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The influence of random effects on the unconditional hazard rate and survival functions

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SUMMARY

The consequences of introducing random effects have been a major issue in models for survival analysis. A general result is derived to establish the underestimation of the unconditional hazard rate when a random effect is present. Also, the survival time is shown to be underestimated. No distributional assumption regarding the random effect is required.

Some key words: Hazard rate; Random effects; Underestimation.

1. INTRODUCTION

The 'random effects survival model' has been a major focus in the recent literature (Heckman & Singer, 1984; Littlewood, 1984; Clayton & Cuzick, 1985; Heckman, Robb & Walker, 1990; Honoré, 1990). When a hazard rate function is estimated, it is conventional practice to assume that observations are taken from a homogeneous group. If they are based on several heterogeneous subgroups, we should estimate their hazard rate functions separately. However, if we could assume that the hazard rate function from one group is parallel to those of other groups, we can deal with all observations at the same time by taking account of covariate variables by setting

$$\lambda_N(t) = \lambda_0(t) \exp(\beta' x),$$

where $\lambda_0(t)$ is a specified hazard rate, x is a vector of fixed covariates, and the subscript N is attached to emphasize that this is a nominal hazard rate, i.e. without heterogeneity. This helps to describe the differences among subgroups. But, if we want to describe all differences exactly, we have to use too many covariates. This is not realistic since the number of observations available is limited. Thus we choose several important covariates and regard the remaining covariates as random.

In order to introduce heterogeneity into the population via a random effect, we let the hazard rate for an individual be $V\lambda_N(t)$ or

$$V\lambda_0(t) \exp(\beta' x),$$

where V is a random variable such that $\mathrm{pr}(V \geqslant 0) = 1$, $E(V) = 1$ and $\mathrm{pr}(V = 1) < 1$. Conditional on $V = v$, an individual hazard rate is $\lambda_C(t \mid v) = v\lambda_N(t)$. The corresponding cumulative distribution functions are:

$$F_C(t \mid v) = 1 - \exp\{-v\Lambda_N(t)\}, \quad F_N(t) = 1 - \exp\{-\Lambda_N(t)\}, \quad F_U(t) = 1 - E[\exp\{-V\Lambda_N(t)\}], \tag{1·1}$$

where $\Lambda_N(t) = \int \lambda_N(s)\, ds$ with the integral over the range $(0, t)$, and the subscripts C, N, U denote the conditional, nominal, and unconditional distributions, respectively. The expectations always exist since $V \geqslant 0$ and $\Lambda_N(t) \geqslant 0$. Using $F_U(t)$ and $F_C(t \mid v)$, by taking an expected value of $f_C(t \mid V)$, the unconditional hazard rate is

$$\lambda_U(t) = \lambda_N(t) \frac{E[V \exp\{-V\Lambda_N(t)\}]}{E[\exp\{-V\Lambda_N(t)\}]}. \tag{1·2}$$

Lancaster (1979) originated the random effects model in the analysis of unemployment data. He used a Weibull hazard rate function and found that the maximum likelihood estimate $\hat{\delta}$ in the hazard function $\lambda_0(t) = \delta t^{\delta - 1}$ increases with an increase of the number of covariates. He showed that, if V has a gamma distribution with mean 1 and variance c, then the unconditional hazard rate is

$$\lambda_U(t) = \{1 - F_U(t)\}^c \lambda_N(t) < \lambda_N(t).$$

If the heterogeneity modelled by V is ignored, the hazard rate function is underestimated. Using this model, Lancaster (1985) proved the inconsistency of maximum likelihood estimators when heterogeneity is ignored. Littlewood (1984) mentioned that mixtures of increasing failure rate distributions do not necessarily have an increasing failure rate even though mixtures of decreasing failure rate distributions have a decreasing failure rate.

A gamma heterogeneity is often used because it is easy to manipulate. Different distributions for heterogeneity such as an inverse Gaussian distribution also need to be considered, but they are not discussed in the literature. Heckman & Singer (1984) used some simulation results to suggest that estimators for the structural parameters, β, are very sensitive to the assumption of a specific heterogeneity distribution. Their suggestion started a discussion on the robustness of the estimators under heterogeneity. Nonparametric estimation was used to solve this problem (Heckman & Singer, 1984; Clayton & Cuzick, 1985; Honoré, 1990). In the next section, we generalize Lancaster (1979).

2. Effects of heterogeneity on the unconditional hazard rate and survival functions

If the heterogeneity modelled by V exists and is ignored, the hazard rate function is underestimated regardless of the heterogeneity distribution. We summarize our results in the following theorem, corollary and lemma. Proofs are given in the Appendix.

Theorem 2·1. *Let T be a nonnegative random variable with probability density function $f_U(t)$. Suppose that* $\mathrm{pr}(V \geqslant 0) = 1$, $E(V) = 1$ *and* $\mathrm{pr}(V = 1) < 1$. *Then*

$$\lambda_U(t) - \lambda_N(t) = \lambda_N(t)\{E(V \mid T > t) - 1\}, \tag{2·1}$$

$$\frac{d}{dt} E(V \mid T > t) = -\mathrm{var}(V \mid T > t), \quad \Lambda_N(t) > 0, \tag{2·2}$$

and so $E(V \mid T > t)$ is nonincreasing in $t > 0$, with $E(V \mid T > 0) = E(V) = 1$.

Equations (2·1) and (2·2) show that the unconditional hazard rate $\lambda_U(t)$ is less than the nominal hazard rate $\lambda_N(t)$ at every point $t > 0$ where $\lambda_N(t) > 0$. They also imply that the difference between two hazard rates goes to 0 as $\mathrm{var}(V)$ goes to 0. If $t_0 = \inf\{t : \Lambda_N(t) > 0\}$ then the conditional expected value goes to 1 as t decreases to t_0. Consequently, $\lambda_U(t)$ is a decreasing multiple of $\lambda_N(t)$. Also, if $F_N(t) = 1$ for some finite value t, then $f_N(t)$ and hence $\lambda_N(t)$ are 0 for that t and all larger values.

Corollary 2·1. *Let T be a nonnegative random variable with a probability density function $f_U(t)$. Suppose that* $\mathrm{pr}(V \geqslant 0) = 1$, $E(V) = 1$ *and* $\mathrm{pr}(V = 1) < 1$. *Then the unconditional survival time is stochastically larger than the nominal survival time. That is,*

$$F_U(t) < F_N(t) \quad \textit{for } t > 0 \textit{ and } \Lambda_N(t) > 0, \tag{2·3}$$

and $F_U(t) \leqslant F_N(t)$ otherwise.

LEMMA 2·1. *Let T be a nonnegative random variable with a probability density function $f_U(t)$. Suppose that* $\mathrm{pr}\,(V \geqslant 0) = 1$, $E(V) = 1$ *and* $\mathrm{pr}\,(V = 1) < 1$. *If* $E\{\exp(uV)\}$ *is finite for u in the neighbourhood of* 0, *then it has a series expansion*

$$\lambda_U(t) = \lambda_N(t) \sum_{j=1}^{\infty} \frac{\kappa_j}{(j-1)!} \{-\Lambda_N(t)\}^{j-1}, \tag{2·4}$$

in the neighbourhood of 0, *where κ_j is the jth cumulant of V.*

Equation (2·4) shows that a large value of $\kappa_2 = \mathrm{var}\,(V)$ contributes to the underestimation of hazard rates.

Example. Assume that V has a gamma distribution with mean 1 and variance c. Then

$$\lambda_U(t) = \lambda_N(t)\{1 + c\Lambda_N(t)\}^{-1}.$$

For example, consider an increasing failure rate, $\lambda_N(t) = 2t$. Then the mixture of these increasing failure rate distributions has an increasing rate for $t < c^{-\frac{1}{2}}$ and a decreasing failure rate for $t > c^{-\frac{1}{2}}$.

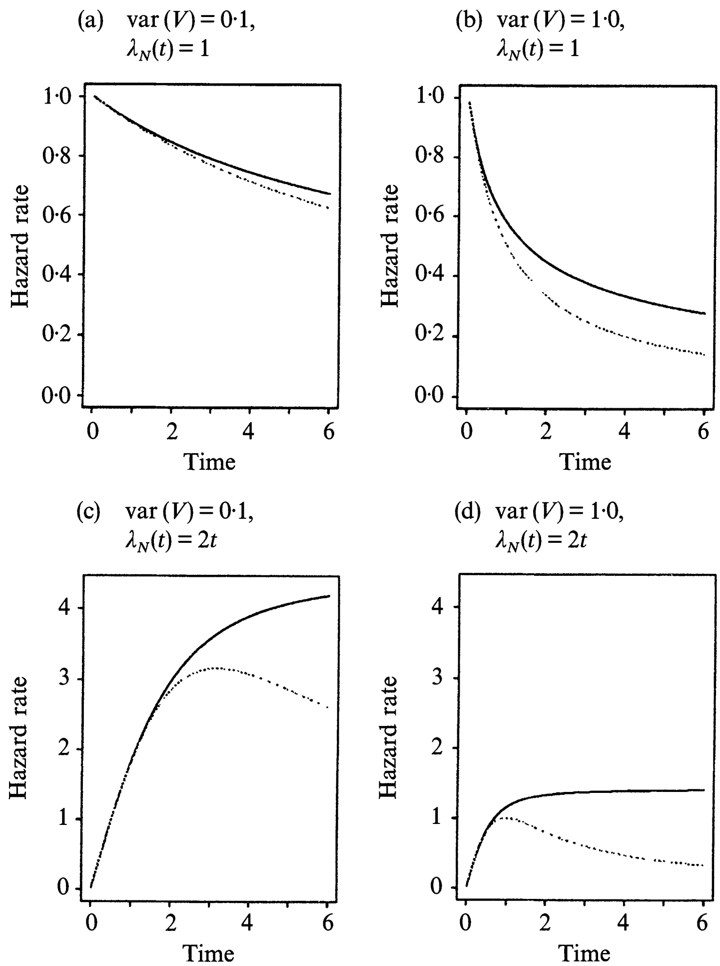

Fig. 1. Comparison of unconditional hazard rates, $\lambda_U(t)$, for different random effects given variance; solid lines, inverse Gaussian; dotted lines, gamma.

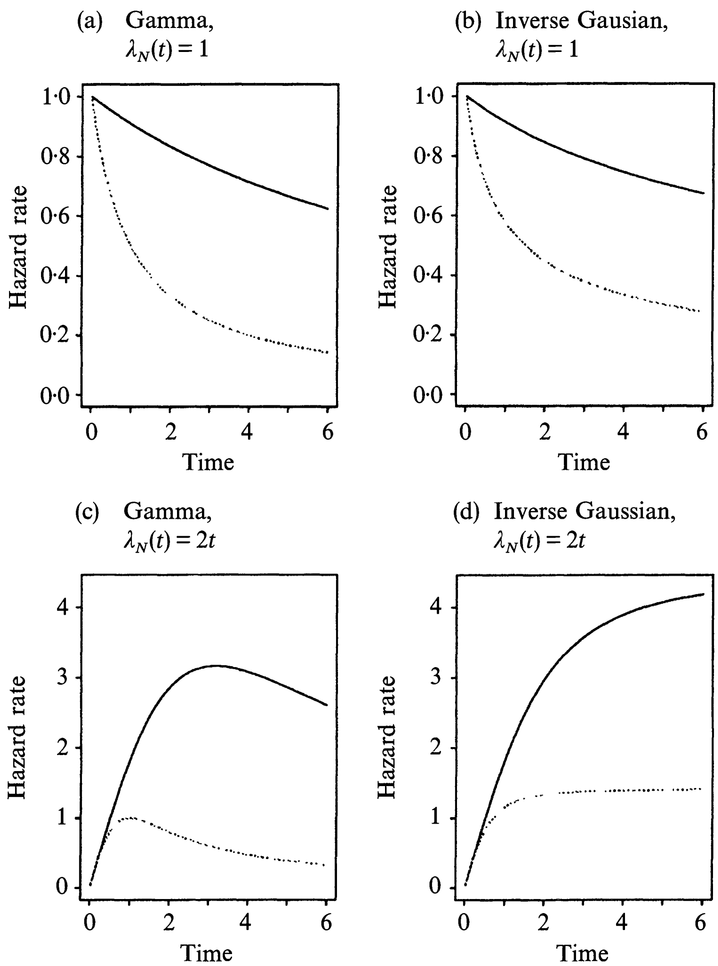

Fig. 2. Comparison of hazard rates, $\lambda_U(t)$, for different random effects given random effects; solid lines, var $(V) = 0{\cdot}1$; dotted lines, var $(V) = 1{\cdot}0$.

Similarly, if V has an inverse Gaussian distribution with mean 1 and variance c, then

$$\lambda_U(t) = \lambda_N(t)\{1 + 2c\Lambda_N(t)\}^{-\frac{1}{2}}.$$

For example, if $\lambda_N(t) = 2t$, the mixture of these increasing failure rate distributions has an increasing failure rate again, but $\lambda_U(t) < (2/c)^{\frac{1}{2}}$. Figures 1 and 2 give examples for the gamma and inverse Gaussian distributions with $\lambda_N(t) = 1$ and $\lambda_N(t) = 2t$ where the effect is more serious for larger t values. Also, the effect of heterogeneity is more serious for the gamma distributions.

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Appendix

Proofs

Proof of Theorem 2·1. Let $I(T > t)$ be the indicator function of the event $T > t$. Then

$$E\{VI(T > t)\} = E[VE\{I(T > t) \mid V = v\}] = E[V\exp\{-V\Lambda_N(t)\}],$$
$$E\{I(T > t)\} = E[E\{I(T > t) \mid V = v\}] = E[\exp\{-V\Lambda_N(t)\}].$$

Hence, by (1·2),

$$\lambda_U(t) - \lambda_N(t) = \lambda_N(t)\left(\frac{E[V\exp\{-V\Lambda_N(t)\}]}{E[\exp\{-V\Lambda_N(t)\}]} - 1\right)$$

$$= \lambda_N(t)\left[\frac{E\{VI(T>t)\}}{E\{I(T>t)\}} - 1\right] = \lambda_N(t)\{E(V\,|\,T>t) - 1\}.$$

For all t where $\Lambda_N(t) > 0$, $\exp\{-v\Lambda_N(t)\}$, $v\exp\{-v\Lambda_N(t)\}$ and $v^2\exp\{-v\Lambda_N(t)\}$ are uniformly bounded. By the dominated convergence theorem,

$$\frac{d}{dt}E(V\,|\,T>t) = -\frac{E[V^2\exp\{-V\Lambda_N(t)\}]}{E[\exp\{-V\Lambda_N(t)\}]} + \frac{E^2[V\exp\{-V\Lambda_N(t)\}]}{E^2[\exp\{-V\Lambda_N(t)\}]} = -\operatorname{var}(V\,|\,T>t).$$

The result follows. □

Proof of Corollary 2·1. By Theorem 2·1, $\lambda_U(t) < \lambda_N(t)$ for $t > 0$ and $\Lambda_N(t) > 0$. Hence, for any such t,

$$F_U(t) = 1 - \exp\left\{-\int_0^t \lambda_U(s)\,ds\right\} < 1 - \exp\left\{-\int_0^t \lambda_N(s)\,ds\right\} = F_N(t).$$ □

Proof of Lemma 2·1. When $E\{\exp(uV)\}$ is finite for all u in a neighbourhood of 0,

$$\psi(u) \equiv \log E\{\exp(uV)\} = \sum_{j=1}^{\infty} \frac{\kappa_j}{j!}u^j.$$

Since

$$\log E[\exp\{-V\Lambda_N(t)\}] = \psi\{-\Lambda_N(t)\},$$

by the dominated convergence theorem,

$$\lambda_U(t) = \lambda_N(t)\frac{E[V\exp\{-V\Lambda_N(t)\}]}{E[\exp\{-V\Lambda_N(t)\}]} = \lambda_N(t)\psi'\{-\Lambda_N(t)\} = \lambda_N(t)\sum_{j=1}^{\infty}\frac{\kappa_j}{(j-1)!}\{-\Lambda_N(t)\}^{j-1},$$

in the neighbourhood of 0 and (2·4) follows.

□

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