)	11.788	51.408 (11)	5.819	8.404 (-)	11.092	19.497 (9)	12.388
Log-normal	126.980 (+)	8.693	135.674 (12)	7.953	21.952 (-)	14.240	36.192 (11)	12.090
Best Parametric	0.001 (-)	8.224	8.224 (6)	6.912	0.055 (-)	12.915	12.970 (7)	11.999
Best SemiNP	4.648 (+)	32.432	37.079 (10)	9.094	2.173 (-)	17.317	19.490 (8)	20.471
\mathcal{M}_P	0.008 (+)	7.834	7.842 (3)	8.057	0.121 (-)	12.601	12.722 (4)	12.804
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.005 (+)	7.896	7.900 (4)	8.126	0.102 (-)	12.738	12.840 (5)	13.363
$\mathcal{M}_P \cup \mathcal{M}_S$	0.003 (+)	7.919	7.922 (5)	8.144	0.102 (-)	12.761	12.862 (6)	13.429

Table A.12: Simulation study. Sample from gamma distribution of size 200 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	var	bias ² (sign)	var	mse(rank)	var
GenGam	0.091 (-)	8.701	8.791 (6)	8.308	0.017 (-)	10.323	10.339 (6)	10.205
Gamma	0.071 (-)	6.672	6.742 (1)	6.536	0.023 (-)	10.271	10.295 (5)	10.139
Weibull	20.930 (+)	9.306	30.237 (9)	7.957	0.000 (+)	11.820	11.820 (8)	10.360
Log-skew-t	0.674 (+)	8.931	9.605 (7)	8.640	0.022 (+)	10.349	10.371 (7)	10.992
Log-t	5.308 (+)	18.045	23.353 (8)	12.525	5.463 (+)	11.428	16.891 (10)	9.884
Log-skew-n	30.653 (+)	8.677	39.330 (10)	5.159	2.982 (+)	14.195	17.177 (11)	9.742
Log-normal	100.255 (+)	4.851	105.106 (12)	7.655	5.904 (+)	11.290	17.194 (12)	9.807
Best Parametric	0.000 (-)	8.416	8.416 (5)	6.735	0.009 (-)	10.153	10.162 (2)	10.141
Best SemiNP	12.995 (+)	26.942	39.937 (11)	8.910	0.069 (-)	12.996	13.065 (9)	13.778
\mathcal{M}_P	0.010 (+)	7.962	7.972 (2)	8.152	0.001 (-)	10.145	10.146 (1)	10.264
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.008 (+)	8.019	8.027 (3)	8.196	0.007 (-)	10.223	10.231 (3)	10.437
$\mathcal{M}_P \cup \mathcal{M}_S$	0.008 (+)	8.056	8.065 (4)	8.214	0.010 (-)	10.225	10.235 (4)	10.476

Table A.13: Simulation study. Sample from gamma distribution of size 500 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	var	bias ² (sign)	var	mse(rank)	var
GenGam	0.003 (-)	3.011	3.014 (2)	2.905	0.006 (+)	4.770	4.775 (6)	5.161
Gamma	0.000 (-)	2.921	2.921 (1)	2.733	0.000 (+)	4.532	4.532 (1)	4.836
Weibull	8.375 (+)	4.496	12.870 (9)	3.272	11.037 (-)	4.658	15.695 (10)	4.429
Log-skew-t	0.986 (+)	3.990	4.976 (7)	3.700	0.020 (-)	4.794	4.814 (7)	5.146
Log-t	0.525 (-)	10.434	10.959 (8)	5.821	19.082 (-)	7.936	27.018 (12)	4.950
Log-skew-n	58.716 (+)	6.430	65.146 (11)	2.452	0.953 (-)	7.168	8.122 (8)	5.078
Log-normal	135.751 (+)	3.446	139.197 (12)	3.188	20.374 (-)	5.443	25.817 (11)	4.873
Best Parametric	0.001 (+)	3.159	3.160 (6)	2.805	0.001 (+)	4.709	4.710 (2)	4.897
Best SemiNP	10.259 (+)	27.962	38.221 (10)	3.578	2.278 (-)	6.816	9.094 (9)	7.378
\mathcal{M}_P	0.005 (+)	3.061	3.066 (4)	3.064	0.001 (-)	4.717	4.718 (3)	5.090
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.005 (+)	3.061	3.066 (5)	3.065	0.001 (-)	4.721	4.721 (5)	5.122
$\mathcal{M}_P \cup \mathcal{M}_S$	0.005 (+)	3.061	3.066 (3)	3.065	0.001 (-)	4.721	4.721 (4)	5.134

Table A.14: Simulation study. Sample from gamma distribution of size 500 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	var	bias ² (sign)	var	mse(rank)	var
GenGam	0.002 (-)	3.432	3.434 (6)	3.305	0.002 (+)	3.874	3.876 (5)	4.087
Gamma	0.001 (+)	2.785	2.785 (1)	2.610	0.001 (+)	3.848	3.849 (1)	4.066
Weibull	23.689 (+)	3.660	27.350 (9)	3.182	0.051 (+)	4.456	4.506 (8)	4.156
Log-skew-t	0.940 (+)	3.720	4.660 (7)	3.438	0.199 (+)	3.825	4.024 (7)	4.214
Log-t	6.021 (+)	7.170	13.190 (8)	4.947	7.398 (+)	5.385	12.784 (12)	3.959
Log-skew-n	46.452 (+)	5.367	51.819 (11)	2.200	1.007 (+)	4.526	5.533 (10)	3.894
Log-normal	103.973 (+)	1.979	105.951 (12)	3.060	6.924 (+)	4.278	11.202 (11)	3.931
Best Parametric	0.002 (+)	3.202	3.204 (5)	2.755	0.008 (+)	3.874	3.882 (6)	4.055
Best SemiNP	21.479 (+)	19.143	40.622 (10)	3.502	0.001 (+)	4.756	4.757 (9)	5.718
\mathcal{M}_P	0.006 (+)	3.072	3.079 (2)	3.160	0.027 (+)	3.829	3.856 (2)	4.103
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.006 (+)	3.073	3.079 (4)	3.160	0.026 (+)	3.830	3.856 (3)	4.109
$\mathcal{M}_P \cup \mathcal{M}_S$	0.006 (+)	3.073	3.079 (3)	3.161	0.026 (+)	3.833	3.859 (4)	4.110

Table A.15: Simulation study. Sample from 75% mixture distribution of size 100 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	2.936 (+)	3.029	5.966 (12)	3.834	11.003 (+)	5.140	16.143 (12)	5.515
Gamma	2.607 (+)	1.712	4.320 (11)	2.762	6.080 (+)	2.872	8.953 (10)	3.757
Weibull	1.946 (+)	1.644	3.589 (10)	2.036	3.438 (+)	2.185	5.623 (5)	2.469
Log-skew-t	1.664 (+)	1.548	3.212 (8)	2.980	6.712 (+)	3.749	10.461 (11)	5.997
Log-t	1.212 (-)	0.973	2.184 (1)	1.090	1.227 (-)	1.111	2.337 (1)	1.257
Log-skew-n	0.926 (+)	1.511	2.437 (3)	2.583	2.768 (+)	2.475	5.243 (4)	3.557
Log-normal	1.277 (-)	1.011	2.288 (2)	1.092	1.396 (-)	1.121	2.517 (2)	1.240
Best Parametric	0.956 (+)	1.608	2.564 (4)	2.578	4.485 (+)	4.276	8.761 (9)	4.057
Best SemiNP	1.158 (-)	2.398	3.556 (9)	1.630	1.710 (-)	3.227	4.937 (3)	5.743
\mathcal{M}_P	1.150 (+)	1.461	2.612 (5)	2.836	5.270 (+)	3.358	8.628 (8)	4.903
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.021 (+)	2.965	2.985 (6)	2.594	1.644 (+)	5.972	7.616 (7)	5.389
$\mathcal{M}_P \cup \mathcal{M}_S$	0.003 (+)	3.041	3.044 (7)	2.541	1.452 (+)	6.144	7.595 (6)	5.470

Table A.16: Simulation study. Sample from 75% mixture distribution of size 100 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	14.788 (-)	5.560	20.349 (8)	8.558	4.224 (-)	7.272	11.495 (2)	10.614
Gamma	15.909 (-)	4.716	20.625 (9)	8.193	7.161 (-)	6.888	14.049 (8)	9.823
Weibull	16.252 (-)	5.590	21.842 (10)	7.692	10.373 (-)	6.925	17.298 (9)	8.635
Log-skew-t	11.396 (-)	4.911	16.307 (4)	8.603	4.187 (-)	6.767	10.954 (1)	10.545
Log-t	16.534 (-)	8.215	24.749 (12)	8.504	17.079 (-)	8.774	25.853 (12)	9.162
Log-skew-n	11.614 (-)	4.995	16.609 (5)	8.433	5.098 (-)	7.129	12.227 (5)	10.266
Log-normal	14.486 (-)	8.256	22.742 (11)	8.243	15.707 (-)	8.865	24.573 (11)	9.058
Best Parametric	11.647 (-)	5.013	16.660 (6)	8.430	4.667 (-)	7.068	11.735 (3)	10.320
Best SemiNP	1.973 (-)	14.199	16.172 (3)	11.348	6.683 (-)	12.490	19.173 (10)	23.085
\mathcal{M}_P	12.142 (-)	5.021	17.163 (7)	8.523	4.930 (-)	6.965	11.895 (4)	10.400
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	5.653 (-)	9.745	15.398 (2)	10.695	3.919 (-)	8.800	12.719 (6)	12.047
$\mathcal{M}_P \cup \mathcal{M}_S$	5.188 (-)	10.095	15.283 (1)	10.827	3.904 (-)	8.848	12.752 (7)	12.303

Table A.17: Simulation study. Sample from 75% mixture distribution of size 200 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	1.808 (+)	1.728	3.536 (10)	1.878	9.306 (+)	3.455	12.760 (12)	2.894
Gamma	4.196 (+)	0.970	5.167 (12)	1.518	8.949 (+)	1.595	10.544 (11)	2.071
Weibull	3.672 (+)	0.978	4.650 (11)	1.140	5.911 (+)	1.263	7.175 (7)	1.384
Log-skew-t	2.333 (+)	0.910	3.243 (9)	1.596	8.304 (+)	2.126	10.430 (10)	2.984
Log-t	0.776 (-)	0.596	1.372 (1)	0.598	0.773 (-)	0.639	1.412 (1)	0.691
Log-skew-n	1.378 (+)	1.240	2.619 (6)	1.375	2.693 (+)	2.594	5.286 (4)	1.786
Log-normal	0.858 (-)	0.609	1.467 (2)	0.597	0.945 (-)	0.658	1.603 (2)	0.679
Best Parametric	1.735 (+)	0.934	2.669 (7)	1.433	6.485 (+)	2.385	8.870 (9)	2.374
Best SemiNP	0.728 (-)	1.394	2.122 (3)	0.907	1.505 (-)	1.657	3.162 (3)	9.550
\mathcal{M}_P	1.774 (+)	0.914	2.688 (8)	1.526	6.694 (+)	2.051	8.746 (8)	2.656
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.004 (+)	2.379	2.383 (5)	1.419	0.984 (+)	6.002	6.985 (5)	3.881
$\mathcal{M}_P \cup \mathcal{M}_S$	0.001 (-)	2.354	2.354 (4)	1.387	0.887 (+)	6.099	6.986 (6)	3.911

Table A.18: Simulation study. Sample from 75% mixture distribution of size 200 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	10.921 (-)	2.767	13.688 (11)	4.349	2.692 (-)	4.188	6.880 (7)	5.463
Gamma	9.878 (-)	2.542	12.419 (9)	4.312	2.925 (-)	3.702	6.627 (6)	5.186
Weibull	8.663 (-)	3.146	11.808 (8)	4.105	4.210 (-)	3.828	8.038 (9)	4.614
Log-skew-t	7.279 (-)	2.651	9.930 (4)	4.439	1.555 (-)	3.752	5.307 (1)	5.507
Log-t	10.246 (-)	4.458	14.704 (12)	4.454	10.336 (-)	4.936	15.272 (12)	4.820
Log-skew-n	7.591 (-)	2.980	10.571 (7)	4.361	2.833 (-)	4.364	7.197 (8)	5.286
Log-normal	8.640 (-)	4.565	13.205 (10)	4.354	9.394 (-)	4.909	14.303 (11)	4.801
Best Parametric	7.334 (-)	2.699	10.033 (5)	4.385	1.752 (-)	3.943	5.695 (2)	5.429
Best SemiNP	0.032 (-)	8.495	8.527 (3)	6.092	2.225 (-)	8.466	10.691 (10)	22.772
\mathcal{M}_P	7.421 (-)	2.724	10.145 (6)	4.403	1.840 (-)	3.896	5.736 (3)	5.455
$\mathcal{M}_P \cup \{\tilde{\mathcal{M}}_S\}$	1.197 (-)	6.691	7.888 (2)	6.057	0.863 (-)	5.470	6.333 (5)	8.312
$\mathcal{M}_P \cup \mathcal{M}_S$	0.953 (-)	6.831	7.783 (1)	6.125	0.838 (-)	5.491	6.329 (4)	8.242

Table A.19: Simulation study. Sample from 75% mixture distribution of size 500 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	1.183 (+)	0.559	1.742 (6)	0.698	7.398 (+)	1.464	8.861 (10)	1.159
Gamma	5.148 (+)	0.381	5.528 (12)	0.635	10.507 (+)	0.641	11.148 (12)	0.864
Weibull	4.755 (+)	0.388	5.143 (11)	0.481	7.373 (+)	0.505	7.878 (7)	0.583
Log-skew-t	2.614 (+)	0.352	2.966 (10)	0.640	8.512 (+)	0.917	9.429 (11)	1.277
Log-t	0.624 (-)	0.250	0.875 (1)	0.251	0.677 (-)	0.264	0.941 (1)	0.284
Log-skew-n	2.099 (+)	0.346	2.445 (7)	0.588	5.112 (+)	0.573	5.685 (4)	0.817
Log-normal	0.657 (-)	0.254	0.911 (2)	0.251	0.750 (-)	0.264	1.014 (2)	0.282
Best Parametric	2.208 (+)	0.367	2.575 (8)	0.600	7.062 (+)	1.069	8.131 (9)	0.998
Best SemiNP	0.032 (-)	0.712	1.107 (3)	0.402	1.131 (-)	1.055	2.186 (3)	2.018
\mathcal{M}_P	2.271 (+)	0.353	2.624 (9)	0.618	7.142 (+)	0.916	8.059 (8)	1.122
$\mathcal{M}_P \cup \{\tilde{\mathcal{M}}_S\}$	0.029 (-)	1.429	1.457 (5)	0.571	0.413 (+)	5.856	6.268 (6)	2.223
$\mathcal{M}_P \cup \mathcal{M}_S$	0.046 (-)	1.362	1.408 (4)	0.577	0.395 (+)	5.872	6.267 (5)	2.375

Table A.20: Simulation study. Sample from 75% mixture distribution of size 500 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	8.852 (-)	1.096	9.949 (12)	1.752	2.187 (-)	1.666	3.853 (9)	2.193
Gamma	7.189 (-)	0.944	8.133 (10)	1.772	1.470 (-)	1.422	2.892 (7)	2.128
Weibull	5.600 (-)	1.179	6.778 (8)	1.698	2.100 (-)	1.453	3.554 (8)	1.906
Log-skew-t	5.281 (-)	1.012	6.293 (4)	1.803	0.724 (-)	1.499	2.223 (1)	2.243
Log-t	6.391 (-)	1.757	8.148 (11)	1.816	6.896 (-)	1.868	8.764 (12)	1.984
Log-skew-n	5.331 (-)	1.032	6.363 (7)	1.786	1.032 (-)	1.514	2.546 (6)	2.191
Log-normal	5.864 (-)	1.768	7.632 (9)	1.797	6.528 (-)	1.884	8.412 (11)	1.982
Best Parametric	5.316 (-)	1.031	6.347 (6)	1.789	0.829 (-)	1.546	2.375 (5)	2.217
Best SemiNP	0.077 (+)	4.105	4.182 (3)	2.502	1.027 (-)	4.058	5.085 (10)	6.089
\mathcal{M}_P	5.314 (-)	1.027	6.340 (5)	1.793	0.826 (-)	1.527	2.353 (2)	2.227
$\mathcal{M}_P \cup \{\tilde{\mathcal{M}}_S\}$	0.024 (-)	3.928	3.952 (2)	2.676	0.106 (-)	2.257	2.363 (4)	5.104
$\mathcal{M}_P \cup \mathcal{M}_S$	0.007 (-)	3.885	3.892 (1)	2.701	0.102 (-)	2.260	2.362 (3)	5.395

Table A.21: Simulation study. Sample from 90% mixture distribution of size 100 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	0.195 (+)	1.824	2.018 (2)	3.181	3.439 (+)	5.291	8.730 (6)	6.285
Gamma	9.658 (+)	2.525	12.182 (11)	4.175	20.351 (+)	4.556	24.907 (12)	5.853
Weibull	11.090 (+)	2.570	13.660 (12)	3.414	17.172 (+)	3.616	20.789 (11)	4.234
Log-skew-t	0.514 (+)	3.010	3.524 (10)	3.690	4.629 (+)	6.323	10.952 (10)	6.521
Log-t	0.338 (-)	1.609	1.948 (1)	1.827	0.245 (-)	1.990	2.235 (1)	2.218
Log-skew-n	0.328 (+)	2.933	3.261 (5)	3.335	1.690 (+)	6.253	7.944 (4)	4.449
Log-normal	0.370 (-)	1.670	2.040 (3)	1.836	0.323 (-)	2.014	2.337 (2)	2.221
Best Parametric	0.091 (+)	3.273	3.364 (7)	2.608	2.790 (+)	7.696	10.486 (9)	3.702
Best SemiNP	0.646 (-)	2.765	3.411 (9)	2.129	0.679 (-)	3.903	4.583 (3)	7.522
\mathcal{M}_P	0.252 (+)	2.653	2.905 (4)	3.339	3.316 (+)	5.445	8.761 (8)	5.803
$\mathcal{M}_P \cup \{\tilde{\mathcal{M}}_S\}$	0.001 (-)	3.350	3.351 (6)	3.221	1.346 (+)	7.405	8.751 (7)	6.938
$\mathcal{M}_P \cup \mathcal{M}_S$	0.036 (-)	3.371	3.407 (8)	3.081	1.016 (+)	7.492	8.508 (5)	7.195

Table A.22: Simulation study. Sample from 90% mixture distribution of size 100 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	11.094 (-)	8.435	19.529 (12)	10.341	5.105 (-)	9.882	14.986 (9)	12.117
Gamma	10.585 (-)	5.649	16.234 (4)	10.155	1.783 (-)	8.675	10.458 (2)	12.275
Weibull	4.851 (-)	7.105	11.956 (1)	10.283	0.910 (-)	9.124	10.034 (1)	11.586
Log-skew-t	10.007 (-)	8.061	18.069 (10)	10.527	3.877 (-)	10.015	13.892 (3)	12.393
Log-t	8.246 (-)	10.587	18.833 (11)	10.706	7.621 (-)	11.669	19.290 (12)	11.829
Log-skew-n	9.783 (-)	8.095	17.878 (9)	10.308	4.537 (-)	10.230	14.767 (7)	12.067
Log-normal	7.125 (-)	10.637	17.762 (8)	10.445	6.925 (-)	11.802	18.727 (11)	11.692
Best Parametric	8.885 (-)	8.658	17.544 (6)	10.217	4.137 (-)	10.534	14.670 (5)	11.789
Best SemiNP	1.495 (-)	14.437	15.933 (3)	12.608	3.702 (-)	14.244	17.946 (10)	20.802
\mathcal{M}_P	9.300 (-)	8.400	17.700 (7)	10.436	4.227 (-)	9.997	14.224 (4)	12.197
$\mathcal{M}_P \cup \{\tilde{\mathcal{M}}_S\}$	4.343 (-)	11.928	16.270 (5)	12.573	3.021 (-)	11.674	14.695 (6)	14.603
$\mathcal{M}_P \cup \mathcal{M}_S$	3.398 (-)	12.161	15.560 (2)	13.021	3.025 (-)	11.822	14.847 (8)	15.735

Table A.23: Simulation study. Sample from 90% mixture distribution of size 200 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	0.176 (+)	0.927	1.103 (3)	1.553	2.059 (+)	2.092	4.151 (5)	2.837
Gamma	12.604 (+)	1.415	14.019 (11)	2.228	25.473 (+)	2.451	27.924 (12)	3.123
Weibull	15.262 (+)	1.495	16.757 (12)	1.840	22.816 (+)	2.011	24.827 (11)	2.277
Log-skew-t	0.160 (+)	1.436	1.597 (7)	1.764	2.775 (+)	3.363	6.139 (10)	3.371
Log-t	0.151 (-)	0.870	1.020 (1)	0.961	0.091 (-)	1.016	1.106 (1)	1.166
Log-skew-n	0.097 (+)	1.443	1.540 (6)	1.645	0.601 (+)	3.117	3.717 (4)	2.209
Log-normal	0.179 (-)	0.904	1.082 (2)	0.969	0.149 (-)	1.040	1.189 (2)	1.165
Best Parametric	0.016 (+)	1.503	1.519 (5)	1.306	1.429 (+)	4.058	5.488 (9)	2.171
Best SemiNP	0.257 (-)	1.636	1.893 (10)	1.217	0.259 (-)	2.080	2.339 (3)	6.849
\mathcal{M}_P	0.038 (+)	1.282	1.320 (4)	1.566	1.700 (+)	3.392	5.092 (6)	3.091
$\mathcal{M}_P \cup \{\tilde{\mathcal{M}}_S\}$	0.061 (-)	1.735	1.795 (9)	1.493	0.382 (+)	4.872	5.254 (8)	5.112
$\mathcal{M}_P \cup \mathcal{M}_S$	0.097 (-)	1.680	1.776 (8)	1.466	0.331 (+)	4.787	5.118 (7)	5.361

Table A.24: Simulation study. Sample from 90% mixture distribution of size 200 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	5.667 (-)	4.607	10.274 (11)	5.414	2.429 (-)	5.115	7.544 (7)	6.175
Gamma	5.891 (-)	2.894	8.785 (6)	5.250	0.163 (-)	4.364	4.526 (1)	6.348
Weibull	1.188 (-)	3.810	4.998 (1)	5.351	0.051 (+)	4.746	4.797 (2)	6.023
Log-skew-t	5.707 (-)	4.719	10.426 (12)	5.441	2.194 (-)	5.188	7.382 (3)	6.274
Log-t	4.100 (-)	5.356	9.456 (7)	5.551	3.537 (-)	5.988	9.526 (12)	6.119
Log-skew-n	5.197 (-)	4.812	10.009 (10)	5.392	2.389 (-)	5.329	7.718 (9)	6.178
Log-normal	3.253 (-)	5.467	8.720 (5)	5.418	3.072 (-)	5.969	9.041 (11)	6.074
Best Parametric	4.579 (-)	5.057	9.636 (8)	5.342	2.202 (-)	5.436	7.638 (8)	6.132
Best SemiNP	0.175 (-)	7.867	8.043 (3)	6.647	1.434 (-)	6.952	8.387 (10)	10.931
\mathcal{M}_P	4.792 (-)	4.894	9.685 (9)	5.459	2.124 (-)	5.329	7.454 (4)	6.266
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	0.919 (-)	7.409	8.328 (4)	6.906	1.109 (-)	6.393	7.503 (6)	8.435
$\mathcal{M}_P \cup \mathcal{M}_S$	0.598 (-)	7.399	7.997 (2)	7.094	1.116 (-)	6.372	7.488 (5)	9.046

Table A.25: Simulation study. Sample from 90% mixture distribution of size 500 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	0.189 (+)	0.400	0.589 (4)	0.596	1.622 (+)	0.904	2.526 (8)	1.289
Gamma	14.429 (+)	0.559	14.988 (11)	0.923	28.453 (+)	1.004	29.457 (12)	1.291
Weibull	17.924 (+)	0.598	18.521 (12)	0.767	26.293 (+)	0.814	27.107 (11)	0.947
Log-skew-t	0.094 (+)	0.557	0.651 (6)	0.675	1.783 (+)	1.481	3.264 (10)	1.322
Log-t	0.079 (-)	0.374	0.453 (1)	0.400	0.053 (-)	0.440	0.494 (1)	0.479
Log-skew-n	0.069 (+)	0.567	0.636 (5)	0.650	0.174 (+)	1.914	2.089 (4)	0.745
Log-normal	0.088 (-)	0.383	0.471 (2)	0.402	0.077 (-)	0.444	0.520 (2)	0.479
Best Parametric	0.037 (+)	0.630	0.667 (7)	0.549	1.187 (+)	1.582	2.769 (9)	1.218
Best SemiNP	0.045 (-)	0.705	0.750 (10)	0.573	0.000 (+)	1.002	1.002 (3)	3.197
\mathcal{M}_P	0.033 (+)	0.525	0.559 (3)	0.625	0.964 (+)	1.513	2.477 (7)	1.314
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	0.026 (-)	0.711	0.737 (9)	0.601	0.377 (+)	2.038	2.414 (6)	3.392
$\mathcal{M}_P \cup \mathcal{M}_S$	0.036 (-)	0.688	0.724 (8)	0.599	0.331 (+)	1.954	2.284 (5)	2.839

Table A.26: Simulation study. Sample from 90% mixture distribution of size 500 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	3.192 (-)	1.799	4.991 (11)	2.201	1.189 (-)	2.105	3.294 (5)	2.528
Gamma	3.751 (-)	1.072	4.822 (9)	2.140	0.016 (+)	1.706	1.722 (1)	2.584
Weibull	0.195 (-)	1.433	1.628 (1)	2.189	0.808 (+)	1.828	2.636 (2)	2.460
Log-skew-t	3.206 (-)	1.915	5.121 (12)	2.243	1.298 (-)	2.157	3.455 (9)	2.516
Log-t	1.829 (-)	2.127	3.956 (6)	2.245	1.670 (-)	2.376	4.046 (12)	2.491
Log-skew-n	2.916 (-)	1.926	4.842 (10)	2.234	1.339 (-)	2.291	3.629 (10)	2.494
Log-normal	1.552 (-)	2.112	3.663 (5)	2.217	1.484 (-)	2.379	3.863 (11)	2.482
Best Parametric	2.596 (-)	1.988	4.584 (7)	2.205	1.196 (-)	2.177	3.373 (7)	2.529
Best SemiNP	0.005 (+)	3.386	3.392 (3)	2.831	0.854 (-)	2.472	3.326 (6)	6.374
\mathcal{M}_P	2.646 (-)	1.958	4.604 (8)	2.252	1.230 (-)	2.204	3.434 (8)	2.527
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	0.019 (-)	3.443	3.462 (4)	2.958	0.833 (-)	2.410	3.243 (3)	5.314
$\mathcal{M}_P \cup \mathcal{M}_S$	0.003 (-)	3.301	3.305 (2)	3.008	0.827 (-)	2.419	3.246 (4)	4.585

Table A.27: Simulation study. Sample from 95% mixture distribution of size 100 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	0.140 (+)	1.952	2.092 (2)	2.973	2.005 (+)	4.224	6.229 (5)	5.645
Gamma	12.680 (+)	2.891	15.571 (11)	4.609	26.497 (+)	5.265	31.761 (12)	6.514
Weibull	15.975 (+)	2.984	18.958 (12)	3.868	24.314 (+)	4.228	28.542 (11)	4.820
Log-skew-t	0.028 (+)	2.804	2.832 (8)	3.417	1.675 (+)	6.150	7.825 (9)	6.610
Log-t	0.197 (-)	1.835	2.032 (1)	2.060	0.111 (-)	2.289	2.400 (1)	2.525
Log-skew-n	0.016 (+)	2.675	2.691 (5)	3.133	0.240 (+)	5.422	5.662 (4)	4.182
Log-normal	0.219 (-)	1.914	2.133 (3)	2.073	0.170 (-)	2.331	2.501 (2)	2.536
Best Parametric	0.006 (-)	2.756	2.762 (6)	2.435	1.021 (+)	7.781	8.801 (10)	3.408
Best SemiNP	0.505 (-)	2.546	3.051 (10)	2.160	0.367 (-)	4.147	4.514 (3)	6.955
\mathcal{M}_P	0.015 (+)	2.468	2.483 (4)	3.096	1.410 (+)	5.431	6.841 (6)	5.719
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.037 (-)	2.736	2.773 (7)	3.024	0.614 (+)	6.635	7.249 (8)	7.077
$\mathcal{M}_P \cup \mathcal{M}_S$	0.107 (-)	2.825	2.931 (9)	2.943	0.406 (+)	6.483	6.889 (7)	7.641

Table A.28: Simulation study. Sample from 95% mixture distribution of size 100 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	8.488 (-)	9.868	18.356 (11)	10.971	4.251 (-)	11.229	15.480 (3)	12.629
Gamma	9.197 (-)	6.112	15.309 (2)	10.699	0.872 (-)	9.400	10.273 (2)	12.941
Weibull	2.446 (-)	7.801	10.247 (1)	11.013	0.034 (-)	10.023	10.057 (1)	12.396
Log-skew-t	7.641 (-)	11.060	18.701 (12)	11.541	4.104 (-)	11.664	15.767 (6)	12.934
Log-t	6.159 (-)	11.781	17.940 (9)	11.407	5.558 (-)	12.979	18.537 (12)	12.689
Log-skew-n	7.137 (-)	10.867	18.004 (10)	11.247	4.146 (-)	12.246	16.392 (9)	12.685
Log-normal	5.148 (-)	11.753	16.901 (5)	11.078	4.874 (-)	13.021	17.895 (11)	12.436
Best Parametric	6.310 (-)	11.058	17.368 (7)	10.990	3.664 (-)	12.288	15.952 (8)	12.437
Best SemiNP	2.065 (-)	14.773	16.837 (4)	12.353	3.143 (-)	14.555	17.699 (10)	18.981
\mathcal{M}_P	6.788 (-)	10.724	17.512 (8)	11.306	3.720 (-)	11.783	15.502 (4)	12.812
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	4.020 (-)	12.994	17.014 (6)	12.611	2.834 (-)	12.870	15.704 (5)	15.342
$\mathcal{M}_P \cup \mathcal{M}_S$	3.037 (-)	13.255	16.292 (3)	13.180	2.826 (-)	12.993	15.818 (7)	16.940

Table A.29: Simulation study. Sample from 95% mixture distribution of size 200 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	0.167 (+)	0.977	1.144 (4)	1.453	1.307 (+)	1.732	3.039 (8)	2.630
Gamma	16.044 (+)	1.557	17.601 (11)	2.446	32.286 (+)	2.706	34.993 (12)	3.452
Weibull	21.072 (+)	1.666	22.738 (12)	2.067	31.100 (+)	2.237	33.337 (11)	2.568
Log-skew-t	0.004 (+)	1.244	1.248 (6)	1.635	0.768 (+)	2.633	3.402 (10)	3.157
Log-t	0.074 (-)	0.948	1.023 (1)	1.072	0.031 (-)	1.096	1.126 (1)	1.309
Log-skew-n	0.001 (+)	1.261	1.262 (7)	1.504	0.051 (+)	2.028	2.078 (4)	1.992
Log-normal	0.087 (-)	0.987	1.074 (2)	1.085	0.063 (-)	1.121	1.185 (2)	1.316
Best Parametric	0.012 (-)	1.204	1.217 (5)	1.217	0.197 (+)	2.926	3.123 (9)	1.858
Best SemiNP	0.150 (-)	1.396	1.546 (10)	1.195	0.076 (-)	1.854	1.930 (3)	15.578
\mathcal{M}_P	0.000 (-)	1.119	1.119 (3)	1.407	0.361 (+)	2.537	2.899 (5)	2.606
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.040 (-)	1.355	1.395 (8)	1.400	0.113 (+)	2.900	3.013 (7)	12.992
$\mathcal{M}_P \cup \mathcal{M}_S$	0.063 (-)	1.409	1.472 (9)	1.421	0.099 (+)	2.836	2.935 (6)	12.632

Table A.30: Simulation study. Sample from 95% mixture distribution of size 200 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	3.807 (-)	4.922	8.729 (11)	5.690	1.606 (-)	5.410	7.016 (3)	6.472
Gamma	4.860 (-)	2.932	7.792 (6)	5.511	0.000 (-)	4.433	4.433 (1)	6.662
Weibull	0.190 (-)	3.955	4.145 (1)	5.701	1.004 (+)	4.905	5.909 (2)	6.406
Log-skew-t	3.512 (-)	5.409	8.920 (12)	5.929	1.936 (-)	5.679	7.614 (9)	6.526
Log-t	2.638 (-)	5.574	8.212 (8)	5.902	2.188 (-)	6.129	8.317 (12)	6.530
Log-skew-n	2.985 (-)	5.410	8.395 (10)	5.835	1.701 (-)	5.860	7.561 (8)	6.463
Log-normal	1.944 (-)	5.682	7.626 (5)	5.729	1.776 (-)	6.102	7.878 (11)	6.433
Best Parametric	2.472 (-)	5.616	8.088 (7)	5.715	1.657 (-)	5.807	7.465 (7)	6.444
Best SemiNP	0.509 (-)	7.004	7.513 (3)	6.356	1.209 (-)	6.477	7.685 (10)	15.145
\mathcal{M}_P	2.807 (-)	5.412	8.219 (9)	5.844	1.628 (-)	5.785	7.413 (6)	6.527
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	1.236 (-)	6.339	7.574 (4)	6.586	1.204 (-)	6.105	7.309 (5)	12.221
$\mathcal{M}_P \cup \mathcal{M}_S$	0.813 (-)	6.468	7.281 (2)	6.886	1.194 (-)	6.108	7.302 (4)	12.651

Table A.31: Simulation study. Sample from 95% mixture distribution of size 500 - estimate of distribution function in the 5% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	0.193 (+)	0.429	0.622 (9)	0.587	1.019 (+)	0.728	1.747 (10)	1.419
Gamma	18.088 (+)	0.642	18.730 (11)	1.010	35.691 (+)	1.172	36.864 (12)	1.423
Weibull	24.357 (+)	0.694	25.051 (12)	0.857	35.388 (+)	0.954	36.342 (11)	1.063
Log-skew-t	0.006 (+)	0.496	0.501 (4)	0.652	0.456 (+)	1.075	1.531 (9)	1.186
Log-t	0.030 (-)	0.407	0.437 (1)	0.443	0.012 (-)	0.490	0.502 (1)	0.535
Log-skew-n	0.004 (+)	0.497	0.501 (5)	0.592	0.001 (-)	0.712	0.714 (3)	0.666
Log-normal	0.034 (-)	0.420	0.454 (2)	0.447	0.025 (-)	0.497	0.522 (2)	0.538
Best Parametric	0.001 (-)	0.522	0.523 (6)	0.494	0.152 (+)	1.204	1.356 (8)	0.794
Best SemiNP	0.018 (-)	0.621	0.639 (10)	0.539	0.009 (+)	0.717	0.726 (4)	1.252
\mathcal{M}_P	0.001 (+)	0.472	0.473 (3)	0.566	0.142 (+)	0.925	1.067 (7)	1.021
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.006 (-)	0.575	0.582 (7)	0.580	0.089 (+)	0.896	0.985 (6)	1.268
$\mathcal{M}_P \cup \mathcal{M}_S$	0.008 (-)	0.591	0.600 (8)	0.598	0.090 (+)	0.871	0.961 (5)	1.426

Table A.32: Simulation study. Sample from 95% mixture distribution of size 500 - estimate of distribution function in the 25% quantile of the log-normal distribution (Results $\times 10^{-4}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	1.915 (-)	1.947	3.863 (11)	2.321	0.611 (-)	2.295	2.906 (2)	2.650
Gamma	2.938 (-)	1.109	4.047 (12)	2.241	0.277 (+)	1.797	2.074 (1)	2.706
Weibull	0.055 (+)	1.529	1.584 (1)	2.324	2.889 (+)	1.960	4.849 (12)	2.607
Log-skew-t	1.533 (-)	2.178	3.711 (10)	2.442	0.843 (-)	2.381	3.224 (10)	2.636
Log-t	0.971 (-)	2.240	3.212 (6)	2.385	0.815 (-)	2.520	3.336 (11)	2.643
Log-skew-n	1.239 (-)	2.172	3.411 (9)	2.401	0.658 (-)	2.493	3.151 (8)	2.623
Log-normal	0.717 (-)	2.220	2.936 (2)	2.337	0.649 (-)	2.517	3.166 (9)	2.622
Best Parametric	1.003 (-)	2.238	3.241 (7)	2.338	0.640 (-)	2.410	3.049 (3)	2.626
Best SemiNP	0.085 (-)	3.032	3.117 (4)	2.645	0.541 (-)	2.521	3.063 (5)	3.750
\mathcal{M}_P	1.152 (-)	2.167	3.319 (8)	2.397	0.670 (-)	2.420	3.090 (7)	2.636
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.271 (-)	2.907	3.178 (5)	2.751	0.604 (-)	2.480	3.084 (6)	3.031
$\mathcal{M}_P \cup \mathcal{M}_S$	0.152 (-)	2.867	3.019 (3)	2.874	0.587 (-)	2.474	3.061 (4)	3.258

Table A.33: Simulation study. Sample from log-normal distribution of size 100 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	0.358 (-)	6.738	7.096 (3)	7.513	0.009 (-)	7.561	7.570 (3)	8.212
Gamma	3.127 (-)	1.935	5.062 (2)	3.129	0.488 (-)	2.429	2.916 (1)	3.164
Weibull	0.044 (-)	2.733	2.778 (1)	3.756	0.371 (+)	3.256	3.627 (2)	3.952
Log Skew t	1.343 (-)	9.095	10.438 (9)	9.525	1.761 (-)	10.554	12.315 (8)	11.209
Log t	0.829 (-)	8.906	9.735 (6)	9.348	0.837 (-)	9.845	10.681 (6)	13.602
Log Skew N	0.340 (-)	9.423	9.762 (7)	8.873	0.682 (-)	12.903	13.585 (10)	11.837
Log-normal	0.083 (-)	9.264	9.347 (5)	8.714	0.085 (-)	10.370	10.455 (4)	10.101
Best Parametric	0.260 (-)	9.699	9.959 (8)	8.784	0.534 (-)	11.184	11.717 (7)	10.098
Best SemiNP	0.137 (-)	13.739	13.876 (12)	9.678	0.752 (-)	16.641	17.394 (12)	16.132
\mathcal{M}_P	0.464 (-)	8.795	9.259 (4)	9.012	0.583 (-)	10.089	10.672 (5)	10.926
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	0.476 (-)	10.710	11.186 (10)	10.081	0.957 (-)	11.674	12.631 (9)	14.194
$\mathcal{M}_P \cup \mathcal{M}_S$	0.233 (-)	11.777	12.009 (11)	11.521	1.100 (-)	12.537	13.637 (11)	18.574

Table A.34: Simulation study. Sample from log-normal distribution of size 100 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	0.691 (-)	1.230	1.921 (4)	1.440	1.049 (-)	1.250	2.299 (4)	1.598
Gamma	18.583 (-)	1.041	19.624 (12)	0.410	18.556 (-)	0.968	19.524 (12)	0.377
Weibull	13.401 (-)	0.716	14.116 (11)	0.469	12.900 (-)	0.680	13.580 (11)	0.441
Log Skew t	0.016 (+)	2.714	2.730 (10)	3.117	0.030 (-)	4.031	4.061 (10)	3.973
Log t	0.009 (+)	1.420	1.429 (2)	1.284	0.003 (+)	1.444	1.447 (2)	1.385
Log Skew N	0.002 (+)	2.387	2.390 (9)	2.147	0.170 (+)	3.220	3.390 (9)	2.651
Log-normal	0.005 (+)	1.219	1.224 (1)	1.098	0.003 (+)	1.254	1.258 (1)	1.117
Best Parametric	0.010 (+)	1.992	2.001 (6)	1.340	0.009 (-)	3.212	3.221 (8)	1.441
Best SemiNP	0.014 (+)	1.974	1.988 (5)	1.476	0.010 (+)	2.138	2.148 (3)	2.316
\mathcal{M}_P	0.002 (-)	1.783	1.785 (3)	1.910	0.039 (-)	2.475	2.514 (5)	2.472
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	0.000 (-)	2.071	2.071 (7)	2.122	0.024 (-)	2.723	2.746 (7)	3.032
$\mathcal{M}_P \cup \mathcal{M}_S$	0.000 (+)	2.178	2.178 (8)	2.380	0.012 (-)	2.668	2.679 (6)	3.428

Table A.35: Simulation study. Sample from log-normal distribution of size 200 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	0.185 (-)	3.370	3.555 (2)	3.804	0.002 (+)	3.705	3.707 (3)	4.247
Gamma	2.840 (-)	0.867	3.707 (3)	1.527	0.354 (-)	1.083	1.438 (1)	1.534
Weibull	0.004 (-)	1.330	1.334 (1)	1.859	0.579 (+)	1.533	2.112 (2)	1.955
Log Skew t	0.793 (-)	4.174	4.967 (11)	4.744	0.747 (-)	4.663	5.411 (9)	5.453
Log t	0.557 (-)	4.141	4.698 (10)	4.757	0.454 (-)	4.780	5.233 (6)	5.779
Log Skew N	0.135 (-)	4.329	4.464 (6)	4.439	0.144 (-)	5.227	5.372 (8)	5.622
Log-normal	0.033 (-)	4.420	4.453 (5)	4.411	0.026 (-)	4.844	4.870 (4)	5.130
Best Parametric	0.135 (-)	4.530	4.664 (9)	4.459	0.154 (-)	5.150	5.304 (7)	5.169
Best SemiNP	0.000 (-)	5.275	5.275 (12)	5.051	0.245 (-)	8.090	8.335 (12)	7.490
\mathcal{M}_P	0.228 (-)	4.219	4.446 (4)	4.591	0.193 (-)	4.730	4.923 (5)	5.434
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	0.118 (-)	4.428	4.547 (7)	5.094	0.319 (-)	5.803	6.122 (10)	6.983
$\mathcal{M}_P \cup \mathcal{M}_S$	0.027 (-)	4.623	4.649 (8)	5.752	0.337 (-)	6.024	6.361 (11)	8.305

Table A.36: Simulation study. Sample from log-normal distribution of size 200 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	0.574 (-)	0.574	1.148 (9)	0.765	0.810 (-)	0.596	1.405 (9)	1.221
Gamma	19.476 (-)	0.503	19.980 (12)	0.195	19.388 (-)	0.476	19.864 (12)	0.178
Weibull	13.776 (-)	0.331	14.107 (11)	0.227	13.239 (-)	0.319	13.559 (11)	0.212
Log Skew t	0.007 (+)	1.169	1.177 (10)	1.223	0.036 (-)	1.749	1.785 (10)	1.738
Log t	0.005 (+)	0.642	0.648 (2)	0.604	0.002 (+)	0.670	0.672 (2)	0.628
Log Skew N	0.000 (+)	1.001	1.002 (7)	1.005	0.031 (+)	1.357	1.388 (8)	1.172
Log-normal	0.002 (+)	0.580	0.582 (1)	0.537	0.001 (+)	0.595	0.597 (1)	0.543
Best Parametric	0.008 (+)	0.904	0.912 (4)	0.653	0.000 (-)	1.358	1.358 (7)	0.747
Best SemiNP	0.000 (-)	1.094	1.094 (8)	0.712	0.001 (+)	1.006	1.007 (3)	0.782
\mathcal{M}_P	0.000 (-)	0.804	0.804 (3)	0.883	0.011 (-)	1.098	1.109 (4)	1.139
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.001 (-)	0.935	0.936 (5)	0.991	0.009 (-)	1.186	1.195 (5)	1.236
$\mathcal{M}_P \cup \mathcal{M}_S$	0.000 (-)	0.947	0.947 (6)	1.106	0.008 (-)	1.196	1.204 (6)	1.354

Table A.37: Simulation study. Sample from log-normal distribution of size 500 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	0.148 (-)	1.344	1.492 (2)	1.534	0.005 (+)	1.604	1.608 (3)	1.733
Gamma	2.672 (-)	0.316	2.988 (12)	0.606	0.296 (-)	0.411	0.707 (1)	0.606
Weibull	0.000 (+)	0.506	0.506 (1)	0.741	0.693 (+)	0.598	1.291 (2)	0.778
Log Skew t	0.420 (-)	1.722	2.142 (9)	1.917	0.363 (-)	1.954	2.318 (8)	2.126
Log t	0.301 (-)	1.846	2.147 (10)	1.923	0.247 (-)	2.108	2.355 (9)	2.380
Log Skew N	0.049 (-)	1.709	1.758 (3)	1.770	0.067 (-)	2.205	2.272 (7)	2.198
Log-normal	0.014 (-)	1.761	1.775 (4)	1.778	0.014 (-)	2.050	2.064 (4)	2.068
Best Parametric	0.051 (-)	1.842	1.893 (6)	1.786	0.055 (-)	2.154	2.209 (6)	2.081
Best SemiNP	0.000 (+)	2.361	2.361 (11)	1.968	0.059 (-)	3.132	3.191 (12)	2.752
\mathcal{M}_P	0.102 (-)	1.726	1.828 (5)	1.859	0.082 (-)	2.049	2.131 (5)	2.187
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.038 (-)	2.008	2.046 (7)	2.076	0.098 (-)	2.397	2.495 (10)	2.564
$\mathcal{M}_P \cup \mathcal{M}_S$	0.005 (-)	2.070	2.075 (8)	2.318	0.099 (-)	2.407	2.506 (11)	2.786

Table A.38: Simulation study. Sample from log-normal distribution of size 500 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	0.509 (-)	0.207	0.716 (10)	0.249	0.667 (-)	0.204	0.871 (10)	0.259
Gamma	19.786 (-)	0.193	19.979 (12)	0.076	19.670 (-)	0.184	19.854 (12)	0.069
Weibull	13.881 (-)	0.120	14.001 (11)	0.089	13.338 (-)	0.116	13.454 (11)	0.083
Log Skew t	0.003 (+)	0.403	0.405 (9)	0.453	0.024 (-)	0.570	0.593 (9)	0.654
Log t	0.004 (+)	0.229	0.233 (2)	0.231	0.002 (+)	0.228	0.231 (2)	0.237
Log Skew N	0.001 (-)	0.360	0.361 (6)	0.350	0.027 (+)	0.425	0.452 (8)	0.427
Log-normal	0.002 (+)	0.212	0.213 (1)	0.213	0.001 (+)	0.213	0.214 (1)	0.214
Best Parametric	0.001 (+)	0.299	0.300 (4)	0.247	0.000 (+)	0.418	0.419 (7)	0.275
Best SemiNP	0.000 (+)	0.377	0.377 (8)	0.274	0.000 (+)	0.285	0.285 (3)	0.238
\mathcal{M}_P	0.000 (-)	0.283	0.284 (3)	0.327	0.002 (-)	0.351	0.353 (4)	0.418
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.001 (-)	0.340	0.341 (5)	0.358	0.001 (-)	0.361	0.362 (5)	0.422
$\mathcal{M}_P \cup \mathcal{M}_S$	0.000 (-)	0.365	0.365 (7)	0.417	0.001 (-)	0.361	0.363 (6)	0.414

Table A.39: Simulation study. Sample from gamma distribution of size 100 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias2 (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias2 (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	0.000 (-)	2.616	2.616 (6)	2.558	0.046 (-)	4.586	4.632 (3)	5.168
Gamma	0.012 (+)	0.861	0.873 (1)	0.839	0.001 (+)	0.996	0.997 (1)	1.062
Weibull	12.807 (+)	1.137	13.944 (10)	1.731	21.082 (+)	1.391	22.473 (9)	1.985
Log Skew t	0.188 (+)	1.544	1.732 (2)	1.402	0.403 (+)	5.284	5.687 (5)	17.055
Log t	27.328 (+)	4.168	31.496 (12)	5.193	117.128 (+)	2.440	119.568 (11)	5.516
Log Skew N	1.180 (+)	3.540	4.720 (8)	1.294	3.531 (+)	2.491	6.022 (6)	2.510
Log-normal	1.351 (+)	4.805	6.156 (9)	1.643	118.133 (+)	2.386	120.519 (12)	5.382
Best Parametric	0.011 (+)	2.152	2.163 (4)	0.933	0.179 (+)	4.609	4.788 (4)	1.129
Best SemiNP	3.047 (+)	11.751	14.798 (11)	5.824	4.521 (-)	99.833	104.353 (10)	62.427
\mathcal{M}_P	0.049 (+)	1.756	1.805 (3)	1.821	0.803 (+)	3.772	4.575 (2)	5.020
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.059 (+)	2.506	2.566 (5)	2.428	0.058 (+)	9.093	9.152 (7)	12.688
$\mathcal{M}_P \cup \mathcal{M}_S$	0.061 (+)	2.739	2.800 (7)	2.662	0.009 (+)	11.928	11.937 (8)	14.946

Table A.40: Simulation study. Sample from gamma distribution of size 100 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias2 (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias2 (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	0.000 (-)	0.362	0.362 (5)	0.344	0.009 (-)	0.831	0.839 (6)	0.860
Gamma	0.008 (+)	0.206	0.214 (1)	0.200	0.005 (+)	0.312	0.317 (1)	0.332
Weibull	0.304 (+)	0.308	0.612 (8)	0.282	2.300 (+)	0.298	2.598 (9)	0.455
Log Skew t	0.035 (-)	0.319	0.354 (4)	0.283	0.004 (-)	0.712	0.716 (4)	1.035
Log t	0.522 (+)	1.031	1.553 (10)	0.777	6.267 (+)	0.591	6.858 (12)	0.907
Log Skew N	0.928 (-)	0.309	1.236 (9)	0.140	0.023 (+)	0.585	0.607 (2)	0.559
Log-normal	1.932 (-)	0.482	2.415 (12)	0.132	6.163 (+)	0.586	6.749 (11)	0.880
Best Parametric	0.000 (-)	0.336	0.336 (3)	0.201	0.007 (+)	0.751	0.758 (5)	0.324
Best SemiNP	0.579 (+)	1.173	1.752 (11)	0.583	0.979 (+)	4.678	5.656 (10)	2.399
\mathcal{M}_P	0.000 (-)	0.285	0.285 (2)	0.293	0.028 (+)	0.675	0.702 (3)	0.712
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.004 (+)	0.394	0.398 (6)	0.366	0.018 (+)	0.865	0.882 (7)	0.972
$\mathcal{M}_P \cup \mathcal{M}_S$	0.009 (+)	0.432	0.441 (7)	0.396	0.015 (+)	0.939	0.954 (8)	1.057

Table A.41: Simulation study. Sample from gamma distribution of size 200 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias2 (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias2 (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	0.000 (+)	1.242	1.243 (8)	1.278	0.005 (-)	2.459	2.464 (3)	2.511
Gamma	0.002 (+)	0.383	0.386 (1)	0.409	0.000 (+)	0.449	0.449 (1)	0.507
Weibull	12.793 (+)	0.496	13.288 (11)	0.855	21.430 (+)	0.626	22.055 (8)	0.949
Log Skew t	0.216 (+)	0.716	0.932 (6)	0.673	0.959 (+)	2.513	3.472 (5)	9.243
Log t	31.015 (+)	1.522	32.536 (12)	2.433	119.204 (+)	1.148	120.352 (11)	2.659
Log Skew N	0.065 (+)	0.737	0.802 (3)	0.431	55.624 (+)	20.910	76.534 (10)	1.979
Log-normal	0.894 (+)	2.429	3.322 (9)	0.798	119.914 (+)	1.098	121.011 (12)	2.606
Best Parametric	0.007 (+)	0.874	0.881 (4)	0.504	0.048 (+)	2.793	2.841 (4)	0.647
Best SemiNP	3.889 (+)	6.130	10.019 (10)	2.607	5.552 (-)	55.384	60.936 (9)	18.724
\mathcal{M}_P	0.013 (+)	0.763	0.777 (2)	0.831	0.267 (+)	1.963	2.231 (2)	2.644
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.011 (+)	0.883	0.895 (5)	0.914	0.042 (+)	4.103	4.145 (6)	4.699
$\mathcal{M}_P \cup \mathcal{M}_S$	0.014 (+)	0.922	0.936 (7)	0.950	0.024 (+)	4.468	4.492 (7)	4.945

Table A.42: Simulation study. Sample from gamma distribution of size 200 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	0.000 (+)	0.162	0.162 (6)	0.173	0.001 (-)	0.420	0.422 (7)	0.431
Gamma	0.002 (+)	0.093	0.095 (1)	0.098	0.001 (+)	0.150	0.151 (1)	0.162
Weibull	0.276 (+)	0.149	0.425 (8)	0.140	2.259 (+)	0.142	2.402 (8)	0.224
Log Skew t	0.036 (-)	0.155	0.190 (7)	0.144	0.000 (-)	0.316	0.316 (2)	0.480
Log t	0.534 (+)	0.516	1.050 (10)	0.393	6.198 (+)	0.295	6.492 (12)	0.447
Log Skew N	0.600 (-)	0.189	0.789 (9)	0.071	2.271 (+)	1.288	3.558 (9)	0.358
Log-normal	2.137 (-)	0.242	2.379 (12)	0.064	6.083 (+)	0.291	6.374 (11)	0.438
Best Parametric	0.000 (-)	0.157	0.158 (5)	0.104	0.002 (+)	0.406	0.408 (4)	0.175
Best SemiNP	0.276 (+)	0.934	1.210 (11)	0.252	2.144 (+)	1.753	3.897 (10)	1.522
\mathcal{M}_P	0.001 (-)	0.128	0.129 (2)	0.152	0.010 (+)	0.332	0.342 (3)	0.368
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.000 (-)	0.145	0.146 (3)	0.165	0.012 (+)	0.403	0.415 (5)	0.538
$\mathcal{M}_P \cup \mathcal{M}_S$	0.000 (-)	0.155	0.155 (4)	0.170	0.013 (+)	0.405	0.418 (6)	0.534

Table A.43: Simulation study. Sample from gamma distribution of size 500 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	0.000 (+)	0.523	0.523 (7)	0.504	0.001 (-)	0.982	0.983 (3)	0.964
Gamma	0.002 (+)	0.161	0.163 (1)	0.163	0.001 (+)	0.187	0.188 (1)	0.199
Weibull	12.806 (+)	0.210	13.016 (11)	0.341	22.187 (+)	0.248	22.435 (8)	0.370
Log Skew t	0.214 (+)	0.281	0.495 (6)	0.254	1.912 (+)	0.984	2.896 (7)	2.423
Log t	32.850 (+)	0.512	33.363 (12)	0.919	120.579 (+)	0.819	121.398 (11)	1.070
Log Skew N	0.169 (+)	0.576	0.745 (8)	0.199	12.584 (+)	12.465	25.049 (9)	0.536
Log-normal	0.465 (+)	1.017	1.481 (9)	0.307	122.418 (+)	0.447	122.865 (12)	1.030
Best Parametric	0.003 (+)	0.367	0.369 (5)	0.217	0.024 (+)	0.987	1.011 (4)	0.341
Best SemiNP	5.204 (+)	2.278	7.482 (10)	0.946	7.247 (-)	24.959	32.206 (10)	4.144
\mathcal{M}_P	0.003 (+)	0.300	0.303 (4)	0.337	0.186 (+)	0.680	0.866 (2)	1.101
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.003 (+)	0.299	0.303 (3)	0.338	0.164 (+)	1.021	1.186 (5)	1.213
$\mathcal{M}_P \cup \mathcal{M}_S$	0.003 (+)	0.299	0.302 (2)	0.338	0.161 (+)	1.035	1.197 (6)	1.250

Table A.44: Simulation study. Sample from gamma distribution of size 500 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	0.000 (+)	0.072	0.072 (6)	0.069	0.000 (-)	0.173	0.174 (7)	0.174
Gamma	0.001 (+)	0.039	0.040 (1)	0.039	0.000 (+)	0.060	0.060 (1)	0.065
Weibull	0.241 (+)	0.063	0.304 (8)	0.056	2.260 (+)	0.058	2.318 (9)	0.090
Log Skew t	0.037 (-)	0.064	0.101 (7)	0.056	0.003 (+)	0.126	0.129 (5)	0.144
Log t	0.503 (+)	0.231	0.734 (9)	0.158	5.916 (+)	0.200	6.116 (11)	0.180
Log Skew N	0.824 (-)	0.091	0.915 (10)	0.027	0.289 (+)	0.871	1.160 (8)	0.118
Log-normal	2.401 (-)	0.097	2.498 (12)	0.024	6.042 (+)	0.115	6.157 (12)	0.176
Best Parametric	0.000 (-)	0.067	0.067 (5)	0.044	0.000 (-)	0.131	0.131 (6)	0.080
Best SemiNP	0.157 (+)	0.867	1.024 (11)	0.087	2.934 (+)	0.471	3.405 (10)	0.286
\mathcal{M}_P	0.000 (-)	0.056	0.056 (2)	0.059	0.001 (+)	0.118	0.119 (2)	0.128
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.000 (-)	0.056	0.056 (3)	0.060	0.001 (+)	0.127	0.127 (3)	0.157
$\mathcal{M}_P \cup \mathcal{M}_S$	0.000 (-)	0.056	0.056 (4)	0.060	0.001 (+)	0.128	0.128 (4)	0.159

Table A.45: Simulation study. Sample from 75% mixture distribution of size 100 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	8.329 (-)	1.512	9.841 (5)	2.649	4.599 (-)	1.695	6.293 (5)	2.579
Gamma	8.712 (-)	1.417	10.129 (6)	2.472	5.130 (-)	1.881	7.012 (6)	2.737
Weibull	8.550 (-)	1.819	10.369 (7)	2.519	6.077 (-)	2.197	8.274 (7)	2.770
Log Skew t	4.408 (-)	2.028	6.435 (3)	3.393	2.713 (-)	2.461	5.173 (3)	3.828
Log t	10.433 (-)	4.492	14.925 (9)	4.698	10.777 (-)	4.842	15.619 (11)	5.123
Log Skew N	3.861 (-)	2.150	6.011 (1)	3.556	1.538 (-)	2.896	4.434 (1)	4.039
Log-normal	9.258 (-)	4.772	14.030 (8)	4.755	10.054 (-)	5.160	15.214 (10)	5.303
Best Parametric	3.988 (-)	2.215	6.203 (2)	3.529	2.142 (-)	2.709	4.851 (2)	3.784
Best SemiNP	2.982 (-)	19.450	22.433 (12)	11.308	10.951 (-)	18.679	29.630 (12)	40.797
\mathcal{M}_P	4.642 (-)	2.176	6.818 (4)	3.510	2.770 (-)	2.481	5.251 (4)	3.751
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	4.065 (-)	11.498	15.563 (11)	8.274	4.497 (-)	9.950	14.447 (8)	11.568
$\mathcal{M}_P \cup \mathcal{M}_S$	3.898 (-)	11.629	15.527 (10)	8.943	4.780 (-)	10.130	14.910 (9)	12.449

Table A.46: Simulation study. Sample from 75% mixture distribution of size 100 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	12.987 (-)	1.124	14.112 (12)	0.870	14.454 (-)	0.695	15.149 (12)	0.583
Gamma	13.127 (-)	0.261	13.388 (11)	0.384	12.042 (-)	0.265	12.307 (11)	0.367
Weibull	11.958 (-)	0.331	12.289 (10)	0.507	10.993 (-)	0.348	11.341 (9)	0.503
Log Skew t	10.182 (-)	0.334	10.516 (9)	0.461	11.129 (-)	0.502	11.631 (10)	0.812
Log t	1.017 (-)	0.780	1.797 (2)	1.028	1.074 (-)	0.810	1.884 (2)	1.066
Log Skew N	8.920 (-)	0.291	9.210 (6)	0.370	8.169 (-)	0.254	8.423 (4)	0.316
Log-normal	0.733 (-)	0.690	1.422 (1)	0.906	0.793 (-)	0.721	1.514 (1)	0.936
Best Parametric	8.945 (-)	0.361	9.306 (7)	0.341	9.584 (-)	0.552	10.136 (5)	0.357
Best SemiNP	0.006 (-)	6.228	6.234 (3)	3.564	0.123 (+)	7.236	7.359 (3)	8.050
\mathcal{M}_P	9.357 (-)	0.346	9.703 (8)	0.522	10.322 (-)	0.392	10.714 (8)	0.619
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	2.788 (-)	6.295	9.082 (5)	2.876	3.670 (-)	6.528	10.198 (7)	3.859
$\mathcal{M}_P \cup \mathcal{M}_S$	2.331 (-)	6.491	8.822 (4)	2.997	3.332 (-)	6.838	10.169 (6)	3.847

Table A.47: Simulation study. Sample from 75% mixture distribution of size 200 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	6.169 (-)	0.979	7.147 (7)	1.539	3.048 (-)	1.010	4.058 (6)	1.465
Gamma	6.084 (-)	0.749	6.834 (6)	1.273	2.963 (-)	0.994	3.957 (5)	1.403
Weibull	5.247 (-)	1.019	6.266 (5)	1.332	3.195 (-)	1.209	4.404 (7)	1.463
Log Skew t	2.634 (-)	1.073	3.707 (3)	1.762	1.152 (-)	1.299	2.451 (2)	1.943
Log t	7.089 (-)	2.540	9.629 (11)	2.515	7.096 (-)	2.846	9.943 (11)	2.767
Log Skew N	2.496 (-)	1.547	4.043 (4)	1.839	0.964 (-)	2.148	3.113 (4)	2.183
Log-normal	6.035 (-)	2.747	8.782 (10)	2.580	6.554 (-)	2.972	9.526 (8)	2.896
Best Parametric	2.337 (-)	1.170	3.507 (1)	1.807	0.866 (-)	1.536	2.403 (1)	1.950
Best SemiNP	0.088 (-)	10.209	10.297 (12)	6.391	7.030 (-)	8.270	15.300 (12)	75.761
\mathcal{M}_P	2.511 (-)	1.176	3.686 (2)	1.830	1.024 (-)	1.438	2.462 (3)	2.016
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	0.635 (-)	6.988	7.623 (8)	5.223	3.269 (-)	6.667	9.936 (10)	15.558
$\mathcal{M}_P \cup \mathcal{M}_S$	0.585 (-)	7.076	7.660 (9)	5.393	3.312 (-)	6.557	9.869 (9)	15.649

Table A.48: Simulation study. Sample from 75% mixture distribution of size 200 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	8.419 (-)	0.789	9.208 (10)	0.577	10.672 (-)	0.587	11.259 (12)	0.382
Gamma	11.741 (-)	0.127	11.867 (12)	0.185	10.700 (-)	0.127	10.827 (11)	0.175
Weibull	10.078 (-)	0.160	10.238 (11)	0.247	9.165 (-)	0.167	9.332 (9)	0.244
Log Skew t	8.811 (-)	0.113	8.924 (9)	0.219	9.506 (-)	0.207	9.713 (10)	0.332
Log t	0.433 (-)	0.349	0.782 (2)	0.495	0.449 (-)	0.374	0.823 (2)	0.500
Log Skew N	7.365 (-)	0.277	7.642 (6)	0.190	5.691 (-)	0.734	6.425 (4)	0.198
Log-normal	0.256 (-)	0.327	0.583 (1)	0.448	0.280 (-)	0.344	0.625 (1)	0.460
Best Parametric	8.023 (-)	0.166	8.189 (8)	0.175	8.498 (-)	0.263	8.761 (7)	0.210
Best SemiNP	0.004 (+)	2.745	2.749 (3)	1.844	0.178 (+)	4.025	4.203 (3)	14.340
\mathcal{M}_P	8.011 (-)	0.175	8.185 (7)	0.242	8.643 (-)	0.209	8.852 (8)	0.292
$\mathcal{M}_P \cup \{\tilde{\mathcal{M}}_S\}$	1.127 (-)	3.887	5.014 (5)	1.816	1.623 (-)	6.035	7.658 (6)	3.375
$\mathcal{M}_P \cup \mathcal{M}_S$	0.885 (-)	3.952	4.837 (4)	1.845	1.489 (-)	6.123	7.612 (5)	3.389

Table A.49: Simulation study. Sample from 75% mixture distribution of size 500 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	4.835 (-)	0.430	5.265 (10)	0.673	2.230 (-)	0.433	2.663 (7)	0.638
Gamma	4.835 (-)	0.273	5.108 (9)	0.519	2.059 (-)	0.373	2.431 (5)	0.570
Weibull	3.815 (-)	0.379	4.194 (7)	0.550	2.062 (-)	0.455	2.516 (6)	0.602
Log Skew t	1.714 (-)	0.418	2.132 (4)	0.725	0.501 (-)	0.533	1.034 (4)	0.825
Log t	4.814 (-)	1.063	5.877 (12)	1.073	5.173 (-)	1.130	6.303 (11)	1.191
Log Skew N	1.501 (-)	0.430	1.931 (1)	0.740	0.167 (-)	0.584	0.751 (1)	0.840
Log-normal	4.437 (-)	1.099	5.535 (11)	1.083	4.922 (-)	1.171	6.093 (10)	1.218
Best Parametric	1.540 (-)	0.434	1.975 (2)	0.736	0.343 (-)	0.601	0.943 (3)	0.810
Best SemiNP	0.138 (+)	4.198	4.336 (8)	2.740	3.356 (-)	4.198	7.554 (12)	16.658
\mathcal{M}_P	1.576 (-)	0.430	2.006 (3)	0.738	0.354 (-)	0.571	0.925 (2)	0.839
$\mathcal{M}_P \cup \{\tilde{\mathcal{M}}_S\}$	0.016 (+)	3.539	3.555 (5)	2.612	1.435 (-)	4.315	5.749 (9)	14.169
$\mathcal{M}_P \cup \mathcal{M}_S$	0.027 (+)	3.546	3.573 (6)	2.665	1.434 (-)	4.263	5.697 (8)	15.408

Table A.50: Simulation study. Sample from 75% mixture distribution of size 500 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	5.960 (-)	0.297	6.257 (6)	0.254	8.298 (-)	0.274	8.572 (11)	0.183
Gamma	10.909 (-)	0.048	10.957 (12)	0.073	9.918 (-)	0.049	9.966 (12)	0.068
Weibull	9.073 (-)	0.056	9.129 (11)	0.098	8.211 (-)	0.059	8.269 (9)	0.096
Log Skew t	7.885 (-)	0.040	7.925 (10)	0.078	8.374 (-)	0.085	8.460 (10)	0.142
Log t	0.124 (-)	0.122	0.245 (2)	0.186	0.139 (-)	0.127	0.266 (2)	0.189
Log Skew N	7.322 (-)	0.036	7.358 (7)	0.065	6.684 (-)	0.033	6.717 (6)	0.058
Log-normal	0.085 (-)	0.117	0.202 (1)	0.178	0.097 (-)	0.124	0.221 (1)	0.183
Best Parametric	7.451 (-)	0.040	7.491 (8)	0.067	7.677 (-)	0.111	7.788 (7)	0.086
Best SemiNP	0.032 (+)	1.410	1.442 (3)	0.775	0.140 (+)	2.867	3.007 (3)	3.010
\mathcal{M}_P	7.513 (-)	0.040	7.553 (9)	0.074	7.716 (-)	0.085	7.801 (8)	0.112
$\mathcal{M}_P \cup \{\tilde{\mathcal{M}}_S\}$	0.136 (-)	2.626	2.762 (5)	0.883	0.598 (-)	5.830	6.428 (5)	2.767
$\mathcal{M}_P \cup \mathcal{M}_S$	0.092 (-)	2.513	2.605 (4)	0.923	0.576 (-)	5.835	6.411 (4)	2.962

Table A.51: Simulation study. Sample from 90% mixture distribution of size 100 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	5.094 (-)	4.183	9.277 (7)	5.253	2.953 (-)	4.135	7.088 (4)	5.152
Gamma	7.320 (-)	1.578	8.898 (4)	2.782	3.212 (-)	2.070	5.281 (2)	2.940
Weibull	3.855 (-)	2.202	6.057 (1)	3.206	1.669 (-)	2.692	4.361 (1)	3.459
Log Skew t	4.559 (-)	4.130	8.689 (3)	5.349	2.082 (-)	4.926	7.008 (3)	5.647
Log t	4.806 (-)	6.419	11.225 (9)	6.674	4.422 (-)	7.137	11.559 (9)	7.486
Log Skew N	3.925 (-)	4.356	8.281 (2)	5.386	1.894 (-)	5.464	7.358 (6)	6.180
Log-normal	3.914 (-)	6.738	10.652 (8)	6.659	3.787 (-)	7.572	11.359 (8)	7.614
Best Parametric	3.979 (-)	4.979	8.958 (5)	5.606	2.590 (-)	5.387	7.976 (7)	5.515
Best SemiNP	1.841 (-)	18.659	20.500 (12)	11.366	6.769 (-)	16.198	22.967 (12)	45.563
\mathcal{M}_P	4.472 (-)	4.553	9.025 (6)	5.536	2.643 (-)	4.676	7.319 (5)	6.659
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	3.765 (-)	12.224	15.990 (10)	9.572	4.480 (-)	9.711	14.192 (10)	17.126
$\mathcal{M}_P \cup \mathcal{M}_S$	3.163 (-)	13.034	16.197 (11)	10.623	4.853 (-)	10.034	14.887 (11)	19.387

Table A.52: Simulation study. Sample from 90% mixture distribution of size 100 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	4.882 (-)	1.154	6.037 (4)	1.530	7.518 (-)	1.505	9.024 (6)	1.612
Gamma	19.437 (-)	0.410	19.847 (12)	0.365	18.501 (-)	0.387	18.889 (12)	0.334
Weibull	15.425 (-)	0.392	15.817 (11)	0.474	14.423 (-)	0.388	14.811 (11)	0.453
Log Skew t	5.826 (-)	2.824	8.650 (10)	2.019	8.504 (-)	2.603	11.106 (10)	1.795
Log t	0.922 (-)	0.804	1.726 (2)	1.008	0.948 (-)	0.799	1.748 (2)	1.019
Log Skew N	5.502 (-)	2.641	8.143 (9)	1.682	5.603 (-)	2.958	8.561 (4)	1.078
Log-normal	0.784 (-)	0.752	1.537 (1)	0.942	0.807 (-)	0.760	1.567 (1)	0.950
Best Parametric	3.941 (-)	2.968	6.909 (8)	0.858	6.197 (-)	3.084	9.281 (8)	0.692
Best SemiNP	0.143 (-)	4.371	4.513 (3)	2.967	0.047 (-)	4.835	4.882 (3)	8.942
\mathcal{M}_P	4.586 (-)	2.174	6.761 (7)	1.600	6.871 (-)	2.035	8.907 (5)	1.500
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	1.752 (-)	4.971	6.723 (6)	3.293	3.235 (-)	6.170	9.405 (9)	4.619
$\mathcal{M}_P \cup \mathcal{M}_S$	1.231 (-)	4.864	6.096 (5)	3.494	2.672 (-)	6.355	9.027 (7)	5.003

Table A.53: Simulation study. Sample from 90% mixture distribution of size 200 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	2.587 (-)	2.428	5.015 (3)	2.944	1.136 (-)	2.456	3.592 (4)	2.974
Gamma	5.009 (-)	0.776	5.785 (8)	1.406	1.637 (-)	0.998	2.635 (2)	1.472
Weibull	1.750 (-)	1.157	2.907 (1)	1.649	0.382 (-)	1.372	1.754 (1)	1.772
Log Skew t	2.732 (-)	2.493	5.225 (6)	2.989	0.927 (-)	2.521	3.447 (3)	3.181
Log t	2.706 (-)	3.306	6.012 (9)	3.531	2.273 (-)	3.824	6.097 (9)	3.959
Log Skew N	2.228 (-)	2.679	4.907 (2)	3.023	0.949 (-)	2.932	3.882 (5)	3.580
Log-normal	1.917 (-)	3.563	5.481 (7)	3.541	1.789 (-)	3.966	5.755 (8)	4.069
Best Parametric	2.207 (-)	2.935	5.142 (5)	3.149	1.207 (-)	2.890	4.098 (7)	3.215
Best SemiNP	0.003 (-)	8.969	8.972 (12)	6.506	1.874 (-)	7.061	8.935 (12)	28.845
\mathcal{M}_P	2.336 (-)	2.778	5.114 (4)	3.156	1.233 (-)	2.688	3.921 (6)	3.308
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	0.306 (-)	7.161	7.466 (11)	6.325	1.669 (-)	5.234	6.903 (10)	17.656
$\mathcal{M}_P \cup \mathcal{M}_S$	0.159 (-)	7.125	7.284 (10)	6.778	1.640 (-)	5.349	6.990 (11)	19.955

Table A.54: Simulation study. Sample from 90% mixture distribution of size 200 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	2.548 (-)	0.501	3.050 (8)	0.799	3.929 (-)	0.666	4.595 (5)	0.835
Gamma	17.907 (-)	0.213	18.120 (12)	0.178	17.066 (-)	0.202	17.268 (12)	0.161
Weibull	13.536 (-)	0.188	13.724 (11)	0.230	12.623 (-)	0.185	12.808 (11)	0.218
Log Skew t	2.509 (-)	1.387	3.896 (10)	1.195	4.798 (-)	1.514	6.312 (10)	1.184
Log t	0.358 (-)	0.389	0.747 (2)	0.504	0.368 (-)	0.385	0.753 (2)	0.504
Log Skew N	2.258 (-)	1.344	3.602 (9)	1.076	2.284 (-)	1.896	4.180 (4)	0.756
Log-normal	0.280 (-)	0.364	0.643 (1)	0.471	0.287 (-)	0.366	0.653 (1)	0.473
Best Parametric	1.537 (-)	1.432	2.969 (7)	0.598	3.058 (-)	1.862	4.919 (8)	0.593
Best SemiNP	0.082 (-)	2.315	2.398 (3)	1.552	0.089 (-)	2.267	2.356 (3)	5.710
\mathcal{M}_P	1.716 (-)	1.047	2.763 (5)	0.957	3.279 (-)	1.444	4.723 (6)	1.030
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.409 (-)	2.474	2.883 (6)	1.724	1.277 (-)	3.649	4.926 (9)	4.081
$\mathcal{M}_P \cup \mathcal{M}_S$	0.292 (-)	2.309	2.601 (4)	1.811	1.210 (-)	3.552	4.762 (7)	4.281

Table A.55: Simulation study. Sample from 90% mixture distribution of size 500 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	1.464 (-)	0.982	2.446 (6)	1.223	0.478 (-)	1.060	1.538 (3)	1.302
Gamma	3.819 (-)	0.280	4.099 (11)	0.567	0.958 (-)	0.377	1.335 (2)	0.590
Weibull	0.894 (-)	0.429	1.323 (1)	0.671	0.053 (-)	0.519	0.571 (1)	0.719
Log Skew t	1.628 (-)	1.019	2.647 (7)	1.263	0.463 (-)	1.144	1.607 (4)	1.337
Log t	1.261 (-)	1.393	2.654 (8)	1.473	1.154 (-)	1.567	2.721 (11)	1.666
Log Skew N	1.318 (-)	1.050	2.369 (2)	1.273	0.636 (-)	1.490	2.126 (7)	1.536
Log-normal	0.989 (-)	1.412	2.400 (3)	1.471	0.937 (-)	1.615	2.551 (8)	1.692
Best Parametric	1.310 (-)	1.119	2.429 (4)	1.308	0.518 (-)	1.219	1.737 (5)	1.359
Best SemiNP	0.476 (+)	3.673	4.150 (12)	2.986	0.505 (-)	2.363	2.868 (12)	18.833
\mathcal{M}_P	1.320 (-)	1.109	2.429 (5)	1.317	0.556 (-)	1.220	1.777 (6)	1.420
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.198 (+)	3.576	3.774 (10)	3.090	0.556 (-)	2.126	2.682 (10)	17.195
$\mathcal{M}_P \cup \mathcal{M}_S$	0.208 (+)	3.245	3.452 (9)	3.166	0.543 (-)	2.105	2.648 (9)	12.123

Table A.56: Simulation study. Sample from 90% mixture distribution of size 500 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	1.546 (-)	0.185	1.731 (10)	0.296	2.461 (-)	0.261	2.722 (8)	0.441
Gamma	16.931 (-)	0.090	17.021 (12)	0.070	16.167 (-)	0.086	16.253 (12)	0.063
Weibull	12.440 (-)	0.072	12.512 (11)	0.091	11.597 (-)	0.072	11.668 (11)	0.086
Log Skew t	1.216 (-)	0.513	1.728 (9)	0.483	2.787 (-)	0.661	3.448 (10)	0.537
Log t	0.115 (-)	0.146	0.261 (2)	0.194	0.121 (-)	0.145	0.267 (2)	0.195
Log Skew N	1.134 (-)	0.504	1.639 (8)	0.457	0.836 (-)	1.108	1.944 (4)	0.262
Log-normal	0.096 (-)	0.140	0.235 (1)	0.189	0.098 (-)	0.141	0.239 (1)	0.189
Best Parametric	0.887 (-)	0.564	1.451 (7)	0.281	2.026 (-)	0.699	2.725 (9)	0.417
Best SemiNP	0.063 (-)	0.873	0.936 (4)	0.712	0.309 (-)	0.766	1.075 (3)	3.744
\mathcal{M}_P	0.882 (-)	0.418	1.300 (6)	0.420	1.796 (-)	0.651	2.447 (7)	0.521
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.111 (-)	0.913	1.023 (5)	0.733	1.035 (-)	1.342	2.377 (6)	3.820
$\mathcal{M}_P \cup \mathcal{M}_S$	0.078 (-)	0.857	0.935 (3)	0.751	0.974 (-)	1.285	2.259 (5)	2.628

Table A.57: Simulation study. Sample from 95% mixture distribution of size 100 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	3.690 (-)	5.227	8.917 (3)	5.984	1.943 (-)	5.480	7.422 (3)	6.204
Gamma	6.969 (-)	1.701	8.671 (2)	2.875	2.779 (-)	2.197	4.976 (2)	2.989
Weibull	2.662 (-)	2.396	5.058 (1)	3.393	0.813 (-)	2.907	3.721 (1)	3.629
Log Skew t	4.236 (-)	6.066	10.301 (7)	6.735	2.494 (-)	6.686	9.180 (5)	7.376
Log t	3.556 (-)	7.331	10.887 (9)	7.400	3.199 (-)	8.125	11.324 (9)	8.416
Log Skew N	3.255 (-)	6.208	9.463 (4)	6.612	2.198 (-)	8.150	10.348 (7)	7.927
Log-normal	2.660 (-)	7.646	10.307 (8)	7.299	2.491 (-)	8.586	11.076 (8)	8.389
Best Parametric	3.145 (-)	6.885	10.030 (6)	6.754	2.495 (-)	7.108	9.603 (6)	6.914
Best SemiNP	1.905 (-)	16.470	18.375 (12)	10.455	5.188 (-)	17.660	22.848 (12)	34.888
\mathcal{M}_P	3.502 (-)	6.302	9.803 (5)	6.714	2.489 (-)	6.527	9.016 (4)	7.069
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	3.019 (-)	10.841	13.860 (10)	9.766	4.164 (-)	10.700	14.864 (10)	19.524
$\mathcal{M}_P \cup \mathcal{M}_S$	2.403 (-)	11.823	14.226 (11)	11.126	4.377 (-)	11.376	15.753 (11)	22.271

Table A.58: Simulation study. Sample from 95% mixture distribution of size 100 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	3.763 (-)	1.054	4.817 (8)	1.313	5.373 (-)	1.309	6.682 (6)	1.561
Gamma	21.542 (-)	0.528	22.071 (12)	0.370	20.815 (-)	0.493	21.308 (12)	0.338
Weibull	16.662 (-)	0.455	17.117 (11)	0.467	15.742 (-)	0.440	16.183 (11)	0.443
Log Skew t	2.631 (-)	3.087	5.718 (10)	2.457	4.565 (-)	3.411	7.976 (10)	2.895
Log t	0.811 (-)	0.924	1.735 (2)	1.049	0.853 (-)	0.914	1.767 (2)	1.068
Log Skew N	2.677 (-)	2.688	5.365 (9)	1.996	2.428 (-)	3.520	5.948 (4)	1.731
Log-normal	0.716 (-)	0.853	1.570 (1)	0.977	0.740 (-)	0.861	1.601 (1)	0.984
Best Parametric	1.797 (-)	2.403	4.200 (5)	1.056	3.400 (-)	3.375	6.775 (7)	0.899
Best SemiNP	0.256 (-)	3.289	3.544 (3)	2.264	0.108 (-)	4.401	4.508 (3)	6.993
\mathcal{M}_P	2.367 (-)	2.030	4.397 (6)	1.752	3.967 (-)	2.427	6.394 (5)	1.941
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	1.246 (-)	3.272	4.518 (7)	2.753	2.030 (-)	5.185	7.215 (9)	5.177
$\mathcal{M}_P \cup \mathcal{M}_S$	0.910 (-)	3.257	4.167 (4)	3.056	1.648 (-)	5.195	6.843 (8)	5.467

Table A.59: Simulation study. Sample from 95% mixture distribution of size 200 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$	bias ² (sign)	var	mse(rank)	$\overline{\text{var}}$
GenGam	1.613 (-)	2.749	4.362 (2)	3.267	0.566 (-)	2.896	3.462 (3)	3.517
Gamma	4.703 (-)	0.779	5.481 (9)	1.448	1.331 (-)	0.984	2.316 (2)	1.489
Weibull	0.964 (-)	1.185	2.149 (1)	1.735	0.050 (-)	1.387	1.437 (1)	1.849
Log Skew t	2.080 (-)	3.183	5.263 (7)	3.623	1.035 (-)	3.413	4.448 (5)	3.987
Log t	1.790 (-)	3.518	5.308 (8)	3.932	1.441 (-)	4.008	5.449 (9)	4.446
Log Skew N	1.456 (-)	3.259	4.715 (3)	3.602	0.791 (-)	3.876	4.666 (7)	4.350
Log-normal	1.066 (-)	3.805	4.871 (5)	3.874	0.951 (-)	4.164	5.115 (8)	4.472
Best Parametric	1.282 (-)	3.611	4.893 (6)	3.713	0.905 (-)	3.684	4.589 (6)	4.044
Best SemiNP	0.186 (-)	6.825	7.011 (12)	5.349	1.355 (-)	8.130	9.485 (12)	71.823
\mathcal{M}_P	1.473 (-)	3.357	4.830 (4)	3.697	0.922 (-)	3.492	4.414 (4)	4.090
$\mathcal{M}_P \cup \{\mathcal{M}_S\}$	0.578 (-)	5.285	5.863 (10)	5.269	1.291 (-)	5.878	7.169 (11)	53.842
$\mathcal{M}_P \cup \mathcal{M}_S$	0.290 (-)	5.671	5.961 (11)	5.986	1.294 (-)	5.852	7.147 (10)	51.809

Table A.60: Simulation study. Sample from 95% mixture distribution of size 200 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	1.906 (-)	0.456	2.362 (10)	0.633	2.649 (-)	0.563	3.212 (9)	0.819
Gamma	19.950 (-)	0.284	20.234 (12)	0.181	19.334 (-)	0.269	19.603 (12)	0.164
Weibull	14.748 (-)	0.220	14.968 (11)	0.227	13.926 (-)	0.214	14.139 (11)	0.214
Log Skew t	0.900 (-)	1.066	1.966 (9)	1.222	1.938 (-)	1.459	3.396 (10)	1.455
Log t	0.267 (-)	0.439	0.705 (2)	0.525	0.282 (-)	0.434	0.717 (2)	0.528
Log Skew N	0.867 (-)	0.988	1.855 (8)	1.018	0.790 (-)	1.408	2.198 (4)	0.877
Log-normal	0.227 (-)	0.411	0.638 (1)	0.491	0.234 (-)	0.413	0.647 (1)	0.492
Best Parametric	0.535 (-)	0.865	1.399 (3)	0.583	1.050 (-)	1.355	2.405 (5)	0.617
Best SemiNP	0.130 (-)	1.420	1.550 (6)	1.050	0.193 (-)	1.628	1.821 (3)	13.650
\mathcal{M}_P	0.714 (-)	0.709	1.423 (4)	0.853	1.285 (-)	1.129	2.414 (6)	1.024
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.377 (-)	1.192	1.569 (7)	1.234	0.811 (-)	1.931	2.742 (8)	10.882
$\mathcal{M}_P \cup \mathcal{M}_S$	0.289 (-)	1.209	1.497 (5)	1.367	0.770 (-)	1.915	2.685 (7)	10.265

Table A.61: Simulation study. Sample from 95% mixture distribution of size 500 - estimate of density function in the 5% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	0.797 (-)	1.126	1.923 (2)	1.368	0.156 (-)	1.296	1.452 (3)	1.552
Gamma	3.542 (-)	0.285	3.827 (12)	0.582	0.723 (-)	0.380	1.103 (2)	0.595
Weibull	0.349 (-)	0.449	0.798 (1)	0.703	0.032 (+)	0.540	0.572 (1)	0.747
Log Skew t	0.987 (-)	1.306	2.292 (8)	1.525	0.441 (-)	1.472	1.912 (6)	1.659
Log t	0.717 (-)	1.512	2.229 (7)	1.631	0.604 (-)	1.716	2.320 (10)	1.846
Log Skew N	0.620 (-)	1.337	1.957 (4)	1.515	0.361 (-)	1.726	2.086 (7)	1.847
Log-normal	0.429 (-)	1.523	1.952 (3)	1.605	0.379 (-)	1.766	2.145 (8)	1.855
Best Parametric	0.545 (-)	1.429	1.974 (5)	1.545	0.306 (-)	1.565	1.871 (4)	1.697
Best SemiNP	0.006 (+)	3.122	3.129 (11)	2.302	0.211 (-)	2.485	2.696 (12)	3.856
\mathcal{M}_P	0.622 (-)	1.369	1.991 (6)	1.546	0.327 (-)	1.556	1.883 (5)	1.735
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.030 (-)	2.601	2.631 (10)	2.375	0.286 (-)	2.076	2.362 (11)	3.094
$\mathcal{M}_P \cup \mathcal{M}_S$	0.000 (-)	2.562	2.562 (9)	2.646	0.269 (-)	2.046	2.315 (9)	3.385

Table A.62: Simulation study. Sample from 95% mixture distribution of size 500 - estimate of density function in the 25% quantile of the log-normal distribution (Results $\times 10^{-2}$).

Censoring	No				Yes			
	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$	bias ² (sign)	var	mse(rank)	$\sqrt{\text{var}}$
GenGam	1.127 (-)	0.170	1.298 (10)	0.263	1.511 (-)	0.200	1.711 (10)	0.556
Gamma	18.924 (-)	0.121	19.045 (12)	0.072	18.395 (-)	0.115	18.510 (12)	0.065
Weibull	13.615 (-)	0.086	13.701 (11)	0.089	12.868 (-)	0.084	12.951 (11)	0.084
Log Skew t	0.345 (-)	0.364	0.709 (9)	0.476	0.872 (-)	0.513	1.386 (9)	0.564
Log t	0.070 (-)	0.166	0.236 (2)	0.205	0.076 (-)	0.165	0.241 (2)	0.206
Log Skew N	0.346 (-)	0.334	0.680 (8)	0.383	0.129 (-)	0.340	0.469 (3)	0.283
Log-normal	0.061 (-)	0.160	0.221 (1)	0.197	0.064 (-)	0.159	0.223 (1)	0.198
Best Parametric	0.211 (-)	0.364	0.575 (4)	0.231	0.491 (-)	0.561	1.052 (8)	0.284
Best SemiNP	0.073 (-)	0.594	0.667 (7)	0.450	0.252 (-)	0.299	0.551 (4)	0.377
\mathcal{M}_P	0.281 (-)	0.276	0.557 (3)	0.341	0.479 (-)	0.375	0.854 (7)	0.447
$\mathcal{M}_P \cup \{\hat{\mathcal{M}}_S\}$	0.133 (-)	0.510	0.643 (6)	0.498	0.428 (-)	0.372	0.801 (6)	0.512
$\mathcal{M}_P \cup \mathcal{M}_S$	0.110 (-)	0.511	0.621 (5)	0.555	0.432 (-)	0.355	0.787 (5)	0.503

Appendix B

Model averaging quantiles

Tables B.1-B.60 give the results of the simulation study as described in Chapter 6. For each setting, the 1%, 5%, 25% and 50% quantiles are estimated for each parametric model separately, and the two approaches (direct and indirect) for model averaging are applied.

Table B.1: Simulation study. Sample from log-normal distribution of size 100 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	3.932 (-)	0.050	3.983 (8)	0.057	4.451 (-)	0.035	4.486 (9)	0.036	5.162 (-)	0.013	5.175 (6)	0.013
Weibull	4.055 (-)	0.025	4.080 (9)	0.025	4.323 (-)	0.021	4.344 (8)	0.020	4.827 (-)	0.014	4.841 (5)	0.012
Log-skew-t	0.001 (+)	0.718	0.718 (6)	1.027	0.036 (-)	1.543	1.579 (7)	1.768	0.183 (+)	16.873	17.056 (8)	54.003
Log-t	0.000 (+)	0.347	0.347 (1)	0.462	0.005 (-)	0.448	0.453 (1)	1.126	0.004 (+)	0.795	0.799 (1)	1.280
Log-skew-n	0.023 (+)	0.720	0.744 (7)	0.639	0.173 (+)	1.183	1.355 (6)	0.968	4.510 (+)	13.726	18.236 (9)	8.008
Log-normal	0.026 (+)	0.370	0.396 (2)	0.365	0.028 (+)	0.438	0.466 (2)	0.444	0.081 (+)	0.869	0.951 (2)	0.938
AIC-selected	0.027 (+)	0.579	0.606 (5)	0.419	0.004 (+)	1.261	1.265 (5)	0.528	1.463 (+)	12.336	13.799 (7)	37.260
$\mathcal{M}^{(1)}$	0.008 (+)	0.503	0.511 (3)	0.603	0.000 (+)	0.925	0.925 (3)	1.029	0.038 (+)	3.924	3.962 (4)	17.110
$\mathcal{M}^{(2)}$	0.002 (+)	0.511	0.514 (4)	0.169	0.024 (-)	1.035	1.059 (4)	0.571	2.547 (-)	0.474	3.021 (3)	2.510

(1) direct method of model averaging (MA_1)

(2) indirect method of model averaging (MA_2)

Table B.2: Simulation study. Sample from log-normal distribution of size 100 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	9.163 (-)	0.833	9.995 (8)	1.064	13.581 (-)	0.800	14.382 (9)	0.831	23.098 (-)	0.484	23.582 (9)	0.441
Weibull	10.820 (-)	0.517	11.337 (9)	0.569	13.162 (-)	0.500	13.662 (8)	0.495	18.736 (-)	0.438	19.174 (7)	0.388
Log-skew-t	0.079 (+)	1.689	1.767 (7)	1.930	0.005 (-)	3.066	3.071 (7)	3.254	0.029 (-)	20.920	20.949 (8)	19.412
Log-t	0.075 (+)	1.300	1.376 (2)	1.328	0.041 (+)	1.506	1.548 (1)	1.609	0.214 (+)	2.807	3.021 (1)	3.130
Log-skew-n	0.060 (+)	1.638	1.698 (6)	1.534	0.238 (+)	2.355	2.593 (5)	2.038	5.121 (+)	13.078	18.199 (6)	9.129
Log-normal	0.065 (+)	1.294	1.359 (1)	1.246	0.069 (+)	1.510	1.579 (2)	1.490	0.197 (+)	2.891	3.087 (2)	3.022
AIC-selected	0.076 (+)	1.467	1.542 (5)	1.307	0.005 (+)	2.762	2.766 (6)	1.568	1.334 (+)	13.283	14.617 (5)	4.887
$\mathcal{M}^{(1)}$	0.051 (+)	1.453	1.505 (3)	1.526	0.001 (+)	2.273	2.274 (3)	2.311	0.108 (-)	4.943	5.051 (3)	13.322
$\mathcal{M}^{(2)}$	0.052 (+)	1.458	1.510 (4)	1.159	0.000 (+)	2.356	2.356 (4)	2.046	2.292 (-)	3.494	5.785 (4)	18.811

(1) direct method of model averaging (MA_1)
 (2) indirect method of model averaging (MA_2)

Table B.3: Simulation study. Sample from log-normal distribution of size 100 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	3.207 (+)	9.784	12.991 (9)	17.060	0.805 (-)	12.739	13.544 (8)	17.134	57.831 (-)	19.226	77.057 (9)	17.908
Weibull	0.602 (-)	9.478	10.080 (8)	12.971	5.367 (-)	10.565	15.932 (9)	12.556	37.872 (-)	13.488	51.360 (8)	12.930
Log-skew-t	0.676 (+)	8.738	9.414 (7)	8.495	0.486 (+)	9.394	9.880 (7)	9.388	0.145 (-)	29.341	29.486 (7)	27.785
Log-t	0.525 (+)	8.488	9.013 (6)	7.957	0.481 (+)	9.214	9.694 (6)	9.406	1.303 (+)	14.796	16.099 (2)	16.472
Log-skew-n	0.293 (+)	8.391	8.684 (3)	7.876	0.150 (+)	8.802	8.952 (1)	8.065	3.162 (+)	16.438	19.600 (5)	15.656
Log-normal	0.149 (+)	8.056	8.205 (1)	7.303	0.147 (+)	8.809	8.956 (2)	8.160	0.422 (+)	14.556	14.978 (1)	14.213
AIC-selected	0.233 (+)	8.373	8.606 (2)	7.473	0.169 (+)	9.315	9.484 (5)	8.671	0.531 (+)	22.247	22.778 (6)	13.714
$\mathcal{M}^{(1)}$	0.350 (+)	8.371	8.721 (5)	7.953	0.185 (+)	9.162	9.347 (4)	9.041	0.955 (-)	16.258	17.213 (3)	28.126
$\mathcal{M}^{(2)}$	0.335 (+)	8.360	8.694 (4)	8.974	0.192 (+)	9.131	9.323 (3)	9.849	0.298 (-)	17.071	17.369 (4)	26.430

(1) direct method of model averaging (MA_1)
 (2) indirect method of model averaging (MA_2)

Table B.4: Simulation study. Sample from log-normal distribution of size 100 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	237.173 (+)	77.151	314.324 (9)	65.347	140.922 (+)	71.895	212.817 (9)	69.342	0.415 (+)	82.118	82.533 (9)	88.795
Weibull	78.867 (+)	53.633	132.500 (8)	61.840	40.779 (+)	55.454	96.233 (8)	62.320	0.591 (-)	66.649	67.239 (8)	69.312
Log-skew-t	0.214 (+)	44.262	44.475 (7)	41.834	0.734 (+)	46.438	47.171 (7)	42.586	0.839 (+)	52.196	53.035 (7)	51.076
Log-t	0.094 (+)	36.906	37.000 (2)	32.595	0.056 (+)	37.573	37.628 (2)	33.829	0.447 (+)	46.200	46.647 (2)	42.430
Log-skew-n	0.349 (+)	43.927	44.276 (6)	38.885	0.015 (-)	43.925	43.940 (5)	36.974	0.096 (+)	44.644	44.739 (1)	39.591
Log-normal	0.095 (+)	36.717	36.812 (1)	32.482	0.087 (+)	37.492	37.579 (1)	33.500	0.275 (+)	47.591	47.866 (4)	43.593
AIC-selected	0.139 (+)	41.282	41.420 (5)	33.512	0.489 (+)	44.288	44.776 (6)	35.035	0.112 (+)	47.737	47.849 (3)	44.357
$\mathcal{M}^{(1)}$	0.316 (+)	40.442	40.758 (4)	37.117	0.583 (+)	42.494	43.078 (4)	39.390	0.115 (+)	52.793	52.907 (6)	52.160
$\mathcal{M}^{(2)}$	0.283 (+)	40.369	40.652 (3)	36.677	0.485 (+)	42.321	42.806 (3)	38.803	0.140 (+)	51.024	51.164 (5)	47.223

(1) direct method of model averaging (MA_1)
 (2) indirect method of model averaging (MA_2)

Table B.5: Simulation study. Sample from 75% mixture of size 100 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	3.305 (-)	0.173	3.479 (9)	0.280	4.041 (-)	0.157	4.198 (9)	0.219	4.943 (-)	0.143	5.086 (8)	0.190
Weibull	2.918 (-)	0.161	3.079 (8)	0.209	3.330 (-)	0.154	3.484 (7)	0.184	3.733 (-)	0.170	3.903 (4)	0.194
Log-skew-t	1.822 (-)	0.303	2.125 (7)	0.591	3.264 (-)	0.343	3.608 (8)	0.942	6.182 (-)	0.146	6.328 (9)	0.822
Log-t	0.508 (+)	0.838	1.346 (1)	0.870	0.544 (+)	0.946	1.490 (1)	1.033	2.240 (+)	1.656	3.895 (3)	1.992
Log-skew-n	1.109 (-)	0.351	1.460 (2)	0.501	1.645 (-)	0.384	2.028 (3)	0.438	0.128 (-)	3.639	3.767 (2)	1.022
Log-normal	0.670 (+)	0.868	1.538 (3)	0.830	0.788 (+)	0.967	1.755 (2)	0.973	2.899 (+)	1.721	4.620 (5)	1.993
AIC-selected	1.125 (-)	0.435	1.560 (4)	0.474	2.065 (-)	0.475	2.540 (4)	0.391	3.042 (-)	1.610	4.652 (6)	0.866
$\mathcal{M}^{(1)}$	1.357 (-)	0.347	1.704 (5)	0.621	2.427 (-)	0.339	2.765 (5)	0.570	2.209 (-)	1.197	3.406 (1)	1.645
$\mathcal{M}^{(2)}$	1.481 (-)	0.317	1.798 (6)	0.372	2.699 (-)	0.348	3.047 (6)	0.495	3.965 (-)	0.731	4.696 (7)	1.682

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.6: Simulation study. Sample from 75% mixture of size 100 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	1.654 (-)	2.541	4.195 (7)	4.043	4.454 (-)	2.733	7.187 (6)	3.634	10.097 (-)	3.119	13.216 (5)	3.701
Weibull	0.991 (-)	2.527	3.518 (6)	3.243	2.196 (-)	2.598	4.794 (2)	3.044	3.896 (-)	3.079	6.975 (1)	3.341
Log-skew-t	0.857 (-)	2.212	3.069 (5)	3.994	4.769 (-)	3.220	7.989 (7)	5.551	28.611 (-)	3.451	32.063 (9)	7.009
Log-t	4.118 (+)	3.460	7.579 (9)	3.359	4.323 (+)	3.780	8.103 (8)	3.758	12.190 (+)	6.112	18.302 (7)	6.713
Log-skew-n	0.304 (-)	2.314	2.618 (1)	3.630	1.496 (-)	2.684	4.179 (1)	3.513	0.003 (-)	12.860	12.862 (3)	4.917
Log-normal	3.937 (+)	3.393	7.330 (8)	3.169	4.448 (+)	3.746	8.193 (9)	3.643	13.041 (+)	6.121	19.162 (8)	6.706
AIC-selected	0.325 (-)	2.478	2.804 (4)	3.616	2.574 (-)	3.679	6.253 (5)	3.523	5.010 (-)	7.954	12.965 (4)	7.379
$\mathcal{M}^{(1)}$	0.448 (-)	2.302	2.750 (2)	3.930	2.933 (-)	3.002	5.935 (3)	4.210	3.363 (-)	5.980	9.343 (2)	9.903
$\mathcal{M}^{(2)}$	0.444 (-)	2.312	2.756 (3)	3.049	2.990 (-)	3.072	6.062 (4)	4.043	5.952 (-)	7.332	13.285 (6)	12.258

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.7: Simulation study. Sample from 75% mixture of size 100 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	131.581 (+)	26.492	158.073 (9)	46.106	77.528 (+)	32.573	110.101 (8)	47.585	21.686 (+)	48.153	69.838 (1)	58.199
Weibull	123.224 (+)	31.518	154.742 (8)	45.434	88.375 (+)	34.860	123.234 (9)	45.428	55.856 (+)	44.811	100.667 (7)	51.680
Log-skew-t	95.098 (+)	26.313	121.410 (7)	43.651	60.485 (+)	32.891	93.376 (7)	51.481	3.041 (-)	86.601	89.641 (6)	102.607
Log-t	36.421 (+)	22.781	59.203 (2)	24.240	37.960 (+)	24.179	62.139 (2)	25.902	80.429 (+)	32.685	113.114 (9)	34.899
Log-skew-n	86.589 (+)	24.127	110.716 (3)	39.481	50.516 (+)	29.307	79.823 (3)	41.921	28.657 (+)	45.555	74.212 (2)	46.835
Log-normal	30.342 (+)	21.160	51.502 (1)	21.740	33.017 (+)	22.683	55.700 (1)	23.512	77.167 (+)	32.254	109.421 (8)	34.175
AIC-selected	87.281 (+)	24.722	112.003 (4)	39.784	54.739 (+)	31.019	85.758 (4)	45.689	31.932 (+)	52.368	84.301 (5)	58.621
$\mathcal{M}^{(1)}$	90.881 (+)	25.388	116.269 (6)	41.653	58.123 (+)	31.259	89.382 (6)	46.877	32.503 (+)	45.561	78.065 (3)	68.293
$\mathcal{M}^{(2)}$	90.200 (+)	25.386	115.587 (5)	35.143	57.784 (+)	31.137	88.921 (5)	40.754	36.292 (+)	44.850	81.142 (4)	58.781

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.8: Simulation study. Sample from 75% mixture of size 100 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	494.980 (+)	109.606	604.587 (8)	151.096	368.057 (+)	112.775	480.831 (5)	158.416	191.488 (+)	132.790	324.278 (4)	186.437
Weibull	397.271 (+)	103.698	500.969 (3)	161.025	312.109 (+)	110.080	422.189 (3)	164.216	221.369 (+)	130.758	352.126 (6)	180.792
Log-skew-t	559.787 (+)	94.493	654.280 (9)	154.065	507.278 (+)	118.075	625.352 (9)	186.922	652.625 (+)	239.503	892.128 (9)	375.632
Log-t	0.730 (+)	80.585	81.315 (2)	113.945	1.062 (+)	82.975	84.037 (2)	116.455	18.823 (+)	95.585	114.408 (2)	123.378
Log-skew-n	495.544 (+)	90.689	586.233 (6)	144.682	369.520 (+)	100.517	470.037 (4)	151.340	96.605 (+)	144.348	240.954 (3)	163.423
Log-normal	0.000 (+)	75.296	75.296 (1)	107.712	0.073 (+)	77.311	77.384 (1)	109.323	15.483 (+)	94.328	109.810 (1)	120.754
AIC-selected	496.121 (+)	97.799	593.919 (7)	142.427	428.187 (+)	114.833	543.020 (8)	161.425	226.534 (+)	148.207	374.741 (8)	217.630
$\mathcal{M}^{(1)}$	485.171 (+)	94.767	579.938 (5)	154.845	414.629 (+)	107.980	522.609 (7)	172.897	219.680 (+)	142.081	361.761 (7)	229.634
$\mathcal{M}^{(2)}$	481.552 (+)	95.558	577.110 (4)	155.839	411.762 (+)	108.234	519.997 (6)	177.192	208.519 (+)	139.336	347.855 (5)	216.685

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.9: Simulation study. Sample from 90% mixture of size 100 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	3.919 (-)	0.071	3.990 (9)	0.102	4.522 (-)	0.057	4.580 (9)	0.069	5.359 (-)	0.029	5.388 (9)	0.035
Weibull	3.821 (-)	0.051	3.872 (8)	0.062	4.163 (-)	0.046	4.209 (8)	0.051	4.709 (-)	0.038	4.747 (7)	0.040
Log-skew-t	0.443 (-)	0.825	1.268 (7)	0.886	1.308 (-)	1.049	2.357 (7)	1.008	4.088 (-)	0.819	4.908 (8)	1.586
Log-t	0.048 (+)	0.493	0.541 (1)	0.528	0.036 (+)	0.573	0.609 (1)	0.628	0.208 (+)	0.981	1.189 (2)	1.194
Log-skew-n	0.264 (-)	0.836	1.100 (4)	0.774	0.416 (-)	1.230	1.646 (3)	0.611	0.366 (+)	1.445	1.811 (4)	1.344
Log-normal	0.096 (+)	0.515	0.611 (2)	0.506	0.096 (+)	0.590	0.686 (2)	0.594	0.387 (+)	1.046	1.433 (3)	1.193
AIC-selected	0.083 (-)	1.063	1.146 (5)	0.446	0.646 (-)	1.669	2.315 (6)	0.363	0.000 (-)	2.312	2.312 (6)	0.962
$\mathcal{M}^{(1)}$	0.202 (-)	0.824	1.025 (3)	0.770	0.827 (-)	1.030	1.857 (4)	0.830	0.072 (-)	1.112	1.184 (1)	2.157
$\mathcal{M}^{(2)}$	0.328 (-)	0.846	1.174 (6)	0.425	1.326 (-)	0.962	2.287 (5)	0.707	1.232 (-)	0.872	2.104 (5)	2.863

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.10: Simulation study. Sample from 90% mixture of size 100 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	6.323 (-)	1.277	7.600 (8)	1.912	10.628 (-)	1.299	11.926 (9)	1.571	19.829 (-)	1.060	20.888 (9)	1.126
Weibull	6.594 (-)	1.025	7.619 (9)	1.271	8.910 (-)	1.027	9.936 (8)	1.136	13.582 (-)	1.033	14.616 (7)	1.052
Log-skew-t	0.131 (-)	2.531	2.662 (4)	2.899	1.891 (-)	3.647	5.538 (6)	3.536	15.553 (-)	4.352	19.905 (8)	8.720
Log-t	0.689 (+)	2.004	2.693 (5)	1.960	0.605 (+)	2.266	2.872 (1)	2.231	1.695 (+)	3.754	5.449 (3)	4.126
Log-skew-n	0.054 (-)	2.469	2.523 (3)	2.636	0.479 (-)	3.858	4.337 (3)	2.521	1.763 (+)	4.778	6.541 (5)	4.304
Log-normal	0.695 (+)	1.999	2.695 (6)	1.898	0.687 (+)	2.265	2.952 (2)	2.200	1.961 (+)	3.825	5.786 (4)	4.150
AIC-selected	0.000 (+)	2.914	2.914 (7)	2.068	0.956 (-)	5.025	5.981 (7)	1.891	0.090 (+)	8.090	8.181 (6)	3.511
$\mathcal{M}^{(1)}$	0.032 (-)	2.456	2.487 (1)	2.695	1.253 (-)	3.505	4.758 (4)	3.180	0.043 (-)	4.557	4.600 (1)	7.560
$\mathcal{M}^{(2)}$	0.031 (-)	2.472	2.503 (2)	2.259	1.375 (-)	3.560	4.935 (5)	3.317	0.363 (-)	4.902	5.264 (2)	8.442

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.11: Simulation study. Sample from 90% mixture of size 100 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	40.039 (+)	16.466	56.505 (9)	28.766	11.941 (+)	20.761	32.701 (9)	29.193	6.930 (-)	30.696	37.626 (4)	33.398
Weibull	19.366 (+)	17.545	36.911 (6)	24.856	7.064 (+)	19.531	26.596 (3)	24.391	0.487 (-)	24.762	25.249 (1)	26.619
Log-skew-t	22.378 (+)	17.159	39.537 (8)	20.120	11.825 (+)	18.211	30.037 (8)	22.878	9.857 (-)	42.028	51.885 (9)	47.342
Log-t	10.787 (+)	13.530	24.318 (2)	13.406	10.163 (+)	14.571	24.734 (2)	14.455	18.406 (+)	21.534	39.940 (6)	22.047
Log-skew-n	21.473 (+)	16.941	38.414 (7)	19.372	11.221 (+)	17.366	28.587 (7)	20.386	16.221 (+)	23.803	40.024 (7)	22.117
Log-normal	9.284 (+)	13.181	22.465 (1)	12.701	9.150 (+)	14.362	23.513 (1)	13.909	17.489 (+)	21.535	39.024 (5)	21.865
AIC-selected	17.906 (+)	16.591	34.497 (3)	17.382	10.561 (+)	17.240	27.801 (4)	20.605	10.113 (+)	29.931	40.044 (8)	23.338
$\mathcal{M}^{(1)}$	18.912 (+)	16.472	35.383 (5)	18.779	10.976 (+)	17.375	28.351 (6)	21.251	6.692 (+)	26.263	32.955 (2)	29.481
$\mathcal{M}^{(2)}$	18.332 (+)	16.341	34.673 (4)	17.968	10.966 (+)	17.236	28.202 (5)	20.681	7.819 (+)	26.201	34.020 (3)	28.257

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.12: Simulation study. Sample from 90% mixture of size 100 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	612.697 (+)	93.483	706.180 (9)	105.132	447.004 (+)	93.602	540.606 (9)	110.951	145.439 (+)	109.621	255.060 (8)	137.094
Weibull	375.009 (+)	78.179	453.188 (8)	106.433	280.477 (+)	82.844	363.321 (7)	108.007	124.276 (+)	99.560	223.836 (7)	120.633
Log-skew-t	215.211 (+)	162.748	377.960 (7)	117.513	255.086 (+)	136.211	391.297 (8)	119.982	165.013 (+)	118.483	283.496 (9)	160.708
Log-t	34.569 (+)	55.185	89.754 (2)	63.188	33.615 (+)	56.718	90.332 (2)	64.740	51.408 (+)	70.086	121.494 (2)	75.923
Log-skew-n	213.679 (+)	157.741	371.420 (6)	110.960	193.640 (+)	146.969	340.609 (6)	100.022	51.151 (+)	71.786	122.938 (3)	77.510
Log-normal	31.627 (+)	54.209	85.836 (1)	61.857	31.344 (+)	56.023	87.367 (1)	63.382	49.780 (+)	70.118	119.898 (1)	75.662
AIC-selected	167.509 (+)	163.553	331.061 (5)	85.356	185.147 (+)	136.862	322.009 (5)	89.631	66.340 (+)	79.259	145.599 (4)	86.517
$\mathcal{M}^{(1)}$	168.236 (+)	134.308	302.544 (4)	106.443	193.763 (+)	115.889	309.653 (4)	108.430	73.483 (+)	79.520	153.003 (6)	95.531
$\mathcal{M}^{(2)}$	162.491 (+)	132.227	294.718 (3)	101.889	186.398 (+)	115.423	301.821 (3)	107.280	70.782 (+)	78.454	149.235 (5)	97.661

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.13: Simulation study. Sample from 95% mixture of size 100 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	3.915 (-)	0.062	3.977 (9)	0.080	4.476 (-)	0.049	4.525 (9)	0.052	5.252 (-)	0.022	5.274 (7)	0.023
Weibull	3.892 (-)	0.039	3.931 (8)	0.044	4.204 (-)	0.035	4.239 (8)	0.035	4.740 (-)	0.026	4.767 (6)	0.025
Log-skew-t	0.079 (-)	0.835	0.914 (7)	0.925	0.491 (-)	1.246	1.738 (5)	1.368	1.862 (-)	6.003	7.865 (9)	499.393
Log-t	0.020 (+)	0.445	0.466 (1)	0.476	0.010 (+)	0.518	0.528 (1)	0.587	0.081 (+)	0.912	0.993 (1)	1.086
Log-skew-n	0.035 (-)	0.775	0.810 (5)	0.737	0.030 (-)	1.362	1.393 (4)	0.764	0.724 (+)	5.111	5.835 (8)	2.086
Log-normal	0.057 (+)	0.471	0.528 (2)	0.445	0.055 (+)	0.544	0.598 (2)	0.527	0.194 (+)	0.974	1.168 (2)	1.058
AIC-selected	0.000 (-)	0.813	0.813 (6)	0.445	0.163 (-)	1.600	1.763 (7)	0.417	0.163 (+)	4.286	4.449 (5)	3.078
$\mathcal{M}^{(1)}$	0.020 (-)	0.695	0.715 (3)	0.713	0.246 (-)	1.119	1.366 (3)	0.918	0.007 (-)	1.617	1.624 (3)	63.129
$\mathcal{M}^{(2)}$	0.055 (-)	0.747	0.802 (4)	0.320	0.557 (-)	1.192	1.749 (6)	0.701	1.310 (-)	0.740	2.050 (4)	3.043

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.14: Simulation study. Sample from 95% mixture of size 100 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	7.324 (-)	1.092	8.416 (8)	1.538	11.701 (-)	1.092	12.793 (9)	1.234	21.139 (-)	0.801	21.939 (9)	0.781
Weibull	8.031 (-)	0.801	8.832 (9)	0.955	10.396 (-)	0.794	11.189 (8)	0.842	15.533 (-)	0.763	16.296 (7)	0.731
Log-skew-t	0.008 (+)	2.244	2.252 (6)	2.467	0.466 (-)	3.525	3.991 (6)	3.615	7.849 (-)	10.875	18.725 (8)	24.028
Log-t	0.385 (+)	1.770	2.155 (4)	1.689	0.310 (+)	2.009	2.320 (1)	1.939	0.812 (+)	3.432	4.244 (2)	3.624
Log-skew-n	0.014 (+)	2.113	2.127 (3)	2.195	0.004 (-)	3.470	3.474 (3)	2.364	1.824 (+)	6.990	8.814 (6)	4.378
Log-normal	0.393 (+)	1.769	2.161 (5)	1.633	0.374 (+)	2.019	2.394 (2)	1.907	0.956 (+)	3.498	4.454 (4)	3.640
AIC-selected	0.089 (+)	2.264	2.352 (7)	1.743	0.188 (-)	4.578	4.766 (7)	1.714	0.565 (+)	7.505	8.070 (5)	3.590
$\mathcal{M}^{(1)}$	0.023 (+)	2.070	2.093 (1)	2.211	0.308 (-)	3.374	3.682 (4)	2.969	0.014 (-)	3.964	3.978 (1)	10.073
$\mathcal{M}^{(2)}$	0.023 (+)	2.080	2.103 (2)	1.742	0.372 (-)	3.489	3.861 (5)	2.936	0.435 (-)	3.934	4.369 (3)	11.157

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.15: Simulation study. Sample from 95% mixture of size 100 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	24.433 (+)	14.170	38.603 (9)	24.314	4.372 (+)	17.951	22.323 (9)	24.557	19.165 (-)	26.694	45.859 (9)	27.168
Weibull	7.452 (+)	14.459	21.911 (5)	20.103	1.064 (+)	16.080	17.144 (1)	19.616	6.806 (-)	20.532	27.338 (3)	20.958
Log-skew-t	10.761 (+)	14.012	24.773 (8)	14.132	6.652 (+)	14.427	21.079 (8)	16.137	5.087 (-)	39.068	44.155 (8)	44.865
Log-t	6.686 (+)	11.841	18.527 (2)	11.167	6.178 (+)	12.756	18.934 (3)	12.174	10.003 (+)	19.429	29.432 (5)	19.057
Log-skew-n	10.083 (+)	13.696	23.779 (7)	13.691	5.966 (+)	13.656	19.622 (7)	14.328	10.104 (+)	20.295	30.399 (6)	18.777
Log-normal	5.617 (+)	11.454	17.071 (1)	10.584	5.417 (+)	12.527	17.943 (2)	11.664	9.188 (+)	19.441	28.628 (4)	18.856
AIC-selected	8.210 (+)	13.195	21.405 (3)	12.290	5.386 (+)	13.954	19.340 (4)	14.761	7.435 (+)	23.311	30.745 (7)	19.107
$\mathcal{M}^{(1)}$	8.890 (+)	13.164	22.054 (6)	13.304	5.586 (+)	13.972	19.559 (6)	15.318	2.740 (+)	21.414	24.154 (1)	27.650
$\mathcal{M}^{(2)}$	8.642 (+)	13.088	21.730 (4)	13.534	5.630 (+)	13.876	19.506 (5)	15.508	3.652 (+)	21.533	25.185 (2)	26.205

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.16: Simulation study. Sample from 95% mixture of size 100 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	536.561 (+)	89.276	625.836 (9)	90.985	380.422 (+)	87.750	468.171 (9)	96.207	88.473 (+)	103.775	192.248 (9)	120.415
Weibull	295.659 (+)	70.760	366.419 (8)	90.131	212.134 (+)	74.458	286.591 (8)	91.259	67.540 (+)	90.564	158.104 (7)	101.904
Log-skew-t	80.392 (+)	105.188	185.580 (7)	81.207	103.869 (+)	103.246	207.115 (7)	88.453	80.707 (+)	100.924	181.630 (8)	114.636
Log-t	29.682 (+)	49.647	79.329 (2)	51.261	28.710 (+)	50.857	79.567 (2)	52.759	38.063 (+)	64.024	102.087 (3)	63.303
Log-skew-n	83.107 (+)	101.269	184.376 (6)	78.555	74.162 (+)	104.074	178.236 (5)	71.847	35.512 (+)	65.805	101.317 (1)	62.880
Log-normal	28.078 (+)	48.811	76.890 (1)	50.462	27.547 (+)	50.393	77.940 (1)	51.850	37.228 (+)	64.202	101.430 (2)	63.558
AIC-selected	62.546 (+)	95.784	158.330 (5)	60.332	82.076 (+)	96.269	178.345 (6)	64.842	40.051 (+)	67.421	107.472 (4)	66.452
$\mathcal{M}^{(1)}$	69.095 (+)	86.332	155.427 (4)	73.272	88.017 (+)	85.812	173.829 (4)	78.883	45.832 (+)	71.705	117.537 (6)	76.024
$\mathcal{M}^{(2)}$	67.109 (+)	85.041	152.150 (3)	71.218	84.189 (+)	84.824	169.013 (3)	77.686	44.286 (+)	70.519	114.805 (5)	75.789

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.17: Simulation study. Sample from gamma distribution of size 100 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	0.000 (+)	0.000	0.000 (1)	0.000	0.000 (+)	0.000	0.000 (1)	0.000	0.000 (+)	0.000	0.000 (1)	0.000
Weibull	0.000 (+)	0.000	0.000 (6)	0.000	0.000 (+)	0.000	0.000 (4)	0.000	0.000 (+)	0.000	0.000 (2)	0.000
Log-skew-t	0.000 (+)	0.000	0.000 (5)	0.000	0.000 (+)	0.000	0.000 (5)	0.000	0.001 (+)	0.084	0.085 (4)	693.827
Log-t	0.000 (+)	0.000	0.000 (7)	0.000	0.006 (+)	0.003	0.008 (8)	0.003	0.113 (+)	0.045	0.158 (7)	0.066
Log-skew-n	0.000 (+)	0.000	0.000 (8)	0.000	0.000 (+)	0.000	0.000 (6)	0.000	0.063 (+)	0.112	0.174 (8)	0.117
Log-normal	0.000 (+)	0.000	0.000 (9)	0.000	0.007 (+)	0.003	0.010 (9)	0.004	0.131 (+)	0.051	0.182 (9)	0.072
AIC-selected	0.000 (+)	0.000	0.000 (3)	0.000	0.000 (+)	0.000	0.000 (2)	0.000	0.053 (+)	0.074	0.127 (6)	0.049
$\mathcal{M}^{(1)}$	0.000 (+)	0.000	0.000 (4)	0.000	0.000 (+)	0.000	0.000 (7)	0.000	0.048 (+)	0.050	0.098 (5)	49.427
$\mathcal{M}^{(2)}$	0.000 (+)	0.000	0.000 (2)	0.000	0.000 (+)	0.000	0.000 (3)	0.000	0.005 (+)	0.014	0.018 (3)	0.209

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.18: Simulation study. Sample from gamma distribution of size 100 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	0.000 (+)	0.000	0.000 (1)	0.000	0.000 (+)	0.000	0.000 (1)	0.000237	0.000 (+)	0.001	0.001 (1)	0.001
Weibull	0.000 (+)	0.000	0.000 (8)	0.000	0.003 (+)	0.003	0.007 (7)	0.003	0.017 (+)	0.016	0.033 (2)	0.018
Log-skew-t	0.000 (+)	0.000	0.000 (5)	0.000	0.000 (+)	0.002	0.002 (4)	0.007	0.009 (+)	0.193	0.202 (3)	126.761
Log-t	0.002 (+)	0.002	0.003 (9)	0.002	0.134 (+)	0.042	0.176 (8)	0.042	1.462 (+)	0.381	1.842 (8)	0.487
Log-skew-n	0.000 (+)	0.000	0.000 (6)	0.000	0.001 (+)	0.003	0.004 (6)	0.004	0.642 (+)	0.798	1.440 (7)	0.379
Log-normal	0.000 (+)	0.000	0.000 (7)	0.000	0.141 (+)	0.043	0.184 (9)	0.043	1.512 (+)	0.385	1.898 (9)	0.496
AIC-selected	0.000 (+)	0.000	0.000 (2)	0.000	0.000 (+)	0.001	0.001 (2)	0.001	0.602 (+)	0.701	1.304 (6)	0.323
$\mathcal{M}^{(1)}$	0.000 (+)	0.000051	0.000064 (4)	0.000074	0.001 (+)	0.002	0.003 (5)	0.004	0.554 (+)	0.453	1.007 (5)	9.627
$\mathcal{M}^{(2)}$	0.000 (+)	0.000045	0.000055 (3)	0.000347	0.000 (+)	0.001	0.001 (3)	0.006	0.290 (+)	0.380	0.671 (4)	1.318

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.19: Simulation study. Sample from gamma distribution of size 100 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	0.051 (+)	0.485	0.536 (4)	0.531	0.095 (+)	1.037	1.132 (1)	1.084	0.263 (+)	2.092	2.355 (1)	2.204
Weibull	0.059 (+)	0.493	0.552 (6)	0.379	2.350 (+)	1.633	3.983 (7)	1.499	8.307 (+)	3.842	12.149 (3)	3.977
Log-skew-t	0.026 (+)	0.543	0.569 (8)	0.579	0.167 (+)	1.151	1.318 (2)	1.687	0.785 (+)	3.950	4.736 (2)	5.413
Log-t	1.676 (+)	3.491	5.167 (9)	1.755	5.622 (+)	1.721	7.342 (9)	1.486	38.120 (+)	6.707	44.827 (9)	7.086
Log-skew-n	0.244 (-)	0.135	0.379 (1)	0.081	0.407 (+)	1.201	1.608 (6)	1.200	14.608 (+)	14.957	29.565 (7)	5.281
Log-normal	0.316 (-)	0.118	0.434 (2)	0.056	5.497 (+)	1.686	7.183 (8)	1.453	37.605 (+)	6.454	44.059 (8)	6.993
AIC-selected	0.049 (+)	0.518	0.567 (7)	0.542	0.181 (+)	1.171	1.351 (3)	1.093	14.568 (+)	14.839	29.407 (6)	5.578
$\mathcal{M}^{(1)}$	0.041 (+)	0.497	0.538 (5)	0.548	0.323 (+)	1.202	1.525 (4)	1.353	15.360 (+)	10.127	25.488 (4)	7.975
$\mathcal{M}^{(2)}$	0.036 (+)	0.491	0.527 (3)	0.603	0.316 (+)	1.227	1.543 (5)	1.215	14.339 (+)	11.156	25.496 (5)	6.734

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.20: Simulation study. Sample from gamma distribution of size 100 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	0.940 (+)	28.374	29.314 (1)	30.243	0.961 (+)	44.961	45.923 (7)	45.967	2.615 (+)	67.875	70.490 (1)	69.606
Weibull	20.170 (-)	19.804	39.974 (6)	17.341	0.947 (+)	35.393	36.340 (3)	31.686	33.444 (+)	56.757	90.201 (6)	54.632
Log-skew-t	0.102 (-)	39.474	39.576 (5)	39.894	0.621 (+)	49.213	49.835 (9)	54.130	1.136 (+)	70.966	72.103 (2)	75.578
Log-t	2.386 (-)	69.375	71.762 (7)	38.477	1.884 (-)	21.664	23.549 (2)	18.952	55.607 (+)	45.879	101.486 (9)	42.302
Log-skew-n	80.807 (-)	13.087	93.894 (8)	9.196	0.006 (+)	38.818	38.824 (4)	40.461	17.256 (+)	72.304	89.560 (5)	57.230
Log-normal	119.953 (-)	6.828	126.781 (9)	7.187	2.194 (-)	21.251	23.445 (1)	18.476	55.179 (+)	44.325	99.504 (8)	41.853
AIC-selected	0.462 (+)	34.904	35.365 (4)	31.786	0.724 (+)	46.694	47.419 (8)	45.811	16.945 (+)	75.567	92.512 (7)	58.763
$\mathcal{M}^{(1)}$	0.065 (+)	31.877	31.942 (3)	35.274	0.478 (+)	43.612	44.090 (6)	44.614	21.855 (+)	63.924	85.779 (3)	61.096
$\mathcal{M}^{(2)}$	0.023 (+)	31.817	31.840 (2)	31.328	0.447 (+)	43.123	43.570 (5)	34.338	24.370 (+)	62.470	86.840 (4)	42.327

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.21: Simulation study. Sample from log-normal distribution of size 200 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	4.135 (-)	0.022	4.157 (8)	0.022	4.644 (-)	0.014	4.658 (9)	0.012	5.282 (-)	0.003	5.285 (7)	0.002
Weibull	4.200 (-)	0.011	4.212 (9)	0.010	4.463 (-)	0.009	4.472 (8)	0.007	4.945 (-)	0.005	4.950 (6)	0.004
Log-skew-t	0.001 (-)	0.325	0.327 (7)	0.395	0.073 (-)	0.663	0.735 (7)	0.816	0.032 (-)	6.819	6.850 (9)	8.108
Log-t	0.002 (-)	0.172	0.174 (1)	0.213	0.012 (-)	0.208	0.220 (2)	0.343	0.000 (-)	0.390	0.390 (1)	0.537
Log-skew-n	0.004 (+)	0.302	0.306 (6)	0.302	0.028 (+)	0.440	0.469 (5)	0.454	0.998 (+)	4.831	5.829 (8)	2.676
Log-normal	0.008 (+)	0.168	0.175 (2)	0.173	0.007 (+)	0.197	0.204 (1)	0.211	0.027 (+)	0.424	0.452 (2)	0.439
AIC-selected	0.009 (+)	0.280	0.289 (5)	0.201	0.002 (+)	0.485	0.488 (6)	0.268	0.158 (+)	3.580	3.738 (5)	1.315
$\mathcal{M}^{(1)}$	0.003 (+)	0.228	0.231 (4)	0.272	0.000 (-)	0.372	0.372 (3)	0.453	0.146 (-)	1.350	1.496 (3)	3.565
$\mathcal{M}^{(2)}$	0.002 (+)	0.226	0.228 (3)	0.056	0.003 (-)	0.412	0.415 (4)	0.181	3.276 (-)	0.230	3.506 (4)	1.539

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.22: Simulation study. Sample from log-normal distribution of size 200 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	10.178 (-)	0.411	10.589 (8)	0.486	14.894 (-)	0.374	15.268 (9)	0.361	24.662 (-)	0.188	24.850 (9)	0.148
Weibull	11.758 (-)	0.251	12.010 (9)	0.253	14.184 (-)	0.231	14.415 (8)	0.215	19.893 (-)	0.195	20.088 (8)	0.156
Log-skew-t	0.025 (+)	0.763	0.788 (7)	0.844	0.022 (-)	1.400	1.422 (7)	1.507	0.242 (-)	9.871	10.112 (7)	12.421
Log-t	0.023 (+)	0.600	0.622 (2)	0.636	0.006 (+)	0.695	0.701 (1)	0.756	0.075 (+)	1.420	1.494 (1)	1.491
Log-skew-n	0.016 (+)	0.740	0.756 (6)	0.738	0.047 (+)	0.975	1.022 (5)	1.026	1.378 (+)	5.395	6.773 (6)	4.127
Log-normal	0.019 (+)	0.598	0.618 (1)	0.604	0.018 (+)	0.688	0.706 (2)	0.724	0.070 (+)	1.429	1.499 (2)	1.465
AIC-selected	0.028 (+)	0.714	0.742 (5)	0.634	0.008 (+)	1.113	1.121 (6)	0.804	0.127 (+)	5.526	5.653 (4)	2.115
$\mathcal{M}^{(1)}$	0.024 (+)	0.660	0.684 (3)	0.706	0.003 (+)	0.974	0.976 (3)	1.049	1.043 (-)	2.276	3.320 (3)	8.408
$\mathcal{M}^{(2)}$	0.024 (+)	0.661	0.685 (4)	0.546	0.002 (+)	0.989	0.992 (4)	0.891	4.134 (-)	2.055	6.189 (5)	14.357

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.23: Simulation study. Sample from log-normal distribution of size 200 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	2.395 (+)	4.740	7.135 (9)	8.514	1.481 (-)	6.128	7.609 (8)	8.561	66.901 (-)	9.935	76.836 (9)	8.735
Weibull	1.330 (-)	4.700	6.029 (8)	6.329	7.386 (-)	5.094	12.481 (9)	6.107	43.916 (-)	6.693	50.608 (8)	6.197
Log-skew-t	0.317 (+)	4.061	4.378 (7)	4.030	0.227 (+)	4.351	4.578 (7)	4.498	0.066 (-)	14.211	14.277 (7)	14.353
Log-t	0.248 (+)	3.926	4.174 (6)	3.892	0.182 (+)	4.336	4.519 (6)	4.331	0.620 (+)	7.630	8.249 (2)	7.596
Log-skew-n	0.102 (+)	3.932	4.034 (5)	3.823	0.049 (+)	4.137	4.186 (2)	4.035	1.096 (+)	8.162	9.258 (3)	8.190
Log-normal	0.045 (+)	3.839	3.884 (1)	3.609	0.038 (+)	4.123	4.161 (1)	4.042	0.167 (+)	7.182	7.349 (1)	7.089
AIC-selected	0.079 (+)	3.881	3.960 (2)	3.667	0.065 (+)	4.273	4.338 (5)	4.147	0.013 (+)	13.645	13.657 (6)	7.064
$\mathcal{M}^{(1)}$	0.123 (+)	3.891	4.013 (4)	3.835	0.082 (+)	4.234	4.316 (4)	4.267	3.055 (-)	8.994	12.049 (5)	20.083
$\mathcal{M}^{(2)}$	0.119 (+)	3.887	4.006 (3)	4.406	0.083 (+)	4.227	4.309 (3)	4.741	1.872 (-)	9.328	11.200 (4)	18.546

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.24: Simulation study. Sample from log-normal distribution of size 200 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	238.457 (+)	37.751	276.208 (9)	32.484	140.605 (+)	35.410	176.015 (9)	34.600	0.125 (+)	41.285	41.410 (9)	44.997
Weibull	74.027 (+)	26.384	100.412 (8)	30.913	36.776 (+)	27.089	63.865 (8)	31.163	1.542 (-)	33.120	34.662 (8)	34.673
Log-skew-t	0.049 (+)	20.548	20.597 (7)	19.124	0.342 (+)	21.863	22.205 (7)	20.280	0.429 (+)	24.726	25.156 (5)	24.266
Log-t	0.025 (+)	17.865	17.890 (1)	16.159	0.006 (+)	18.163	18.169 (1)	16.742	0.205 (+)	23.358	23.562 (3)	21.137
Log-skew-n	0.101 (+)	20.127	20.228 (6)	18.898	0.001 (-)	20.961	20.962 (6)	18.336	0.045 (+)	22.656	22.701 (1)	20.743
Log-normal	0.025 (+)	17.896	17.921 (2)	16.130	0.020 (+)	18.161	18.180 (2)	16.645	0.133 (+)	23.372	23.505 (2)	21.804
AIC-selected	0.016 (+)	19.340	19.356 (5)	16.590	0.055 (+)	20.771	20.825 (5)	17.196	0.030 (+)	24.562	24.592 (4)	22.787
$\mathcal{M}^{(1)}$	0.034 (+)	18.805	18.839 (4)	17.802	0.076 (+)	19.981	20.057 (4)	18.520	0.018 (+)	26.886	26.905 (7)	27.452
$\mathcal{M}^{(2)}$	0.032 (+)	18.798	18.830 (3)	17.661	0.067 (+)	19.942	20.009 (3)	18.298	0.030 (+)	25.928	25.958 (6)	24.945

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.25: Simulation study. Sample from 75% mixture of size 200 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	3.902 (-)	0.067	3.969 (9)	0.098	4.668 (-)	0.056	4.724 (9)	0.070	5.631 (-)	0.046	5.678 (8)	0.049
Weibull	3.562 (-)	0.063	3.625 (8)	0.070	3.991 (-)	0.057	4.048 (8)	0.060	4.481 (-)	0.061	4.541 (5)	0.058
Log-skew-t	2.053 (-)	0.145	2.198 (7)	0.258	3.663 (-)	0.188	3.851 (7)	0.300	6.691 (-)	0.053	6.744 (9)	0.647
Log-t	0.198 (+)	0.380	0.577 (1)	0.371	0.205 (+)	0.395	0.600 (1)	0.434	1.294 (+)	0.723	2.017 (1)	0.864
Log-skew-n	1.244 (-)	0.477	1.721 (3)	0.219	1.370 (-)	0.738	2.108 (3)	0.216	0.125 (+)	2.457	2.582 (3)	0.652
Log-normal	0.320 (+)	0.381	0.700 (2)	0.358	0.376 (+)	0.430	0.806 (2)	0.422	1.717 (+)	0.786	2.502 (2)	0.869
AIC-selected	1.568 (-)	0.191	1.759 (4)	0.208	2.858 (-)	0.317	3.175 (4)	0.173	4.331 (-)	0.440	4.771 (7)	0.152
$\mathcal{M}^{(1)}$	1.639 (-)	0.173	1.812 (5)	0.263	3.017 (-)	0.221	3.238 (5)	0.261	3.671 (-)	0.429	4.100 (4)	0.524
$\mathcal{M}^{(2)}$	1.686 (-)	0.165	1.851 (6)	0.160	3.167 (-)	0.225	3.392 (6)	0.281	4.514 (-)	0.202	4.716 (6)	0.485

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.26: Simulation study. Sample from 75% mixture of size 200 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	3.600 (-)	1.112	4.712 (9)	1.678	7.488 (-)	1.171	8.659 (9)	1.459	15.086 (-)	1.294	16.380 (8)	1.338
Weibull	2.970 (-)	1.094	4.064 (8)	1.268	4.869 (-)	1.093	5.961 (4)	1.169	7.679 (-)	1.268	8.947 (1)	1.230
Log-skew-t	1.659 (-)	1.057	2.716 (5)	1.753	6.444 (-)	1.587	8.031 (8)	2.164	32.991 (-)	1.692	34.683 (9)	5.003
Log-t	2.115 (+)	1.567	3.682 (7)	1.472	2.170 (+)	1.725	3.896 (1)	1.659	7.452 (+)	2.782	10.234 (4)	3.015
Log-skew-n	0.771 (-)	1.789	2.560 (4)	1.590	1.624 (-)	2.626	4.250 (3)	1.550	1.212 (+)	8.645	9.857 (3)	2.598
Log-normal	2.071 (+)	1.537	3.609 (6)	1.403	2.334 (+)	1.715	4.049 (2)	1.619	8.030 (+)	2.829	10.858 (6)	3.018
AIC-selected	1.131 (-)	1.125	2.256 (1)	1.618	4.840 (-)	1.976	6.816 (7)	1.686	8.448 (-)	2.656	11.104 (7)	2.197
$\mathcal{M}^{(1)}$	1.196 (-)	1.094	2.290 (3)	1.726	5.033 (-)	1.632	6.665 (5)	1.953	6.919 (-)	2.411	9.330 (2)	3.381
$\mathcal{M}^{(2)}$	1.193 (-)	1.096	2.289 (2)	1.485	5.048 (-)	1.645	6.694 (6)	2.072	7.866 (-)	2.487	10.352 (5)	4.080

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.27: Simulation study. Sample from 75% mixture of size 200 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	86.340 (+)	12.418	98.758 (9)	21.330	42.294 (+)	15.370	57.665 (8)	22.008	3.522 (+)	22.682	26.204 (1)	26.806
Weibull	69.545 (+)	14.721	84.266 (8)	20.308	43.309 (+)	16.130	59.439 (9)	20.228	18.621 (+)	20.473	39.094 (5)	22.867
Log-skew-t	61.409 (+)	11.610	73.019 (7)	19.501	31.196 (+)	14.904	46.099 (7)	22.255	10.778 (-)	39.200	49.979 (7)	43.621
Log-t	18.758 (+)	10.255	29.013 (2)	10.693	19.105 (+)	11.306	30.412 (2)	11.300	47.492 (+)	15.221	62.713 (9)	16.059
Log-skew-n	54.365 (+)	10.583	64.948 (3)	17.772	25.872 (+)	13.913	39.785 (3)	18.222	25.190 (+)	23.057	48.248 (6)	18.655
Log-normal	14.941 (+)	9.939	24.881 (1)	9.856	16.332 (+)	10.723	27.056 (1)	10.695	45.589 (+)	14.955	60.545 (8)	15.832
AIC-selected	57.715 (+)	11.572	69.286 (4)	18.425	29.422 (+)	14.511	43.933 (4)	21.053	13.463 (+)	22.648	36.112 (3)	24.176
$\mathcal{M}^{(1)}$	58.106 (+)	11.650	69.755 (6)	18.777	30.093 (+)	14.630	44.723 (6)	21.243	14.630 (+)	20.908	35.539 (2)	26.293
$\mathcal{M}^{(2)}$	57.899 (+)	11.678	69.576 (5)	16.598	30.021 (+)	14.614	44.634 (5)	19.434	15.271 (+)	20.866	36.137 (4)	23.923

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.28: Simulation study. Sample from 75% mixture of size 200 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	337.472 (+)	49.871	387.343 (5)	71.454	229.612 (+)	52.861	282.473 (5)	75.143	84.256 (+)	62.215	146.471 (6)	89.556
Weibull	228.630 (+)	48.518	277.148 (3)	76.063	162.054 (+)	51.919	213.973 (3)	77.569	88.842 (+)	60.914	149.756 (7)	85.800
Log-skew-t	379.094 (+)	42.533	421.628 (9)	74.132	314.072 (+)	49.939	364.011 (9)	83.938	288.112 (+)	98.337	386.449 (9)	160.351
Log-t	7.907 (-)	36.480	44.387 (1)	51.559	7.600 (-)	38.027	45.627 (1)	52.130	0.088 (+)	43.972	44.059 (2)	57.075
Log-skew-n	301.988 (+)	57.044	359.032 (4)	69.887	164.587 (+)	93.159	257.746 (4)	70.386	7.132 (+)	70.533	77.665 (3)	66.766
Log-normal	12.752 (-)	35.321	48.073 (2)	49.299	11.384 (-)	36.465	47.849 (2)	50.119	0.000 (-)	43.229	43.229 (1)	56.192
AIC-selected	345.975 (+)	47.284	393.259 (8)	70.765	282.511 (+)	51.470	333.981 (8)	78.083	89.381 (+)	63.561	152.942 (8)	93.259
$\mathcal{M}^{(1)}$	342.877 (+)	47.893	390.770 (7)	74.588	276.552 (+)	50.196	326.748 (7)	81.459	82.760 (+)	60.926	143.687 (5)	95.106
$\mathcal{M}^{(2)}$	341.727 (+)	48.355	390.082 (6)	73.309	275.657 (+)	50.303	325.960 (6)	84.424	80.948 (+)	60.544	141.492 (4)	93.979

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.29: Simulation study. Sample from 90% mixture of size 200 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	4.244 (-)	0.027	4.271 (9)	0.036	4.838 (-)	0.019	4.857 (9)	0.021	5.620 (-)	0.007	5.628 (9)	0.007
Weibull	4.153 (-)	0.019	4.172 (8)	0.021	4.484 (-)	0.016	4.500 (8)	0.017	5.031 (-)	0.013	5.044 (8)	0.011
Log-skew-t	0.245 (-)	0.394	0.639 (7)	0.450	1.013 (-)	0.501	1.514 (7)	0.538	4.255 (-)	0.300	4.555 (7)	0.653
Log-t	0.004 (+)	0.220	0.224 (1)	0.235	0.001 (+)	0.238	0.239 (1)	0.279	0.069 (+)	0.443	0.511 (1)	0.532
Log-skew-n	0.142 (-)	0.417	0.559 (6)	0.405	0.231 (-)	0.618	0.849 (3)	0.350	0.141 (+)	0.938	1.078 (4)	0.593
Log-normal	0.028 (+)	0.222	0.250 (2)	0.225	0.025 (+)	0.254	0.279 (2)	0.265	0.153 (+)	0.494	0.647 (2)	0.532
AIC-selected	0.045 (-)	0.504	0.550 (5)	0.253	0.377 (-)	0.985	1.362 (5)	0.241	0.009 (-)	1.415	1.424 (5)	0.448
$\mathcal{M}^{(1)}$	0.059 (-)	0.395	0.454 (3)	0.381	0.460 (-)	0.715	1.175 (4)	0.511	0.181 (-)	0.687	0.867 (3)	1.395
$\mathcal{M}^{(2)}$	0.079 (-)	0.420	0.499 (4)	0.145	0.692 (-)	0.774	1.467 (6)	0.382	1.482 (-)	0.664	2.146 (6)	2.044

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.30: Simulation study. Sample from 90% mixture of size 200 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	8.224 (-)	0.550	8.774 (8)	0.798	13.041 (-)	0.537	13.578 (9)	0.627	23.141 (-)	0.399	23.540 (9)	0.367
Weibull	8.756 (-)	0.426	9.182 (9)	0.500	11.309 (-)	0.411	11.720 (8)	0.438	16.641 (-)	0.411	17.052 (7)	0.376
Log-skew-t	0.036 (-)	1.176	1.212 (6)	1.338	1.304 (-)	1.848	3.152 (6)	1.841	15.621 (-)	2.501	18.122 (8)	4.058
Log-t	0.243 (+)	0.870	1.113 (1)	0.880	0.184 (+)	0.981	1.165 (1)	1.008	0.717 (+)	1.767	2.485 (1)	1.884
Log-skew-n	0.013 (-)	1.174	1.187 (5)	1.238	0.202 (-)	1.824	2.025 (3)	1.341	0.747 (+)	2.174	2.920 (3)	1.961
Log-normal	0.256 (+)	0.871	1.127 (2)	0.853	0.237 (+)	0.984	1.221 (2)	0.995	0.843 (+)	1.823	2.667 (2)	1.893
AIC-selected	0.002 (+)	1.291	1.293 (7)	1.021	0.499 (-)	2.863	3.362 (7)	1.077	0.002 (+)	5.612	5.614 (6)	1.635
$\mathcal{M}^{(1)}$	0.001 (+)	1.158	1.159 (3)	1.198	0.640 (-)	2.286	2.926 (4)	1.753	0.366 (-)	2.854	3.220 (4)	5.135
$\mathcal{M}^{(2)}$	0.001 (+)	1.161	1.162 (4)	0.942	0.691 (-)	2.331	3.022 (5)	1.738	1.033 (-)	3.181	4.214 (5)	6.439

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.31: Simulation study. Sample from 90% mixture of size 200 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	22.948 (+)	7.368	30.316 (9)	13.175	3.500 (+)	9.253	12.753 (8)	13.362	21.217 (-)	14.727	35.944 (9)	14.983
Weibull	6.550 (+)	7.798	14.348 (5)	10.965	0.668 (+)	8.525	9.192 (1)	10.710	7.650 (-)	11.270	18.920 (6)	11.490
Log-skew-t	9.368 (+)	7.376	16.744 (8)	7.922	5.229 (+)	7.579	12.807 (9)	9.117	13.380 (-)	22.380	35.760 (8)	22.888
Log-t	4.628 (+)	5.908	10.535 (2)	6.030	4.089 (+)	6.494	10.583 (3)	6.499	8.191 (+)	10.320	18.511 (5)	10.164
Log-skew-n	8.434 (+)	7.233	15.667 (7)	7.671	4.465 (+)	7.382	11.847 (7)	7.979	7.293 (+)	9.862	17.155 (3)	10.242
Log-normal	3.680 (+)	5.859	9.538 (1)	5.731	3.518 (+)	6.339	9.858 (2)	6.309	7.666 (+)	10.260	17.926 (4)	10.111
AIC-selected	6.958 (+)	7.396	14.354 (6)	6.989	4.199 (+)	7.527	11.726 (6)	8.257	3.309 (+)	17.487	20.796 (7)	10.317
$\mathcal{M}^{(1)}$	6.981 (+)	7.052	14.033 (4)	7.338	4.151 (+)	7.294	11.445 (5)	8.454	1.120 (+)	13.329	14.449 (1)	16.262
$\mathcal{M}^{(2)}$	6.834 (+)	7.002	13.836 (3)	7.432	4.150 (+)	7.255	11.405 (4)	8.553	1.608 (+)	13.314	14.922 (2)	15.774

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.32: Simulation study. Sample from 90% mixture of size 200 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	461.396 (+)	42.435	503.831 (9)	48.641	317.499 (+)	42.552	360.051 (9)	51.504	65.367 (+)	53.064	118.430 (8)	64.634
Weibull	241.069 (+)	35.614	276.683 (8)	48.993	165.634 (+)	37.507	203.141 (8)	49.682	45.927 (+)	46.953	92.880 (7)	55.569
Log-skew-t	56.431 (+)	61.179	117.610 (7)	50.095	89.607 (+)	61.851	151.458 (7)	53.894	69.104 (+)	52.896	122.000 (9)	67.417
Log-t	9.378 (+)	24.873	34.251 (2)	28.325	8.718 (+)	25.656	34.374 (2)	28.989	16.380 (+)	33.141	49.521 (2)	34.658
Log-skew-n	52.986 (+)	58.886	111.872 (6)	47.933	49.657 (+)	65.026	114.683 (4)	43.453	16.384 (+)	35.253	51.637 (3)	35.045
Log-normal	8.084 (+)	24.554	32.638 (1)	27.790	7.870 (+)	25.256	33.126 (1)	28.546	15.697 (+)	32.997	48.694 (1)	34.640
AIC-selected	40.109 (+)	63.122	103.230 (5)	40.271	56.937 (+)	66.031	122.968 (6)	40.379	19.864 (+)	34.973	54.837 (4)	38.313
$\mathcal{M}^{(1)}$	38.250 (+)	54.423	92.673 (4)	44.876	59.253 (+)	57.290	116.542 (5)	48.256	24.434 (+)	37.190	61.624 (6)	43.369
$\mathcal{M}^{(2)}$	37.595 (+)	53.812	91.407 (3)	42.005	57.226 (+)	56.709	113.936 (3)	46.399	23.299 (+)	36.622	59.921 (5)	43.966

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.33: Simulation study. Sample from 95% mixture of size 200 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	4.197 (-)	0.022	4.219 (9)	0.028	4.746 (-)	0.014	4.761 (9)	0.016	5.456 (-)	0.004	5.460 (9)	0.004
Weibull	4.166 (-)	0.014	4.181 (8)	0.015	4.466 (-)	0.011	4.477 (8)	0.011	4.989 (-)	0.008	4.997 (8)	0.007
Log-skew-t	0.053 (-)	0.332	0.385 (7)	0.435	0.348 (-)	0.529	0.878 (7)	0.667	2.181 (-)	2.020	4.201 (7)	4.133
Log-t	0.000 (+)	0.193	0.193 (1)	0.214	0.000 (-)	0.204	0.205 (1)	0.265	0.015 (+)	0.377	0.392 (1)	0.495
Log-skew-n	0.019 (-)	0.321	0.341 (6)	0.357	0.024 (-)	0.478	0.503 (3)	0.387	0.257 (+)	3.415	3.672 (6)	0.990
Log-normal	0.014 (+)	0.191	0.205 (2)	0.199	0.011 (+)	0.216	0.227 (2)	0.237	0.062 (+)	0.427	0.489 (2)	0.477
AIC-selected	0.000 (-)	0.313	0.313 (5)	0.216	0.033 (-)	0.652	0.685 (5)	0.239	0.033 (+)	1.521	1.554 (4)	0.503
$\mathcal{M}^{(1)}$	0.002 (-)	0.264	0.266 (3)	0.306	0.068 (-)	0.516	0.584 (4)	0.439	0.132 (-)	0.796	0.928 (3)	1.802
$\mathcal{M}^{(2)}$	0.004 (-)	0.272	0.276 (4)	0.078	0.128 (-)	0.609	0.737 (6)	0.248	1.789 (-)	0.505	2.294 (5)	2.226

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.34: Simulation study. Sample from 95% mixture of size 200 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	9.085 (-)	0.458	9.543 (8)	0.643	13.876 (-)	0.428	14.303 (9)	0.490	23.938 (-)	0.261	24.199 (9)	0.243
Weibull	10.012 (-)	0.325	10.337 (9)	0.376	12.534 (-)	0.305	12.838 (8)	0.324	18.133 (-)	0.281	18.413 (8)	0.259
Log-skew-t	0.004 (+)	0.896	0.900 (6)	1.083	0.277 (-)	1.502	1.780 (6)	1.700	6.818 (-)	5.159	11.977 (7)	13.135
Log-t	0.111 (+)	0.729	0.839 (1)	0.760	0.071 (+)	0.810	0.881 (1)	0.879	0.277 (+)	1.497	1.774 (1)	1.672
Log-skew-n	0.007 (+)	0.871	0.878 (5)	0.971	0.002 (-)	1.242	1.244 (3)	1.158	0.633 (+)	3.889	4.522 (6)	2.167
Log-normal	0.117 (+)	0.728	0.845 (2)	0.737	0.101 (+)	0.812	0.913 (2)	0.866	0.333 (+)	1.549	1.882 (2)	1.675
AIC-selected	0.044 (+)	0.873	0.917 (7)	0.796	0.014 (-)	1.835	1.849 (7)	0.913	0.192 (+)	3.166	3.358 (4)	1.669
$\mathcal{M}^{(1)}$	0.033 (+)	0.819	0.853 (3)	0.907	0.044 (-)	1.563	1.607 (4)	1.347	0.392 (-)	2.001	2.393 (3)	5.820
$\mathcal{M}^{(2)}$	0.034 (+)	0.821	0.855 (4)	0.680	0.053 (-)	1.613	1.665 (5)	1.216	1.382 (-)	2.234	3.616 (5)	9.318

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.35: Simulation study. Sample from 95% mixture of size 200 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	12.684 (+)	6.016	18.700 (9)	11.104	0.466 (+)	7.604	8.070 (8)	11.211	37.285 (-)	12.068	49.353 (9)	12.106
Weibull	1.215 (+)	6.192	7.407 (3)	8.833	0.337 (-)	6.722	7.060 (2)	8.580	19.150 (-)	8.810	27.960 (8)	8.999
Log-skew-t	3.739 (+)	5.417	9.156 (8)	5.741	2.442 (+)	5.695	8.136 (9)	6.452	4.195 (-)	20.186	24.382 (7)	21.609
Log-t	2.460 (+)	4.848	7.309 (2)	5.013	2.096 (+)	5.266	7.362 (6)	5.455	3.828 (+)	8.633	12.461 (5)	8.901
Log-skew-n	3.222 (+)	5.361	8.583 (7)	5.574	1.962 (+)	5.500	7.461 (7)	5.828	3.645 (+)	8.724	12.369 (4)	8.940
Log-normal	1.850 (+)	4.824	6.674 (1)	4.769	1.716 (+)	5.158	6.874 (1)	5.280	3.334 (+)	8.583	11.917 (3)	8.741
AIC-selected	2.510 (+)	5.249	7.759 (4)	5.086	1.795 (+)	5.494	7.289 (3)	5.847	2.659 (+)	11.366	14.025 (6)	8.731
$\mathcal{M}^{(1)}$	2.707 (+)	5.137	7.844 (6)	5.342	1.829 (+)	5.499	7.328 (5)	6.025	0.056 (+)	10.162	10.218 (1)	16.865
$\mathcal{M}^{(2)}$	2.669 (+)	5.116	7.785 (5)	5.765	1.838 (+)	5.475	7.314 (4)	6.373	0.237 (+)	10.140	10.378 (2)	15.806

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.36: Simulation study. Sample from 95% mixture of size 200 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	403.707 (+)	39.630	443.337 (9)	41.791	269.586 (+)	38.803	308.389 (9)	44.352	33.522 (+)	46.989	80.510 (9)	56.502
Weibull	186.451 (+)	30.987	217.438 (8)	41.174	121.323 (+)	32.331	153.654 (8)	41.658	18.408 (+)	40.122	58.530 (7)	46.564
Log-skew-t	18.787 (+)	30.724	49.511 (7)	31.648	27.736 (+)	35.514	63.250 (7)	34.759	25.588 (+)	38.128	63.716 (8)	47.647
Log-t	8.219 (+)	21.264	29.484 (2)	22.817	7.610 (+)	21.753	29.363 (2)	23.427	11.665 (+)	28.220	39.885 (2)	28.816
Log-skew-n	18.902 (+)	30.309	49.211 (6)	30.334	16.267 (+)	35.398	51.665 (6)	28.828	10.870 (+)	29.350	40.220 (4)	28.862
Log-normal	7.553 (+)	21.142	28.695 (1)	22.537	7.291 (+)	21.575	28.866 (1)	23.188	11.279 (+)	28.254	39.533 (1)	28.982
AIC-selected	13.176 (+)	28.735	41.911 (5)	25.308	16.888 (+)	32.245	49.133 (3)	26.672	11.371 (+)	28.730	40.101 (3)	29.628
$\mathcal{M}^{(1)}$	13.857 (+)	27.008	40.865 (4)	28.085	18.673 (+)	31.563	50.236 (5)	30.546	14.203 (+)	31.606	45.809 (6)	34.909
$\mathcal{M}^{(2)}$	13.739 (+)	26.894	40.633 (3)	27.654	18.169 (+)	31.346	49.515 (4)	30.041	13.685 (+)	31.038	44.723 (5)	34.206

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.37: Simulation study. Sample from gamma distribution of size 200 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	0.000 (+)	0.000	0.000 (1)	0.000	0.000 (+)	0.000	0.000 (1)	0.000	0.000 (+)	0.000	0.000 (1)	0.000
Weibull	0.000 (+)	0.000	0.000 (7)	0.000	0.000 (+)	0.000	0.000 (6)	0.000	0.000 (+)	0.000	0.000 (2)	0.000
Log-skew-t	0.000 (+)	0.000	0.000 (3)	0.000	0.000 (+)	0.000	0.000 (4)	0.000	0.000 (+)	0.000	0.000 (3)	0.001
Log-t	0.000 (+)	0.000	0.000 (8)	0.000	0.005 (+)	0.001	0.006 (8)	0.001	0.100 (+)	0.022	0.123 (6)	0.029
Log-skew-n	0.000 (+)	0.000	0.000 (6)	0.000	0.002 (+)	0.001	0.003 (7)	0.001	0.116 (+)	0.055	0.170 (9)	0.223
Log-normal	0.000 (+)	0.000	0.000 (9)	0.000	0.005 (+)	0.001	0.007 (9)	0.001	0.111 (+)	0.024	0.135 (8)	0.030
AIC-selected	0.000 (+)	0.000	0.000 (5)	0.000	0.000 (+)	0.000	0.000 (3)	0.000	0.097 (+)	0.029	0.126 (7)	0.028
$\mathcal{M}^{(1)}$	0.000 (+)	0.000	0.000 (4)	0.000	0.000 (+)	0.000	0.000 (5)	0.000	0.077 (+)	0.023	0.100 (5)	0.057
$\mathcal{M}^{(2)}$	0.000 (+)	0.000	0.000 (2)	0.000	0.000 (+)	0.000	0.000 (2)	0.000	0.020 (+)	0.013	0.033 (4)	0.201

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.38: Simulation study. Sample from gamma distribution of size 200 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	0.000 (+)	0.000	0.000 (1)	0.000	0.000 (+)	0.000	0.000 (1)	0.000	0.000 (+)	0.000	0.000 (1)	0.000
Weibull	0.000 (+)	0.000	0.000 (8)	0.000	0.002 (+)	0.001	0.003 (6)	0.001	0.012 (+)	0.006	0.018 (3)	0.006
Log-skew-t	0.000 (+)	0.000	0.000 (5)	0.000	0.000 (+)	0.000	0.001 (5)	0.001	0.001 (+)	0.005	0.006 (2)	0.026
Log-t	0.001 (+)	0.001	0.002 (9)	0.001	0.117 (+)	0.017	0.133 (8)	0.018	1.335 (+)	0.191	1.526 (7)	0.224
Log-skew-n	0.000 (+)	0.000	0.000 (6)	0.000	0.040 (+)	0.025	0.065 (7)	0.009	1.366 (+)	0.241	1.608 (9)	0.322
Log-normal	0.000 (+)	0.000	0.000 (7)	0.000	0.122 (+)	0.017	0.139 (9)	0.019	1.345 (+)	0.196	1.541 (8)	0.225
AIC-selected	0.000 (+)	0.000	0.000 (3)	0.000	0.000 (+)	0.000	0.000 (3)	0.000	1.205 (+)	0.256	1.461 (6)	0.213
$\mathcal{M}^{(1)}$	0.000 (+)	0.000	0.000 (4)	0.000015	0.000 (+)	0.000	0.000 (4)	0.0005	0.977 (+)	0.189	1.166 (5)	0.322
$\mathcal{M}^{(2)}$	0.000 (+)	0.000	0.000 (2)	0.000070	0.000 (+)	0.000	0.000 (2)	0.0008	0.720 (+)	0.182	0.903 (4)	0.951

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.39: Simulation study. Sample from gamma distribution of size 200 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	0.018 (+)	0.220	0.238 (5)	0.224	0.026 (+)	0.405	0.430 (1)	0.436	0.083 (+)	0.878	0.961 (1)	0.851
Weibull	0.023 (+)	0.222	0.246 (6)	0.158	1.935 (+)	0.699	2.635 (6)	0.665	7.080 (+)	1.880	8.960 (3)	1.804
Log-skew-t	0.003 (+)	0.218	0.222 (3)	0.227	0.111 (+)	0.481	0.592 (3)	0.755	0.485 (+)	1.573	2.058 (2)	3.303
Log-t	1.116 (+)	1.080	2.195 (9)	0.623	5.088 (+)	0.774	5.862 (9)	0.693	36.221 (+)	3.421	39.642 (9)	3.439
Log-skew-n	0.225 (-)	0.085	0.311 (7)	0.048	2.223 (+)	0.782	3.005 (7)	0.621	35.282 (+)	3.494	38.776 (8)	3.396
Log-normal	0.385 (-)	0.050	0.435 (8)	0.021	4.979 (+)	0.762	5.741 (8)	0.683	35.185 (+)	3.450	38.635 (7)	3.393
AIC-selected	0.011 (+)	0.219	0.231 (4)	0.215	0.060 (+)	0.526	0.586 (2)	0.447	33.050 (+)	4.134	37.183 (6)	3.305
$\mathcal{M}^{(1)}$	0.008 (+)	0.211	0.219 (2)	0.225	0.108 (+)	0.503	0.611 (4)	0.572	29.062 (+)	3.602	32.665 (4)	4.339
$\mathcal{M}^{(2)}$	0.007 (+)	0.210	0.216 (1)	0.240	0.105 (+)	0.510	0.615 (5)	0.492	29.304 (+)	3.668	32.973 (5)	3.632

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.40: Simulation study. Sample from gamma distribution of size 200 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	0.460 (+)	14.364	14.824 (1)	14.679	0.340 (+)	21.878	22.217 (8)	22.523	0.921 (+)	36.391	37.312 (1)	34.137
Weibull	23.371 (-)	9.712	33.084 (7)	8.176	0.349 (+)	16.807	17.156 (3)	15.262	27.695 (+)	29.618	57.313 (3)	26.629
Log-skew-t	0.677 (-)	17.949	18.625 (5)	18.501	0.043 (+)	22.232	22.275 (9)	23.880	0.503 (+)	37.995	38.498 (2)	37.540
Log-t	4.496 (-)	26.188	30.684 (6)	17.304	2.718 (-)	10.274	12.991 (1)	9.042	52.480 (+)	23.297	75.778 (9)	20.631
Log-skew-n	48.475 (-)	9.881	58.356 (8)	5.972	0.854 (-)	17.411	18.265 (4)	13.886	50.218 (+)	23.635	73.853 (7)	20.637
Log-normal	125.454 (-)	3.288	128.742 (9)	3.307	3.044 (-)	10.116	13.160 (2)	8.920	50.189 (+)	23.639	73.828 (6)	20.648
AIC-selected	0.077 (+)	16.120	16.197 (4)	14.612	0.217 (+)	21.439	21.656 (7)	22.148	49.332 (+)	24.577	73.910 (8)	21.095
$\mathcal{M}^{(1)}$	0.000 (-)	15.405	15.405 (2)	16.662	0.146 (+)	20.720	20.866 (6)	21.958	46.155 (+)	25.217	71.372 (4)	22.346
$\mathcal{M}^{(2)}$	0.004 (-)	15.494	15.498 (3)	14.864	0.139 (+)	20.581	20.720 (5)	16.685	46.852 (+)	25.059	71.911 (5)	14.750

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.41: Simulation study. Sample from log-normal distribution of size 500 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	4.236 (-)	0.007	4.244 (8)	0.007	4.735 (-)	0.004	4.739 (9)	0.004	5.348 (-)	0.000	5.349 (9)	0.000
Weibull	4.274 (-)	0.004	4.278 (9)	0.003	4.528 (-)	0.003	4.531 (8)	0.002	5.018 (-)	0.001	5.019 (8)	0.001
Log-skew-t	0.005 (-)	0.107	0.111 (7)	0.150	0.068 (-)	0.233	0.301 (7)	0.333	0.417 (-)	1.339	1.757 (6)	2.179
Log-t	0.002 (-)	0.063	0.066 (1)	0.081	0.008 (-)	0.081	0.089 (2)	0.130	0.001 (-)	0.150	0.151 (1)	0.196
Log-skew-n	0.000 (+)	0.106	0.106 (6)	0.110	0.016 (+)	0.166	0.182 (6)	0.163	0.216 (+)	0.886	1.102 (5)	0.978
Log-normal	0.002 (+)	0.065	0.067 (2)	0.067	0.003 (+)	0.079	0.081 (1)	0.082	0.005 (+)	0.154	0.158 (2)	0.167
AIC-selected	0.001 (+)	0.089	0.089 (5)	0.077	0.001 (+)	0.169	0.170 (5)	0.104	0.008 (+)	0.881	0.889 (4)	0.442
$\mathcal{M}^{(1)}$	0.000 (+)	0.078	0.078 (3)	0.101	0.000 (-)	0.126	0.126 (3)	0.173	0.459 (-)	0.373	0.832 (3)	1.691
$\mathcal{M}^{(2)}$	0.000 (+)	0.078	0.078 (4)	0.018	0.000 (-)	0.129	0.129 (4)	0.055	3.865 (-)	0.060	3.925 (7)	0.946

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.42: Simulation study. Sample from log-normal distribution of size 500 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	10.658 (-)	0.162	10.820 (8)	0.186	15.476 (-)	0.146	15.622 (9)	0.134	25.716 (-)	0.054	25.770 (9)	0.041
Weibull	12.229 (-)	0.097	12.327 (9)	0.094	14.661 (-)	0.089	14.750 (8)	0.080	20.655 (-)	0.066	20.721 (8)	0.053
Log-skew-t	0.006 (+)	0.279	0.285 (7)	0.322	0.021 (-)	0.506	0.528 (7)	0.593	0.747 (-)	3.084	3.831 (6)	4.405
Log-t	0.008 (+)	0.235	0.243 (2)	0.247	0.002 (+)	0.279	0.281 (1)	0.294	0.013 (+)	0.528	0.541 (2)	0.577
Log-skew-n	0.002 (+)	0.269	0.271 (6)	0.279	0.028 (+)	0.394	0.422 (6)	0.393	0.384 (+)	1.562	1.946 (3)	1.760
Log-normal	0.006 (+)	0.233	0.239 (1)	0.237	0.006 (+)	0.280	0.286 (2)	0.285	0.011 (+)	0.528	0.539 (1)	0.571
AIC-selected	0.006 (+)	0.253	0.260 (5)	0.248	0.006 (+)	0.386	0.392 (5)	0.314	0.003 (+)	2.238	2.241 (4)	0.848
$\mathcal{M}^{(1)}$	0.005 (+)	0.246	0.25176 (4)	0.270	0.003 (+)	0.343	0.3461 (3)	0.389	1.992 (-)	0.925	2.918 (5)	5.674
$\mathcal{M}^{(2)}$	0.005 (+)	0.246	0.25175 (3)	0.215	0.004 (+)	0.343	0.3463 (4)	0.322	5.602 (-)	0.880	6.482 (7)	10.926

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.43: Simulation study. Sample from log-normal distribution of size 500 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	2.029 (+)	1.790	3.819 (9)	3.382	1.810 (-)	2.465	4.275 (8)	3.408	74.277 (-)	3.792	78.068 (9)	3.418
Weibull	1.810 (-)	1.808	3.618 (8)	2.490	8.429 (-)	2.012	10.441 (9)	2.401	48.641 (-)	2.479	51.120 (8)	2.401
Log-skew-t	0.139 (+)	1.570	1.709 (7)	1.580	0.106 (+)	1.724	1.830 (7)	1.734	0.239 (-)	5.244	5.483 (4)	5.788
Log-t	0.101 (+)	1.549	1.650 (6)	1.523	0.070 (+)	1.711	1.781 (6)	1.697	0.135 (+)	2.747	2.882 (2)	3.003
Log-skew-n	0.036 (+)	1.523	1.559 (4)	1.507	0.015 (+)	1.635	1.650 (1)	1.582	0.340 (+)	3.246	3.587 (3)	3.514
Log-normal	0.011 (+)	1.456	1.467 (1)	1.430	0.011 (+)	1.641	1.652 (2)	1.603	0.019 (+)	2.657	2.675 (1)	2.822
AIC-selected	0.028 (+)	1.536	1.564 (5)	1.456	0.021 (+)	1.663	1.685 (3)	1.617	0.004 (-)	5.922	5.926 (5)	2.883
$\mathcal{M}^{(1)}$	0.045 (+)	1.503	1.548 (3)	1.512	0.032 (+)	1.665	1.696 (5)	1.650	5.024 (-)	3.641	8.665 (7)	14.903
$\mathcal{M}^{(2)}$	0.044 (+)	1.502	1.546 (2)	1.747	0.031 (+)	1.664	1.695 (4)	1.850	3.533 (-)	3.784	7.317 (6)	13.160

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.44: Simulation study. Sample from log-normal distribution of size 500 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	234.162 (+)	14.322	248.483 (9)	12.814	137.839 (+)	13.541	151.380 (9)	13.671	0.014 (-)	15.010	15.024 (9)	17.999
Weibull	70.325 (+)	9.534	79.859 (8)	12.270	34.254 (+)	10.022	44.275 (8)	12.371	3.026 (-)	11.981	15.007 (8)	13.779
Log-skew-t	0.006 (+)	7.620	7.625 (7)	7.510	0.111 (+)	7.968	8.079 (7)	7.889	0.108 (+)	8.849	8.957 (5)	9.443
Log-t	0.000 (+)	6.632	6.632 (2)	6.400	0.002 (-)	6.871	6.874 (2)	6.592	0.010 (+)	8.359	8.369 (2)	8.529
Log-skew-n	0.046 (+)	7.535	7.581 (6)	7.266	0.039 (-)	7.452	7.491 (6)	7.177	0.001 (-)	8.204	8.205 (1)	8.437
Log-normal	0.000 (+)	6.591	6.591 (1)	6.399	0.000 (+)	6.863	6.863 (1)	6.601	0.001 (+)	8.482	8.483 (3)	8.692
AIC-selected	0.003 (+)	7.114	7.117 (5)	6.577	0.000 (+)	7.433	7.433 (5)	6.744	0.003 (-)	8.739	8.743 (4)	8.902
$\mathcal{M}^{(1)}$	0.007 (+)	6.916	6.9235 (4)	6.948	0.000 (+)	7.243	7.243 (4)	7.138	0.029 (-)	9.845	9.874 (7)	11.245
$\mathcal{M}^{(2)}$	0.007 (+)	6.916	6.9227 (3)	6.911	0.000 (+)	7.242	7.242 (3)	7.077	0.016 (-)	9.514	9.530 (6)	10.195

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.45: Simulation study. Sample from 75% mixture of size 500 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	4.197 (-)	0.020	4.217 (9)	0.031	4.962 (-)	0.017	4.978 (9)	0.021	6.012 (-)	0.009	6.021 (8)	0.011
Weibull	3.881 (-)	0.019	3.899 (8)	0.022	4.305 (-)	0.017	4.322 (8)	0.019	4.883 (-)	0.015	4.898 (4)	0.016
Log-skew-t	2.091 (-)	0.048	2.139 (7)	0.087	3.693 (-)	0.095	3.788 (7)	0.144	7.127 (-)	0.005	7.132 (9)	0.073
Log-t	0.141 (+)	0.131	0.272 (1)	0.133	0.160 (+)	0.146	0.305 (1)	0.157	0.907 (+)	0.226	1.133 (1)	0.315
Log-skew-n	1.714 (-)	0.044	1.758 (3)	0.072	2.421 (-)	0.044	2.465 (3)	0.061	0.052 (+)	1.880	1.932 (3)	0.243
Log-normal	0.182 (+)	0.132	0.314 (2)	0.131	0.222 (+)	0.147	0.369 (2)	0.155	1.110 (+)	0.232	1.342 (2)	0.317
AIC-selected	1.786 (-)	0.056	1.842 (4)	0.074	3.082 (-)	0.147	3.229 (4)	0.072	4.917 (-)	0.017	4.934 (5)	0.017
$\mathcal{M}^{(1)}$	1.840 (-)	0.049	1.889 (5)	0.082	3.140 (-)	0.102	3.242 (5)	0.110	4.910 (-)	0.024	4.935 (6)	0.030
$\mathcal{M}^{(2)}$	1.846 (-)	0.049	1.895 (6)	0.051	3.199 (-)	0.108	3.307 (6)	0.131	5.015 (-)	0.020	5.035 (7)	0.061

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.46: Simulation study. Sample from 75% mixture of size 500 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	4.825 (-)	0.364	5.190 (9)	0.604	9.164 (-)	0.389	9.553 (9)	0.515	18.338 (-)	0.341	18.679 (8)	0.426
Weibull	4.295 (-)	0.349	4.645 (8)	0.441	6.469 (-)	0.349	6.818 (7)	0.404	10.197 (-)	0.357	10.554 (4)	0.406
Log-skew-t	2.089 (-)	0.356	2.445 (7)	0.629	6.848 (-)	0.644	7.491 (8)	0.869	38.585 (-)	0.356	38.942 (9)	0.760
Log-t	1.294 (+)	0.543	1.837 (2)	0.531	1.424 (+)	0.596	2.019 (1)	0.610	5.116 (+)	0.869	5.985 (1)	1.125
Log-skew-n	1.612 (-)	0.355	1.967 (3)	0.591	3.975 (-)	0.404	4.378 (3)	0.561	6.639 (+)	6.551	7.190 (3)	0.973
Log-normal	1.289 (+)	0.538	1.827 (1)	0.521	1.487 (+)	0.592	2.079 (2)	0.604	5.410 (+)	0.870	6.280 (2)	1.127
AIC-selected	1.713 (-)	0.379	2.092 (4)	0.600	5.600 (-)	0.804	6.404 (6)	0.654	10.436 (-)	0.417	10.853 (5)	0.435
$\mathcal{M}^{(1)}$	1.777 (-)	0.362	2.139 (6)	0.616	5.679 (-)	0.664	6.343 (4)	0.765	10.573 (-)	0.403	10.976 (6)	0.556
$\mathcal{M}^{(2)}$	1.777 (-)	0.362	2.138 (5)	0.564	5.681 (-)	0.666	6.347 (5)	0.843	10.767 (-)	0.424	11.192 (7)	0.822

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.47: Simulation study. Sample from 75% mixture of size 500 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	65.491 (+)	4.271	69.762 (9)	8.109	28.138 (+)	5.430	33.568 (9)	8.366	0.038 (+)	7.239	7.277 (1)	10.172
Weibull	47.649 (+)	4.902	52.551 (8)	7.599	26.569 (+)	5.441	32.009 (8)	7.558	6.379 (+)	6.459	12.837 (5)	8.491
Log-skew-t	45.357 (+)	4.056	49.413 (7)	7.234	19.893 (+)	5.332	25.224 (7)	8.204	22.294 (-)	12.769	35.064 (8)	16.368
Log-t	9.612 (+)	3.556	13.168 (2)	3.835	10.465 (+)	3.798	14.263 (2)	4.130	30.345 (+)	4.964	35.310 (9)	6.088
Log-skew-n	43.083 (+)	3.971	47.053 (3)	6.918	18.167 (+)	5.078	23.245 (3)	7.410	14.762 (+)	11.082	25.844 (6)	7.020
Log-normal	8.547 (+)	3.492	12.039 (1)	3.713	9.591 (+)	3.750	13.342 (1)	4.040	29.561 (+)	4.900	34.460 (7)	6.042
AIC-selected	43.607 (+)	3.982	47.589 (4)	6.987	19.111 (+)	5.214	24.325 (4)	7.883	5.902 (+)	6.853	12.755 (4)	8.562
$\mathcal{M}^{(1)}$	43.920 (+)	4.005	47.925 (6)	7.046	19.184 (+)	5.227	24.410 (6)	7.916	5.608 (+)	6.595	12.203 (2)	9.165
$\mathcal{M}^{(2)}$	43.908 (+)	4.006	47.913 (5)	6.373	19.169 (+)	5.225	24.394 (5)	7.429	5.676 (+)	6.587	12.263 (3)	8.548

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.48: Simulation study. Sample from 75% mixture of size 500 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	254.572 (+)	18.507	273.079 (4)	27.422	162.215 (+)	19.719	181.934 (4)	28.866	37.768 (+)	22.246	60.014 (8)	34.771
Weibull	152.996 (+)	17.061	170.058 (3)	29.209	99.405 (+)	18.427	117.832 (3)	29.782	37.509 (+)	20.854	58.363 (4)	33.082
Log-skew-t	284.443 (+)	14.499	298.941 (9)	28.373	223.546 (+)	17.547	241.093 (9)	31.967	161.240 (+)	32.920	194.160 (9)	57.675
Log-t	29.097 (-)	12.855	41.952 (1)	19.001	27.290 (-)	13.204	40.493 (1)	19.300	5.592 (-)	15.394	20.986 (1)	21.695
Log-skew-n	261.469 (+)	14.872	276.341 (5)	27.604	175.866 (+)	16.619	192.486 (5)	28.492	0.039 (-)	34.495	34.535 (3)	25.372
Log-normal	32.226 (-)	12.593	44.819 (2)	18.673	30.029 (-)	13.082	43.111 (2)	18.996	6.392 (-)	15.186	21.578 (2)	21.507
AIC-selected	267.842 (+)	14.453	282.295 (6)	27.750	205.616 (+)	17.825	223.441 (6)	30.095	37.938 (+)	20.977	58.915 (5)	33.360
$\mathcal{M}^{(1)}$	270.499 (+)	14.522	285.020 (8)	28.126	206.195 (+)	17.308	223.502 (8)	30.963	38.364 (+)	20.884	59.248 (7)	33.821
$\mathcal{M}^{(2)}$	270.453 (+)	14.531	284.983 (7)	26.984	206.132 (+)	17.309	223.441 (7)	32.099	38.212 (+)	20.835	59.046 (6)	34.478

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.49: Simulation study. Sample from 90% mixture of size 500 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	4.416 (-)	0.008	4.424 (9)	0.011	4.996 (-)	0.005	5.001 (9)	0.006	5.765 (-)	0.001	5.766 (9)	0.001
Weibull	4.325 (-)	0.006	4.331 (8)	0.007	4.644 (-)	0.005	4.649 (8)	0.005	5.211 (-)	0.003	5.214 (8)	0.003
Log-skew-t	0.189 (-)	0.137	0.326 (7)	0.176	0.802 (-)	0.227	1.029 (7)	0.220	4.346 (-)	0.140	4.486 (7)	0.254
Log-t	0.001 (+)	0.074	0.075 (1)	0.086	0.000 (+)	0.088	0.088 (1)	0.102	0.020 (+)	0.159	0.178 (1)	0.195
Log-skew-n	0.130 (-)	0.145	0.275 (6)	0.165	0.086 (-)	0.436	0.523 (3)	0.112	0.051 (+)	0.155	0.206 (3)	0.197
Log-normal	0.007 (+)	0.077	0.084 (2)	0.084	0.006 (+)	0.090	0.096 (2)	0.099	0.050 (+)	0.155	0.205 (2)	0.196
AIC-selected	0.056 (-)	0.203	0.260 (5)	0.116	0.191 (-)	0.488	0.680 (6)	0.116	0.269 (-)	1.391	1.661 (5)	0.141
$\mathcal{M}^{(1)}$	0.051 (-)	0.154	0.205 (3)	0.157	0.214 (-)	0.390	0.604 (4)	0.222	0.568 (-)	0.490	1.058 (4)	0.995
$\mathcal{M}^{(2)}$	0.056 (-)	0.156	0.212 (4)	0.050	0.264 (-)	0.411	0.675 (5)	0.150	2.269 (-)	0.450	2.719 (6)	1.326

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.50: Simulation study. Sample from 90% mixture of size 500 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	9.324 (-)	0.187	9.511 (8)	0.287	14.342 (-)	0.182	14.524 (9)	0.219	25.269 (-)	0.101	25.370 (9)	0.103
Weibull	10.003 (-)	0.142	10.145 (9)	0.173	12.627 (-)	0.135	12.763 (8)	0.150	18.528 (-)	0.117	18.645 (8)	0.120
Log-skew-t	0.032 (-)	0.396	0.428 (6)	0.488	0.939 (-)	0.807	1.746 (7)	0.731	15.592 (-)	1.345	16.937 (7)	1.772
Log-t	0.093 (+)	0.305	0.398 (1)	0.324	0.072 (+)	0.354	0.426 (1)	0.377	0.281 (+)	0.604	0.885 (1)	0.708
Log-skew-n	0.021 (-)	0.398	0.418 (5)	0.463	0.055 (-)	1.135	1.190 (3)	0.452	0.336 (+)	0.587	0.923 (3)	0.714
Log-normal	0.096 (+)	0.305	0.401 (2)	0.319	0.090 (+)	0.353	0.443 (2)	0.375	0.335 (+)	0.586	0.922 (2)	0.711
AIC-selected	0.001 (-)	0.457	0.458 (7)	0.405	0.185 (-)	1.230	1.415 (6)	0.487	0.700 (-)	5.550	6.250 (6)	0.539
$\mathcal{M}^{(1)}$	0.000 (-)	0.409	0.409 (4)	0.443	0.211 (-)	1.104	1.315 (4)	0.690	1.675 (-)	2.049	3.724 (4)	3.886
$\mathcal{M}^{(2)}$	0.000 (-)	0.409	0.409 (3)	0.349	0.216 (-)	1.115	1.331 (5)	0.642	3.002 (-)	2.271	5.273 (5)	4.967

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.51: Simulation study. Sample from 90% mixture of size 500 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	15.304 (+)	2.525	17.829 (9)	4.980	1.021 (+)	3.328	4.349 (4)	5.054	34.310 (-)	4.825	39.135 (9)	5.574
Weibull	2.380 (+)	2.633	5.013 (3)	4.062	0.030 (-)	2.940	2.969 (1)	3.960	16.027 (-)	3.623	19.650 (7)	4.187
Log-skew-t	4.264 (+)	2.509	6.772 (8)	2.762	2.532 (+)	2.651	5.183 (9)	3.115	15.571 (-)	9.500	25.071 (8)	9.294
Log-t	1.817 (+)	2.107	3.924 (2)	2.205	1.684 (+)	2.324	4.007 (3)	2.410	3.511 (+)	3.484	6.995 (5)	3.866
Log-skew-n	3.882 (+)	2.492	6.374 (7)	2.720	1.859 (+)	2.512	4.371 (5)	2.718	3.305 (+)	3.421	6.726 (4)	3.856
Log-normal	1.540 (+)	2.058	3.598 (1)	2.152	1.488 (+)	2.299	3.787 (2)	2.376	3.306 (+)	3.419	6.725 (3)	3.854
AIC-selected	3.218 (+)	2.645	5.863 (6)	2.535	1.997 (+)	2.570	4.567 (8)	2.828	0.014 (+)	11.418	11.432 (6)	3.922
$\mathcal{M}^{(1)}$	3.124 (+)	2.499	5.623 (5)	2.624	1.970 (+)	2.554	4.524 (7)	2.860	0.178 (-)	6.121	6.299 (2)	9.402
$\mathcal{M}^{(2)}$	3.091 (+)	2.494	5.584 (4)	2.763	1.959 (+)	2.548	4.507 (6)	2.972	0.043 (-)	6.133	6.176 (1)	9.217

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.52: Simulation study. Sample from 90% mixture of size 500 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	378.153 (+)	16.102	394.255 (9)	18.451	250.127 (+)	16.339	266.467 (9)	19.568	30.259 (+)	18.770	49.029 (9)	24.861
Weibull	176.366 (+)	12.534	188.900 (8)	18.557	113.274 (+)	13.439	126.713 (8)	18.812	16.615 (+)	16.068	32.683 (7)	21.074
Log-skew-t	16.406 (+)	16.846	33.252 (7)	16.206	31.067 (+)	19.746	50.813 (7)	18.718	29.577 (+)	17.299	46.876 (8)	23.818
Log-t	1.638 (+)	8.876	10.513 (2)	10.499	1.520 (+)	9.310	10.830 (2)	10.765	4.029 (+)	11.564	15.593 (3)	13.133
Log-skew-n	15.934 (+)	16.563	32.497 (6)	15.931	11.419 (+)	24.091	35.510 (3)	14.196	3.852 (+)	11.530	15.382 (1)	13.136
Log-normal	1.402 (+)	8.794	10.196 (1)	10.412	1.363 (+)	9.262	10.626 (1)	10.687	3.862 (+)	11.528	15.390 (2)	13.137
AIC-selected	11.278 (+)	18.777	30.055 (5)	14.195	16.228 (+)	25.077	41.305 (6)	15.261	6.398 (+)	13.943	20.342 (4)	15.464
$\mathcal{M}^{(1)}$	10.256 (+)	16.756	27.012 (4)	15.374	16.091 (+)	22.216	38.307 (5)	17.108	7.850 (+)	13.714	21.565 (6)	17.269
$\mathcal{M}^{(2)}$	10.202 (+)	16.731	26.933 (3)	14.867	15.851 (+)	22.191	38.042 (4)	16.164	7.381 (+)	13.499	20.880 (5)	17.387

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.53: Simulation study. Sample from 95% mixture of size 500 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	4.340 (-)	0.007	4.347 (9)	0.009	4.875 (-)	0.004	4.879 (9)	0.005	5.559 (-)	0.001	5.559 (9)	0.001
Weibull	4.307 (-)	0.005	4.312 (8)	0.005	4.594 (-)	0.004	4.598 (8)	0.004	5.125 (-)	0.002	5.127 (8)	0.002
Log-skew-t	0.046 (-)	0.106	0.152 (7)	0.172	0.262 (-)	0.199	0.461 (7)	0.260	2.186 (-)	0.384	2.570 (6)	0.579
Log-t	0.000 (-)	0.067	0.067 (1)	0.079	0.001 (-)	0.080	0.082 (1)	0.097	0.001 (+)	0.141	0.142 (1)	0.180
Log-skew-n	0.023 (-)	0.107	0.130 (6)	0.138	0.001 (-)	0.146	0.147 (3)	0.126	0.021 (+)	0.341	0.361 (3)	0.235
Log-normal	0.003 (+)	0.069	0.071 (2)	0.075	0.002 (+)	0.082	0.084 (2)	0.090	0.012 (+)	0.145	0.158 (2)	0.177
AIC-selected	0.002 (-)	0.116	0.118 (5)	0.086	0.007 (-)	0.216	0.223 (6)	0.100	0.007 (-)	0.504	0.511 (4)	0.171
$\mathcal{M}^{(1)}$	0.005 (-)	0.092	0.097 (3)	0.114	0.015 (-)	0.153	0.168 (4)	0.168	0.474 (-)	0.192	0.666 (5)	1.085
$\mathcal{M}^{(2)}$	0.005 (-)	0.093	0.099 (4)	0.024	0.021 (-)	0.169	0.191 (5)	0.072	2.725 (-)	0.276	3.001 (7)	1.325

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.54: Simulation study. Sample from 95% mixture of size 500 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	10.051 (-)	0.165	10.216 (8)	0.232	14.998 (-)	0.155	15.153 (9)	0.172	25.667 (-)	0.071	25.738 (9)	0.065
Weibull	11.128 (-)	0.114	11.242 (9)	0.130	13.685 (-)	0.107	13.792 (8)	0.111	19.720 (-)	0.086	19.805 (8)	0.082
Log-skew-t	0.000 (-)	0.304	0.304 (6)	0.398	0.199 (-)	0.568	0.767 (7)	0.634	5.820 (-)	1.959	7.779 (7)	2.257
Log-t	0.033 (+)	0.262	0.295 (3)	0.283	0.019 (+)	0.309	0.328 (1)	0.331	0.070 (+)	0.530	0.600 (1)	0.632
Log-skew-n	0.000 (-)	0.297	0.297 (5)	0.355	0.006 (+)	0.417	0.423 (3)	0.390	0.107 (+)	0.765	0.873 (3)	0.713
Log-normal	0.034 (+)	0.262	0.297 (4)	0.277	0.029 (+)	0.309	0.338 (2)	0.328	0.086 (+)	0.533	0.620 (2)	0.633
AIC-selected	0.008 (+)	0.308	0.315 (7)	0.302	0.000 (-)	0.559	0.559 (6)	0.364	0.004 (-)	1.964	1.968 (4)	0.602
$\mathcal{M}^{(1)}$	0.006 (+)	0.286	0.293 (2)	0.328	0.001 (-)	0.461	0.462 (4)	0.472	1.537 (-)	0.828	2.365 (5)	4.291
$\mathcal{M}^{(2)}$	0.007 (+)	0.286	0.293 (1)	0.252	0.001 (-)	0.465	0.466 (5)	0.395	3.394 (-)	1.097	4.491 (6)	6.923

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.55: Simulation study. Sample from 95% mixture of size 500 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	7.747 (+)	2.105	9.852 (9)	4.190	0.006 (-)	2.839	2.845 (7)	4.233	52.143 (-)	4.188	56.331 (9)	4.470
Weibull	0.039 (+)	2.158	2.197 (1)	3.261	2.125 (-)	2.414	4.539 (9)	3.161	29.829 (-)	2.966	32.795 (8)	3.256
Log-skew-t	1.392 (+)	1.913	3.305 (8)	2.076	0.896 (+)	2.082	2.978 (8)	2.274	3.559 (-)	7.250	10.809 (7)	7.017
Log-t	0.802 (+)	1.762	2.564 (3)	1.846	0.688 (+)	1.961	2.649 (6)	2.022	1.198 (+)	2.967	4.165 (3)	3.352
Log-skew-n	1.146 (+)	1.886	3.032 (7)	2.026	0.589 (+)	1.965	2.555 (2)	2.033	1.031 (+)	3.017	4.048 (2)	3.382
Log-normal	0.601 (+)	1.725	2.326 (2)	1.789	0.553 (+)	1.938	2.491 (1)	1.987	0.994 (+)	2.969	3.963 (1)	3.332
AIC-selected	0.869 (+)	1.887	2.756 (5)	1.883	0.612 (+)	1.985	2.597 (3)	2.071	0.300 (+)	5.478	5.778 (6)	3.327
$\mathcal{M}^{(1)}$	0.928 (+)	1.834	2.762 (6)	1.950	0.643 (+)	1.994	2.637 (5)	2.095	1.088 (-)	3.742	4.830 (5)	11.211
$\mathcal{M}^{(2)}$	0.922 (+)	1.830	2.752 (4)	2.162	0.641 (+)	1.991	2.632 (4)	2.268	0.603 (-)	3.706	4.309 (4)	10.229

(1) direct method of model averaging (MA₁)
 (2) indirect method of model averaging (MA₂)

Table B.56: Simulation study. Sample from 95% mixture of size 500 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	330.421 (+)	14.887	345.308 (9)	15.762	211.319 (+)	14.697	226.017 (9)	16.759	11.291 (+)	16.682	27.973 (9)	21.638
Weibull	133.628 (+)	10.840	144.469 (8)	15.505	79.930 (+)	11.552	91.481 (8)	15.679	3.177 (+)	13.826	17.002 (7)	17.532
Log-skew-t	5.041 (+)	9.993	15.034 (7)	11.034	7.851 (+)	10.872	18.723 (7)	11.674	7.298 (+)	12.141	19.439 (8)	14.736
Log-t	1.641 (+)	7.599	9.241 (2)	8.443	1.484 (+)	7.957	9.441 (2)	8.677	2.488 (+)	9.812	12.300 (3)	10.876
Log-skew-n	5.214 (+)	9.742	14.956 (6)	10.506	2.196 (+)	9.478	11.673 (3)	9.299	2.305 (+)	9.924	12.229 (2)	10.932
Log-normal	1.520 (+)	7.558	9.078 (1)	8.395	1.445 (+)	7.929	9.374 (1)	8.638	2.353 (+)	9.858	12.211 (1)	10.942
AIC-selected	3.218 (+)	9.794	13.012 (5)	9.145	2.986 (+)	10.124	13.110 (6)	9.308	2.407 (+)	10.102	12.509 (4)	11.406
$\mathcal{M}^{(1)}$	3.344 (+)	9.029	12.373 (4)	9.817	3.167 (+)	9.526	12.693 (5)	10.194	3.452 (+)	11.309	14.761 (6)	13.589
$\mathcal{M}^{(2)}$	3.333 (+)	9.021	12.355 (3)	9.789	3.128 (+)	9.516	12.645 (4)	10.134	3.288 (+)	11.071	14.359 (5)	13.198

(1) direct method of model averaging (MA_1)
 (2) indirect method of model averaging (MA_2)

Table B.57: Simulation study. Sample from gamma distribution of size 500 - estimate of 1% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	0.000 (+)	0.000	0.000 (1)	0.000	0.000 (+)	0.000	0.000 (1)	0.000	0.000 (+)	0.000	0.000 (1)	0.000
Weibull	0.000 (+)	0.000	0.000 (6)	0.000	0.000 (+)	0.000	0.000 (6)	0.000	0.000 (+)	0.000	0.000 (3)	0.000
Log-skew-t	0.000 (+)	0.000	0.000 (5)	0.000	0.000 (+)	0.000	0.000 (5)	0.000	0.000 (+)	0.000	0.000 (2)	0.000
Log-t	0.000 (+)	0.000	0.000 (7)	0.000	0.004 (+)	0.000	0.004 (8)	0.000	0.088 (+)	0.007	0.096 (8)	0.010
Log-skew-n	0.000 (+)	0.000	0.000 (8)	0.000	0.000 (+)	0.001	0.001 (7)	0.000	0.031 (+)	0.036	0.067 (7)	0.006
Log-normal	0.000 (+)	0.000	0.000 (9)	0.000	0.005 (+)	0.000	0.005 (9)	0.000	0.096 (+)	0.008	0.104 (9)	0.011
AIC-selected	0.000 (+)	0.000	0.000 (3)	0.000	0.000 (+)	0.000	0.000 (4)	0.000	0.031 (+)	0.036	0.066 (6)	0.006
$\mathcal{M}^{(1)}$	0.000 (+)	0.000	0.000 (4)	0.000	0.000 (+)	0.000	0.000 (3)	0.000	0.025 (+)	0.027	0.052 (5)	0.011
$\mathcal{M}^{(2)}$	0.000 (+)	0.000	0.000 (2)	0.000	0.000 (+)	0.000	0.000 (2)	0.000	0.009 (+)	0.013	0.021 (4)	0.065

(1) direct method of model averaging (MA_1)
 (2) indirect method of model averaging (MA_2)

Table B.58: Simulation study. Sample from gamma distribution of size 500 - estimate of 5% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	0.000 (+)	0.000	0.000 (1)	0.000	0.000 (+)	0.000	0.000 (1)	0.000	0.000 (+)	0.000	0.000 (1)	0.000
Weibull	0.000 (+)	0.000	0.000 (8)	0.000	0.002 (+)	0.000	0.002 (6)	0.000	0.009 (+)	0.002	0.011 (3)	0.002
Log-skew-t	0.000 (+)	0.000	0.000 (5)	0.000	0.000 (+)	0.000	0.000 (5)	0.001	0.001 (+)	0.001	0.001 (2)	0.002
Log-t	0.001 (+)	0.000	0.001 (9)	0.000	0.104 (+)	0.007	0.110 (8)	0.006	1.206 (+)	0.069	1.275 (8)	0.083
Log-skew-n	0.000 (+)	0.000	0.000 (6)	0.000	0.006 (+)	0.014	0.020 (7)	0.001	0.378 (+)	0.408	0.786 (7)	0.048
Log-normal	0.000 (+)	0.000	0.000 (7)	0.000	0.109 (+)	0.006	0.115 (9)	0.007	1.222 (+)	0.068	1.290 (9)	0.083
AIC-selected	0.000 (+)	0.000	0.000 (2)	0.000	0.000 (+)	0.000	0.000 (4)	0.000	0.376 (+)	0.407	0.783 (6)	0.048
$\mathcal{M}^{(1)}$	0.000 (+)	0.00000174	0.00000199 (4)	0.0000020	0.000 (+)	0.00007	0.00012 (3)	0.000149	0.316 (+)	0.315	0.630 (5)	0.090
$\mathcal{M}^{(2)}$	0.000 (+)	0.00000169	0.00000192 (3)	0.0000103	0.000 (+)	0.00004	0.00006 (2)	0.000175	0.242 (+)	0.272	0.514 (4)	0.265

(1) direct method of model averaging (MA_1)
 (2) indirect method of model averaging (MA_2)

Table B.59: Simulation study. Sample from gamma distribution of size 500 - estimate of 25% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	0.001 (+)	0.080	0.081 (4)	0.076	0.002 (+)	0.122	0.125 (1)	0.145	0.012 (+)	0.256	0.268 (1)	0.264
Weibull	0.004 (+)	0.080	0.084 (6)	0.053	1.623 (+)	0.232	1.856 (7)	0.241	6.149 (+)	0.651	6.800 (3)	0.664
Log-skew-t	0.000 (-)	0.079	0.080 (1)	0.077	0.092 (+)	0.172	0.264 (5)	0.242	0.292 (+)	0.493	0.785 (2)	0.889
Log-t	0.837 (+)	0.344	1.181 (9)	0.201	4.445 (+)	0.337	4.782 (8)	0.258	33.569 (+)	1.332	34.900 (9)	1.330
Log-skew-n	0.327 (-)	0.023	0.350 (7)	0.012	0.498 (+)	0.572	1.070 (6)	0.196	10.173 (+)	9.498	19.671 (6)	0.856
Log-normal	0.453 (-)	0.016	0.469 (8)	0.006	4.549 (+)	0.269	4.818 (9)	0.259	33.087 (+)	1.265	34.351 (8)	1.320
AIC-selected	0.001 (+)	0.082	0.083 (5)	0.076	0.010 (+)	0.164	0.174 (2)	0.151	10.205 (+)	9.539	19.744 (7)	1.145
$\mathcal{M}^{(1)}$	0.001 (+)	0.079	0.080 (3)	0.078	0.028 (+)	0.155	0.183 (3)	0.191	9.890 (+)	7.601	17.491 (4)	1.620
$\mathcal{M}^{(2)}$	0.001 (+)	0.079	0.080 (2)	0.083	0.029 (+)	0.156	0.184 (4)	0.155	9.654 (+)	7.925	17.579 (5)	1.203

(1) direct method of model averaging (MA₁)

(2) indirect method of model averaging (MA₂)

Table B.60: Simulation study. Sample from gamma distribution of size 500 - estimate of 50% quantile (Results $\times 10^{-4}$).

Censoring	No				Censoring 1				Censoring 2			
	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$	bias ²	var	mse(rank)	$\overline{\text{var}}$
Gamma	0.008 (+)	5.971	5.980 (1)	5.558	0.008 (+)	8.104	8.112 (8)	8.716	0.108 (+)	13.644	13.752 (1)	13.326
Weibull	28.086 (-)	3.817	31.903 (7)	3.049	0.021 (+)	6.165	6.186 (1)	5.849	22.394 (+)	11.067	33.461 (3)	10.349
Log-skew-t	1.601 (-)	7.305	8.906 (5)	6.932	0.217 (-)	7.536	7.753 (3)	8.435	0.053 (+)	13.997	14.050 (2)	14.699
Log-t	6.559 (-)	9.431	15.991 (6)	6.347	4.575 (-)	4.683	9.258 (9)	3.441	45.553 (+)	9.281	54.835 (9)	8.102
Log-skew-n	70.143 (-)	4.660	74.803 (8)	1.913	0.913 (-)	6.829	7.742 (2)	6.785	9.985 (+)	28.057	38.042 (6)	10.710
Log-normal	132.546 (-)	1.277	133.822 (9)	1.215	4.247 (-)	3.748	7.994 (6)	3.431	44.725 (+)	8.918	53.644 (8)	8.109
AIC-selected	0.000 (+)	6.343	6.343 (4)	5.714	0.001 (-)	7.997	7.998 (7)	8.591	10.158 (+)	28.230	38.387 (7)	11.399
$\mathcal{M}^{(1)}$	0.011 (-)	6.099	6.110 (2)	6.168	0.022 (-)	7.776	7.798 (5)	8.518	11.585 (+)	24.472	36.057 (4)	12.740
$\mathcal{M}^{(2)}$	0.013 (-)	6.119	6.132 (3)	5.461	0.024 (-)	7.770	7.793 (4)	6.324	12.164 (+)	24.169	36.333 (5)	8.514

(1) direct method of model averaging (MA₁)

(2) indirect method of model averaging (MA₂)

Implementation codes

We performed statistical analyses of Chapters 3 to 6 using SAS 9.2 (SAS Institute Inc., Cary, NC, USA) and R 2.14 (R Foundation for Statistical Computing, Vienna, Austria). The package **stats4** in R is used for maximum likelihood estimation.

C.1 Parametric models

Suppose y is a matrix consisting of two columns. For uncensored, left-censored and right-censored data, first and second column contain the observed value. For interval-censored data, the first entry is the left-end value and the second entry the right-end value of the interval. ind , $d1$, dr , di are vectors representing the indicator variables. They have the value 1 if the corresponding observation is respectively uncensored, left-censored, right-censored and interval-censored and 0 otherwise.

Example for fitting the log-normal and gamma distribution.

```
# log-normal distribution
## starting values
p1=mean(log(y[,2]))
p2=sqrt(var(log(y[,2])))
## maximum likelihood
minusloglikLN <- function(par1,par2){
  -sum(
    log((dnorm(log(y[,2])), mean = par1, sd = abs(par2))/y[,2])^ind)
    +log(pnorm(log(y[,2]), mean = par1, sd = abs(par2))^d1)
    +log((1-pnorm(log(y[,1]), mean = par1, sd = abs(par2)))^dr)
```

```

+log((pnorm(log(y[,2]), mean = par1, sd = abs(par2))-
      pnorm(log(y[,1]), mean = par1, sd = abs(par2)))^di)
)
}
fitLN <- mle(minusloglikLN,start=list(par1=p1,par2=p2))

# gamma distribution
## starting values
p1=mean(y[,2])/var(y[,2])
p2=mean(y[,2])^2/var(y[,2])
## maximum likelihood
minusloglikGA <- function(par1,par2){
-sum(
log(dgamma(y[,2], shape = abs(par1), rate = abs(par2))^ind)+
log(pgamma(y[,2], shape = abs(par1), rate = abs(par2))^dl)+
log((1-pgamma(y[,1], shape = abs(par1), rate = abs(par2)))^dr)+
log((pgamma(y[,2], shape = abs(par1), rate = abs(par2))-
      pgamma(y[,1], shape = abs(par1), rate = abs(par2)))^di)
)
}
fitGA <- mle(minusloglikGA,start=list(par1=p1,par2=p2))

```

The R packages **sn** and **VGAM** are used for the skewed distributions and the generalized gamma distribution.

R Development Core Team (2011). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL <http://www.R-project.org/>.

Azzalini, A. (2011). R package 'sn': The skew-normal and skew-t distributions (version 0.4-17). URL <http://azzalini.stat.unipd.it/SN>

Thomas W. Yee (2010). The VGAM Package for Categorical Data Analysis. *Journal of Statistical Software*, 32(10), 1-34. URL <http://www.jstatsoft.org/v32/i10/>.

C.2 SemiNP models

The macro to fit the SemiNP models is included in **goftest8.sas**.

```
%include 'C:\...\goftest8.sas';
/*
left censored: llim = 0, rlim = value, dl = 1
right censored: llim = value, rlim = fixed, dr = 1
interval censored: llim = value 1, rlim = value 2, di = 1
non censored: llim = rlim = value, ind = 1
*/
%SNPmacrointB(data=cadb, depl=llim,depr=rlim, delta=ind,
              deltal=dl, deltar=dr, deltai=di);
proc iml; load;
/*parameter estimates and corresponding likelihoods
(similar for N_3, ..., N_7)*/
print N_1 N_2;
/*only max likelihood for eg N_1
(similar for N_2, ..., N_7)*/
%let para1 = 3; /*&para1 = number of parameters*/
loca=N_1[<:>,&para1+1];
best=N_1[loca,];
print best;
quit;
```

C.3 Model averaging distribution functions

Suppose `aicMA` is a matrix with all AIC values: each column represents a candidate model. `Fhat` and `sef` represent the estimated values and their standard error for each candidate model (column).

```
bestaic=apply(aicMA,1,min)
bestaic=as.matrix(bestaic)%*%matrix(nrow=1,ncol=ncol(aicMA),1)
delta=aicMA-bestaic
num=exp((-1/2)*delta)
den=apply(num,1,sum)
den=den%*%matrix(nrow=1,ncol=ncol(aicMA),1)
weights=t(num/den)
```

```

Fhatavg=diag(Fhat%*(weights))
var_Fhat=sef^2
bias_tocompute_MA=(Fhat-Fhatavg%*matrix(1,nrow=1,ncol=ncol(aicMA)))^2
comp1=sqrt(var_Fhat+bias_tocompute_MA)
std_Fhatavg=diag(comp1%*(weights))

```

C.4 Model averaging quantiles

The codes for approach 1 are similar to the model averaging of distribution functions, by changing the Fhat to Qhat. The R code to obtain the model average of the second approach is given here.

```

pMA_temp=function(x,p1LN,p2LN,...)
{
  cbind(
    plnorm(x,meanlog=p1LN,sdlog=p2LN),
    ...
  )%*t(weights)-xmed
}
#quantile with root
medMA=function(p) uniroot(pMA_temp,c(10e-35,5),p[1],p[2],...
  ,tol=10e-10)$root

xihatavg2=rep(0,length(xvalmed));dim(xihatavg2)=c(length(xihatavg2),1)
for(i in 1:length(xvalmed)){
  xmed=xvalmed[i]
  xihatavg2[i]=medMA(unlist(coeff))
}

#var of F(quantile) with MA
#we need every single distribution for the calculation of
#the MAvariance, evaluated in Fhatavg
Fhat=cbind(
  plnorm(xihatavg2, meanlog = coeff$LN[1], sdlog = coeff$LN[2]),
  ...
)
colnames(Fhat)=colnames(weights)

```

```

FLN=function(x) plnorm(xx,meanlog=x[1],sdlog=x[2])
...

Fse=matrix(nrow=length(xihatavg2),ncol=ncol(weights))
for(i in 1:length(xihatavg2)){
xx=xihatavg2[i]
Fse[i,1]=sqrt(t(as.matrix(grad(FLN,coeff$LN)))*%
  vcov(fitLN)*%as.matrix(grad(FLN,coeff$LN)))
...
}
colnames(Fse)=colnames(weights)

FMA=Fhat*%t(weights)
var_Fhat=Fse^2
bias=(Fhat-FMA*%matrix(1,nrow=1,ncol=length(aic)))^2
comp1=sqrt(var_Fhat+bias)
FMAse=comp1*%t(weights)

#inverse with Taylor
dMA=function(x){
cbind(
dlnorm(x, meanlog = coeff$LN[1], sdlog = coeff$LN[2]),
...
)*%t(weights)
}
var_xihatavg2=1/dMA(xihatavg)^2*FMAse^2;var_xihatavg2
std_xihatavg2=sqrt(var_xihatavg2)

```


Samenvatting

Toxische stoffen zijn schadelijk voor de gezondheid. De aanwezigheid van deze stoffen in ons voedsel moet beperkt blijven en hierop wordt streng toegezien. Op het niveau van de Europese Unie wordt dit onderzoek geleid door de Europese autoriteit voor voedselveiligheid (EFSA, European Food Safety Authority). Voor ons onderzoek beschikken we over gegevens omtrent de aanwezigheid van Cadmium in bepaalde delen van de voedselketen (EFSA, 2010). Bij het meten van de concentratie van zulke stoffen, wordt men geconfronteerd met links- en interval-gecensureerde gegevens (beneden de detectielimiet en kwantificatielimiet respectievelijk), m.a.w. de concentratie is te laag om gedetecteerd of precies gemeten te kunnen worden.

Een eerste groep gegevens (zie Hoofdstuk 2), bestaat uit 99 stalen waarbij de concentratie van Cadmium in 42 stalen onder de detectielimiet ligt en dus niet detecteerbaar is. Dat wil zeggen dat we in bijna de helft van de stalen geen precieze gegevens hebben over de concentratie Cadmium en we enkel weten dat de concentratie heel laag is. In een tweede steekproef zijn er 114 stalen, waarbij er in 3 stalen geen Cadmium gedetecteerd wordt (concentratie onder de detectielimiet) en in 17 stalen geen precieze concentratie gemeten wordt (tussen de detectielimiet en de kwantificatielimiet).

Om uitspraken te kunnen doen over de veiligheid van ons voedsel, worden statistische modellen gebruikt. Daarbij is het belangrijk om een 'goed' model te selecteren.

Een model dat vaak gebruikt wordt in de context van toxische stoffen, is de log-normale verdeling. Deze verdeling dankt zijn populariteit vooral aan het verband (via een logaritmische transformatie) met de bekende normale of Gauss verdeling. De log-normale verdeling wordt getypeerd door twee parameters, μ en σ^2 , die respectievelijk het gemiddelde en de variantie voorstellen op de logaritmisches-getransformeerde schaal. Naast de log-normale verdeling, bekijken we ook andere parametrische verdelingen. Deze

verdelingen kunnen allemaal gelinkt worden aan de log-normale verdeling, maar ze hebben bijvoorbeeld meer parameters en zijn daardoor flexibeler. Een andere manier om de log-normale verdeling uit te breiden en zo meer flexibiliteit te geven aan de verdeling, is het beschouwen van een semi-parametrische familie van verdelingen. Hierbij worden, op een vooraf bepaalde manier, parameters toegevoegd aan de log-normale verdeling of aan een andere basisverdeling. Wij gebruiken de semi-parametrische familie SemiNP van Fenton en Gallant (1996), Gallant en Nychka (1987) en Zhang en Davidian (2008).

In Hoofdstuk 3 stellen we deze verdelingen voor en tonen we hoe waarschijnlijk het is dat de steekproeven van Cadmium concentraties komen uit een populatie met voren genoemde verdeling. Hiervoor berekenen we de meest aannemelijke schatters (maximum likelihood). Daarbij moeten we de aannemelijkheidsfunctie aanpassen, omdat sommige gegevens gecensureerd zijn. Een globale vergelijking van de verdelingen gebeurt met Akaike's informatie criterium (AIC). We zien dat de log-normale verdeling het niet slecht doet in vergelijking met de andere verdelingen, maar dat bijvoorbeeld de semi-parametrische familie van verdelingen een betere globale weerspiegeling van de gegevens geeft.

Om de mogelijke sterktes en zwaktes van een verdeling te onderzoeken, kan men gebruik maken van statistische toetsen die aanpassingstoetsen (goodness-of-fit test) genoemd worden. Met een aanpassingstoets onderzoekt men of de verdeling waaruit de steekproef is getrokken, afwijkt van een bekende verdeling, zoals de log-normale verdeling. In Hoofdstuk 4 van deze verhandeling, onderzoeken we een aanpassingstoets die werd voorgesteld door Aerts et al. (1999). De toets onderzoekt of een parametrische verdeling, ook wel basismodel genoemd, past bij een gegeven steekproef. Daartoe wordt een familie van verdelingen gedefinieerd waartoe het basismodel behoort. Vervolgens wordt binnen die familie van verdelingen de beste verdeling gekozen. Als de beste verdeling een aanzienlijke verbetering is ten opzichte van het basismodel, dan besluiten we dat het basismodel geen goed model is.

De toets werd nog niet eerder gebruikt voor gecensureerde gegevens. Wij maken deze uitbreiding in deze verhandeling en gebruiken daarvoor de SemiNP familie van verdelingen. Hoewel de toets kan gebruikt worden voor een willekeurig basismodel, leggen wij de nadruk op de log-normale verdeling. Uit de resultaten van de simulatie studie blijkt dat de toets eerder conservatief is, maar in staat is om lokale en globale afwijkingen van de log-normale verdeling te detecteren.

Multimodel inferentie is een methodologie om naast de variabiliteit die eigen is aan steekproefgegevens ook de onzekerheid over een geschikt statistisch model in rekening te brengen in de statistische besluitvorming. Deze methodologie werd nog niet toegepast in

en aangepast aan de setting van gecensureerde gegevens. Wij hebben ons gebaseerd op de techniek van model uitmiddeling (model averaging) die beschreven wordt door Burnham en Anderson (2002). Hierbij wordt een familie van kandidaatmodellen beschouwd en wordt informatie van elk model gebruikt, waarbij meer belang wordt gehecht aan een goed model.

In Hoofdstuk 5 zijn we geïnteresseerd in het schatten van de verdelingsfunctie op een vooraf vastgelegde plaats in de gegevens. De kandidaten voor de familie van kandidaatmodellen werden beschreven in Hoofdstuk 3. Er zijn echter verschillende mogelijkheden om de SemiNP familie te beschouwen. Ten eerste kunnen we ons beperken tot enkel de familie van parametrische modellen. Die kunnen we uitbreiden met het 'beste' model uit de SemiNP familie, resulterend in een tweede familie. Of we kunnen een derde familie van kandidaatmodellen definiëren door alle parametrische en alle (tot een bepaalde graad) modellen uit de SemiNP familie in te sluiten. Voor de Cadmium gegevens schatten we op deze drie manieren bijvoorbeeld de kans dat een concentratie onder de gemiddelde detectielimiet ligt. In een simulatie studie bestuderen we het gedrag van de schattingen gebaseerd op deze drie families. We beschouwen verschillende scenario's: met en zonder censurering, verschillende modellen waaruit gegevens gegenereerd worden, verschillende steekproefgroottes en andere plaatsen waar de verdelingsfunctie wordt geschat. De conclusie van de simulatiestudie is afhankelijk van het scenario dat wordt onderzocht.

In Hoofdstuk 6 werken we verder met de techniek van model uitmiddeling, maar zijn we op zoek naar een schatting voor een kwantiel. Als we veronderstellen dat het onderliggende model continu is, dan kunnen we een kwantiel berekenen door de verdelingsfunctie te inverteren. Wanneer we opnieuw de onzekerheid over het geschikte statistische model in rekening willen brengen, dan zijn er twee manieren om het model uit te middelen. In de eerste manier wordt voor elk model in de familie van kandidaatmodellen een schatting gedaan voor het kwantiel. Vervolgens wordt een gewogen gemiddelde berekend van deze kwantielen, waarbij een goed model meer invloed heeft. Een tweede manier om uit te middelen bestaat erin eerst een gemiddelde verdeling te bepalen en deze vervolgens te inverteren. We gebruiken beide manieren om het 5% en 25% kwantiel van de Cadmium concentraties te schatten. Uit de simulatie studie blijkt dat er geen favoriete methode is van uitmiddelen. In sommige scenario's is de eerste manier te verkiezen, terwijl de tweede manier de voorkeur heeft in andere scenario's.

In het laatste hoofdstuk worden voorbeelden uit andere disciplines gebruikt om de methodologie te illustreren. Het eerste voorbeeld gaat over de concentratie van de bacterie *Yersinia enterocolitica*, die gedurende 4 dagen wordt gemeten. In het algemeen kunnen we de groei van de concentratie van een bacterie opsplitsen in drie fasen. In de eerste

fase is er nog geen groei; vervolgens zal de concentratie snel toenemen, vaak exponentieel snel; in de derde fase stopt de groei en wordt een maximale concentratie bereikt. Een populair model om deze groei te beschrijven, is het model van Baranyi en Roberts (1994).

Het tweede voorbeeld gaat over een serologische studie waarin antilichamen tegen de vijfde kindenziekte (Parvovirus B19) worden opgespoord in het bloed. Ook hier bestaan vele modellen om het voorkomen van antilichamen te modelleren afhankelijk van de leeftijd van de onderzochte persoon. Wij gebruiken het model van Farrington (1990) om de gegevens te beschrijven.

In beide voorbeelden wordt verondersteld dat er steeds een toename is of m.a.w. dat het model monotoon is: de concentratie van de bacterie kan niet afnemen; en hoe ouder een persoon is, hoe groter de kans dat hij antilichamen heeft tegen een ziekte.

Zowel het model van Baranyi en Roberts (1994) als van Farrington (1990) kan voorgesteld worden aan de hand van één of meerdere differentiaalvergelijkingen. Voor zulke modellen stelden Ramsay et al. (2007) een veralgemeende afvlakkende (smoothing) schattingsmethode voor om de parameters van de differentiaalvergelijking(en) te schatten. De methode laat toe om af te wijken van het model, maar de mate waarin afwijkingen zijn toegestaan, wordt bepaald door een penalisatieparameter. Aangezien het bepalen van de beste penalisatieparameter een belangrijke stap is in het schattingsproces, stellen wij een manier voor om de penalisatieparameter te bepalen, waarbij we gebruik maken van eenzijdige cross-validatie (Hart en Yi, 1998). Daarnaast breiden we de methode van Ramsay et al. (2007) uit zodat de oplossing nog steeds kan afwijken van het model, maar moet voldaan aan bepaalde beperkingen qua vorm, bijvoorbeeld het monotoon zijn van de oplossing. Tot slot gebruiken we bootstrap methodes om betrouwbaarheidsintervallen te bepalen rond de oplossing, en om te testen of het onderliggende model geschikt is om de gegevens te beschrijven alsook om de hypothese van monotonie te toetsen. Het model van Baranyi en Roberts (1994) blijkt geschikt te zijn voor de *Yersinia enterocolitica* gegevens, terwijl het model van Farrington (1990) onvoldoende flexibiliteit heeft voor de Parvovirus B19 gegevens. De assumptie van een monotoon gedrag is aanvaardbaar voor de *Yersinia enterocolitica* gegevens, maar niet voor de Parvovirus B19 gegevens.