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Crossing Hazard Functions in Common Survival Models

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Abstract

Crossing hazard functions have extensive applications in modeling survival data. However, existing studies in the literature mainly focus on comparing crossed hazard functions and estimating the time at which the hazard functions cross, and there is little theoretical work on conditions under which hazard functions from a model will have a crossing. In this paper, we investigate crossing status of hazard functions from the proportional hazards (PH) model, the accelerated hazard (AH) model, and the accelerated failure time (AFT) model. We provide and prove conditions under which the hazard functions from the AH and the AFT models have no crossings or a single crossing. A few examples are also provided to demonstrate how the conditions can be used to determine crossing status of hazard functions from the three models.

Keywords

accelerated hazard model; accelerated failure time model; monotone hazard; U-shape hazard; bell-shape hazard

1 Introduction

Hazard function is commonly used in modeling survival data. The most popular model for survival data is the proportional hazards (PH) model. The hazard functions in this model are proportional for patients with different covariates and they do not cross. Other survival models may produce crossed hazard functions. There are numerous papers in the literature on estimating the point at which the hazard functions cross or comparing two crossed hazard functions (e.g. 9;12;8). However, there is very little study in the literature on the conditions under which the hazard functions will cross in these models and on how they will cross. It is of practical and theoretical importance to investigate this issue formally.

In this paper, we will examine the hazard functions under several commonly used survival models, including the PH model, the accelerated hazard (AH) model, and the accelerated failure time (AFT) model. We will present conditions under which the hazard functions of the models have no crossing, one crossing or more than one crossing. The paper is organized as follows. Section 2 provides a few definitions about the shape of a hazard function and crossing status of hazard functions. Notations used throughout the paper are also given in this section. The main results about the conditions that govern the crossing status of the hazard functions of the three models are given in Section 3. We demonstrate the application of the main results in determining the crossing status of the hazards when the baseline hazard function is from some

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special distributions in Section 4. We also demonstrate two situations not covered by the results in Section 3 via examples. The main results of this paper are summarized in Section 5.

2 Notations and Definitions

Let T be the random variable of survival time and $S(t)$, $F(t)$, $f(t)$, $H(t)$, $h(t)$ be the survival, cumulative, density, cumulative hazard and hazard functions respectively. We assume the distribution of T may depend on a covariate x (we only consider a single covariate case in this paper and generalizing to more than one covariate should be straightforward in most cases). The corresponding baseline survival, cumulative, density, cumulative hazard and hazard functions at $x = 0$ will be denoted by the same letters with a subscript “0”. For example, $h_0(t)$ is the baseline hazard function when $x = 0$.

We first describe a few commonly used survival models that we will discuss throughout the paper. The first model is the popular PH model (4) defined as:

$$h(t|x) = h_0(t) e^{\beta x} \quad (1)$$

The baseline hazard function in this model is usually an unspecified arbitrary function.

Chen and Wang (3); Chen (1) recently proposed another class of survival model named the AH model. This model is defined as

$$h(t|x) = h_0(e^{\beta x} t) \quad (2)$$

They proposed a nonparametric estimation method to estimate the parameters in the model.

The AFT model is another popular model in survival analysis (7). It is defined as

$$h(t|x) = h_0(e^{\beta x} t) e^{\beta x} \quad (3)$$

Unlike the PH and AH models, the covariate effect acts both on the time scale and the hazard rate in the AFT model. The baseline hazard function can be specified parametrically or nonparametrically, the latter is getting popular in recent years due to advances in nonparametric estimation methods (5;6;14).

To simplify the discussion, we assume the baseline hazard function in these models is continuous and differentiable up to the second order, and the r th order derivative of $h_0(t)$ is denoted as $h_0^{(r)}(t)$. We also consider the hazard function in the following shapes.

DEFINITION 1 The hazard function $h(t)$ is said to be an increasing [decreasing] hazard function if $h^{(1)}(t) \geq 0$ [$h^{(1)}(t) \leq 0$] for all t . If the strict inequality holds, the hazard function $h(t)$ is said to be a strictly increasing [decreasing] function.

DEFINITION 2 The hazard function $h(t)$ is said to be a U-shape hazard function if there exist r_1 and r_2 such that $0 < r_1 \leq r_2 < \infty$, and the hazard function is strictly decreasing in the interval $0 \leq t < r_1$, constant in $r_1 \leq t \leq r_2$, and strictly increasing in $t > r_2$.

DEFINITION 3 The hazard function $h(t)$ is said to be a bell-shape (inverse U-shape) hazard function if $-h(t)$ is a U-shape function.

The above definitions do not imply that the U-shape and the bell shape hazard functions will respectively have a unique minimum or maximum value.

DEFINITION 4 The two hazard functions $h_1(t)$ and $h_2(t)$ have a single crossing if there exist $0 < r_1 \leq r_2 < \infty$ such that $h_1(t) - h_2(t) > 0$ (or < 0) for $t < r_1$ (with strictly inequality for some $t < r_1$), $h_1(t) - h_2(t) = 0$ for $r_1 \leq t \leq r_2$, and $h_1(t) - h_2(t) < 0$ (or > 0) for $t > r_2$ (with strictly inequality for some $t > r_2$).

DEFINITION 5 The hazard functions from a model, defined by $h(t|x)$, do not have a crossing, have a single crossing, or have more than one crossings if for any $x_1 \neq x_2$, the two hazard functions $h(t|x_1)$ and $h(t|x_2)$ do not have a crossing, have a single crossing, or have more than one crossing.

3 Crossing Hazard Functions in Survival Models

In the survival model (1), (2), and (3), the hazard functions from subjects with different covariate values, denoted as x_1 and x_2 ($x_1 \neq x_2$), are usually different unless $\beta = 0$. If we denote the corresponding hazard functions as $h(t|x_1)$ and $h(t|x_2)$, we will investigate the conditions under which $h(t|x_1)$ and $h(t|x_2)$ have a crossing.

3.1 PH model

It is relatively straightforward to show that $h(t|x_1)$ and $h(t|x_2)$ in the PH model do not have any crossing regardless of the shape of the baseline hazard function $h_0(t)$. To show this, we consider $h(t|x_1) - h(t|x_2) = h_0(t)e^{\beta x_1} - h_0(t)e^{\beta x_2} = h_0(t)[e^{\beta x_1} - e^{\beta x_2}]$. If $e^{\beta x_1} \geq e^{\beta x_2}$, $h(t|x_1) - h(t|x_2) \geq 0$ for $0 < t < \infty$. If $e^{\beta x_1} < e^{\beta x_2}$, $h(t|x_1) - h(t|x_2) \leq 0$ for $0 < t < \infty$. Therefore the condition of crossing in Definition 4 is not satisfied and the hazard functions in the PH model do not have crossings.

3.2 AH Model

THEOREM 1 The hazard functions of the AH model (2) do not have any crossings if and only if the baseline hazard function $h_0(t)$ is monotone.

We only show the proof when $h_0(t)$ is a decreasing function. The proof for the increasing baseline hazard function case is similar.

Proof. Suppose that $h_0(t)$ is a decreasing function. Consider $h(t|x_1) - h(t|x_2) = h_0(te^{\beta x_1}) - h_0(te^{\beta x_2})$. If $e^{\beta x_1} \geq e^{\beta x_2}$, $h(t|x_1) - h(t|x_2) \leq 0$ for $0 < t < \infty$. If $e^{\beta x_1} < e^{\beta x_2}$, $h(t|x_1) - h(t|x_2) \geq 0$ for $0 < t < \infty$. Therefore the condition of crossing in Definition 4 is not satisfied and the hazard functions in the AH model do not have crossings.

To prove that no crossings in the AH model implies a monotone baseline hazard function, we use the contradiction method. That is, we will show that if the baseline hazard function is not monotone, the hazard functions of the AH model will have crossings. If $h_0(t)$ is not monotone, it will be either bell-shape or U-shape locally. For local bell-shape there are two cases: 1) There exist $t_0 > 0$ and $\delta > 0$ such that $h_0(t)$ is strictly increasing in $[t_0 - \delta, t_0]$ and strictly decreasing in $[t_0, t_0 + \delta]$. 2) There exist $t_1 < t_2$ and $\delta > 0$ such that $h_0(t)$ is strictly increasing in $[t_1 - \delta, t_1]$, constant in $[t_1, t_2]$ and strictly decreasing in $[t_2, t_2 + \delta]$. For case 1), choose x such that $e^{\beta x} > 1$, $t_0 e^{\beta x} < t_0 + \delta$, and $t_0 / e^{\beta x} > t_0 - \delta$. Then

$$h(t_0) = h_0(t_0) < h_0(t_0 e^{\beta x}) \quad \text{and} \quad h(t_0 / e^{\beta x}) = h_0(t_0) > h_0(t_0 e^{\beta x}).$$

Because of the continuity of the hazard functions there is a crossing in $[t_0 / e^{\beta x}, t_0]$.

For case 2), choose x such that $e^{\beta x} > 1$, $t_1 / e^{\beta x} > t_1 - \delta$, and $t_2 e^{\beta x} < t_2 + \delta$. Then

$$h(t_2) = h_0(t_2 e^{\beta x}) < h_0(t_2) \quad \text{and} \quad h(t_1/e^{\beta x}) = h_0(t_1) > h_0(t_1/e^{\beta x}).$$

Because of the continuity of the hazard functions there is a crossing in $[t_1/e^{\beta x}, t_2]$.

For local U-shape, the proof is similar. Therefore the monotonicity of the baseline hazard function is also a necessary condition for non-crossing hazard functions in the AH model.

To consider conditions under which the hazard functions from the AH model have a single crossing, we require the following lemmas.

LEMMA 1 *If the hazard function $h_0(t)$ is a decreasing, increasing, U-shape or bell-shape function, the hazard function $h_0(e^{\beta x}t)$ is also a decreasing, increasing, U-shape or bell-shape function.*

LEMMA 2 *If the hazard function $h_0(t)$ is a U-shape with r_1 and r_2 as defined in Definition 2, then $h_0(te^{\beta x})$ is also a U-shape function with $\frac{r_1}{e^{\beta x}}$ and $\frac{r_2}{e^{\beta x}}$ as r_1 and r_2 in Definition 2.*

The proofs of the lemmas are straightforward and thus skipped.

THEOREM 2 *The hazard function in the AH model (2) has a single crossing if and only if the baseline hazard function $h_0(t)$ is a U-shape or bell-shape function.*

Proof. The proof for the bell-shape hazard function is very similar to that of the U-shape hazard function, and we will only show the proof for the U-shape hazard function. Suppose $h_0(t)$ is the U-shaped function with r_1 and r_2 as defined in Definition 2. Following Lemma 1 and 2,

$h_0(e^{\beta x_1}t)$ and $h_0(e^{\beta x_2}t)$ are also U-shape functions with $\frac{r_1}{e^{\beta x_1}}, \frac{r_2}{e^{\beta x_1}}$ and $\frac{r_1}{e^{\beta x_2}}, \frac{r_2}{e^{\beta x_2}}$ as the corresponding r_1 and r_2 in Definition 2. Assume $e^{\beta x_1} > e^{\beta x_2}$, then $\frac{r_1}{e^{\beta x_1}} < \frac{r_1}{e^{\beta x_2}}$ and $\frac{r_2}{e^{\beta x_1}} < \frac{r_2}{e^{\beta x_2}}$.

Without loss of generality, we assume $\frac{r_1}{e^{\beta x_2}} \leq \frac{r_2}{e^{\beta x_1}}$ and $h_0(t) = a$ when $t \in [r_1, r_2]$. Consider $h(t|x_1) - h(t|x_2) = h_0(te^{\beta x_1}) - h_0(te^{\beta x_2})$ in the following five cases.

When $t < \frac{r_1}{e^{\beta x_1}}$,

$$h(t|x_1) - h(t|x_2) = h_0(te^{\beta x_1}) - h_0(te^{\beta x_2}) < 0$$

since $h_0(t)$ is a strictly decreasing function when $te^{\beta x_2} < te^{\beta x_1} < r_1$.

When $\frac{r_1}{e^{\beta x_1}} \leq t < \frac{r_1}{e^{\beta x_2}}$,

$$h(t|x_1) - h(t|x_2) = h_0(te^{\beta x_1}) - h_0(te^{\beta x_2}) < 0$$

since $h(t|x_1)$ is a constant a , which is also the minimum value of $h(t|x_2)$, when

$$te^{\beta x_1} \in \left[r_1, \frac{te^{\beta x_1}}{e^{\beta x_2}} \right).$$

When $\frac{r_1}{e^{\beta x_2}} \leq t < \frac{r_2}{e^{\beta x_1}}$,

$$h(t|x_1) - h(t|x_2) = h_0(te^{\beta x_1}) - h_0(te^{\beta x_2}) = 0$$

since $h_0(t)$ is a constant a when $r_1 \leq te^{\beta x_2} < te^{\beta x_1} < r_2$.

When $\frac{r_2}{e^{\beta x_1}} \leq t \leq \frac{r_2}{e^{\beta x_2}}$,

$$h(t|x_1) - h(t|x_2) = h_0(te^{\beta x_1}) - h_0(te^{\beta x_2}) > 0$$

since $h(t|x_2)$ is a constant a , which is also the minimum value of $h(t|x_1)$, when

$$te^{\beta x_2} \in \left(\frac{te^{\beta x_2}}{e^{\beta x_1}}, r_2 \right].$$

When $\frac{r_2}{e^{\beta x_2}} < t$,

$$h(t|x_1) - h(t|x_2) = h_0(te^{\beta x_1}) - h_0(te^{\beta x_2}) > 0$$

since $h_0(t)$ is a strictly increasing function when $r_2 < te^{\beta x_2} < te^{\beta x_1}$. Therefore the condition of crossing in Definition 4 is satisfied and the hazard functions in the AH model have a single crossing.

To prove that a single crossing in the hazard functions of the AH model implies a U-shape or bell shape baseline hazard function, we use the contradiction method. That is, we will show that if the baseline hazard function is not U-shape or bell shape, the hazard functions of the AH model will have either no crossing or more than one crossing.

It is easy to see from Theorem 1 that the hazard functions of the AH model have no crossing if the baseline hazard function is monotone.

If the baseline hazard function is not monotone, U-shape or bell shape, there exist $t_0 > t_0^* > 0$ and δ such that $h_0(t)$ is strictly decreasing in $[t_0^* - \delta, t_0^*]$ and strictly increasing in $[t_0^*, t_0^* + \delta]$, where $t_0^* - \delta > 0$ and $h_0(t)$ is strictly increasing in $[t_0 - \delta, t_0]$ and strictly decreasing in $[t_0, t_0 + \delta]$, where $t_0 - \delta > 0$. That is, t_0^* is a local minimum and t_0 is a local maximum of $h_0(t)$. Other cases include that t_0^* is a local maximum and t_0 is a local minimum of $h_0(t)$, both t_0^* and t_0 are local maxima,

or both are local minima. Let $e^{\beta x} = 1 + \frac{\delta}{t_0}$. We have

$$h(t_0^*|x) = h_0(t_0^*e^{\beta x}) = h_0\left(t_0^* + \frac{t_0^*}{t_0}\delta\right) > h_0(t_0^*)$$

which means $h(t_0^*|x) - h(t_0^*|x=0) > 0$. And

$$h(t_0^* - \delta | x) = h_0 \left[(t_0^* - \delta) e^{\beta x} \right] = h_0 \left(t_0^* + \frac{t_0^*}{t_0} \delta - \delta - \frac{\delta^2}{t_0} \right) < h_0(t_0^* - \delta)$$

since $t_0 - \delta < t_0^* + \frac{t_0^*}{t_0} \delta - \delta - \frac{\delta^2}{t_0} < t_0^*$, which means $h(t_0^* - \delta | x) - h(t_0^* - \delta | x=0) < 0$. Because of the continuity of the hazard functions, $h(t|x) - h(t|x=0)$ must have a crossing in $[t_0^* - \delta, t_0^*]$. Similar to the proof in Theorem 1, we can show that there is a crossing in $[t_0 - \delta, t_0]$. Therefore, the hazard functions of the AH model have at least two crossings in this case. The same results can be shown for the other three cases. Therefore, a U-shape or bell shape the baseline hazard function is also a necessary condition for a single crossing in the hazard functions of the AH model.

3.3 AFT Model

THEOREM 3 *The hazard functions in the AFT model (3) do not have any crossings if and only if the baseline hazard function satisfies $h_0^{(1)}(t) \geq -h_0(t)$ or $h_0^{(1)}(t) \leq -h_0(t)$.*

Proof. Let $g_0(t) = h_0(t)t$. If $h_0^{(1)}(t) \geq -h_0(t)$ or $h_0^{(1)}(t) \leq -h_0(t)$, then $g_0^{(1)}(t) = h_0(t) + h_0^{(1)}(t)t > 0$ or $g_0^{(1)}(t) = h_0(t) + h_0^{(1)}(t)t < 0$. That is, $g_0(t)$ is a monotone function in t . Consider a new model with the hazard function $g(t|x) = g_0(e^{\beta x}t)$. It is an AH model with $g_0(t)$ as the baseline hazard function. Following Theorem 1, the hazard functions from $g(t|x) = h_0(e^{\beta x}t)e^{\beta x}t$ do not have any crossings, which implies that the hazard functions of the AFT model $h_0(e^{\beta x}t)e^{\beta x}$ do not have any crossings either. Therefore the hazard functions from the AFT model do not have any crossings under the condition $h_0^{(1)}(t) \geq -h_0(t)$ or $h_0^{(1)}(t) \leq -h_0(t)$.

A sufficient condition for no crossing hazard functions in the AFT model can be obtained from above theorem.

COROLLARY 1 *If the baseline hazard function $h_0(t)$ is increasing in t or $h_0(t)t$ is increasing in t , the hazard functions from the AFT model do not have any crossings.*

REMARK 1 When the baseline hazard function is decreasing, the hazard functions from the AFT model may have a crossing. See an example in Section 4.

THEOREM 4 *The hazard functions from the AFT model (3) have a single crossing if and only if $h_0(t)t$ is a U-shape or bell shape function in t .*

Proof. The result follows immediately from Theorem 2 after treating $h_0(t)t$ as the baseline hazard function in the AH model.

Unfortunately when the baseline hazard function in the AFT model is U-shape or bell-shape, the crossing status of the hazard functions in the AFT model is more complicated than the other two models. We will demonstrate in Section 4 different numbers of crossings when the baseline hazard function is U-shape (or bell-shape).

4 Example

In this section, we demonstrate the crossing status of hazard functions from the AH and AFT models when the baseline hazard function is from a particular distribution or is in a particular shape.

4.1 Weibull Baseline Distribution

We first consider the Weibull distribution with the hazard function $\alpha\lambda t^{\alpha-1}$. The first derivative of the hazard function of the Weibull distribution is $\alpha(\alpha-1)\lambda t^{\alpha-2}$. Therefore the hazard function is constant if $\alpha = 1$, increasing if $\alpha > 1$ and decreasing if $0 < \alpha < 1$.

Following Theorem 2, the hazard functions in the AH model do not have any crossings if the baseline hazard function is $h_0(t) = \alpha\lambda t^{\alpha-1}$ with $\alpha \neq 1$. When $\alpha = 1$, the hazard function in the AH model is λ regardless of the values of covariate x .

For the AFT model with the baseline hazard function $h_0(t) = \alpha\lambda t^{\alpha-1}$, it is easy to see the first derivative of the function $h_0(t)t = \alpha\lambda t^{\alpha-1}t$ is $\alpha^2\lambda t^{\alpha-1} > 0$ for $t > 0$. Therefore, following Corollary 1, the hazard functions in the AFT model do not have any crossings.

4.2 Log-logistic Baseline Distribution

The log-logistic distribution has the hazard function $\frac{\alpha t^{\alpha-1} \lambda}{1 + \lambda t^\alpha}$. The first derivative of the log-

logistic hazard function is $\frac{\alpha\lambda t^{\alpha-2}(\alpha - 1 - \lambda t^\alpha)}{(1 + \lambda t^\alpha)^2}$. When $0 < \alpha < 1$, the hazard function is monotone decreasing function. When $\alpha > 1$, the hazard function has the bell shape with the

maximum achieved at $\left(\frac{\alpha - 1}{\lambda}\right)^{\frac{1}{\alpha}}$.

It is clear that the hazard functions of the AH model do not have crossings if the baseline hazard function is from the log-logistic distribution with $0 < \alpha < 1$. Or the hazard functions have only one crossing if the baseline hazard function is from the log-logistic distribution with $\alpha > 1$.

For the AFT model with $h_0(t) = \frac{\alpha t^{\alpha-1} \lambda}{1 + \lambda t^\alpha}$, the first derivative of the function $h_0(t)t = \frac{\alpha t^\alpha \lambda}{1 + \lambda t^\alpha}$ is $\frac{\alpha^2 \lambda t^{\alpha-1}}{(1 + \lambda t^\alpha)^2} > 0$. Thus the function $h_0(t)t$ is the increasing function and the hazard functions from such an AFT model do not have crossings.

4.3 Generalized Weibull Baseline Distribution

The hazard function of the generalized Weibull distribution (10) is given by

$$h_0(t) = \frac{(t/\sigma)^{1/\alpha-1}}{\alpha\sigma(1 - \lambda(t/\sigma)^{1/\alpha})}$$

When $\alpha > 1, \lambda > 0$, the hazard function is U-shape; when $\alpha < 1, \lambda < 0$, it is bell-shape; when $\alpha \geq 1, \lambda \leq 1$, it is decreasing; and when $\alpha \leq 1, \lambda \geq 0$, it is increasing function. Therefore, the generalized Weibull distribution greatly extends the applicability of the Weibull distribution.

Following Theorem 1, the hazard functions from the AH model do not have any crossings when the baseline hazard is from the generalized Weibull distribution with $\alpha \geq 1$ and $\lambda \leq 1$, or

$\alpha \leq 1$ and $\lambda \geq 0$. Following Theorem 2, the hazard functions have a single crossing when $\alpha > 1$ and $\lambda > 0$, or $\alpha < 1$ and $\lambda < 0$.

For the AFT model with the baseline hazard function $h_0(t)$ above, we consider $h_0(t)t$ and obtain its first derivative

$$\frac{\sigma(t/\sigma)^{1/\alpha-1}}{(\alpha\sigma(1-\lambda(t/\sigma)^{1/\alpha}))^2},$$

which is greater than 0. Following Corollary 1, the hazard functions from the AFT model do not have any crossing.

4.4 AFT Model with a Decreasing Baseline Hazard Function

Corollary 1 shows that an increasing baseline hazard function in the AFT model implies its hazard functions have no crossing. However, this result cannot be extended to a decreasing baseline hazard function in the AFT model. As an example, suppose that the baseline hazard

function of an AFT model is $h_0(t) = \frac{1}{(1+t)^2}$. It is a decreasing hazard function with

$h_0^{(1)}(t) = -\frac{2}{(1+t)^3}$, and $h_0(t) + h_0^{(1)}(t)t = \frac{1-t}{(1+t)^3}$. When $\beta = 1$, the hazard function of the two groups, defined by $x = 0$ (control) and $x = 1$ (treatment), have one crossing (see the left panel of Figure 1). If the baseline hazard function of the AFT model is $h_0(t) = \alpha\lambda t^{\alpha-1}$ with $\alpha = 0.8$, $\lambda = 0.2$ (a hazard function from the Weibull distribution) and $\beta = 1$, it is easy to see that $h(t|x = 1) > h_0(t)$ and the two hazard functions do not have any crossings (see the right panel of Figure 1). Therefore the crossing status of the hazard function in the AFT model is more complicated than the AH model when the baseline hazard function is decreasing.

4.5 AFT Model with a U-shape/bell-shape Baseline Hazard Function

When the baseline hazard function in the AFT model is U-shape or bell-shape, the crossing status cannot be determined either. For example, suppose that a U-shape baseline hazard function is given by $h_0(t) = 0.1(t-2)^2 + 0.2$, and $\beta = -0.5$, the hazard functions of two groups with $x = 0$ (control) and $x = 1$ (treatment) have two crossings (see the left panel in Figure 2).

If the baseline hazard function is $\frac{\alpha t^{\alpha-1}\lambda}{1+\lambda t^\alpha}$ with $\lambda = 0.2$, $\alpha = 3$ (a hazard function from the log-logistic distribution), and $\beta = -0.5$, the hazard functions of two groups with $x = 0$ (control) and $x = 1$ (treatment) do not have any crossings (see the right panel in Figure 2). Therefore the crossing status of the hazard function is more complicated than the AH model when the baseline distribution is U-shape or bell-shape.

5 Conclusions

We investigated the crossing status of the hazard functions from three popular survival models, the PH model, the AH model and the AFT model. The hazard functions of the PH model do not have any crossing, regardless of covariate values. For the AH model, we proved that a sufficient and necessary condition for the hazard functions from the model to have no crossing is a monotone baseline hazard function, and that a sufficient and necessary condition for the hazard functions from the model to have a single crossing is a U-shape or bell-shape baseline hazard function. For the AFT model, we also obtained sufficient and necessary conditions under which the hazard functions from the model have no crossing, or have a single crossing. The conditions are based on a function of the baseline hazard function of the AFT model and

is less straightforward than the conditions for the AH model. The results of this paper will be helpful for practitioners to quickly determine whether the model they consider will produce crossing hazard functions or not if their model is one of the PH, AH and the AFT models.

As one reviewer pointed out, the multiplier $\exp(\beta x)$ in the three models can be replaced with any nonnegative continuous functions of βx , and the results will still hold.

This paper only focuses on the three popular survival models and zero or a single crossing in the hazard functions. Further work is required if a model is beyond the three models considered in this paper, such as the general model proposed in (2), or if the number of crossings in the hazard functions is more than 1. However, the three models still find applications in real world problems in spite of their rigid assumptions. We briefly demonstrate this via a breast cancer data set of Tooele, Utah from the SEER (13) program. The data set includes 101 patients diagnosed between 1995-2004. We are interested in the impact of tumour stage of breast cancer on cancer survival. For illustration purpose, we only consider two stages: local and regional, and they form two groups. We first estimated the hazard functions of the two groups by a nonparametric kernel based smooth estimator (11), and the survival functions of the two groups by the Kaplan-Meier survival estimator. We then fit the data by the AFT model with Weibull baseline distribution. The estimated nonparametric and parametric hazard and survival functions are given in Figure 3. A visual inspection of the figure demonstrates an adequate fit of the AFT model to the data. The estimated baseline hazard function is increasing. Following Corollary 1, the two hazard function will not have any crossings.

References

- [1]. Chen YQ. Accelerated Hazards Regression Model and Its Adequacy for Censored Survival Data. *Biometrics* 2001;57:853–860. [PubMed: 11550937]
- [2]. Chen YQ, Jewell N-P. On a general class of semiparametric hazards regression models. *Biometrika* 2000;88:687–702.
- [3]. Chen YQ, Wang M-C. Analysis of Accelerated Hazards Models. *Journal of the American Statistical Association* 2000;95:608–618.
- [4]. Cox DR. Regression Models and Life-Tables. *Journal of the Royal Statistical Society, Series B* 1972;34:187–220.
- [5]. Jin Z, Lin DY, Wei LJ, Ying Z. Rank-based inference for the accelerated failure time model. *Biometrika* 2003;90:341–353.
- [6]. Jin Z, Lin DY, Ying Z. On least-squares regression with censored data. *Biometrika* 2006;93:147–161.
- [7]. Kalbfleisch, JD.; Prentice, RL. *The Statistical Analysis of Failure Time Data*. John Wiley & Sons; Hoboken, NJ: 2002.
- [8]. Liu K, Qiu P, Sheng J. Comparing two crossing hazard rates by Cox proportional hazards modeling. *Statistics in Medicine* 2007;26:375391.
- [9]. Mantel N, Stablein DM. The Crossing Hazard Function Problem. *The Statistician: Journal of the Institute of Statisticians* 1988;37:59–64.
- [10]. Mudholkar GS, Srivastava DK, Kollia GD. A Generalization of the Weibull Distribution With Application to the Analysis of Survival Data. *Journal of the American Statistical Association* 1996;91:1575–1583.
- [11]. Müller HG, Wang JL. Hazard rate estimation under fandon censoring with varying kernels and bandwidths. *Biometrics* 1994;50:61–76. [PubMed: 8086616]
- [12]. O'Quigley J. On a two-sided test for crossing hazards. *The Statistician: Journal of the Institute of Statisticians* 1994;43:563–569.
- [13]. Surveillance, Epidemiology, and End Results (SEER) Program. Limited-Use Data, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch; Apr. 2008 www.seer.cancer.gov/releasedbased on the November 2007 submission, 1973-2005

- [14]. Zeng D, Lin D. Efficient Estimation for the Accelerated Failure Time Model. *Journal of the American Statistical Association* 2007;102:1387–1396.

Figure 1. Decreasing Hazard function: solid line denote the treatment group and dash line is the control group

Figure 2. U-shape and Bell-shape Hazard function: solid line denote the treatment group and dash line is the control group

Figure 3.
Estimated hazard function and estimated survival function.