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Appelbaum, Elie and Prisman, Eliezer, Z.

York University, York University

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Elie Appelbaum* and Eliezer Z. Prisman†

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Abstract

Hazard function applications in medical research are problematic for two reasons. First, they are not cast within a decision theory framework. Second, they often adopt severe self-imposed restrictive structures (e.g., in the constant hazard ratio models). The disadvantage of an excessively restrictive structure is self-evident. The disadvantage of the lack of a theoretical basis, which is more subtle, is that treatment choice itself becomes unnecessarily restrictive because decision theory insights remain untapped.

This paper uses a decision-theory-based framework for treatment choice, thus addressing the two issues above. It shows that high-order stochastic dominance tools, in conjunction with risk preference attributes, can often be used to compare treatments under weaker conditions than the ones currently used. The paper compares treatments by using what we call high-order hazard functions. These high-order hazard functions are obtained by calculating areas under low-order hazard functions (such as standard and cumulative hazard functions). The paper provides necessary and sufficient conditions for treatment comparisons based on these high-order hazard functions. These conditions are shown to be weaker than the ones currently used because we are able to exploit theoretical tools that are otherwise unavailable. Thus, for example, it shows that our framework often allows treatment comparisons even when hazard functions cross. An example using real-world data shows that the use of high-order stochastic dominance and risk preference attributes allows us to identify a preferred treatment even if low-order hazard functions cross.

KEYWORDS: High-Order Hazard Functions, Treatment Choice, Survival Functions, High-Order Stochastic Dominance, Risk Preferences.

*Department of Economics, York University, Toronto, Canada
†Schulich School of Business, York University, Toronto, Canada

1 Introduction

In his seminal paper, Cox (1972) provided what became known as the Cox regression model. The Cox model assumed that "on each individual are available values of one or more explanatory variables. The hazard function (age-specific failure rate) is taken to be a function of the explanatory variables and unknown regression coefficients multiplied by an arbitrary and unknown function of time." He uses a parametric framework to estimate the hazard function (HF), hazard ratio (HR) and their sensitivity to various exogenous variables. Cox's model's ability to study and test the effects of the independent variables makes it invaluable in medical research. Unfortunately, the Cox regression model is based on very restrictive hazard functions (HFs) that are multiclipably separable, yielding a constant HR. Admittedly, having a constant HR is very convenient, making global testing possible and simple. But, given the restrictiveness of his assumption, the validity of the model's results is questionable.[1,2]

Several alternative models were introduced in the literature to address this issue. The feature they all have in common is that they suggest HFs that yield time-dependent hazard ratios (HRs).[3] Nevertheless, the constancy of HRs is only one of the problems with this approach to the choice between treatments. The other, more fundamental problem is that this approach is not cast within a decision-making framework. However, to choose a treatment is to make a decision, and to make decisions, we need an objective function. By not casting the problem within a decision-making framework, insights that decision theory can provide are lost and left unexploited. Some of these insights allow us to compare treatments under far less restrictive conditions than those required when comparing standard HFs. Consequently, comparing treatments under such a weaker condition is possible even when HFs cross. Several papers have attempted to address the crossing hazard function problem, however, thus far, no satisfactory solution has been proposed.[4]

[1] For recent examples of studies using hazard functions, see Li et al. (2025), Dai et al. (2025) and Judge et al. (2025).

[2] Recently, other methods of producing hazard functions have been proposed. For example, see Mamun et al. (2023), Locey et al. (2024) and Nath et al. (2023), who use machine learning, the Rush Regression Workbench and an interactive web-based tool, respectively, to obtain hazard functions.

[3] Time-varying covariates in the context of Cox regression are also considered by Yao et al. (2022), who propose a general framework for estimating a survival function in the presence of time-varying covariates. They compare the performance of this framework with that of the Cox model and transformation forest, which has been adapted to accommodate time-varying covariates. Austin et al. (2021) describe two methods to allow a regression coefficient—and, consequently, the hazard ratio—to vary as a flexible function of time.

[4] Dormuth, Liu, et al. (2022) examine the crossing hazard functions problem and suggest that total areas (not

This paper aims to cast the comparison of HFs within a standard decision-making framework and use that framework to define necessary and sufficient conditions for treatment comparisons. In doing so, we show that "crossing curves" (including Kaplan-Meier curves) are not necessarily an insurmountable problem. As an example, we apply the standard theory of decision under uncertainty, first developed by von Neumann and Morgenstern (von Neumann and Morgenstern, (1944)). Within that framework, we use common risk preference attributes which enable us to apply higher-order stochastic dominance (SD) tools[5] to compare treatments by comparing what we call high-order HFs. This SD approach is well-known in finance and economics and can provide the theoretical foundation for comparing treatments using high-order HFs. In conjunction with patients' preference attributes, this approach allows us to extract information from the underlying HFs that is otherwise unexploited. Consequently, in many cases, we are able to resolve the "crossing-HFs-problem," namely, an HR that is not always higher or lower than 1. An intuitive way to view this approach is that it "substitutes" risk preference attributes for properties of the underlying HFs. Namely, as we adopt additional risk preference attributes, the restrictions required to rank treatments conclusively become weaker (for example, intersections may no longer be a problem). For example, the HFs literature takes it as given that, say, treatment B is preferred to treatment A if and only if A's HF is always higher than B's. No example in the literature challenges this criterion. However, our SD approach shows that if we make the obvious assumptions that a later event occurrence - say death - is better (an assumption that is already implicit in the HFs literature), the requirement that one HF should always be higher than the other is no longer necessary; it is still a sufficient condition, but it is not a necessary one. Instead, we show that the necessary and sufficient conditions for treatment B to be preferred to treatment A are weaker.

In general, all decision problems require and are based on objective functions. Each objective function, in turn, is defined by its properties. We focus on risk preference attributes because health-related decisions involve a great deal of uncertainty. The uncertainty is due to diagnostic and treatment risks, co-morbidity risks, potential future morbidity risks and background eco-

the absolute differences) under the KMCs over the whole range (again, from the initial point to the endpoint, usually taken as the truncation point) should be used. Unfortunately (as shown in this paper), neither method is capable of comparing crossing survival distributions.Crossing survival functions and the problems they raise regarding the use of hazard ratios are discussed in Dehbi et al. (2018). Park et al. (2014) emphasize the importance of crossing hazard functions when evaluating treatment effects, particularly in studies involving longitudinal data. However, no general solution was provided.

[5]For a good survey and discussion of stochastic dominance, see Levy (1992).

nomics, financial and other risks. It is, therefore, clear that risk preference attributes play an important role in health-related decisions, such as treatment choices, as captured by comparing HFs. Hence, as Attemaa, l'Haridonb et al. (2019) state, "it is widely recognized that risk preferences are an important determinant of health-related decisions."

This paper explores three possible risk preference attributes: risk aversion or discounting, prudence and temperance (in addition to the trivial property that a longer survival time is better than a shorter one). All three properties have been well-studied and demonstrated in numerous empirical studies in medical and other fields (e.g. finance, economics, political science, psychology and biology).

We show that by using "high-order" risk preference attributes, we can apply well-known high-order SD tools to compare HFs even if they intersect. Specifically, we propose a procedure that successively calculates "higher-order" HFs whenever they intersect. This procedure is based on higher-order SD, which, in turn, is applicable if we use higher-order risk preference attributes. These higher-order HFS are obtained by calculating the areas under "lower order HFs." Starting with standard HFs, if, at any round, there is no intersection, there is no need to proceed; treatments can be ranked. On the other hand, if we encounter an intersection, we construct the next-order HFs and compare them. We repeat these steps until we find no intersection or reach SD of order four. If we still find intersections after reaching fourth-order SD, we conclude that (given the available risk preference attributes SD orders) it is impossible to rank the treatments. At each step, the move to higher-order HFs is facilitated by adopting more risk preference attributes, allowing us to apply a higher-order SD. Applying this process, we provide necessary and sufficient conditions for ranking treatments using high-order HFs at each step.[6]

We provide an empirical example, based on real-world data from Arenal et al. (2022), to show that, indeed, using high-order SD (in this case, third-order), a preferred treatment can be found even if low-order hazard functions cross.

2 Survival and Hazard Functions

A patient faces a choice between two treatments, defined as treatment A and treatment B (TA and TB, hereafter). The treatments start at the same point in time, which we call zero. Under

[6] Appelbaum et al. (2024) use a somewhat similar approach to study the properties of Kaplan-Meier curves.

both treatments, an event may occur after the treatment begins. The event could be a biochemical recurrence, a clinical recurrence, death, etc. The time at which the event occurs is denoted by x. We assume that x is a continuous random variable whose probability distribution depends on the treatment given to a patient and the patient's characteristics, denoted by the vector q. Some characteristics may be fixed, and others may be time-dependent.[7] We define the density functions of x under TA and TB as $f^A(x;q)$ and $f^B(x;q)$,[8] respectively, and the closed interval $[0,b]$ is their support.[9] Define the corresponding cumulative distribution functions (CDFs) as $F^A(z,q) = \int_0^z f^A(x;q)dx$, $0 \leq z \leq a$ and $F^B(z;q) = \int_0^z f^B(x;q)dx$, $0 \leq z \leq b$. These CDFs give us the probability that the event will occur before time z. Define the corresponding survival functions (SFs)[10] as $S^A(z;q) = 1 - F^A(z;q)$ and $S^B(z;q) = 1 - F^B(z;q)$. The SFs give us the probability that the event will occur after time z. The hazard functions corresponding to TA and TB are given by,

$$h^i(z;q) = \frac{f^i(z;q)}{S^i(z;q)} = \frac{f^i(z;q)}{1-F^i(z;q)} - \frac{d\ln[1-F^i(z;q)]}{dz} = -\frac{d\ln[S^i(z;q)]}{dz},\ i = A,\ B \qquad (1)$$

Thus, the HF gives us the rate of change of the survival function at each z.

Alternatively, we can define the HF as,

$$h^i(z;q) \ = \ \lim_{\Delta z \to 0}\{\frac{P(z \leq x < z + \Delta z / x \geq z)}{\Delta z}\}.$$

In other words, $h^i(z;q)$ gives us the probability that you will not survive for another $\Delta z \to 0$ period, given that you already survived until period z. Thus, we can think of it as the instantaneous probability that the event in question will occur in period z, given that it has not yet occurred.

[7] Alternatively, we can consider comparing (i) a given treatment between two groups of patients with different characteristics, which may be fixed or time-dependent, and (ii) two treatments to two groups of patients with different characteristics.

[8] With the alternative interpretation, the density functions of x for the two patients are then given by $f^A(x;q^A)$ and $f^B(x;q^B)$, respectively. In the following, we use the first interpretation. Namely, we consider a patient's choice between two treatments.

[9] The sample space may not be the same, but following the stochastic dominance literature, we assume it is. So, for both treatments, the random variables are supported on the finite interval$[0,b]$, $0 < b < +\infty$. For a sufficiently large b, any reasonable possible upper bound for the two treatments can be accommodated.

[10] The probability that the event will occur after time z.

Now, integrating both sides in equation (1) above, we get:

$$\int_0^z h^i(v;q)dv = -\ln[S^i(z;q)], \tag{2}$$

or,

$$\ln[S^i(z;q)] = -\int_0^z h^i(v;q)dv = -H^i(z;q),\ i = A,\ B., \tag{3}$$

where $H^i(z;q)$ is the the cumulative HF. Therefore, equation (3) can be alternatively written as,

$$S^i(z;q) = \exp^{-H^i(z;q)} \tag{4}$$

Equations (3) and (4) provide the explicit relationship between survival, hazard and cumulative hazard functions (CHFs). It shows that $S^i(z;q)$ and $H^i(z;q)$, indeed, determine each other. They provide a clear link between the two most common approaches to treatment choice in medical research. The two approaches consist of the Kaplan-Meier Curves (KMCs) literature, which focuses on the estimation and comparison of SFs and the HF literature (the Cox regression being its most common example), which focuses on the estimation and comparison of HFs. The two approaches are inseparably related. If you have information about hazard functions, you can calculate survival functions and vice versa.

3 Hazard Functions and the Hazard Ratio

Define the hazard ratio as

$$hr(z,q) = \frac{h^B(z;q)}{h^A(z;q)}. \tag{5}$$

Generally, there is no compelling reason why the HR should be time-independent, namely, why it should be constant (i.e., why we should have $\frac{\partial hr(z,q)}{\partial z} = 0$, or $\frac{\partial h^B(z,q)}{\partial z} / \frac{\partial h^A(z,q)}{\partial z} = hr(z,q)$). First, the vector of characteristics (q) includes time-dependent variables. Second, even if all characteristics were time-independent, the functions $h^B(z;q)$ and $h^A(z;q)$ are not necessarily multiplicably and identically separable in z. Namely, they are not of the form $h^i(z;q) = w(z)v^i(q)$. Even if the HFs were given by the multiplicably separable functions $h^i(z;q) = w^i(z)v^i(q)$, the two treatments may, generally, endow the $w^i(z)$ functions with different time-properties (i.e., the HFs functions would not be *identically* separable). Therefore, there is no reason why we should have

$w^A(z) = w^B(z) = w(z)$. Indeed, in the Cox regression model, the HR is $\frac{w(z)v^A(q)}{w(z)v^B(q)} = \frac{v^A(q)}{v^B(q)}$, and the characteristic vector, q, do not depend on z; thus, the HR is constant.

Therefore, we must conclude that, generally, we should not expect HRs to be constant. This conclusion means that the commonly used Cox regression model is a very special case, and generally, we would expect it to be incorrect. Why, then, is it so popular? The answer must be that having a constant HR is very convenient and lends itself to simple testing. However, convenience is not a good enough reason.

What about crossing HFs? HFs cross if and only if there exists a value $z^* = z(q)$ such that,

$$\begin{aligned} h^B(z^*;q) &= h^A(z^*;q) \\ \frac{dh^B(z^*;q)}{dz} &\neq \frac{dh^A(z^*;q)}{dz} \end{aligned} \tag{6}$$

Since hazard ratios are generally non-constant, there is no reason why these conditions in equations (6) should not be satisfied for one or more values of z^*. Hence, generally, we should expect HFs to cross.

The medical literature discusses the "crossing-HFs problem" extensively,[11] yet, thus far, no satisfactory solution has been proposed. However, the issue is not as important as it may seem because, as shown below, treatments may still be ranked even if HFs cross. Moreover, they may be ranked even if cumulative HFs cross.

4 Risk Preference Attributes and the Choice of Treatments

To choose between TA and TB, we need what all decision problems require: an objective function.[12] The most obvious and commonly used framework that provides an objective function for choice under uncertainty is the expected utility model introduced by von Neumann and Morgenstern (1944)). While some reservations have been raised over the years about using this model (and several non-expected utility alternative models have been introduced), it has been and still is the main workhorse for dealing with choice under uncertainty, theoretically and

[11] For example, Kristiansen (2012) reviewed all publications in five major journals and found 175, about 47%, survival studies in which KMCs crossed.

[12] This paper does not discuss whose objective function should be used, the doctor's or the patient's. For a discussion of this issue, see Makins (2023)).

empirically, including a wide range of medical fields. In this paper, we also apply the expected utility model.

Thus, we assume that the decision-maker chooses a treatment by comparing the expected utilities of the outcomes, given the two distribution functions. Define the utility of outcomes (z) as $u(z)$.[13] Then, the expected utilities of x under TA and TB are given by $E_A[u(x)] = \int_0^b u(x)\, f^A(x;q)dx$ and $E_B[u(x)] = \int_0^b u(x)\, f^B(x;q)dx$, respectively. Since, generally, the treatments' underlying distribution functions differ, so do the corresponding expected utilities. The decision-maker, therefore, chooses a treatment by comparing the expected utilities $E^A[u(x)]$ and $E^B[u(x)]$. It is, therefore, clear that the expected utility of a given treatment depends not only on the properties of its distribution function but also on the properties of the utility function.

Four common utility function properties have been observed and discussed in the theoretical and empirical decision theory literature, as well as medical research.[14] This paper will refer to them as properties of orders one to four. Each of these properties implies a specific individual's preferences and characteristics and thus gives rise to a particular type of behaviour when making decisions involving risk. We now summarize these four properties.

The first property is trivial; it says u must be an increasing function (in x). In other words, a later event occurrence is always preferred to an earlier one.[15] This property says, "it is better to have more years." If this property holds, we say that the utility function satisfies the first-order property (P1).

The second property determines whether an individual is risk-averse or not.[16]. Risk aversion (with respect to the timing of the event occurrence) means that patients attach value to certainty and are willing to "pay a risk-premium" to avoid risk. An alternative interpretation of this property (which is observationally equivalent) is that patients apply a discount factor to later years. In the following, we do not differentiate between the two interpretations and refer to both as the second-order property, P2, or, sometimes, simply risk aversion.

Admittedly, not all patients are risk-averse. However, some, perhaps even most, are, as is the

[13] Where $u(x)$ is the utility of outcome x, and u is a continuous differentiable function.

[14] Utility functions' common properties are captured by their derivatives. In practice, only the first four derivatives (denoted as $u'(x)$, $u''(x)$, $u'''(x)$ and $u''''(x)$) have been considered (since it is unclear what higher-order derivatives represent). The signs of these derivatives capture and imply a specific characteristic of an individual's preferences. In particular, the signs of the second, third and fourth derivatives capture risk preference attributes. The second-order derivative may also capture future-discounting attributes.

[15] Thus, u must be an increasing function, i.e., $u'(x) > 0$.

[16] An individual is risk-averse if $u''(x) < 0$, i.e., if the utility functions are concave. She could also be risk-neutral or risk loving if $u''(x) = 0$ or $u''(x) > 0$, respectively

case with investors - not all are risk-averse, but most are. Practically all of finance theory is based on the assumption that individuals are risk averse, as are most economic models that deal with choice under uncertainty. The medical literature also recognizes the validity and importance of risk aversion (see, for example, Cykert, S., (2004), Klein and Stefanek (2007), Deakin, Alexander et al., (2009) and Riddel and Hales (2018)). The alternative interpretation of the second-order property is also intuitive and is related to "time-substitution" or "time discounting," in this case, current years versus future years. Generally, a year today is worth more than a year in the future. In the context of survival, this idea becomes even more important since we often think in terms of "quality years," and quality deteriorates over time; hence, later years are worth less than earlier ones. The discounting of future "rewards" underlies most economic and finance theories and appears even in neuroscience and animal behaviour (see Glasziou, Simes and Gelber, (1990), Berridge and Kringelbach, (2015) and Schultz (2015)). For example, it was even suggested that the neurotransmitter serotonin might play an important role in modulating future discounting (Mobini, Chiang, et al. (2000)).

It has been recognized that individuals tend to exhibit prudence. Prudence refers to the sensitivity of an individual's actions in the presence of risk, whereas risk aversion refers to an individual's dislike of risk. Thus, prudence implies that an individual will take precautionary or preventive actions in the face of uncertainty. Prudence captures a "propensity to prepare and forearm oneself when facing uncertainty" (Kimball (1990)). The economic, finance and medical literature has noted and discussed its importance (see Ebert and Wiesen (2011) and Crawford (2022)).

A classic example is that intertemporal saving decisions suggest that an individual will have precautionary savings. In the context of health, it means that an individual will act to ameliorate health risks. If prudence is satisfied, we say that the utility function satisfies the third-order property, P3.[17]

Finally, temperance, P4, is another property of utility function that has been noted, addressed and used in economics and finance (for a finance example, see Colasante and Riccetti (2020); for an economics example, see Deck and Schlesinger (2010)). Temperance means that an individual will reduce exposure to risky treatments if her independent background risk (from other risky choices) increases the degree of moderation in accepting risk. Several studies in various medical fields found that temperance plays an important role in patients' decisions regarding

[17] Prudence is defined by the condition $u'''(x) > 0$.

risky treatments while facing unrelated risks (see Felder and Mayrhofer (2014)).[18]

We compare two treatments by comparing the properties of the HFs given the utility function and its properties. Specifically, we apply the concept of stochastic dominance (discussed below) of orders one to four in conjunction with the utility function properties P1 to P4.[19]

5 Stochastic Dominance: Definitions

To place the approach used in medical research within the framework of choice under uncertainty, we start with the definitions of stochastic dominance of orders 1 to 4 with respect to the cumulative hazard functions $H^B(z;q)$ and $H^A(z;q)$. We denote stochastic dominance of order $i = 1..4$, with respect to $H^B(z;q)$ and $H^A(z;q)$ as SDi^H. The definitions are as follows,

Definition 1: SD1^H $H^B(z;q)$ exhibits SD1^H over $H^A(z;q)$ *if and only if* $H^A(z;q) \geq H^B(z;q)$ *for all* z, *with strict inequality for at least some* z *values.*

Definition 2: SD2^H $H^B(z;q)$ exhibits SD2^H over $H^A(z;q)$ *if and only if* $H_2^A(v;q) \equiv \int_0^z H^A(v;q)dv \geq \int_0^z H^B(v;q)dv \equiv H_2^A(v;q)$, *for all* z, *with strict inequality for at least some* z *values.*

Definition 3: SD3^H $H^B(z;q)$ exhibits SD3^H over $H^A(z;q)$ *if and only if* $H_3^A(v;q) \equiv \int_0^z H_2^A(v;q)dv \geq \int_0^z H_2^B(z;q)dv \equiv H_3^B(z;q)$, *for all* z, *with strict inequality for at least some* z *values and* $H^A(z;b) \geq H^B(z;b)$.[20]

Definition 4: SD4^H $H^B(z;q)$ exhibits SD4^H over $H^A(z;q)$ *if and only if* $H_4^A(v;q) \equiv \int_0^z H_3^A(v;q)dv \geq \int_0^z H_3^B(z;q) \equiv H_4^B(v;q)$, *for all* z, *with strict inequality for at least some* z *values and* $H^A(z;b) \geq H^B(z;b)$.

[18] Temperance is present if $u''''(x) < 0$.

[19] For a discussion of stochastic dominance, see Levy (1992).

[20] The requirement that we should have $H^A(z;b) \geq H^B(z;b)$ ensures that the condition for SD2^H hold when $z = b$. Rothschild and Stiglitz (1970) show that this requirement ensures that $E^B(x) \geq E^A(x)$.

In Definition 1, we compare the areas under the standard hazard functions $h^A(z;q)$ and $h^B(z;q)$. In Definition 2, we compare the areas under the cumulative hazard functions. We can think of these as second-order areas. In Definition 3, we compare the areas under the second-order hazard functions, which give us the third-order areas. We do the same for Definition 4.

What is most important to note is that the conditions for stochastic dominance become weaker as we move from SD1^H to SD4^H. Thus, if the stochastic dominance of order r is satisfied, then the stochastic dominance of all orders higher than r is also satisfied. The converse, however, is not true.

6 Stochastic Dominance and Treatment Ranking

6.1 First-Order Stochastic Dominance

Given the definitions above, we can now show how stochastic dominance, in conjunction with risk preference attributes, can be used to rank treatments. The first result is given by Proposition 1.

Proposition 1: *If property P1 is satisfied, then TB is preferred TA, if and only if $H^B(z;q)$ exhibits SD1^H over $H^A(z;q)$.*

Proof: *From the relationship between survival and cumulative hazard functions (shown in equations (3) and (4)), it follows that $H^B(z;q)$* exhibits SD1^H over $H^A(z;q)$ *if and only if the condition $S^B(z;q)] \geq S^A(z;q)$ for all z, with strict inequality for some z values holds. The latter condition is known as SD1 with respect to the SFs. It was shown and proven, for example, by Rothschild and Stiglitz (1970) and Levy (1992), that the latter condition, in conjunction with P1, guarantees that treatment B is preferred to treatment A.*[21]

Note that the necessary and sufficient condition provided in Proposition 1 is much weaker than the condition $h^A(z;q) > h^B(z;q)$ *for all* z, which is used in standard medical research using hazard functions. Denote this condition as C1. By construction, condition C1 does not allow hazard functions to intersect. The ranking requirement in Proposition 1 is strikingly weaker and

[21] Proofs and discussions of all the propositions below can also be found in Rothschild and Stiglitz (1970) and Levy (1992).

allows treatment comparisons even when hazard functions cross, hence even if the HR is sometimes smaller but other times greater than 1. Proposition 1 implies that the medical literature self-imposed stronger-than-necessary conditions. Moreover, the standard Cox regression with a constant HR makes the self-imposed restrictions even stronger.[22]

In practice, given hazard functions, $H^A(z;q)$ and $H^B(z;q)$ need to be calculated by integrating the hazard functions $h^A(z;q)$ and $h^B(z;q)$, Namely by calculating the areas under $h^A(z;q)$ and $h^B(z;q)$ for all z values. If it turns out that $H^A(z;q) \geq H^B(z;q)$ for all z, *with strict inequality for at least some z values,* we conclude that TB is preferred to TA. Otherwise, second-order stochastic needs to be considered.

6.2 Second-Order Hazard Functions

If $H^A(z;q)$ and $H^B(z;q)$ intersect, the weaker restrictions required for SD2^H are enough for treatment comparisons if we assume that also P2 (risk-aversion) holds. For SD2^H to hold, the area under the cumulative hazard function $H^A(z;q)$ must be greater than the area under the cumulative function $H^B(z;q)$ for all z, with strict inequality for at least some z values. Hence, the condition for SD2^H is weaker than the condition for SD1^H. Namely, SD1^H implies SD2^H, but SD2^H does not imply SD1^H.

We now have the following proposition:

Proposition 2: *If properties P1 and P2 hold, TB is preferred to TA if and only if* $H^B(z;q)$ exhibits SD2^H over $H^A(z;q)$.

Proof: *If* $\int_0^z H^A(v;q)dv \geq \int_0^z H^B(v;q)dv$, *for all z for all z, with strict inequality for at least some z values, and since* $-H^i(z;q) = \ln[S^i(z;q)]$, *we also have* $\int_0^z S^B(v;q)dv \geq \int_0^z S^A(v;q)dv$, *for all z for all z, with strict inequality for at least some z values. However, the latter condition is the standard requirement for SD2 with respect to the SFs, which*

[22] For a constant hazard ratio, as in the Cox regression, comparing hazard functions is easy because the hazard ratio is $\frac{w(z)v^1(q)}{w(z)v^2(q)} = \frac{v^1(q)}{v^2(q)}$ and the characteristic vector, q, do not depend on z. In this case, we have either $v^2(q) > v^1(q)$ or $v^2(q) < v^1(q)$ (or $v^2(q) = v^1(q)$) for all z. However, the question still is how using the constant ratio is related to the underlying decision theory, the properties of the survival functions, and stochastic dominance.

was shown to be a necessary and sufficient condition for comparing risky alternatives if P1 and P2 hold (see Rothschild and Stiglitz (1970) and Levy (1992)).

It follows from Proposition 2 that we can compare treatments even if their cumulative hazard functions intersect. We can use the second-order area curves $H_2^A(z;q)$ and $H_2^B(z;q)$ to re-write Proposition 2 as,

Proposition 2a: *If properties P1 and P2 hold, TB is preferred to TA if and only if $H_2^A(z;q) \geq H_2^B(z;q)$, for all z, with strict inequality for at least some z values.*

Proposition 2a allows us to compare the heights of the $H_2^A(z;q)$ and $H_2^B(z;q)$ curves (for a given z) rather than the areas under the $H^A(z;q)$ and $H^B(z;q)$ curves, which makes it visually easier to observe and test.

Propositions 2 and 2a allow us to compare treatments under weaker restrictions, even if cumulative hazard functions cross. We can do so because SD2 extracts additional information from the underlying hazard functions, which, in conjunction with the risk aversion property, allows us to compare otherwise non-comparable treatments.

7 Third-Order Hazard Functions

If $H_2^A(z;q)$ and $H_2^B(z;q)$ intersect, we can weaken the conditions for treatment ranking by assuming that P3 (prudence) holds. We now have the following result.

Proposition 3: *If properties P1, P2 and P3 hold, TB is preferred to TA if and only if $H^B(z;q)$ exhibits $SD3^H$ over $H^A(z;q)$.*

Proof. *The proof is identical to the proof of Proposition 2. It follows from (i) the relationship $H^i(z;q) = \ln[S^i(z;q)]$ and (ii) the standard definition and proof of SD3 for SFs.* ■

Proposition 3 can then be re-stated by using the third-order functions $H_3^A(z;q)$ and $H_3^B(z;q)$. It is given as,

Proposition 3a: *$H^B(z;q)$ exhibits $SD3^H$ over $H^A(z;q)$ if and only if $H_3^A(z;q) \geq H_3^B(z;q)$, for all z, with strict inequality for at least some z values and $H^A(z;b) \geq H^B(z;b)$.*

The conditions for SD3^H in Proposition 3a are the same as the ones in Definition 3; hence Proposition 3 still applies.

To conclude, if $H_2^A(z;q)$ and $H_2^B(z;q)$ intersect, assuming that the patient is prudent, we calculate $H_3^A(z;q)$ and $H_3^B(z;q)$. If they satisfy $SD3^H$, we conclude that treatment B is preferred to treatment A. If not, we have to consider fourth-order stochastic dominance (SD4), following the same steps as above. However, since we were unable to find examples where $SD3^H$ did not hold, but $SD4^H$ did, we do not pursue the $SD4^H$ case further.

8 An Empirical Example

This section applies our model to the real-world data of Arenal et al. (2022). Catheter ablation (ABL) and antiarrhythmic drugs (AAD) reduce ICD shocks in patients with ischemic cardiomyopathy and an implantable cardioverter-defibrillator, but the most effective approach remains uncertain. The study compares the efficacy and safety of ABL (treatment B) and AAD (treatment A). Patients (144) were randomized to ABL or AAD. The two groups' SF specifications are displayed in Table 1. They represents S^A and S^B.

ABL		AAD	
Months	Probability	Months	Probability
0.474	1	0.378	1
2.104	0.98484848	0.755	0.98611111
4.775	0.95146379	1.912	0.95710784
5.987	0.91622439	4.803	0.94088568
6.566	0.89825921	6.537	0.92346187
9.071	0.87784422	7.116	0.90535477
10.228	0.85589812	12.148	0.85770452
14.852	0.82533033	13.256	0.83171347
18.899	0.77678149	14.991	0.80200942
25	0.77678149	20.194	0.74854213
		25	0.74854213

ABL: Catheter ablation. AAD: Antiarrhythmic drugs (AAD).

The HFs and the corresponding high-order HFs H^i, H_2^i, and H_3^i, $i = A,\ B$ are obtained by using equation (3) above. The graphs in Figures 1, 2 and 3, respectively, show (the differences): $H^A - H^B$, $H_2^A - H_2^B$, and $H_3^A - H_3^B$.[23]

[23]It should be noted that since the survival and hazard functions are estimated based on a discrete sample, they are piecewise linear step functions. The areas under the standard and higher-order curves are generated by calculating the indefinite integrals of the corresponding lower-order curves.

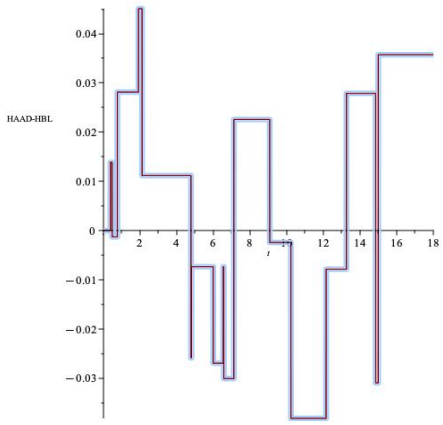

Figure 1: $H^A - H^B$.

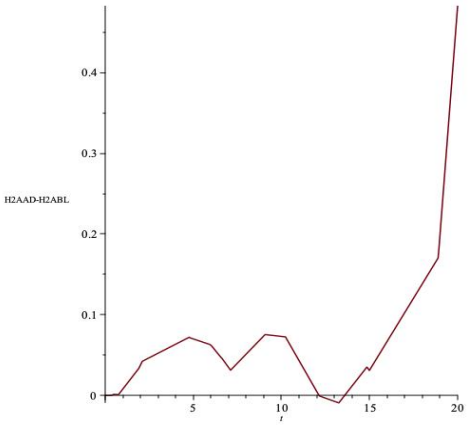

Figure 2: $H_2^A - H_2^B$.

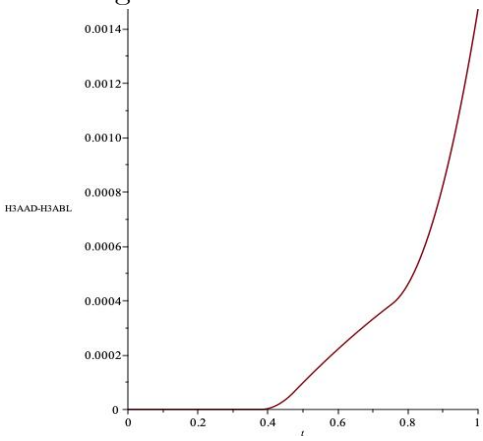

Figure 3: $H_3^A - H_3^B$.

Using S^A and S^B, we obtain the high-order KMCs by calculating the areas under the lower-order KMCs. We define the high-order KMCs as S_i^j, $i = 2,\ 3,\ j = A, B$. Figures 4, 5, and 6, respectively, show the differences, $S^B - S^A$, $S_2^B - S_2^A$ and $S_3^B - S_3^A$.

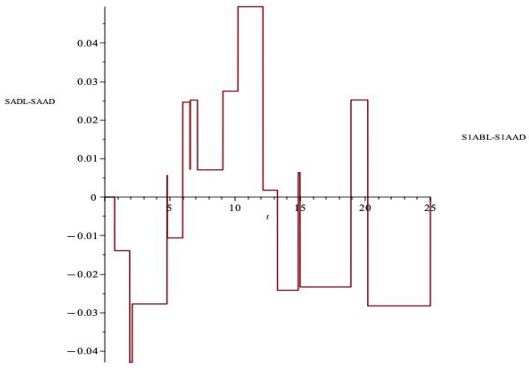

Figure 4: $S^B - S^A$.

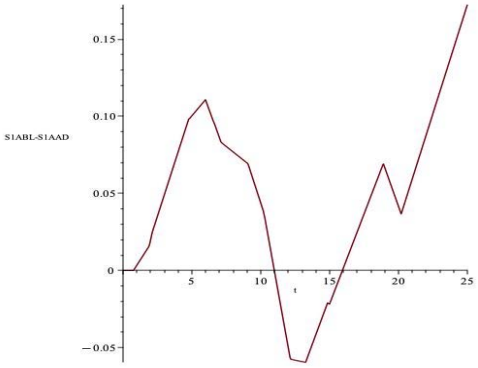

Figure 5: $S_2^B - S_2^A$.

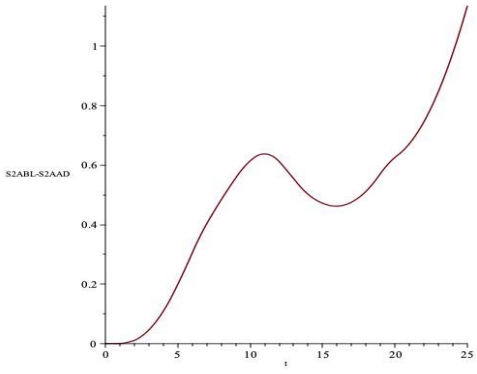

Figure 6: $S_3^B - S_3^A$.

First, Figure 1 shows that H^A and H^B intersect. Therefore, Figure 1 implies that standard HFs, h^A and h^B (not shown in the Figures above), must also intersect. Why? Because if h^A and h^B did not intersect, neither would H^A and H^B.

Second, the Figures also show that whether we use HFs or KMCs, SD1 and SD2 are not satisfied. However, SD3 is satisfied when using HFs or KMCs. The consistency of the results obtained from HFs and KMCs should be expected, given the relationships between SFs and HFs. Based on SD3, and assuming that properties P1 to P3 hold, we conclude that TB (ABL) is preferred to TA (AAD).

9 Conclusion

This paper shows that standard applications of HFs (and the HRs) are based on severe self-imposed conditions, which are much stronger than necessary. This conclusion does not refer only to the self-imposed severe constant HR condition of the Cox regression literature; it also applies to non-constant hazard ratios.

We provide necessary and sufficient conditions for treatment comparisons based on what we term high-order hazard functions. This procedure allows us to apply standard concepts of high-order stochastic dominance in conjunction with patients' risk preference attributes to compare treatments even if hazard functions intersect. The procedure also allows us to compare treatments even if high-order hazard functions intersect. Using high-order hazard functions allows us to obtain all the extractable information embedded in the underlying distribution functions. This additional information is not obtainable when we only use standard hazard functions, thus resulting in information loss. Such information loss means that, with standard medical research, treatment comparisons are sometimes impossible or even wrong.

An example based on real-world data is provided, showing that using $SD3^H$ and prudence, the preferred treatment can be determined even if low-order hazard functions cross.

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