Genetic Versus Non-Genetic Weibull Log-Normal Sire Frailty Models: A Simulation Study

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Abstract

Models used worldwide for sire evaluations of longevity are known to be inconsistent with assumption of the additive genetic infinitesimal model, because three quarter of the additive genetic variance is ignored. The objective of this study was to test that parameters estimated using Weibull log-normal sire frailty models without genetic interpretation are inconsistent with parameters defined by the additive genetic infinitesimal model. Two simulation studies were carried out, and in both simulation studies data were simulated according to a Weibull log-normal sire frailty model with genetic interpretation. In the first simulation study four different data sets were generated. The data sets were balanced in the number of daughters per sire, but differed in the level of censoring (0 %, 25 %, 50 %, 75 %). The four data sets were analyzed with the model used to generate data, and with a Weibull log-normal sire frailty model without genetic interpretation. Parameter estimates obtained from analysis based on the non-genetic sire model were strongly biased, in particular, the sire variance was downward biased, and parameter estimates, including sire effects, were highly influenced by the level of censoring. Parameter estimates obtained from analysis based on genetic sire models were consistent with the true values used to simulate data. The second simulation study mimics the data structure encountered in dairy breeding, where daughter group size and level of censoring heavily increase when sires have their second crop daughters. Data was analyzed using a Weibull log-normal sire frailty model with and without genetic interpretation. In the non-genetic sire model, the estimated sire effects of proven bulls with second crop daughters were decreased (improved) when level of censoring increased from 20 % to about 86 % (daughter group size increased from 100 to 1000) without changing estimated sire effects of remaining (young) bulls. This jump of sire effects for proven bulls with second crop daughters is not observed in the sire model with genetic interpretation. This study suggest that the problem with unstable sire effects observed in practise, and described in VanRaden and Powell (2002), is due to the fact that sires are ranked for longevity based on models without genetic interpretation.

Keywords: Survival models; prediction of breeding values; estimations of parameters; simulation study; model with genetic interpretation; model without genetic interpretation

Introduction

The routine genetic evaluation of bulls on length of productive life implemented in several countries over the last couple of years is based on Weibull log-normal sire frailty models or sire-maternal grand-sire models (Ducrocq and Sölkner, 1998a). These models do not have a genetic interpretation, in the sense that they are inconsistent with assumptions of the additive genetic infinitesimal model (Fisher, 1918; Bulmer, 1971), as notified by Ducrocq and Casella (1996) and formally proved by Andersen et al. (2000) and Korsgaard et al. (2000). Andersen et al. (2000) also defined Weibull log-normal sire frailty models consistent with assumptions of the additive genetic infinitesimal model. Sire models with genetic interpretation are characterized by inclusion of a normally distributed error term on the log frailty scale,

which account for the remaining part of the additive genetic variance (e.g. 3/4 in sire model), and residual sources of variation influencing the hazard function. We will distinguish between sire models without and with genetic interpretation by referring to non-genetic sire models and genetic sire models.

In this study, ranking of sires and bias of parameter estimates obtained using Weibull log-normal sire frailty models without genetic interpretation were addressed by simulation. The objective was to test that parameters, including sire effects, estimated using a Weibull log-normal sire frailty model without genetic interpretation are inconsistent with parameters defined by the additive genetic infinitesimal model.

Materials and Methods

This study consists of two simulation studies. The first simulation study address bias of parameter estimates in balanced data sets with different levels of censoring. The second simulation study mimics the data structure encountered in dairy breeding, where daughter group size and level of censoring increase heavily, when sires get their second crop daughters. In this study only Weibull log-normal frailty models without systematic effects and without time dependent random effects were considered. The sire model with genetic interpretation and the sire model without genetic interpretation are defined below.

Genetic sire model

Let $\boldsymbol{\eta}$ denote a vector with elements (s_i+e_{ij}) for i=1,...,q and j=1,...,n_i, where q is the number of sires and n_i is the number of daughters of sire i. Now consider the genetic Weibull log-normal sire frailty model, for survival times T_{ij} (i=1,...,q and j=1,...,n_i), where the hazard function for T_{ij}, conditional on $\boldsymbol{\eta}$, is given by

$$\lambda_{ij}(t \mid \boldsymbol{\eta}) = \rho t^{(\rho-1)} \exp(\beta + s_i + e_{ij}) \qquad (1)$$

where ρ and β are parameters characterizing the baseline hazard function, and s_i is a sire transmitting ability, with $\mathbf{s} \sim N_q(\mathbf{0}, \mathbf{I}\sigma_s^2)$ (sires are unrelated). Here e_{ij} is a residual effect, with $\mathbf{e} \sim N_n(\mathbf{0}, \mathbf{I}\sigma_e^2)$. It is assumed that $\sigma_e^2 \geq 3\sigma_s^2$. The two vectors **s** and **e** are assumed to be independent, and conditional on the vector $\boldsymbol{\eta}$, all the lifetimes are assumed to be independent. This model is consistent with assumptions of the additive genetic infinitesimal model (Andersen et al., 2000). The genetic Weibull log-normal sire frailty model is a log linear model for T_{ij} (e.g. Kalbfleisch and Prentice 1980) given by

$$\log(T_{ij}) = \frac{1}{\rho}(-\beta - s_i - e_{ij} + \varepsilon_{ij}) \qquad (2)$$

where ε_{ij} follows an extreme value distribution, with $E(\varepsilon_{ij}) = \gamma_E$ (γ_E is Euler's constant), and $Var(\varepsilon_{ij}) = \frac{\pi^2}{6}$. All of the ε_{ij}'s are independent, and independent of **s** and **e**.

Non-genetic sire model

The Weibull log-normal sire frailty model without genetic interpretation is here defined exactly as the genetic sire model, except that the residual effect on the normally distributed scale is missing. The hazard function for a survival time $\widetilde{T}_{ij}$, conditional on $\widetilde{\mathbf{s}}$, is given by

$$\widetilde{\lambda}_{ij}(t \mid \widetilde{\mathbf{s}}) = \widetilde{\rho} t^{(\widetilde{\rho}-1)} \exp(\widetilde{\beta} + \widetilde{s}_i) \qquad (3)$$

where $\widetilde{\mathbf{s}}$ is a vector with elements $(\widetilde{s}_i)_{i=1,...q}$. Here $\widetilde{\mathbf{s}}$ is a random effect (not a sire transmitting ability) specific for each sire, with $\widetilde{\mathbf{s}} \sim N_q(\mathbf{0}, \mathbf{I}\sigma_{\widetilde{s}}^2)$ (random effects are independent). The non-genetic sire model is like the genetic sire model a log linear model for $\widetilde{T}_{ij}$ and this model is inconsistent with assumption of the additive genetic infinitesimal model (Ducrocq and Casella, 1996; Korsgaard et al., 2000; Andersen et al., 2000).

Simulation study 1

Lifetimes of 10,000 animals after 100 unrelated sires, each having 100 offspring, were generated from a Weibull log-normal sire frailty model (1) based on the model parameters: $\rho = 2.4$,

$\beta = -15.5$, $\sigma_s^2 = 0.375$ and $\sigma_e^2 = 2.625$. The parameter values correspond to a heritability on the normally distributed scale ($h_{nor}^2 = \frac{4\sigma_s^2}{\sigma_s^2+\sigma_e^2}$) equal to 0.5, and expected value and variance of log lifetime are E(log(T))=6.22 and Var(log(T))=0.81 (expected value and variance of lifetime are E(T)=734 and Var(T)=739^2 (Hougaard, 2000)). Four different levels of censoring (0 %, 25 %, 50 % and 75 %) were introduced by right censoring. Each of the 4 data sets was analyzed with two models: a Weibull log-normal sire frailty model without genetic interpretation (non-genetic sire model), and a Weibull log-normal sire frailty model with genetic interpretation (genetic sire model). In both models parameter estimates were obtained from a Bayesian analysis using Gibbs sampling together with adaptive rejective sampling, and for the non-genetic sire model, parameter estimates were also obtained using the software Survival Kit (Ducrocq and Sölkner, 1998b).

Simulation study 2

The second simulation study includes three steps. All data generated in simulation study 2 are based on the genetic sire model with parameter values as given in simulation study 1.

Step 1
Lifetimes of 10,000 animals after 100 unrelated sires each having 100 offspring were generated from a Weibull log-normal sire frailty model (1) with an average of 20 % censored records. This data set was analyzed with the non-genetic sire model (Survival Kit). Based on results from Survival Kit, the 10 best sires were identified, and selected for having second crop daughters.

Step 2
The data set from Step 1 was supplied with lifetimes (20 % censoring) of 10,000 new animals after 100 new unrelated sires, unrelated with the first 100 sires. These new sires were considered as a new generation of young sires. This data set, with 20,000 records, was analyzed with a non-genetic sire model (Survival Kit).

Step 3
The data set from Step 2 was supplied with lifetimes (censored at time 265) of 9000 daughters after the 10 sires selected in Step 1 (900 daughters per sire). The level of censoring of daughter groups (with 100+900 daughters) of selected sires varied from 82 % to 90 %. The 10 sires with large daughter groups were considered as proven bulls with second crop daughters. This data set was analyzed with the non-genetic sire model (Survival Kit). The estimated sire effects, with specific focus on proven bulls with second crop daughters, were compared with the sire effects obtained in Step 2.

The three steps described above were now repeated in a slightly changed version, such that data was analyzed using genetic sire models instead of non-genetic sire models. The data was the same as described above except for the 9,000 animals added to the 10 best sires selected in Step 1 (the 10 best sires identified based on the genetic sire model do not necessarily correspond to the 10 best sires identified based on the non-genetic sire model).

This whole scenario was repeated three times. The results were basically the same, therefore only results from one of the repetitions are presented.

Results (Simulation study 1)

Parameter estimates obtained using a non-genetic sire model

Parameter estimates obtained from a Bayesian analysis using Gibbs sampling were very similar to estimates obtained using the software Survival Kit (Table 1). Mode and mean values of marginal posterior distributions of model parameters obtained using a non-genetic sire model were numerically lower than the corresponding true values, and the true values were far outside the corresponding 95 % central posterior density (CPD) regions (Gelman et al., 1995) defined by the 2.5 % and 97.5 % quantiles (Table 1). In the non-genetic sire model, censoring not only increased the 95 % CPD regions, but also mode and mean values of the marginal posterior distributions of $\tilde{\rho}$ and $\sigma_{\tilde{s}}^2$ were increased and of $\tilde{\beta}$ decreased with increasing level of censoring. Because $\sigma_{\tilde{s}}^2$ was increasing with increasing level of censoring, then the empirical mean of the 10 best estimated sire effects was decreasing (improved), and the empirical variance of all

estimated sire effects was increasing (results not shown). For the Weibull baseline parameters the 9 % CPD regions did not overlap for any of the four different levels of censoring. The true average log lifetime was within the 95 % CPD regions at 0 % and 25 % censoring, but outside for the two remaining levels of censoring. The estimated variance of log lifetime decreased with increasing level of censoring, and the 95 % CPD regions did not overlap for any levels of censoring. The true variance of log lifetime was only within the 95 % CPD region at 25 % censoring.

Parameter estimates obtained using a genetic sire model

Mode and mean values of marginal posterior distributions of model parameters obtained using a genetic sire model were close to the true parameter values, i.e. the true values of all model parameters were within the 95 % CPD regions (Table 2). With increasing level of censoring the 95 % CPD regions were increased. The true values of expected log lifetime and variance of log lifetime were also within the corresponding 95 % CDF regions.

Ranking of sires

The Spearman rank correlations between estimated sire transmitting abilities (genetic sire model)/sire effects (non-genetic sire model) and true sire transmitting abilities were basically the same independently of the model used for estimation (Table 3). The only exception was for data not censored, where Spearman rank correlation was slightly higher for the genetic sire model. With increasing level of censoring the correlation decreased.

Table 1**.** Results from a Bayesian analysis of data (from simulation study 1) with the non-genetic sire model using Gibbs sampling and the software Survival Kit (S. Kit). True values, mode, mean, 2.5 % and 97.5 % quantiles of the marginal posterior distributions of model parameters ($\tilde{\rho}$, $\tilde{\beta}$, $\sigma^2_{\tilde{s}}$), and the derived quantities $E(\log(\tilde{T})) = \frac{1}{\tilde{\rho}}(-\tilde{\beta} - \gamma_E)$ and $Var(\log(\tilde{T})) = \frac{1}{\tilde{\rho}^2}(\sigma^2_{\tilde{s}} + \frac{\pi^2}{6})$.

Non-genetic sire model							
Parameter	Cens.	True	S.Kit	Mode	Mean	2.5%Q	97.5%Q
$\tilde{\rho}$	0 %	2.4	1.25	1.25	1.24	1.23	1.26
$\tilde{\rho}$	25 %	-	1.47	1.48	1.47	1.44	1.50
$\tilde{\rho}$	50 %	-	1.65	1.65	1.64	1.60	1.68
$\tilde{\rho}$	75 %	-	1.89	1.88	1.88	1.81	1.95
$\tilde{\beta}$	0 %	-15.5	-8.26	-8.25	-8.26	-8.40	-8.12
$\tilde{\beta}$	25 %	-	-9.65	-9.55	-9.64	-9.83	-9.44
$\tilde{\beta}$	50 %	-	-10.65	-10.55	-10.62	-10.89	-10.36
$\tilde{\beta}$	75 %	-	-11.95	-11.85	-11.90	-12.31	-11.49
$\sigma^2_{\tilde{s}}$	0 %	0.375	0.10	0.11	0.10	0.08	0.14
$\sigma^2_{\tilde{s}}$	25 %	-	0.10	0.11	0.11	0.08	0.15
$\sigma^2_{\tilde{s}}$	50 %	-	0.13	0.14	0.14	0.10	0.19
$\sigma^2_{\tilde{s}}$	75 %	-	0.16	0.17	0.17	0.12	0.25
$E(\log(\tilde{T}))$	0 %	6.22	-	6.18	6.17	6.12	6.23
$E(\log(\tilde{T}))$	25 %	-	-	6.17	6.17	6.12	6.22
$E(\log(\tilde{T}))$	50 %	-	-	6.13	6.12	6.07	6.17
$E(\log(\tilde{T}))$	75 %	-	-	6.03	6.02	5.97	6.08
$Var(\log(\tilde{T}))$	0 %	0.81	-	1.14	1.13	1.09	1.17
$Var(\log(\tilde{T}))$	25 %	-	-	0.82	0.81	0.78	0.85
$Var(\log(\tilde{T}))$	50 %	-	-	0.67	0.66	0.63	0.70
$Var(\log(\tilde{T}))$	75 %	-	-	0.52	0.52	0.47	0.56

Table 2**.** Results from a Bayesian analysis of data (from simulation study 1) with the genetic sire model using Gibbs sampling. True values, mode, mean, 2.5 % and 97.5 % quantiles of the marginal posterior distributions of model parameters (ρ, β, σ_s^2, σ_e^2), and the derived quantities $E(\log(T)) = \frac{1}{\rho}(-\beta - \gamma_E)$ and $Var(\log(T)) = \frac{1}{\rho^2}(\sigma_s^2 + \sigma_e^2 + \frac{\pi^2}{6})$.

Genetic sire model						
Parameter	Cens.	True	Mode	Mean	2.5%Q	97.5%Q
ρ	0 %	2.4	2.36	2.37	2.19	2.56
ρ	25 %	-	2.40	2.41	2.22	2.65
ρ	50 %	-	2.44	2.42	2.18	2.72
ρ	75 %	-	2.36	2.41	2.12	2.77
β	0 %	-15.5	-15.15	-15.31	-16.48	-14.20
β	25 %	-	-15.15	-15.59	-17.06	-14.36
β	50 %	-	-15.51	-15.66	-17.54	-14.13
β	75 %	-	-14.97	-15.51	-17.85	-13.62
σ_s^2	0 %	0.375	0.35	0.36	0.25	0.51
σ_s^2	25 %	-	0.35	0.38	0.26	0.54
σ_s^2	50 %	-	0.35	0.39	0.26	0.58
σ_s^2	75 %	-	0.33	0.36	0.22	0.57
σ_e^2	0 %	2.625	2.58	2.51	1.95	3.13
σ_e^2	25 %	-	2.58	2.68	1.99	3.57
σ_e^2	50 %	-	2.58	2.74	1.81	4.02
σ_e^2	75 %	-	2.28	2.60	1.28	4.45
$E(\log(T))$	0 %	6.22	6.22	6.22	6.17	6.27
$E(\log(T))$	25 %	-	6.22	6.22	6.17	6.27
$E(\log(T))$	50 %	-	6.22	6.22	6.16	6.28
$E(\log(T))$	75 %	-	6.21	6.21	6.13	6.28
$Var(\log(T))$	0 %	0.81	0.81	0.80	0.77	0.84
$Var(\log(T))$	25 %	-	0.81	0.81	0.77	0.84
$Var(\log(T))$	50 %	-	0.82	0.81	0.76	0.86
$Var(\log(T))$	75 %	-	0.79	0.79	0.69	0.89

Table 3. Spearman rank correlations between true and mean values of marginal posterior distributions of sire transmitting abilities (sire effects).

	Censoring			
Model	0 %	25 %	50 %	75 %
Genetic	0.93	0.92	0.90	0.84
Non-genetic	0.91	0.92	0.90	0.84

Simulation study 2

Non-genetic sire model

Estimated sire effects, obtained in Step 2, of the 10 selected sires from Step 1 were far away from the true sire transmitting abilities (Figure 1). Furthermore, estimated sire effects of the 10 selected sires were decreased (improved) when level of censoring was increased from 20 % to about 86 % and daughter group size was increased from 100 to 1000. Estimated sire effects of the remaining 190 sires were basically not influenced by changes in size of daughter groups (and level of censoring) of the 10 selected sires (results not shown). The improved sire values of proven bulls with second crop daughters obtained from Step 2 to Step 3 imply that these bulls contribute with a too large proportion of the top sires, which is in agreement with what has been observed in practice (VanRaden and Powell, 2002).

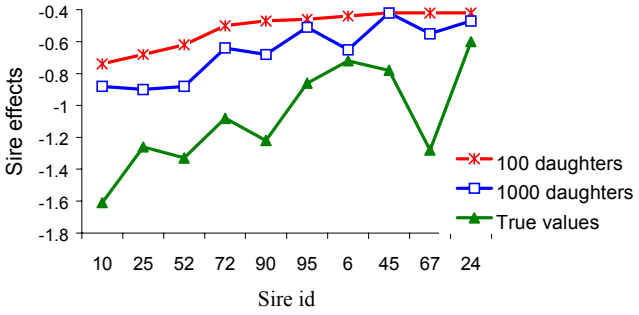

Figure 1. Estimated sire effects of the 10 proven bulls with second crop daughters (see Material and Methods) obtained from Step 2 (100 daughters) and Step 3 (1000 daughters), using the non-genetic sire model. True sire transmitting abilities are also shown in the Figure.

Genetic sire model

The estimated sire transmitting abilities were in agreement with the true sire transmitting abilities, and the agreement was improved from Step 2 to Step 3 as daughtergroup size was increased from 100 to 1000 (see Figure 2).

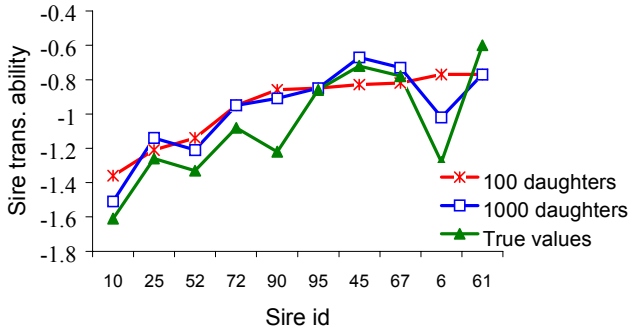

Figure 2. Estimated sire transmitting (trans.) abilities of the 10 proven bulls with second crop daughters (see Material and Methods) obtained from Step 2 (100 daughters) and Step 3 (1000 daughters), using the genetic sire model. True sire transmitting abilities are also shown in the Figure**.**

Discussion

Simulation study 1

Simulation study 1 established that parameters estimated using a Weibull log-normal sire frailty model without genetic interpretation deviate considerably from the true values used for simulating data. The sire variance and the Weibull parameter $\tilde{\rho}$ were downward biased, and the Weibull parameter $\tilde{\beta}$ was upward biased. Furthermore estimated parameters, including sire effects, were highly influenced by the level of censoring.

In contrast to this study, Ducrocq and Casella (1996) presented a simulation study where the sire variance, estimated using a non-genetic sire model, was consistent with the value used for simulation (Ducrocq and Casella, 1996). Simonsen and Dalsgaard (2002) presented another simulation study where this was not the case. Hence, the non-genetic sire model does not, in general, allow for correct genetic inferences from data.

Several other simulation studies have been presented where data were generated according to Weibull frailty models without genetic interpretation (Ducrocq and Casella, 1996; Yazdi et al., 2002). These studies can therefore not be used to justify that non-genetic models provide parameter estimates consistent with the additive genetic model.

In spite of the biased parameter estimates obtained using non-genetic sire models the efficiency to rank sires was basically the same for the non-genetic and for the genetic sire model in simulation study 1, and only for the case with no censoring, the genetic sire model was slightly superior. The ability of the non-genetic sire model to provide nearly optimal ranking of sires, has also been reported in previous studies (Ducrocq and Casella, 1996; Ducrocq, 2001). This result may at first suggest that the non-genetic sire model together with Survival Kit (Ducrocq and Sölkner, 1998b) can be used to rank sires for selection. However, problems occur when selection is across generations and the proportion of censored daughters differs significantly between sires. This is because parameter estimates are highly influenced by the level of censoring when estimated using non-genetic sire models. This is further illustrated in Simulation study 2.

Simulation study 2

In the second simulation study, estimated sire effects obtained from the non-genetic sire model were decreased (improved) when the daughter group size and level of censoring were increased (i.e. from Step 2 to Step 3). The jump in estimated sire effects of proven bulls with second crop daughters imply that they make up a too large proportion of the top sires. This problem with the non-genetic sire model is in close agreement with experiences collected from routine genetic evaluations of bulls on length of productive life (VanRaden and Powell, 2002). This study suggest, that problems with unstable sire effects are due to the fact that sires today are ranked for longevity based on models without genetic interpretation.

Conclusions

The Bayesian analysis of simulated data with genetic sire models lead to parameter estimates consistent with the true parameter values used for simulating data, independently of the level of censoring, daughter group size and the balanced and unbalanced data sets analyzed in this study. This is not the case when simulated data were analyzed with non-genetic models. This study suggest that the problem with unstable sire effects observed in practice, and described in VanRaden and Powell (2002), is due to the fact that sires are ranked for longevity based on models without genetic interpretation.

Based on this study we conclude that there are good reasons to use frailty models that allow for an additive genetic interpretation.

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