On Hadamard differentiability in k-sample semiparametric models - with applications to the assessment of structural relationships

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February 29, 2004

Running title: "Assessment of structural relationships"

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Abstract

Semiparametric models to describe the functional relationship between k groups of observations are broadly applied in statistical analysis, ranging from nonparametric ANOVA to proportional hazard rate models in survival analysis. In this paper we deal with the empirical assessment of the validity of such a model, which will be denoted as a "structural relationship model". To this end Hadamard differentiability of a suitable goodness-of-fit measure in the k-sample case is proved. This yields asymptotic limit laws which are applied to construct tests for various semiparametric models, including the Cox proportional hazards model. Two types of asymptotics are obtained, first when the hypothesis of the semiparametric model under investigation holds true, and second for the case when a fixed alternative is present. The latter result can be used to validate the presence of a semiparametric model instead of simply checking the null hypothesis "the model holds true". Finally, various bootstrap approximations are numerically investigated and a data example is analyzed.

Key Words:
semiparametric model, Hadamard differentiability, quadratic differentiability, weak convergence, k-sample problem, goodness-of-fit, proportional hazard rates, nonlinear approximation, multivariate empirical process

AMS subject classification: 62E20, 62G10, 62G99, 62J105

1 Introduction

The asymptotics of many goodness-of-fit statistics can be derived by proving some sort of smoothness (such as Hadamard differentiability) of the corresponding functional together with the weak convergence of the underlying stochastic process. This approach has been successfully applied in various one-sample goodness-of-fit problems where the presence of a certain class of parametric distribution functions is to be investigated (cf. e.g. [23, 39, 9, 5, 6, 50]).

However, many practical problems of testing the goodness-of-fit occur in cases where more than one sample is observed. For example, the semiparametric analysis of linear models (cf. [1]), the analysis of acceleration models (cf. e.g. [38, 40, 2]), or of the Cox proportional hazards model [12] fit into that framework. Our aim is to present a general methodology to obtain goodness-of-fit tests for the assessment of the validity of these models. The approach is based on the Hadamard differentiability of the minimum distance between two cumulative distribution functions (c.d.f.s) *up to a semiparametric model*, i.e. the remaining distance between the two c.d.f.s after fitting the model. For the sake of brevity, in this paper we focus on Mallows distance [33] between two c.d.f.s. However, other smooth distances can be treated analogously.

In the following we assume that we observe two independent real valued samples $\{X_1, ..., X_m\}$ and $\{Y_1, ..., Y_n\}$, the $\{X_i\}$ being independent identically distributed (i.i.d.) according to F and the $\{Y_j\}$ being i.i.d. according to G. Here F and G denote two unknown distribution functions, which are elements of the set

$$\mathcal{F}^2 := \{F : F \text{ is a c.d.f. and } \int t^2 dF(t) < \infty\}. \tag{1.1}$$

We will restrict our investigations to one-dimensional observations, however, our results can be extended to multivariate observations (cf. section 7). Furthermore, we introduce a trimmed version of Mallows distance [33] between F and G viz.

$$d(F, G) := \left\{ \frac{1}{b-a} \int_a^b \left(F^{-1}(u) - G^{-1}(u)\right)^2 du \right\}^{\frac{1}{2}}, \tag{1.2}$$

where the quantile function of $F \in \mathcal{F}^2$ is defined as

$$F^{-1}(u) = \inf\{t : F(t) \geq u\}, \quad u \in (0, 1),$$

and a, b are two fixed trimming bounds, with $0 \leq a < b \leq 1$.

Example 1.1 (*Location-scale and related models*). One of the most popular models of semiparametric inference is the location-scale model (cf. e.g. [27, 54]), where F and G belong to the class

$$\mathcal{F}_{LS} := \Big\{(F,G)\ \Big|\ F(t)=G\Big(\frac{t-\mu}{\sigma}\Big)=:G(t,\theta),\ t\in\mathbb{R},\ \text{for some } \theta=(\mu,\sigma)^T, \sigma>0\Big\}. \tag{1.3}$$

Hence, in order to assess whether F and G are related by a location scale model it is tempting to consider the (trimmed) Mallows distance between F and G up to a location-scale transformation, which is given by

$$\begin{aligned} d_{LS}(F,G) &:= \min_{\theta\in\Theta} d\left(F, G(\cdot,\theta)\right) \\ &= \min_{(\mu,\sigma)^T\in\Theta} \left\{ \frac{1}{b-a}\int_a^b \left(F^{-1}(u) - \sigma G^{-1}(u) - \mu\right)^2 du \right\}^{\frac{1}{2}}, \end{aligned} \tag{1.4}$$

with $G(\cdot,\theta)$ from (1.3). For the case $\sigma = 1$, (1.3) reduces to a location model (cf. [29]), whereas $\mu = 0$ corresponds to an acceleration model (cf. [52]). Observe that for the case of distributions with support $\mathbb{R}^+$ the location model of [37] results, which is used to model the logarithmic survival times in a random censorship model. This corresponds to a scale model for the survival times (cf. [53, 51, 32]). For testing procedures in location and scale models see e.g. [26, 11]. From (1.4) it becomes transparent why Mallows distance is an appropriate criterion to measure the deviation between F and G up to $\mathcal{F}_{LS}$. This distance allows an interpretation in terms of the difference of the quantile functions (up to a straight line). Thus, we have a natural extension of the popular QQ-plot of two c.d.f.s (cf. e.g. [17]).

Example 1.2 (*Lehmann alternatives*). Two c.d.f.s F and G are related by a Lehmann alternative [31], if they are in the class

$$\mathcal{F}_{Leh} := \Big\{(F,G)\ \Big|\ F(t)=1-(1-G(t))^{1/\theta}=:G(t,\theta),\ t\in\mathbb{R},\ \text{for some } \theta>0\Big\}. \tag{1.5}$$

The model equation from (1.5) can be also expressed in terms of the quantile functions as

$$F^{-1}(u) = G^{-1}\big(1-(1-u)^\theta\big), \quad u\in(0,1),\ \theta>0. \tag{1.6}$$

Hence we obtain for the minimal Mallows distance between F and G up to $\mathcal{F}_{Leh}$

$$\begin{aligned} d_{Leh}(F,G) &:= \inf_{\theta\in\Theta} d\left(F, G(\cdot,\theta)\right) \\ &= \inf_{\theta\in\Theta} \left\{ \frac{1}{b-a}\int_a^b \left(F^{-1}(u) - G^{-1}(1-(1-u)^\theta)\right)^2 du \right\}^{\frac{1}{2}}, \end{aligned} \tag{1.7}$$

with $G(\cdot, \theta)$ from (1.5). Observe that (1.5) is equivalent to the situation of proportional hazard rates in the two-sample case, where the relation

$$h_G(t) = \theta\, h_F(t), \quad t \in \mathbb{R}, \tag{1.8}$$

holds for the hazard rates h_F and h_G corresponding to F and G, respectively.

In the following we investigate the Hadamard differentiability of minimum distance functionals such as (1.4) and (1.7) in the two sample case under the assumption that the corresponding semiparametric model holds true, as well as under model violations. This will be used to consider the full power curve of the corresponding test instead of solely the p-value under the null hypothesis "H_0 : The semiparametric model holds true". According to the quadratic nature of the proposed functional we find that the asymptotics under this hypothesis is a complicated χ^2-law, whereas under model deviations asymptotic normality holds. The analysis under alternatives turns out to be technically more sophisticated, due to the fact that in semiparametric models uniqueness and existence of a minimum distance has to be guaranteed - a problem which is well known in nonlinear approximation theory and robust statistics.

The paper is organized as follows. In section 2 we present a general model for the semiparametric relationship between two distribution functions which helps to unify several special cases. Semiparametric relationships between various samples will be denoted as *structural relationships*. In section 3 the main result on Hadamard differentiability of the semiparametric functional under investigation is presented. In section 4 the weak convergence of the corresponding test statistic is derived under the model as well as under a fixed alternative. Section 5 provides details on the practical implementation of bootstrap tests for the two testing problems at hand and some results of a Monte-Carlo study on their finite sample behavior. Some recommendations on their proper use are provided. Section 6 illustrates our methods, where the Cox proportional hazards model and the acceleration model are investigated for the difference between treatment groups in the COMPASS clinical trial, where 2 thrombolytic therapies were compared with respect to survival after acute myocardial infarction (cf. [49]). The paper closes with several remarks and possible extensions in section 7. Technical proofs are postponed to the appendix.

2 A general model of structural relationships

The above examples can be regarded as generic in the sense that they cover two essential aspects of semiparametric models for the relationship between two distribution functions, namely a parameterized transformation of the quantile function itself (cf. (1.3)) and a transformation of the argument of the quantile function as in (1.6). This motivates the following definition of a general structural relationship model between F and G.

Definition 2.1 Let $\Theta \subseteq \mathbb{R}^l$, and let $\phi_1 : \mathbb{R} \times \Theta \to \mathbb{R}$, $\phi_2 : [0,1] \times \Theta \to [0,1]$, both continuous with respect to both parameters. We say that F and G in $\mathcal{F}^2$ (cf. (1.1)) are related by a *structural relationship* induced by ϕ_1 and ϕ_2, if $(F,G) \in \mathcal{U}_{\phi_1,\phi_2} =: \mathcal{U}$, where the model class $\mathcal{U}$ is given by

$$\mathcal{U} := \Big\{ \big(F,G\big) \in \mathcal{F}^2 \times \mathcal{F}^2 \;\Big|\; \exists\, \theta \in \Theta \text{ s.t. } F^{-1}(u) = \phi_1\big(G^{-1}\big(\phi_2(u,\theta)\big), \theta\big),\ u \in [0,1] \Big\}. \tag{2.1}$$

Note that in Definition 2.1 no specific parametric assumption on F or G is made. Hence, in this paper we are not concerned with the question whether F and G are jointly normal, say. Here F and G vary in the entire class $\mathcal{F}^2$, restricted to the structural relationship $F^{-1}(u) = \phi_1\big(G^{-1}\big(\phi_2(u,\theta)\big), \theta\big)$.

Observe that in a location model we have $\phi_1(t,\theta) = t + \theta$, whereas in an acceleration model $\phi_1(t,\theta) = \theta\, t$, and in a location-scale model $\phi_1(t, (\theta_1, \theta_2)^T) = \theta_1 + \theta_2\, t$. For these models, $\phi_2(u,\theta) \equiv u$. For the case of Lehmann alternatives (Example 1.2) we obtain $\phi_1(t,\theta) \equiv t$ and $\phi_2(u,\theta) = 1 - (1-u)^\theta$.

In the following we use the notations $D_1 H(t,\theta) := \frac{\partial}{\partial t} H(t,\theta)$ and $D_2 H(t,\theta) := \frac{\partial}{\partial \theta} H(t,\theta)$ for the partial derivatives of functions H on $\mathbb{R} \times \Theta$ whenever they exist; higher derivatives $D_{ij} H(t,\theta)$ are defined analogously. Further, we introduce a (fixed) interval $[p,q]$ for the given trimming bounds a, b, for which

$$[a,b] \subseteq [p,q] \subseteq [0,1] \tag{2.2}$$

holds. For the subsequent asymptotic analysis we require the following technical assumption.

Assumptions 2.2 For $F \in \mathcal{F}^2$ and $\theta \in \Theta$ it holds that $\phi_1\big(F^{-1}\big(\phi_2(\cdot,\theta)\big), \theta\big) \in \mathcal{F}^2$. For the trimming bounds a, b, let $l(\theta) := \phi_2(a,\theta)$ and $u(\theta) := \phi_2(b,\theta)$ for $\theta \in \Theta$. It is assumed that $\phi_2(\cdot,\theta)$ is strictly isotonic for all $\theta \in \Theta$, i.e. there is a map $\phi_2^- : [l(\theta), u(\theta)] \times \Theta \to [a,b]$ with

$$\phi_2\big(\phi_2^-(v,\theta), \theta\big) = v, \qquad v \in [l(\theta), u(\theta)]. \tag{2.3}$$

Likewise, there is an inverse $\phi_1^- : \mathbb{R} \times \Theta \to \mathbb{R}$, i.e. for all $\theta \in \Theta$,

$$\phi_1\big(\phi_1^-(t,\theta),\theta\big) = t, \qquad t \in \mathbb{R}. \tag{2.4}$$

Observe that with (2.3) and (2.4) the structural relationship model from (2.1) can also be expressed in terms of the c.d.f.s, viz.

$$F(t) = \phi_2^-\big(G(\phi_1^-(t,\theta)),\theta\big) =: G(t,\theta). \tag{2.5}$$

Thus, the functionals (1.4) and (1.7) can be considered as special cases of a general class of minimum distance functionals of the form

$$\begin{aligned} T(F,G) := d^2(F,G;\mathcal{U}) \ &:= \ \inf_{\theta\in\Theta} d^2\Big(F, G(\cdot,\theta)\Big) \qquad (2.6)\\ &= \ \inf_{\theta\in\Theta} \left\{ \frac{1}{b-a} \int_a^b \Big(F^{-1}(u) - \phi_1\big(G^{-1}(\phi_2(u,\theta)),\theta\big)\Big)^2 du \right\}, \end{aligned}$$

with $G(\cdot,\theta)$ from (2.5). The use of trimming in (2.6) is often required for technical reasons (cf. the case of Lehmann alternatives in Remark 2.8), but it also permits to assess the validity of the model under investigation as restricted to specific regions of interest. This will be illustrated in the example in section 6.

Remark 2.3 Note that often it might be more suitable to express the discrepancy between F and G up to $\mathcal{U}$ in terms of a general measure of distance Δ between c.d.f.s,

$$\Delta(F,G;\mathcal{U}) := \inf_{\theta\in\Theta} \Delta\big(F, G(\cdot,\theta)\big).$$

However, for the sake of brevity, we restrict ourselves in this paper to the case $\Delta = d$ (with d from (1.2)). This choice of Δ has some practical appeal [35] and is related to the Wasserstein distance between probability distributions. In the context of goodness-of-fit testing for parametric models in the one sample case, see [16, 15] and the references given there. Note, however, that all results of the next section can be immediately transferred to a general Δ, provided that appropriate smoothness and boundedness assumptions on Δ and the model class $\mathcal{U}$ as well as certain requirements on the existence and uniqueness of minimizing values are satisfied.

For a given pair (F,G) of distribution functions we will require the following assumption regarding the existence of a minimizing value of $d^2(F, G(\cdot,\theta))$.

Assumption 2.4 1. There exists a minimizing value θ_0 of $d\big(F, G; \mathcal{U}\big)$ in the interior of Θ. For each minimizing point θ_0 there exists a neighborhood $\Theta_0 \subset \Theta$ of θ_0, such that θ_0 is the unique minimizing value for $d\big(F, G; \mathcal{U}\big)$ on Θ_0, i.e.

$$\theta_0 = \text{argmin}_{\theta \in \Theta_0} \left\{ \frac{1}{b-a} \int_a^b \Big(F^{-1}(u) - \phi_1\big(G^{-1}(\phi_2(u,\theta)), \theta\big) \Big)^2 du \right\}^{\frac{1}{2}}.$$

2. If $(F, G) \in \mathcal{U}$, then there exists a unique parameter value θ_0, such that the model relation in (2.1) holds; hence this value θ_0 is the unique minimizing point for $d\big(F, G(\cdot, \theta)\big)$.

3. If $d(F, G; \mathcal{U}) > 0$, then the set of minimizing values lies in a compact subset Θ_1 of Θ.

Remark 2.5 Under Assumption 2.4 we have that the set of minimizing values

$$\theta_M := \big\{ \theta \in \Theta \,:\, d(F, G; \mathcal{U}) = d(F, G(\cdot, \theta)) \big\}$$

is finite.

Finally, we need the following assumptions in order to guarantee suitable smoothness properties of the distance functional from (2.6).

Assumption 2.6 For the constants p and q from (2.2) and Θ_1 from Assumption 2.4, the functions ϕ_1 and ϕ_2 are twice continuously differentiable with respect to both arguments on $\mathbb{R} \times \Theta_1$ and on $[p, q] \times \Theta_1$, respectively. The derivative $D_1\phi_2$ is bounded away from zero on $[p, q] \times \Theta_1$. The continuous densities f of F and g of G are strictly positive on the intervals $[F^{-1}(p), F^{-1}(q)]$ and $[G^{-1}(p), G^{-1}(q)]$, respectively. Further, it holds that $G \in \mathbf{C}_2[p, q]$, i.e. G is twice continuously differentiable with bounded second derivative on $[p, q]$. It is assumed that the condition $l(\theta), u(\theta) \in [p, q]$, $\theta \in \Theta_1$, is satisfied, with $l(\theta)$ and $u(\theta)$ from Assumption 2.2. Without loss of generality we will in the following write Θ for the closure $\bar{\Theta}_1$ of Θ_1.

We will briefly comment on the above assumptions.

Remark 2.7 Assumption 2.4 is fulfilled for given c.d.f.s F and G and model $\mathcal{U}$, e.g., if $d(F, G(\cdot, \theta))$ is a strictly convex function of θ. This holds for the location, acceleration, and location-scale model, respectively (for any $F, G \in \mathcal{F}^2$). Here the (unique) minimizing parameter vector θ_0 can be calculated explicitly, cf. Remark 4.1.
If Assumptions 2.4.1,2 are satisfied, a set of sufficient conditions for Assumption 2.4.3 is given by

(a) $d(F, G(\cdot, \theta))$ is continuous in θ;

(b) $d(F, G(\cdot, \theta)) \to \infty$ as $\|\theta\| \to \infty$.

For the model of Lehmann alternatives this would be the case e.g. if $G^{-1}(1) = \infty$, i.e. if the support of the c.d.f. G is not bounded.

Remark 2.8 For the location model, acceleration model, and the location-scale model the assumptions on ϕ_1 and ϕ_2 from Assumption 2.6 are obviously satisfied, even when $[p, q] = [0, 1]$. For the case of Lehmann alternatives the additional condition $0 < p < q < 1$ has to be satisfied in order to fulfill the requirements on ϕ_1 and ϕ_2 in Assumption 2.6, hence trimming is required in this case. This condition is also required for the proportional odds model for survival times (cf. [4]), which is given by

$$\ln \frac{F(t)}{1 - F(t)} = \ln \frac{G(t)}{1 - G(t)} + \theta,$$

i.e. for which $\phi_1(t, \theta) = t$ and

$$\phi_2(u, \theta) = \frac{u/(1-u)}{\exp(\theta) + u/(1-u)} \, .$$

3 Hadamard differentiability of $d(\cdot, \cdot; \mathcal{U})$

For the definition of Hadamard differentiability and its use in a functional delta method for the derivation of the asymptotics of statistical functionals we refer to [41, 22, 25]. Further applications can be found in [42, 45, 43, 50], among others.

In the following we will require several notations. We denote by $\mathbf{D}[\mathbb{I}]$ the space of right continuous functions with left limits (*càdlàg*) on a closed interval $\mathbb{I} \subset \mathbb{R}$. Analogously, $\mathbf{D}_-[\mathbb{I}]$ is the space of left continuous functions with right limits on $\mathbb{I}$. The space of continuous functions on $\mathbb{I}$ is denoted by $\mathbf{C}[\mathbb{I}]$. All function spaces will be equipped with the supremum norm $\|f\|_\infty := \sup_{t \in \mathbb{I}} |f(t)|$. For finite product spaces, e.g.

$$\mathbf{D}^k[\mathbb{I}] := \big(\mathbf{D}[\mathbb{I}]\big)^k = \big\{ f = (f_1, ..., f_k)^T : f_i \in \mathbf{D}[\mathbb{I}], 1 \leq i \leq k \big\}$$

we will use the maximum-supremum norm

$$\|f\|_\infty := \max_{i=1,\dots,k} \left\{ \sup_{t \in \mathbb{I}} |f_i(t)| \right\} .$$

Weak convergence in these spaces will be understood in the sense of [18, 19], i.e. by using the σ-algebra of open balls of the respective space as the underlying σ-algebra. The set $\mathbf{BV}_M[p,q]$ is defined as the subset of $\mathbf{D}_{-}[p,q]$ with total variation bounded by the constant $M < \infty$,

$$\mathbf{BV}_M[p,q] := \Big\{ S \in \mathbf{D}_{-}[p,q] \,:\, \int_p^q \big|dS(u)\big| \leq M \Big\}.$$

Let

$$\mathbf{D}_M[\bar{\mathbb{R}}] := \Big\{ S \in \mathbf{D}[\bar{\mathbb{R}}] : S^{-1}I_{[p,q]} \in \mathbf{BV}_M[p,q] \Big\},$$

and define $\mathbf{BV}_{M,C}[p,q] := \mathbf{BV}_M[p,q] \cap \mathbf{C}[p,q]$ and $\mathbf{D}_{M,C}[\bar{\mathbb{R}}] := \mathbf{D}_M[\bar{\mathbb{R}}] \cap \mathbf{C}[\bar{\mathbb{R}}]$. For a function $f : \Theta \to \mathbb{R}$ we denote the vector of derivatives with respect to θ by $\nabla f(\theta) = (D_1 f(\theta), ..., D_l f(\theta))^T$, where x^T shall denote the transpose of a vector x. The Hessian corresponding to f will be denoted by $\nabla^2 f(\theta)$. We need the following abbreviations,

$$\begin{aligned} \tilde{\beta}(v,\theta) &:= \Big\{ D_1\phi_2\big(\phi_2^{-}(v,\theta),\theta\big) \Big\}^{-1}, \qquad && v \in [l(\theta), u(\theta)],\ \theta \in \Theta, \\ \beta(v,\theta) &:= D_2\phi_2\big(\phi_2^{-}(v,\theta),\theta\big)\,\tilde{\beta}(v,\theta), && v \in [l(\theta), u(\theta)],\ \theta \in \Theta. \end{aligned}$$

Finally, we shall make use of the function $\Phi : \Theta \to \mathbb{R}^l$,

$$\Phi(\theta) \;:=\; \frac{b-a}{2}\,\nabla d^2\Big(F, G(\cdot,\theta)\Big), \tag{3.1}$$

the function $\Phi_{(S_1,S_2)} : \Theta \to \mathbb{R}^l$,

$$\begin{aligned} \Phi_{(S_1,S_2)}(\theta) = \; & -\int_{l(\theta)}^{u(\theta)} S_1\big(\phi_2^{-}(v,\theta)\big) D_1\phi_1\big(S_2(v),\theta\big)\beta(v,\theta)\,dS_2(v) \\ & + \int_{l(\theta)}^{u(\theta)} \phi_1\big(S_2(v),\theta\big) D_1\phi_1\big(S_2(v),\theta\big)\beta(v,\theta)\,dS_2(v) \\ & - \int_{l(\theta)}^{u(\theta)} \Big\{ S_1\big(\phi_2^{-}(v,\theta)\big) - \phi_1\big(S_2(v),\theta\big) \Big\} D_2\phi_1\big(S_2(v),\theta\big)\tilde{\beta}(v,\theta)\,dv\,, \end{aligned} \tag{3.2}$$

where $(S_1, S_2) \in \mathbf{D}_{-}[p,q] \times \mathbf{BV}_M[p,q]$, and of the matrix

$$A_\theta := \nabla\Phi(\theta),\ \theta \in \Theta. \tag{3.3}$$

Note that we have $\Phi \equiv \Phi_{(\tilde{F},\tilde{G})}$, where

$$\tilde{F} := F^{-1}I_{[p,q]},\ \tilde{G} := G^{-1}I_{[p,q]}.$$

We will now present the two main results of this paper, which will be used for the derivation of weak convergence results of an estimator of $d(F,G;\mathcal{U})$ and for the construction of corresponding testing procedures. First, we state the Hadamard differentiability (tangentially to a subspace) of the functional under investigation, if certain regularity conditions are satisfied. Here we use the fact that each minimizing value $\theta \in \Theta$ of $d(F, G(\cdot, \theta))$ will be a zero of its first derivative, i.e. of the function Φ given by (3.1). Thus, we formulate our result in terms of a given zero of Φ, assuming that it exists and is well separated from possible other zeros. The second result contains the quadratic Hadamard differentiability of the functional (cf. Definition 3.3), if additionally the underlying distribution functions F and G are related by a structural relationship as defined by $\mathcal{U}$, i.e. for the case where $(F, G) \in \mathcal{U}$ holds.

■ **Theorem 3.1** *Suppose the following assumptions hold for a given interval* $[p, q]$ *with (2.2).*

(1) *We have* $F,\, G \in \mathbf{D}_M[\bar{\mathbb{R}}]$ *for an* $M > 0$. *The class* $\mathcal{U}$ *is given by (2.1), and the Assumptions 2.2 and 2.6 are satisfied.*

(2) *There exists a minimizing value* θ_0 *of* $d(F, G; \mathcal{U})$ *according to Assumption 2.4 (and hence a zero of the function* Φ *in (3.1)) such that* Φ *is locally homeomorphic at* θ_0*, and the matrix* A_θ *in (3.3) is non-singular and bounded for* $\theta = \theta_0$.

Then, there exist for θ_0 *a neighborhood* $\mathbf{U}$ *of* (F, G) *in* $\mathbf{D}[\bar{\mathbb{R}}] \times \mathbf{D}_M[\bar{\mathbb{R}}]$ *and a functional* $T : \mathbf{D}[\bar{\mathbb{R}}] \times \mathbf{D}_M[\bar{\mathbb{R}}] \to \mathbb{R}$ *with*

$$T(S_1, S_2) = d^2\Big(S_1, S_2\big(\cdot, \theta(S_1^{-1} I_{[p,q]}, S_2^{-1} I_{[p,q]})\big)\Big), \tag{3.4}$$

where the functional $\theta : \mathbf{D}_{-}[p, q] \times \mathbf{BV}_M[p, q] \to \Theta$ *is defined by Lemma 8.1, for which* $\theta(S_1^{-1} I_{[p,q]}, S_2^{-1} I_{[p,q]})$ *is for every pair* $(S_1, S_2) \in \mathbf{U} \cap \big(\mathbf{C}[\bar{\mathbb{R}}] \times \mathbf{D}_{M,C}[\bar{\mathbb{R}}]\big)$ *a zero of* $\Phi_{(S_1^{-1} I_{[p,q]}, S_2^{-1} I_{[p,q]})}$ *in (3.2), and* $\theta(\tilde{F}, \tilde{G}) = \theta_0$. *Every functional* T *with these properties is Hadamard differentiable at* (F, G) *tangentially to* $\mathbf{C}^2[\bar{\mathbb{R}}]$*, with the derivative given by*

$$\begin{aligned} & T'_{(F,G)}(h_1, h_2) \\ = \ & \frac{2}{b-a} \int_a^b \Big(F^{-1}(u) - \phi_1\big(G^{-1}(\phi_2(u, \theta_0)), \theta_0\big)\Big) \Big[\tilde{h}_1(u) - D_2\phi_1\big(G^{-1}(\phi_2(u, \theta_0)), \theta_0\big)^T \theta'_{(\tilde{F}, \tilde{G})}\big(\tilde{h}_1, \tilde{h}_2\big) \\ & - D_1\phi_1\big(G^{-1}(\phi_2(u, \theta_0)), \theta_0\big)\Big\{\tilde{h}_2\big(\phi_2(u, \theta_0)\big) + \tilde{G}'\big(\phi_2(u, \theta_0)\big) D_2\phi_2(u, \theta_0)^T \theta'_{(\tilde{F}, \tilde{G})}\big(\tilde{h}_1, \tilde{h}_2\big)\Big\}\Big] \, du, \end{aligned} \tag{3.5}$$

where $\tilde{h}_1(u) := -\frac{h_1(F^{-1}(u))}{f(F^{-1}(u))}$, $\tilde{h}_2(u) := -\frac{h_2(G^{-1}(u))}{g(G^{-1}(u))}$, $u \in [a, b]$, *and the derivative* $\theta'_{(\tilde{F}, \tilde{G})}\big(\tilde{h}_1, \tilde{h}_2\big)$ *is given by (8.2).*

Remark 3.2 Note that the functional T constructed in Theorem 3.1 is equal to $d^2(F,G;\mathcal{U})$ from (2.6) at the given c.d.f.s (F,G). It is also equal to $d^2(S_1,S_2;\mathcal{U})$ at pairs $(S_1,S_2)\in \mathbf{U}\cap\big(\mathbf{C}[\bar{\mathbb{R}}]\times \mathbf{D}_{M,C}[\bar{\mathbb{R}}]\big)$. At the other points in **U** the functional is at least 'close' to the corresponding minimum value of the distance, due to the extension lemma (Lemma 1 of [25]; cf. the proof of Theorem 3.1 in Section 8.1). An essential observation is that in case of several minima the properties of the functional depend to a large extent on the choice of the particular minimizing value θ_0.

For the statement of the second result we require the map, $\tilde{T}:\mathbf{BV}^2_M[p,q]\to\mathbb{R}$,

$$\tilde{T}(S_1,S_2)=\frac{1}{b-a}\int_a^b\Big(S_1(u)-\phi_1\big(S_2(\phi_2(u,\theta(S_1,S_2))),\theta(S_1,S_2)\big)\Big)^2du, \tag{3.6}$$

where the functional θ is given by Theorem 3.1. Clearly, for $S_1,S_2\in \mathbf{D}_M[\bar{\mathbb{R}}]$ the relationship $T(S_1,S_2)=\tilde{T}(S_1^{-1}I_{[p,q]},S_2^{-1}I_{[p,q]})$ holds. We will use the following definition of quadratic Hadamard differentiability tangentially to a subspace, which is based on the definition of 'second order ρ-Hadamard differentiability' in [47].

Definition 3.3 Let **V**, **W** be normed spaces. A functional $T:\mathbf{V}\to\mathbf{W}$ is called *quadratic Hadamard differentiable at* $x\in\mathbf{V}$ tangentially to the subspace $\mathbf{V}_0\subset\mathbf{V}$, if there is a continuous, bilinear functional $T_x^{(2)}:\mathbf{V}_0\times\mathbf{V}_0\to\mathbf{W}$, such that for all sequences $t_n\to 0$ ($t_n\in\mathbb{R}$) and $h_n\to h\in\mathbf{V}_0$ with $x+t_nh_n\in\mathbf{V}, n\geq 1$, it holds that

$$\lim_{n\to\infty}\frac{T(x+t_nh_n)-T(x)}{t_n^2}-T_x^{(2)}(h)=0. \tag{3.7}$$

Here we used the abbreviation $T_x^{(2)}(h,h)=:T_x^{(2)}(h)$.

Note that, in contrast to [44], for instance, this definition does not include the (first order) Hadamard differentiability of the functional. It is suitable especially for 'purely quadratic' functionals, i.e. for functionals which can be locally approximated by quadratic functionals.

■ **Theorem 3.4** *If the pair $(F,G)\in\mathcal{U}$, and the conditions of Theorem 3.1 are satisfied, then the functional $\tilde{T}$ is quadratic Hadamard differentiable at $(\tilde{F},\tilde{G})$ tangentially to $\mathbf{C}^2[p,q]$. The derivative $\tilde{T}^{(2)}_{(\tilde{F},\tilde{G})}$ is then given by*

$$\begin{aligned}\tilde{T}^{(2)}_{(\tilde{F},\tilde{G})}(h_1,h_2)=&\frac{1}{b-a}\int_a^b\Big[h_1(u)-D_2\phi_1(G^{-1}(\phi_2(u,\theta_0)),\theta_0)\theta'_{(\tilde{F},\tilde{G})}(h_1,h_2)\\&-D_1\phi_1(G^{-1}(\phi_2(u,\theta_0)),\theta_0)\big\{\tilde{G}'(\phi_2(u,\theta_0))D_2\phi_2(u,\theta_0)\theta'_{(\tilde{F},\tilde{G})}(h_1,h_2)+h_2(\phi_2(u,\theta_0))\big\}\Big]^2du.\end{aligned}$$

The above results indicate that there are two cases to be distinguished which yield qualitatively different features of the functional under investigation. Suppose that the conditions of Theorem 3.1 hold. If the Hadamard derivative $T'_{(F,G)}$ is not identically zero, the functional T can be approximated by this linear functional in a neighborhood of (F,G). This will be called the *regular case* in the following. On the other hand, if a structural relationship according to the model $\mathcal{U} = \mathcal{U}_{\phi_1,\phi_2}$ holds for the given pair (F,G), then the derivative $T'_{(F,G)}$ vanishes. In this *nonregular case* we can deduce from Theorem 3.4 that the functional T can be approximated by a quadratic functional, which is defined with help of $\tilde{T}^{(2)}_{(\tilde{F},\tilde{G})}$. These properties will be used in the next section in the derivation of the large sample behavior of our test statistic.

4 The test statistic and its weak convergence results

In order to use $d(F,G;\mathcal{U})$ as a measure of the goodness-of-fit of a structural relationship model $\mathcal{U}$, the unknown c.d.f.'s F and G have to be estimated properly. In the case of i.i.d. observations as described in section 2 this can be simply done by the empirical c.d.f., which is given by

$$F_m(t) = \frac{1}{m}\sum_{i=1}^{m} X_i \, I_{\{X_i \le t\}} \tag{4.1}$$

for the estimation of F; the estimator G_n for G is defined analogously. Smoothed variants of F_m and G_n would be appropriate, too. Under a more complicated sampling scheme, such as independent right censoring, one could use the Kaplan-Meier estimators of the distribution functions. For the sake of briefness we will only focus on the simplest case of two independent samples of i.i.d. observations without censoring. Then the Donsker theorem yields the weak convergence of the empirical processes,

$$\begin{aligned} \sqrt{m}(F_m - F)(\cdot) &\overset{\mathcal{D}}{\Longrightarrow} \mathbb{B}_F(F(\cdot)), \\ \sqrt{n}(G_n - G)(\cdot) &\overset{\mathcal{D}}{\Longrightarrow} \mathbb{B}_G(G(\cdot)), \end{aligned} \tag{4.2}$$

in $\mathbf{D}[\bar{\mathbb{R}}]$, where $\mathbb{B}_F(\cdot)$ and $\mathbb{B}_G(\cdot)$ are two independent Brownian Bridges on $[0,1]$. Together with the differentiability properties from section 3, this will be used for deriving the weak convergence of the estimated discrepancy $\hat{d}(F,G;\mathcal{U}) := d(F_m, G_n;\mathcal{U})$. Here we will have to distinguish between the two cases according to whether $(F,G) \in \mathcal{U}$ or not.

Remark 4.1 Note that for the location, acceleration, and location-scale model the (unique) minimum distance estimators $\hat{\theta} = \theta(F_m^{-1}, G_n^{-1})$ with θ from Theorem 3.1 can be calculated explicitly. For instance, for the location model we obtain $\hat{\theta} = \frac{1}{b-a}\int_a^b (F_m^{-1}(u) - G_n^{-1}(u))du$. For the lengthy formulae in case of the location-scale model see [24]. In contrast, for the model of Lehmann alternatives there is no explicit expression for the minimizing parameter value, and there could be even more than one minimizing value, depending on the underlying distribution functions. Here the parameter has to be estimated numerically.

4.1 Regular case

The following result holds under the given conditions, no matter if the structural relationship under investigation is satisfied. However, in case $(F, G) \in \mathcal{U}$ it yields a degenerate asymptotic distribution of our statistic, which cannot be used for practical purposes. For that case we refer to the next paragraph.

■ **Theorem 4.2** *Assume that the assumptions of Theorem 3.1 are satisfied for the interval $[p, q]$ and a locally unique minimizing value θ_0. Let F_m and G_n be two independent empirical estimators according to (4.1) for F and G, respectively, and let the independent limits of the respective empirical processes be given by (4.2). T is supposed to be the functional corresponding to θ_0 given by Theorem 3.1. Let $m \wedge n \to \infty$ and $n/(m+n) \to \rho$ for some $\rho \in (0,1)$. Then we have the convergence in distribution*

$$\sqrt{\frac{mn}{m+n}}\big(T(F_m, G_n) - T(F,G)\big) \xrightarrow{\mathcal{D}} L_{F,G} \tag{4.3}$$

$$= \frac{2}{b-a}\int_a^b \Big(F^{-1}(u) - \phi_1\big(G^{-1}(\phi_2(u,\theta_0)),\theta_0\big)\Big)\Big[\tilde{\mathbb{X}}_F(u) - D_2\phi_1\big(G^{-1}(\phi_2(u,\theta_0)),\theta_0\big)^T\theta'_{(\tilde{F},\tilde{G})}\big(\tilde{\mathbb{X}}_F, \tilde{\mathbb{X}}_G\big)$$

$$- D_1\phi_1\big(G^{-1}(\phi_2(u,\theta_0)),\theta_0\big)\Big\{\tilde{\mathbb{X}}_G\big(\phi_2(u,\theta_0)\big) + \tilde{G}'\big(\phi_2(u,\theta_0)\big)D_2\phi_2(u,\theta_0)^T\theta'_{(\tilde{F},\tilde{G})}\big(\tilde{\mathbb{X}}_F, \tilde{\mathbb{X}}_G\big)\Big\}\Big]du,$$

where

$$\tilde{\mathbb{X}}_F := -\sqrt{\rho}\,\frac{\mathbb{B}_F}{f\circ F^{-1}}, \quad \tilde{\mathbb{X}}_G := -\sqrt{1-\rho}\,\frac{\mathbb{B}_G}{g\circ G^{-1}},$$

and $\theta'_{(\tilde{F},\tilde{G})}\big(\tilde{\mathbb{X}}_F, \tilde{\mathbb{X}}_G\big)$ is given by inserting $(\tilde{\mathbb{X}}_F, \tilde{\mathbb{X}}_G)$ for $(\tilde{h}_1, \tilde{h}_2)$ in $\theta'_{(\tilde{F},\tilde{G})}\big(\tilde{h}_1, \tilde{h}_2\big)$ in (8.2).

Note that the limiting random element $L_{F,G}$ is given by a linear functional applied to a zero mean Gaussian process, hence $L_{F,G}$ is normally distributed with mean 0 and a limiting variance $\sigma^2_{F,G}$

(provided it exists), which depends on the unknown distribution functions F and G, the particular structural relationship model $\mathcal{U}$, the trimming bounds a, b, and the chosen minimizing value θ_0.

4.2 Nonregular case

■ **Theorem 4.3** *In addition to the conditions of Theorem 4.2, suppose that* $(F, G) \in \mathcal{U}$ *holds, i.e.* $T(F, G) = 0$. *Then we obtain the convergence in distribution*

$$\frac{mn}{m+n} T(F_m, G_n) \xrightarrow{\mathcal{D}} L_0 \tag{4.4}$$

$$= \frac{1}{b-a} \int_a^b \Bigg[\tilde{\mathbb{X}}_F(u) - D_2\phi_1(G^{-1}(\phi_2(u, \theta_0)), \theta_0)\, \theta'_{(\tilde{F},\tilde{G})}(\tilde{\mathbb{X}}_F, \tilde{\mathbb{X}}_G)$$

$$- D_1\phi_1(G^{-1}(\phi_2(u, \theta_0)), \theta_0) \Big\{ \tilde{G}'(\phi_2(u, \theta_0)) D_2\phi_2(u, \theta_0)\, \theta'_{(\tilde{F},\tilde{G})}(\tilde{\mathbb{X}}_F, \tilde{\mathbb{X}}_G) + \tilde{\mathbb{X}}_G(\phi_2(u, \theta_0)) \Big\} \Bigg]^2 du.$$

Observe that the limiting random variable L_0 is in this case obtained by applying a quadratic functional to a mean zero Gaussian process. Thus it is distributed according to a complicated distribution given by an infinite convolution of scaled and shifted χ^2-random variables. This limiting distribution also depends on the unknown distribution functions F and G, the model $\mathcal{U}$, the trimming bounds a, b, and on the corresponding parameter vector θ_0.

5 Bootstrap tests and some simulation results

The results of the preceding section provide the means of constructing tests of the validity of the model $\mathcal{U}$ for the underlying distribution functions F and G. The *classical* formulation of goodness-of-fit hypotheses would lead to the problem of testing

$$H_0 : d(F, G; \mathcal{U}) = 0 \quad \text{vs} \quad H_A : d(F, G; \mathcal{U}) > 0. \tag{5.1}$$

Under the null hypothesis H_0 we have the nonregular case described above, hence an appropriate asymptotic level α test would be given by rejecting H_0 if $mn/(m+n)d^2(F_m, G_n; \mathcal{U})$ exceeds the $(1-\alpha)$-quantile of the distribution of L_0 (cf. (4.4)). However, this distribution depends on unknown parameters, and we suggest using a bootstrap approximation of this distribution. To this end bootstrap versions of the empirical distribution functions have to be calculated from independent bootstrap samples X_i^*, $i = 1, ..., m^*$, and Y_j^*, $j = 1, ..., n^*$, from the original samples

$X_i,\ i=1,...,m$, and $Y_j,\ j=1,...,n$, respectively. Observe that the bootstrap sample sizes have to be chosen smaller than the original sample sizes, as will be stated in the following theorem, which gives the justification for the application of the bootstrap method in this case. This is essentially based on the ideas of [46] and [47] which were formulated for specific Fréchet differentiable functionals. For the definition of the weak consistency of bootstrap approximations we refer to [47]. The conditional distribution, given the original samples, will be denoted by $\mathcal{L}^*$.

■ **Theorem 5.1** *Suppose the conditions of Theorem 4.3 are satisfied. Let $F^*_{m^*}$ and $G^*_{n^*}$ be bootstrap versions of F_m and G_n, respectively, where $m^*, n^* \to \infty$, $m^* = o(m)$, $n^* = o(n)$, and $n^*/(m^*+n^*) \to \rho$. Then the sequence of bootstrap distributions*

$$\mathcal{L}^*\left[\tfrac{m^*n^*}{m^*+n^*}\Big(T(F^*_{m^*}, G^*_{n^*}) - T(F_m, G_n)\Big)\right]$$

is weakly consistent for the distribution of the limiting random variable L_0 from (4.4).

Thus, the $(1-\alpha)$-quantile of the distribution of L_0 can be approximated by the empirical $(1-\alpha)$-quantile $T_{B,1-\alpha}$ from B bootstrap versions $T(F^*_{m^*}, G^*_{n^*})$, $b = 1, ..., B$, of $T(F_m, G_n)$. A test of the problem (5.1) rejects the null hypothesis at level α if $T(F_m, G_n) > T_{B,1-\alpha}$. The choice of the bootstrap sample size in this so-called *m-out-of-n bootstrap* is a complicated theoretical problem, see also [8, 7, 30]. A practicable suggestion for the choice of the bootstrap sample size is given in Paragraph 5.1.2 on the simulation results for this testing problem.

However, in addition to problem (5.1) we suggest to consider the following class of testing problems for the actual *validation* of the model $\mathcal{U}$ (cf. also [35]),

$$H_\Delta : d(F, G; \mathcal{U}) > \Delta_0 \quad \text{vs} \quad K_\Delta : d(F, G; \mathcal{U}) \leq \Delta_0. \tag{5.2}$$

Here Δ_0 is a fixed bound the experimenter is willing to tolerate for the distance between F and G up to the model $\mathcal{U}$. Note that this approach automatically yields confidence intervals for d (cf. section 6). For testing H_Δ, we need the asymptotic distribution of the estimated discrepancy at the hypothesis margin, i.e. at $d(F, G; \mathcal{U}) = \Delta_0$. Hence, we have the regular case and we can use the result of section 4.1. Thus, an appropriate asymptotic level α test of H_Δ would amount to rejecting H_Δ if $\sqrt{mn/(m+n)}(d^2(F_m, G_n; \mathcal{U}) - \Delta_0^2)$ falls below the α-quantile of the centered normal distribution with variance $\sigma^2_{F,G}$. Since $\sigma^2_{F,G}$ is not known, we suggest using a bootstrap approximation of the distribution of $L_{F,G}$, which is based on the following result. Note that here we can use the bootstrap sample sizes equal to the original sample sizes.

■ **Theorem 5.2** *Suppose the conditions of Theorem 4.2 hold. Let F_m^* and G_n^* be bootstrap versions of F_m and G_n, respectively. Then the sequence of bootstrap distributions*

$$\mathcal{L}^*\Big[\sqrt{\frac{mn}{m+n}}\big(T(F_m^*, G_n^*) - T(F_m, G_n)\big)\Big]$$

is weakly consistent for the distribution of the limiting random variable $L_{F,G}$ from (4.3).

Thus, under the above conditions we can use e.g. the bootstrap percentile (PC) or the bias-corrected accelerated (BC$_a$) method for testing H_Δ (cf. [21]). For example, the PC method amounts to rejecting H_Δ at level α if the empirical $(1-\alpha)$-quantile $T_{B,1-\alpha}$ from B bootstrap versions $T(F_m^*, G_n^*)$, $b = 1, ..., B$, of $T(F_m, G_n)$ is less than Δ_0^2.

Further, instead of simply testing the hypothesis for a pre-specified value of Δ_0, we suggest looking at the whole p-value curve for the problem $H_\Delta \; vs. \; K_\Delta$, i.e. at the plot of the resulting p-values in dependence on the value of Δ_0 (cf. [35]), which can serve as a valuable diagnostic tool in model checking and in comparing different models.

Remark 5.3 Note that the minimum discrepancy functional $d(F,G;\mathcal{U})$ is not necessarily symmetric in F and G. Therefore, it is tempting to work with a symmetrized version of it, i.e. with

$$\tilde{d}(F,G;\mathcal{U}) := \sqrt{\frac{1}{2}\big(d^2(F,G;\mathcal{U}) + d^2(G,F;\mathcal{U})\big)}. \tag{5.3}$$

The corresponding weak convergence results and bootstrap tests can readily be obtained from those for $d(F,G;\mathcal{U})$.

5.1 Simulation results (Tests for Lehmann's alternative)

5.1.1 Test of the hypothesis H_Δ in (5.2)

In the following we present a short study on how well the test of (5.2) with $\mathcal{U} = \mathcal{F}_{Leh}$ (cf. (1.5)) keeps its nominal level. The distribution F was chosen as the exponential distribution with parameter $\theta = 0.5$, i.e. $F(t) = 1 - \exp(-0.5t)$. In setting (a), the distribution G was chosen as the exponential distribution with parameter $\theta = 1.5$, shifted by a $\delta > 0$, whereas in the other settings, (b) and (c), G was the Weibull distribution with parameters $\theta_1 = 1.5$ and $\theta_2 > 1$ in case (b) and $\theta_2 < 1$ in case (c), respectively (cf. Table 1). The free parameters δ and θ_2, respectively, where chosen such that a true distance $\tilde{d}^2 = 1$ resulted (cf. (5.3)), thus yielding the margin $\Delta_0^2 = 1$. Note that for $\delta = 0$ and $\theta_2 = 1$, respectively, the model of Lehmann alternatives would hold, such that $d^2 = d_{Leh}^2(F, G) = 0$ (cf. (1.7)). The sample sizes in both groups were $m = n = 50, 100, 200$, and trimming bounds $[a, b] = [0.05, 0.95]$ and $[a, b] = [0.10, 0.90]$ were used. For each setting, 1000 simulations with $B = 1000$ bootstrap replications were realized, and both the PC and the BC$_a$bootstrap tests were performed. In Table 1 the resulting empirical levels are presented for the nominal levels $\alpha = 0.05, 0.1$.

Table 1: Test of H_Δ for $\mathcal{F}_{Leh}$: $\Delta_0^2 = 1$, $\tilde{d}^2 = 1$

In the simulation settings described above, the PC test turns out to be rather conservative, whereas the BC$_a$test is mostly liberal, and sometimes conservative. A stronger trimming improves the PC test in case (b), whereas in case (c) it becomes even more conservative. The BC$_a$test is in most cases improved under a stronger trimming, and its overall performance is better than that of the PC test.

5.1.2 *Test of the classical null hypothesis H_0 in (5.1)*

This test was investigated with respect to maintaining the nominal level for a small selection of Lehmann's alternatives in two Weibull distributions $W(\theta_1, \theta_2)$. For F the parameters $\theta_1 = 0.5$ and $\theta_2 = 1.2, 0.6$ were chosen, and for G the parameters $\theta_1 = 1.5$ and $\theta_2 = 1.2, 0.6$. We considered sample sizes $m = n = 100, 200$ and trimming bounds $[a, b] = [0.05, 0.95], [0.1, 0.9]$. For each setting, 1000 simulations with $B = 1000$ bootstrap replications were performed.

The Figures 1 to 3 show the simulated levels of the test for the different settings, in dependence of the bootstrap sample size m^*, for the nominal levels $\alpha = 0.05, 0.1$. The curves are mostly antitonic, which was also seen in further simulation studies on other models. For this test a stronger trimming on both sides ($a = 0.1,\ b = 0.9$) yields better results, since in that case the test keeps its nominal level for almost all values of m^*. For an underlying sample size of $m = 100$ and stronger trimming, suitable values for m^* seem to be around $m^* = 10$.

However, the choice of the bootstrap sample size given as $m^* = m$ was found numerically to almost always keep the nominal level. Thus, we suggest using this for practical applications.

Figure 1: Test of H_0 for $\mathcal{F}_{Leh}$: $F = W(0.5, 1.2)$, $G = W(1.5, 1.2)$, $m = 100$.

Figure 2: Test of H_0 for $\mathcal{F}_{Leh}$: $F = W(0.5, 1.2)$, $G = W(1.5, 1.2)$, $m = 200$.

Figure 3: Test of H_0 for $\mathcal{F}_{Leh}$: $F = W(0.5, 0.6)$, $G = W(1.5, 0.6)$, $m = 100$.

6 A data example

In order to illustrate the methods described above, we present an example from the COMPASS clinical trial on the thrombolytic therapy of acute myocardial infarction [49]. Here a new thrombolytic agent, saruplase, was compared with the (former) standard therapy streptokinase. The aim of the study was to show that saruplase is not relevantly inferior to streptokinase with respect to the 30-day mortality rate (*noninferiority trial*; cf. e.g. [20], or [13, 14, 28]). Noninferiority was then assessed with help of the odds ratio of the 30-day mortality rates in the two groups, which were found to be 5.7% with saruplase and 6.7% with streptokinase (odds ratio 0.84, p<0.01 for noninferiority). However, it would be more reliable if the entire estimated survival curves during the first 30 days would be taken into account instead of the single values at 30 days.

If it was known, in addition, that the hazard functions of the two treatment groups are proportional, i.e. (1.8) holds, an assessment on the mortality rate as a function of survival time could be performed with help of an estimate of the proportionality factor θ from (1.8) (cf. e.g. [10]). Likewise, under the assumption of accelerated failure times between the two groups (cf. Example 1.1), noninferiority could be assessed with help of an estimate of the acceleration constant σ. Hence, our aim is to investigate now whether one of these models is appropriate.

In Figure 4 the Kaplan-Meier estimates of the survival functions are displayed for the two treatments throughout the whole follow-up period of 1 year. In Figure 5 the estimated hazard functions are displayed for the two treatment groups from this trial. (The two curves were obtained with help of the kernel estimator presented in [34], using a fixed bandwidth of 55.) The corresponding estimated hazard ratio curve is displayed in Figure 6. Note that for these data the proportional hazards (ph) model seems not to be appropriate for the period of 1 year.

Figure 4: Estimated survival functions for saruplase (—) and streptokinase (– –) from the COMPASS trial.

Figure 5: Estimated hazard functions for saruplase (—) and streptokinase (– –) from the COMPASS trial (bandwidth=55).

Figure 6: Estimated hazard ratio curve from the COMPASS trial. The dashed line marks the estimated constant hazard ratio ($\hat{\delta}_{hr} = 1.02$) obtained from the ph model.

However, we will now focus on a comparison of the two curves only over the period of the first 30 days as it was the initial goal of the COMPASS trial. Note that, since our model validation method relies on the comparison of quantile functions, we have to specify an according range of quantiles (the trimming interval $[a, b]$) for which we want to assess the fit of the model. From previous information on the standard treatment streptokinase it was known that the 30 days mortality rate is about 0.067. Therefore, we choose three different right trimming bounds near that estimate, i.e. $b = 0.05,\ 0.06,\ 0.07$. Further, in order to assess the effect of trimming on the left side, we compare three different values of that boundary, i.e. $a = 0,\ 0.001,\ 0.005$. We compare the fit of two different models, i.e. that of the acceleration model and that of the ph model.

Figures 7 and 8 show the p-value curves for the PC and the BC$_a$test of the acceleration model and of the ph model, respectively. Note that an upper $(1-\alpha)$-confidence bound for the 'distance to the model', $\tilde{d}$, can be read off as the cut-point of the p-value curve with the line $p = \alpha$. This corresponds to the smallest value of Δ_0 for which the test of H_Δ would yield a significant result.

Figure 7: P-value curves for PC and BC$_a$tests of the acceleration model for the COMPASS data (a=0.00).

Figure 8: P-value curves for PC and BC$_a$tests of the ph model for the COMPASS data (a=0.00).

In agreement with the simulation results from section 5, the BC$_a$test yields smaller upper confidence bounds for $\tilde{d}$. However, the comparison of the two models gives the same results with both bootstrap methods. Here we show only the results for $a = 0$, since slight trimming on the left side does not show a noticeable effect. On the other hand, the choice of the trimming bound b does have a strong impact on the resulting p-value curves, as was to be expected from Figures 4 to 6. When using $b = 0.05$, the acceleration model produces a better fit than the ph model, whereas for $b = 0.06$ or 0.07 the ph model seems to be better. Overall, less trimming on the right tail results in larger upper confidence bounds $\tilde{d}$, and for $b = 0.07$ both models yield already a very bad fit. In addition, when applying the tests of the corresponding null hypotheses H_0, highly significant results (p<0.001) are obtained for each choice of the trimming bounds, which underlines the rather bad fit of both models to the data even for short time periods of about 30 days.

In summary, for this data example we do not get clear evidence in favour of one of the models under investigation. Rather it seems to be worthwhile to apply purely nonparametric methods for the comparison of the whole survivor curves in this case.

7 Remarks and extensions

The findings of this paper for two independent samples can be generalized to the k-sample case with distributions $F_i,\ i = 1, ..., k$, as follows. For checking whether all pairs (F_i, F_j) belong to the model $\mathcal{U}$, the distance $d(F, G; \mathcal{U})$ can be replaced by the 'sum' of pairwise distances,

$$d(F_1, ..., F_k; \mathcal{U}) := \left\{ \frac{1}{k(k-1)} \sum_{i,j=1, i\neq j}^{k} d^2(F_i, F_j; \mathcal{U}) \right\}^{\frac{1}{2}}.$$

Thus, the asymptotic properties of $d(F_1, ..., F_k; \mathcal{U})$ can be immediately derived from those of the $d(F_i, F_j; \mathcal{U})$. Observe that this distance is symmetric with respect to the ordering of the $F_1, ..., F_k$.

The case of multivariate outcomes with marginals $F_1, ..., F_k$ can be treated in a similar way. Here results on the weak convergence of the multivariate empirical process have to be combined with those on the Hadamard differentiability on $\mathbf{D}[0, 1]^k$ (cf. [43]).

Further, our results can readily be extended to the case of independent randomly right censored data. This follows immediately from the Hadamard differentiability results obtained above and from the weak convergence of the corresponding product limit processes and from the validity of the bootstrap approximation of these processes (cf. e.g. [3]).

8 Appendix

8.1 Proofs of the results in section 3

Proof of Theorem 3.1:

We will investigate the functional T from (3.4) by viewing it as the composition of several partial mappings and handling these separately.

$$\begin{aligned}(F,G) &\xrightarrow{\psi_1} (\tilde F,\tilde G) \xrightarrow{\psi_2} \Big(\tilde F,\tilde G,\theta(\tilde F,\tilde G)\Big) \\ &\xrightarrow{\psi_3} \frac{1}{b-a}\int_a^b \Big\{F^{-1}(u)-\phi_1\Big(G^{-1}\big(\phi_2(u,\theta(\tilde F,\tilde G))\big),\theta(\tilde F,\tilde G)\Big)\Big\}^2\,du.\end{aligned} \tag{8.1}$$

Under the conditions of the theorem the map ψ_1 is Hadamard differentiable at (F,G) tangentially to $\mathbf{C}^2[\bar{\mathbb{R}}]$ (cf. Lemma 3.9.23 in [50]), with the derivative

$$\psi'_{1(F,G)}(h_1,h_2) = -I_{[p,q]}\left(\frac{h_1\circ F^{-1}}{F'\circ F^{-1}},\frac{h_2\circ G^{-1}}{G'\circ G^{-1}}\right).$$

We will examine the maps ψ_2 and ψ_3 in the following Lemmata 8.1 and 8.2. For the investigation of ψ_2 it is sufficient to consider the component mapping θ.

Lemma 8.1 *Under the conditions of Theorem 3.1 there exist for the local minimizing value* θ_0 *a neighborhood* $\mathbf{U}$ *of* (F,G) *in* $\mathbf{D}[\bar{\mathbb{R}}]\times\mathbf{D}_M[\bar{\mathbb{R}}]$ *and a map* $\theta:\mathbf{D}_{-}[p,q]\times\mathbf{BV}_M[p,q]\to\Theta$ *with* $\theta(\tilde F,\tilde G)=\theta_0$ *and*

$$\Phi_{(S_1^{-1}I_{[p,q]},S_2^{-1}I_{[p,q]})}\Big(\theta(S_1^{-1}I_{[p,q]},S_2^{-1}I_{[p,q]})\Big)=0 \text{ for all } (S_1,S_2)\in\mathbf{U}\cap\big(\mathbf{C}[\bar{\mathbb{R}}]\times\mathbf{D}_{M,C}[\bar{\mathbb{R}}]\big),$$

where the map $\Phi_{(S_1^{-1}I_{[p,q]},S_2^{-1}I_{[p,q]})}$ *is given by (3.2), such that* θ *is Hadamard differentiable at* $(\tilde F,\tilde G)$ *tangentially to* $\mathbf{C}^2[p,q]$*, with the derivative*

$$\begin{aligned}&\theta'_{(\tilde F,\tilde G)}(h_1,h_2) \\ =\;& A_{\theta_0}^{-1}\Bigg\{\int_{l(\theta_0)}^{u(\theta_0)}\Big[h_1\big(\phi_2^-(v,\theta_0)\big)-D_1\phi_1\big(\tilde G(v),\theta_0\big)h_2(v)\Big]D_1\phi_1\big(\tilde G(v),\theta_0\big)\,\beta(v,\theta_0)\,d\tilde G(v) \\ &+\int_{l(\theta_0)}^{u(\theta_0)}\Big[\tilde F\big(\phi_2^-(v,\theta_0)\big)-\phi_1\big(\tilde G(v),\theta_0\big)\Big]D_{11}\phi_1\big(\tilde G(v),\theta_0\big)h_2(v)\beta(v,\theta_0)\,d\tilde G(v) \\ &+\int_{l(\theta_0)}^{u(\theta_0)}\Big[\tilde F\big(\phi_2^-(v,\theta_0)\big)-\phi_1\big(\tilde G(v),\theta_0\big)\Big]D_1\phi_1\big(\tilde G(v),\theta_0\big)\beta(v,\theta_0)\,dh_2(v) \\ &+\int_{l(\theta_0)}^{u(\theta_0)}\Big[h_1\big(\phi_2^-(v,\theta_0)\big)-D_1\phi_1\big(\tilde G(v),\theta_0\big)h_2(v)\Big]D_2\phi_1\big(\tilde G(v),\theta_0\big)\tilde\beta(v,\theta_0)\,dv \\ &+\int_{l(\theta_0)}^{u(\theta_0)}\Big[\tilde F\big(\phi_2^-(v,\theta_0)\big)-\phi_1\big(\tilde G(v),\theta_0\big)\Big]D_{12}\phi_1\big(\tilde G(v),\theta_0\big)h_2(v)\tilde\beta(v,\theta_0)\,dv\Bigg\}.\end{aligned} \tag{8.2}$$

Note that the above expression is defined via partial integration, if the function h_2 *is not of finite variation.*

Proof of Lemma 8.1:

The (yet unknown) map θ can be formally written as a composition of two functionals, where we restrict ourselves for the moment to continuous arguments,

$$\begin{aligned} \theta: \quad & \mathbf{C}[p,q] \times \mathbf{BV}_{M,C}[p,q] \to \Theta, & \theta(S_1,S_2) &= \phi_4 \circ \phi_3(S_1,S_2), \\ \phi_3: \quad & \mathbf{C}[p,q] \times \mathbf{BV}_{M,C}[p,q] \to \mathbf{C}^l[\Theta], & \phi_3(S_1,S_2)(\cdot) &= \Phi_{(S_1,S_2)}(\cdot), \\ \phi_4: \quad & \mathbf{C}^l[\Theta] \to \Theta, & \phi_4(S) &= Z(S). \end{aligned} \tag{8.3}$$

Here $Z : \mathbf{C}^l[\Theta] \to \Theta$ with $f(Z(f)) = 0,\ f \in \mathbf{V}$, denotes a Z-functional, where $\mathbf{V}$ is a certain neighborhood of Φ from (3.1), and we have $Z\big(\phi_3(\tilde{F},\tilde{G})\big) = \theta_0$. The existence of this functional will be ascertained below with help of Theorem 1.4.2 in [45] (cf. the investigation of the map ϕ_4 further on). First, however, we will consider the map ϕ_3.

(i) Investigation of the map ϕ_3:

We shall in the following show that the map ϕ_3 is Hadamard differentiable at $(\tilde{F},\tilde{G})$ tangentially to $\mathbf{C}^2[p,q]$. According to (3.2), ϕ_3 is given by

$$\begin{aligned} \phi_3(S_1,S_2)(\cdot) &= -\int_{l(\cdot)}^{u(\cdot)} S_1\big(\phi_2^-(v,\cdot)\big) D_1\phi_1\big(S_2(v),\cdot\big)\beta(v,\cdot)dS_2(v) \\ &\quad + \int_{l(\cdot)}^{u(\cdot)} \phi_1\big(S_2(v),\cdot\big) D_1\phi_1\big(S_2(v),\cdot\big)\beta(v,\cdot)dS_2(v) \\ &\quad - \int_{l(\cdot)}^{u(\cdot)} \Big\{ S_1\big(\phi_2^-(v,\cdot)\big) - \phi_1\big(S_2(v),\cdot\big)\Big\} D_2\phi_1\big(S_2(v),\cdot\big)\tilde{\beta}(v,\cdot)dv \\ &=: I_1(S_1,S_2)(\cdot) + I_2(S_2)(\cdot) + I_3(S_1,S_2)(\cdot). \end{aligned} \tag{8.4}$$

Analogous to the function spaces defined in section 3, we will consider the space $\mathbf{C}^l\big[[p,q]\times\Theta\big]$ of bounded and continuous, $\mathbb{R}^l$-valued functions on $[p,q]\times\Theta$, equipped with the supremum norm, denoted by $\|f\|_{\infty,\infty} := \sup_{v\in[p,q],\,\theta\in\Theta} \big|f(v,\theta)\big|_l$, where $|x|_l := \max\{|x_i| : i = 1,...,l\}$ for $x \in \mathbb{R}^l$. The map $I_1 : \mathbf{C}[p,q] \times \mathbf{BV}_{M,C}[p,q] \to \mathbf{C}^l[\Theta]$ from (8.4) is decomposed into the following maps,

$$(S_1,S_2) \longrightarrow (\gamma\circ S_1, S_2) \longrightarrow (\gamma\circ S_1, \eta\circ S_2, S_2) \longrightarrow \int_{l(\cdot)}^{u(\cdot)} \gamma\circ S_1(v,\cdot)\, \eta\circ S_2(v,\cdot)\, dS_2(v),$$

where

$$\begin{aligned} \gamma: \quad & \mathbf{C}[p,q] \to \mathbf{C}\big[[p,q]\times\Theta\big], & \gamma(S)(v,\theta) &:= -S\circ\phi_2^-(v,\theta); \\ \eta: \quad & \mathbf{BV}_{M,C}[p,q] \to \mathbf{C}^l\big[[p,q]\times\Theta\big], & \eta(S)(v,\theta) &:= D_1\phi_1\big(S(v),\theta\big)\,\beta(v,\theta). \end{aligned}$$

We shall show first the Fréchet differentiability of γ and η, then we will investigate the integral operator. The map γ is linear and continuous, hence it is Fréchet differentiable at $S = \tilde{F}$, with the derivative $\gamma'_{\tilde{F}}(h_1) = -h_1 \circ \phi_2^-$. For the investigation of η it is sufficient to consider the map

$$\kappa : \mathbf{BV}_{M,C}[p,q] \to \mathbf{C}\big[[p,q] \times \Theta\big], \quad \kappa(S)(v,\theta) = D_1\phi_1\big(S(v),\theta\big),$$

since β is simply a fixed, bounded factor in $\mathbf{C}^l\big[[p,q]\times\Theta\big]$ according to the assumptions of Theorem 3.1. The derivative of κ at $S = \tilde{G}$ is given by

$$\kappa'_{\tilde{G}}(h_2)(v,\theta) = D_{11}\phi_1\big(\tilde{G}(v),\theta\big)\, h_2(v).$$

To verify the differentiability of κ, note that

$$\begin{aligned}
&\big\|\kappa(\tilde{G}+h_2) - \kappa(\tilde{G}) - \kappa'_{\tilde{G}}(h_2)\big\|_{\infty,\infty} \\
&= \sup_{v\in[p,q],\theta\in\Theta} \Big| D_1\phi_1\big(\tilde{G}(v)+h_2(v),\theta\big) - D_1\phi_1\big(\tilde{G}(v),\theta\big) - D_{11}\phi_1\big(\tilde{G}(v),\theta\big)\, h_2(v)\Big| \\
&= \sup_{v\in[p,q],\theta\in\Theta} \Big| D_{11}\phi_1\big(\tilde{G}(v)+\xi(v,\theta)h_2(v),\theta\big)h_2(v) - D_{11}\phi_1\big(\tilde{G}(v),\theta\big)\, h_2(v)\Big| \\
&\le \sup_{v\in[p,q],\theta\in\Theta} \Big| D_{11}\phi_1\big(\tilde{G}(v)+\xi(v,\theta)h_2(v),\theta\big) - D_{11}\phi_1\big(\tilde{G}(v),\theta\big)\Big|\, \|h_2\|_\infty \\
&= o(1)\, O(\|h_2\|_\infty) = o(\|h_2\|_\infty), \qquad \|h_2\|_\infty \to 0,
\end{aligned}$$

using assumption (1) from Theorem 3.1. In the second equality we applied the mean value theorem ($0 \le \xi(v,\theta) \le 1,\ v \in [p,q], \theta \in \Theta$).

Now we consider the integral operator

$$I : \mathbf{C}^l\big[[p,q]\times\Theta\big] \times \mathbf{BV}_{M,C}[p,q] \to \mathbf{C}^l[\Theta], \quad I(S_1,S_2)(\cdot) = \int_{l(\cdot)}^{u(\cdot)} S_1(v,\cdot)\, dS_2(v). \qquad (8.5)$$

Under the assumptions of Theorem 3.1, the integrands of the maps I_1 and I_2 in (8.4) are each of bounded total variation at $(S_1,S_2) = (\tilde{F},\tilde{G})$ and $S_2 = \tilde{G}$, respectively; without loss of generality they are bounded by M from Theorem 3.1. In the following we will show the map I in (8.5) to be Hadamard differentiable tangentially to $\mathbf{C}^l\big[[p,q]\times\Theta\big] \times \mathbf{C}[p,q]$ at each $(S_1,S_2) \in \mathbf{C}^l\big[[p,q]\times\Theta\big] \times \mathbf{BV}_{M,C}[p,q]$, for which $\big|\int_p^q |dS_1(v,\theta)|\,\big|_l < M,\ \theta\in\Theta$, holds. The derivative is given by

$$I'_{(S_1,S_2)}(h_1,h_2)(\cdot) = \int_{l(\cdot)}^{u(\cdot)} h_1(v,\cdot)\, dS_2(v) + \int_{l(\cdot)}^{u(\cdot)} S_1(v,\cdot)\, dh_2(v),$$

where the right-hand side is defined by partial integration in case h_2 is not of bounded variation. To this end we define sequences $\{t_n\} \subset \mathbb{R}^+$, $\{h_{1n}\} \subset \mathbf{C}^l\big[[p,q]\times\Theta\big]$, and $\{h_{2n}\} \subset \mathbf{BV}_{M,C}[p,q]$, where $t_n \to 0$, $h_{1n} \to h_1 \in \mathbf{C}^l\big[[p,q]\times\Theta\big]$, $h_{2n} \to h_2 \in \mathbf{C}[p,q]$ for $n\to\infty$, and $S_{kn} = S_k + t_n h_{kn}$, $k=1,2$, for which $(S_{1n}, S_{2n}) \in \mathbf{C}^l\big[[p,q]\times\Theta\big] \times \mathbf{BV}_{M,C}[p,q]$ holds. Then we have to show that

$$R_n := \frac{I(S_{1n},S_{2n}) - I(S_1,S_2)}{t_n} - I'_{(S_1,S_2)}(h_{1n},h_{2n}) \underset{n\to\infty}{\longrightarrow} 0\,.$$

First, we obtain with the triangle inequality,

$$\begin{aligned}
\|R_n\|_\infty &= \sup_{\theta\in\Theta}\Big|\int_{l(\theta)}^{u(\theta)} h_{1n}(v,\theta) t_n dh_{2n}(v)\Big|_l \\
&\le \sup_{\theta\in\Theta}\Big|\int_{l(\theta)}^{u(\theta)} h_1(v,\theta)\big(dS_{2n}(v)-dS_2(v)\big)\Big|_l \\
&+ \sup_{\theta\in\Theta}\Big|\int_{l(\theta)}^{u(\theta)}\big(h_{1n}(v,\theta)-h_1(v,\theta)\big)\big(dS_{2n}(v)-dS_2(v)\big)\Big|_l\,.
\end{aligned} \tag{8.6}$$

For the second term in (8.6) we get

$$\sup_{\theta\in\Theta}\Big|\int_{l(\theta)}^{u(\theta)}\big(h_{1n}(v,\theta)-h_1(v,\theta)\big)\big(dS_{2n}(v)-dS_2(v)\big)\Big|_l \le 2M\sup_{\theta\in\Theta}\big\|h_{1n}-h_1\big\|_{\infty,\infty} \underset{n\to\infty}{\longrightarrow} 0.$$

For the first term of the right-hand side of (8.6) we show the convergence to zero for each coordinate of this vector. Since we have $h_1 \in \mathbf{C}^l\big[[p,q]\times\Theta\big]$, it follows for the ith coordinate that $h_{1_i} \in \mathbf{C}\big[[p,q]\times\Theta\big]$. For this continuous function on $\mathbb{R}^{l+1}$, there is for each $\varepsilon>0$ a simple function $h^\varepsilon_{1_i}$ of the form $h^\varepsilon_{1_i}(\cdot,\cdot) = \sum_{j=1}^{N_\varepsilon}\alpha_j I_{R_j}(\cdot,\cdot)$, where N_ε is a positive integer, the R_j are rectangles in $\mathbb{R}^{l+1}$, and the $\alpha_j\in\mathbb{R}$, such that $\|h_{1_i} - h^\varepsilon_{1_i}\|_{\infty,\infty}\le\varepsilon$ holds (cf. [36], p. 1288). We obtain

$$\begin{aligned}
&\sup_{\theta\in\Theta}\Big|\int_{l(\theta)}^{u(\theta)} h_{1_i}(v,\theta)\big(dS_{2n}(v)-dS_2(v)\big)\Big| \\
\le\ &\sup_{\theta\in\Theta}\Big|\int_{l(\theta)}^{u(\theta)}\big(h_{1_i}(v,\theta)-h^\varepsilon_{1_i}(v,\theta)\big)\big(dS_{2n}(v)-dS_2(v)\big)\Big| \\
&+\sup_{\theta\in\Theta}\Big|\int_{l(\theta)}^{u(\theta)} h^\varepsilon_{1_i}(v,\theta)\big(dS_{2n}(v)-dS_2(v)\big)\Big| \\
\le\ &\Big\|h_{1_i}(v,\theta)-h^\varepsilon_{1_i}(v,\theta)\Big\|_{\infty,\infty}\bigg(\int_p^q|dS_{2n}(v)|+\int_p^q|dS_2(v)|\bigg) \\
&+\sup_{\theta\in\Theta}\Big[2\|h^\varepsilon_{1i}(\cdot,\theta)\|_\infty\|S_{2n}-S_2\|_\infty + \|S_{2n}-S_2\|_\infty\int_p^q|\,dh^\varepsilon_{1i}(v,\theta)|\Big] \\
\le\ &2\,\varepsilon M + 4\,N_\varepsilon\max_{1\le j\le N_\varepsilon}\big|\alpha_j\big|\big\|S_{2n}-S_2\big\|_\infty \underset{n\to\infty}{\longrightarrow} 2\,\varepsilon M.
\end{aligned}$$

Since ε can be chosen arbitrarily small, the convergence to zero of the left-hand side follows for $n\to\infty$. (For similar proofs for the differentiability of integral operators cf. also [43], [25] and [50].)

Now, the map I_2 from (8.4) can be treated analogously to I_1. These 2 maps differ only in the first factor of the integrand, and that of I_2 can obviously be handled in the same way as the above map η. For the map I_3 we are left to investigate the factor $D_2\phi_1(S_2(t),\cdot)$. This can be done similarly to the proof of the differentiability of η (because of assumption (1) from Theorem 3.1).

Overall, this yields the Hadamard derivative of ϕ_3 at $(\tilde{F},\tilde{G})$ as

$$\begin{aligned}
&\phi'_{3(\tilde{F},\tilde{G})}(h_1,h_2)\\
&= \int_{l(\cdot)}^{u(\cdot)} \Big[D_1\phi_1\big(\tilde{G}(v),\cdot\big)h_2(v) - h_1\big(\phi_2^-(v,\cdot)\big)\Big] D_1\phi_1\big(\tilde{G}(v),\cdot\big)\,\beta(v,\cdot)\,d\tilde{G}(v)\\
&+ \int_{l(\cdot)}^{u(\cdot)} \Big[\phi_1\big(\tilde{G}(v),\cdot\big) - \tilde{F}\big(\phi_2^-(v,\cdot)\big)\Big] D_{11}\phi_1\big(\tilde{G}(v),\cdot\big)h_2(v)\beta(v,\cdot)\,d\tilde{G}(v)\\
&+ \int_{l(\cdot)}^{u(\cdot)} \Big[\phi_1\big(\tilde{G}(v),\cdot\big) - \tilde{F}\big(\phi_2^-(v,\cdot)\big)\Big] D_1\phi_1\big(\tilde{G}(v),\cdot\big)\beta(v,\cdot)\,dh_2(v)\\
&+ \int_{l(\cdot)}^{u(\cdot)} \Big[D_1\phi_1\big(\tilde{G}(v),\cdot\big)h_2(v) - h_1\big(\phi_2^-(v,\cdot)\big)\Big] D_2\phi_1\big(\tilde{G}(v),\cdot\big)\tilde{\beta}(v,\cdot)\,dv\\
&+ \int_{l(\cdot)}^{u(\cdot)} \Big[\phi_1\big(\tilde{G}(v),\cdot\big) - \tilde{F}\big(\phi_2^-(v,\cdot)\big)\Big] D_{12}\phi_1\big(\tilde{G}(v),\cdot\big)h_2(v)\tilde{\beta}(v,\cdot)\,dv.
\end{aligned}$$

Again, if h_2 is not of bounded variation, then the last expression is defined via partial integration.

(ii) Investigation of the map ϕ_4 from (8.3):

For the map ϕ_4 in (8.3) we can apply the Theorem 1.4.2 from [45]. The criterion function Φ (cf. (3.1)) can be written with help of the map ϕ_3 from (8.4),

$$\Phi:\Theta\to\mathbb{R}^l,\quad \Phi(\theta) = \phi_3\big(\tilde{F},\tilde{G}\big)(\theta).$$

Under the assumptions of Theorem 3.1 we have $\Phi\in\mathbf{C}^l[\Theta]$. From the Theorem of Rieder we get for maps from $\mathbf{C}^l[\Theta]$ in a neighborhood $\mathbf{V}$ of Φ a functional Z with $Z(\Phi)=\theta_0$ and $f(Z(f))=0$ for $f\in\mathbf{V}$. This functional Z is Hadamard differentiable at Φ tangentially to $\mathbf{C}^l[\Theta]$, with the derivative

$$Z'_\Phi(h) = -A_{\theta_0}^{-1}h(\theta_0),\quad h\in\mathbf{C}^l[\Theta],$$

where A_{θ_0} is given by inserting $\theta=\theta_0$ into A_θ from (3.3). Because of the Hadamard differentiability (and thus continuity) of the map ϕ_3, there is a neighborhood $\mathbf{U}'\subset\mathbf{C}[p,q]\times\mathbf{BV}_{M,C}[p,q]$ of $(\tilde{F},\tilde{G})$, such that $\Phi_{(S_1,S_2)}=\phi_3(S_1,S_2)\in\mathbf{V}$ for all $(S_1,S_2)\in\mathbf{U}'$. For these $(S_1,S_2)\in\mathbf{U}'$, let the map θ be defined as $\theta(S_1,S_2):=Z(\Phi_{(S_1,S_2)})$. Thus, θ is Hadamard differentiable at $(\tilde{F},\tilde{G})$

tangentially to $\mathbf{C}^2[p,q]$, with the derivative

$$\theta'_{(\tilde{F},\tilde{G})}(h_1,h_2) = \phi'_{4_{(\phi_3(\tilde{F},\tilde{G}))}} \circ \phi'_{3_{(\tilde{F},\tilde{G})}}(h_1,h_2) = -A_{\theta_0}^{-1} \cdot \left\{ \phi'_{3_{(\tilde{F},\tilde{G})}}(h_1,h_2) \circ \theta(\tilde{F},\tilde{G}) \right\}. \qquad (8.7)$$

Furthermore, it follows from Lemma 1 of [25] that there exists an extension of the map θ onto $\mathbf{D}_{\text{-}}[p,q] \times \mathbf{BV}_M[p,q]$, such that θ is Hadamard differentiable at $(\tilde{F},\tilde{G})$ tangentially to $\mathbf{C}^2[p,q]$, with the derivative (8.7). In order to conclude the proof of Lemma 8.1, define the set

$$\mathbf{U}'' := \Big\{ (f_1,g_1) \in \mathbf{D}_{\text{-}}[p,q] \times \mathbf{BV}_M[p,q] \;\Big|\; \exists (f_2,g_2) \in \mathbf{U}' : \big\|(f_1,g_1) - (\tilde{F},\tilde{G})\big\|_\infty \le \big\|(f_2,g_2) - (\tilde{F},\tilde{G})\big\|_\infty \Big\}.$$

Then, because of the Hadamard differentiability of ψ_1 from (8.1), there is also a neighborhood $\mathbf{U}$ of (F,G) in $\mathbf{D}[\bar{\mathbb{R}}] \times \mathbf{D}_M[\bar{\mathbb{R}}]$, such that $(S_1^{-1}I_{[p,q]}, S_2^{-1}I_{[p,q]}) \in \mathbf{U}''$ for all $(S_1,S_2) \in \mathbf{U}$. Thus, the assertion of Lemma 8.1 is shown. □

For completing the proof of Theorem 3.1 it remains to show the Hadamard differentiability of the map ψ_3 from the composition (8.1) of the functional T.

Lemma 8.2 *Under the conditions of Theorem 3.1, the map $\psi_3 : \mathbf{D}_{\text{-}}^2[p,q] \times \Theta \to \mathbb{R}$,*

$$\psi_3(S_1,S_2,\theta) = \frac{1}{b-a}\int_a^b \Big\{ S_1(u) - \phi_1\big(S_2\big(\phi_2(u,\theta)\big),\theta\big) \Big\}^2 du,$$

is Hadamard differentiable at $(\tilde{F},\tilde{G},\theta_0)$ tangentially to $\mathbf{D}_{\text{-}}[p,q] \times \mathbf{C}[p,q] \times \Theta$, with the derivative

$$\begin{aligned} &\psi'_{3_{(\tilde{F},\tilde{G},\theta_0)}}(h_1,h_2,h_3) \qquad (8.8)\\ &= \frac{2}{b-a}\int_a^b \Big(\tilde{F}(u) - \phi_1\big(\tilde{G}(\phi_2(u,\theta_0)),\theta_0\big)\Big)\Big[h_1(u) - D_2\phi_1\big(\tilde{G}(\phi_2(u,\theta_0)),\theta_0\big)^T h_3 \\ &- \; D_1\phi_1\big(\tilde{F}(\phi_2(u,\theta_0)),\theta_0\big)\Big\{h_2\big(\phi_2(u,\theta)\big) + S_2'\big(\phi_2(u,\theta_0)\big)D_2\phi_2(u,\theta_0)^T h_3\Big\}\Big]du. \end{aligned}$$

Proof of Lemma 8.2:

We split ψ_3 into suitable partial maps as follows,

$$\begin{aligned} (S_1,S_2,\theta) &\xrightarrow{\psi_3^1} (S_1,S_2,\theta,\phi_2(\cdot,\theta)I_{[a,b]}(\cdot)) \xrightarrow{\psi_3^2} (S_1, S_2 \circ [\phi_2(\cdot,\theta)I_{[a,b]}(\cdot)],\theta) \\ &\xrightarrow{\psi_3^3} \big(S_1, \phi_1 \circ (S_2 \circ [\phi_2(\cdot,\theta)I_{[a,b]}(\cdot)],\theta)\big) \\ &\xrightarrow{\psi_3^4} \frac{1}{b-a}\int_a^b \Big\{ S_1(u) - \phi_1\big(S_2\big(\phi_2(u,\theta)\big),\theta\big) \Big\}^2 du. \end{aligned}$$

The maps $\psi_3^1, \psi_3^3, \psi_3^4$ can even be shown to be Fréchet differentiable, along similar lines as in the treatment of the map κ in the proof of Lemma 8.1. For the investigation of the map ψ_3^2, we define the set

$$\mathcal{T} := \big\{ f \mid f : [a,b] \to [p,q], f(\cdot) \text{ continuous} \big\}$$

and the map

$$\tilde{\phi}_2 : \mathbf{D}_{\_}[p,q] \times \mathcal{T} \to \mathbf{D}_{\_}[p,q], \qquad \tilde{\phi}_2(S_1, S_2) := S_1 \circ S_2.$$

In the following we will show that ϕ_2 is Hadamard differentiable at $\big(\tilde{G}, \phi_2(\cdot,\theta_0) I_{[a,b]}(\cdot)\big)$ tangentially to $\mathbf{C}[p,q] \times \mathcal{T}$.

Under the assumptions for G, the inverse $\tilde{G} =: S_1$ is continuously differentiable on the interval $[p,q]$. Further, for $S_2(\cdot) := \phi_2(\cdot,\theta_0) I_{[a,b]}(\cdot)$ we have under the assumptions for ϕ_2, that $S_2 \in \mathcal{T}$ holds. The Gateaux derivative of $\tilde{\phi}_2$ at (S_1, S_2) is given by

$$\tilde{\phi}'_{2_{(S_1,S_2)}}(h_1, h_2) = (S_1' \circ S_2)\, h_2 + h_1 \circ S_2.$$

Now we have to show that for each real $t_n \to 0$ and for each sequence (h_{1_n}, h_{2_n}) in $\mathbf{D}_{\_}[p,q] \times \mathcal{T}$ with $(h_{1_n}, h_{2_n}) \stackrel{\|\cdot\|_\infty}{\longrightarrow} (h_1, h_2) \in \mathbf{C}[p,q] \times \mathcal{T}$, $n \to \infty$, and $S_2 + t_n h_{2_n} \in \mathcal{T},\ \forall n$, it holds that

$$\frac{\tilde{\phi}_2((S_1,S_2) + t_n(h_{1_n}, h_{2_n})) - \tilde{\phi}_2(S_1,S_2)}{t_n} \underset{n\to\infty}{\longrightarrow} (S_1' \circ S_2)\, h_2 + h_1 \circ S_2. \tag{8.9}$$

For the left-hand side of (8.9) we obtain

$$\begin{aligned}
&\frac{\tilde{\phi}_2((S_1,S_2) + t_n(h_{1_n}, h_{2_n})) - \tilde{\phi}_2(S_1,S_2)}{t_n} \\
&= \frac{S_1 \circ (S_2 + t_n h_{2_n}) - S_1 \circ S_2}{t_n} + h_{1_n} \circ (S_2 + t_n h_{2_n}) \\
&= (S_1' \circ \xi_n)\, h_{2_n} + h_{1_n} \circ (S_2 + t_n h_{2_n}),
\end{aligned}$$

where ξ_n is a function in $\mathcal{T}$ with $S_2(u) \le \xi_n(u) \le S_2(u) + t_n h_{2_n}(u)$, $u \in [a,b]$. Thus we have $\xi_n \stackrel{\|\cdot\|_\infty}{\longrightarrow} S_2$. According to the assumptions, the function S_1' is continuous and thus uniformly continuous on $[p,q]$, thus we have

$$S_1' \circ \xi_n \stackrel{\|\cdot\|_\infty}{\longrightarrow} S_1' \circ S_2, \quad n \to \infty.$$

Since $h_1 \in \mathbf{C}[p,q]$, the function h_1 is uniformly continuous on $[p,q]$. We obtain

$$\|h_{1_n} \circ (S_2 + t_n h_{2_n}) - h_1 \circ S_2\|_\infty$$

$$\leq \|h_{1_n} \circ (S_2 + t_n h_{2_n}) - h_1 \circ (S_2 + t_n h_{2_n})\|_\infty + \|h_1 \circ (S_2 + t_n h_{2_n}) - h_1 \circ S_2\|_\infty$$
$$= \|h_{1_n} - h_1\|_\infty + \sup_{u \in [a,b]} \left| h_1(S_2(u) + t_n h_{2_n}(u)) - h_1(S_2(u)) \right| \underset{n\to\infty}{\longrightarrow} 0,$$

using the properties of the sequence (h_{1_n}, h_{2_n}).

With help of the chain rule for Hadamard differentiability we get the expression (8.8) for the Hadamard derivative of ψ_3, thus Lemma 8.2 is proved. □

Now we return to the proof of Theorem 3.1. Overall we can conclude the Hadamard differentiability of the map T given by (3.4), with θ from Lemma 8.1, at (F, G) tangentially to **C**$^2[\bar{\mathbb{R}}]$. Using the decomposition (8.1), the Hadamard derivative of T at (F, G) can be calculated as

$$T'_{(F,G)}(h_1, h_2) = \psi'_{3\left(\psi_2 \circ \psi_{1(F,G)}\right)} \circ \psi'_{2(\psi_{1(F,G)})} \circ \psi'_{1(F,G)}(h_1, h_2),$$

thus yielding the expression (3.5) and completing the proof of Theorem 3.1. □

Proof of Theorem 3.4:

With the component maps ψ_2 and ψ_3 of T (cf. (8.1)) we have $\tilde{T} = \psi_3 \circ \psi_2$ (cf. (3.6)). Thus, under the assumptions of the theorem and using the results from the proof of Theorem 3.1 we get immediately the Hadamard differentiability of $\tilde{T}$ tangentially to **C**$^2[p, q]$. However, because of the condition $(F, G) \in \mathcal{U}$, the derivative of $\tilde{T}$ vanishes at $(\tilde{F}, \tilde{G})$, i.e. $\tilde{T}'_{(\tilde{F},\tilde{G})} \equiv 0$. We use the notations $\tilde{F}_n := \tilde{F} + t_n h_{1n}$, $\tilde{G}_n := \tilde{G} + t_n h_{2n}$, $\theta_n := \theta(\tilde{F}_n, \tilde{G}_n)$, and $c := \frac{1}{b-a}$. For the left-hand side of (3.7) in the definition of quadratic Hadamard differentiability we obtain

$$\frac{\tilde{T}(\tilde{F}_n, \tilde{G}_n) - \tilde{T}(\tilde{F}, \tilde{G}) - \tilde{T}^{(2)}_{(\tilde{F},\tilde{G})}(t_n(h_{1n}, h_{2n}))}{t_n^2} \tag{8.10}$$
$$= \frac{c}{t_n^2} \int_a^b \Bigg[\Bigg(\tilde{F}(u) + t_n h_{1n}(u) - \phi_1 \left(\tilde{G}(\phi_2(u, \theta_n)) + t_n h_{2n}(\phi_2(u, \theta_n)), \theta_n \right) \Bigg)^2$$
$$- \Bigg(t_n h_{1n}(u) - D_2\phi_1(\tilde{G}(\phi_2(u, \theta_0)), \theta_0)\theta'_{(\tilde{F},\tilde{G})}(t_n(h_{1n}, h_{2n}))$$
$$- D_1\phi_1(\tilde{G}(\phi_2(u, \theta_0)), \theta_0) \Big\{ t_n h_{2n}(\phi_2(u, \theta_0))$$
$$+ \tilde{G}'(\phi_2(u, \theta_0)) D_2\phi_2(u, \theta_0)\theta'_{(\tilde{F},\tilde{G})}(t_n(h_{1n}, h_{2n})) \Big\} \Bigg)^2 \Bigg] du.$$

Now we shall make use of the Hadamard differentiability at $(\tilde{F}, \tilde{G})$, tangentially to **C**$^2[p, q]$, of the map $H : \mathbf{D}_-^2[p,q] \to \mathbf{D}_-[p,q]$,

$$H(\tilde F,\tilde G)(u) := \phi_1\big(\tilde G(\phi_2(u,\theta(\tilde F,\tilde G))),\theta(\tilde F,\tilde G)\big).$$

This follows from the Hadamard differentiability of the map θ (cf. Lemma 8.1) and from that of the partial maps ψ_3^1 to ψ_3^3 of ψ_3 (cf. Lemma 8.2). The Gateaux derivative of H at $(\tilde F,\tilde G)$ is

$$\begin{aligned} H'_{(\tilde F,\tilde G)}(h_1,h_2)(u) &= D_2\phi_1(\tilde G(\phi_2(u,\theta_0)),\theta_0)\theta'_{(\tilde F,\tilde G)}((h_1,h_2)) \\ &\quad - D_1\phi_1(\tilde G(\phi_2(u,\theta_0)),\theta_0)\Big\{\tilde G'(\phi_2(u,\theta_0))D_2\phi_2(u,\theta_0)\theta'_{(\tilde F,\tilde G)}((h_1,h_2)) + h_2(\phi_2(u,\theta_0))\Big\}. \end{aligned}$$

We denote $H := H(\tilde F,\tilde G)$ and $H_n := H(\tilde F_n,\tilde G_n)$. Thus, we can write the expression (8.10) as

$$\frac{c}{t_n^2}\int_a^b\left[\Big(\tilde F(u) - H_n(u) + t_n h_{1n}(u)\Big)^2 - \Big(t_n h_{1n}(u) - H'_{(\tilde F,\tilde G)}\left(t_n(h_{1n},h_{2n})\right)(u)\Big)^2\right]du.$$

Further calculations yield (using the equality $\tilde F(u) = H(\tilde F,\tilde G)(u)$, since $(F,G)\in\mathcal U$),

$$\begin{aligned} &\frac{c}{t_n^2}\int_a^b\left[\Big(H(u) - H_n(u) + t_n h_{1n}(u)\Big)^2 - \Big(t_n h_{1n}(u) - H'_{(\tilde F,\tilde G)}\left(t_n(h_{1n},h_{2n})\right)(u)\Big)^2\right]du \\ &= \frac{c}{t_n^2}\int_a^b\Bigg[\Big(H(u) - H_n(u)\Big)^2 + 2(H(u)-H_n(u))t_n h_{1n}(u) \\ &\quad -\Big(H'_{(\tilde F,\tilde G)}\left(t_n(h_{1n},h_{2n})\right)(u)\Big)^2 + 2H'_{(\tilde F,\tilde G)}\left(t_n(h_{1n},h_{2n})\right)(u)t_n h_{1n}(u)\Bigg]du \\ &= \frac{c}{t_n^2}\int_a^b\Bigg[2t_n h_{1n}(u)\Big(H(u) - H_n(u) + H'_{(\tilde F,\tilde G)}\left(t_n(h_{1n},h_{2n})\right)(u)\Big) \\ &\quad +\Big(H(u)-H_n(u)-H'_{(\tilde F,\tilde G)}\big(t_n(h_{1n},h_{2n})\big)(u)\Big)\Big(H(u)-H_n(u)+H'_{(\tilde F,\tilde G)}\big(t_n(h_{1n},h_{2n})\big)(u)\Big)\Bigg]du \\ &= \frac{c}{t_n^2}\int_a^b\Bigg[\Big(H(u) - H_n(u) + H'_{(\tilde F,\tilde G)}\left(t_n(h_{1n},h_{2n})\right)(u)\Big) \\ &\qquad \cdot\Big(H(u) - H_n(u) - H'_{(\tilde F,\tilde G)}\left(t_n(h_{1n},h_{2n})\right)(u) + 2t_n h_{1n}(u)\Big)\Bigg]du. \end{aligned}$$

The absolute value of the above expression can be bounded by

$$\begin{aligned} &\frac{c}{t_n^2}\big\|H_n - H - H'_{(\tilde F,\tilde G)}\left(t_n(h_{1n},h_{2n})\right)\big\|_\infty \\ &\cdot\int_a^b\Big[\big|H_n(u)-H(u)-H'_{(\tilde F,\tilde G)}\left(t_n(h_{1n},h_{2n})\right)(u)\big| + 2t_n\big|H'_{(\tilde F,\tilde G)}\left(h_{1n},h_{2n}\right)(u)+h_{1n}(u)\big|\Big]du \\ =\;\; &\frac{c}{t_n^2}\cdot o(t_n)\cdot O(t_n) = o(1), \end{aligned}$$

due to the Hadamard differentiability of H and the boundedness of the second summand in the above integral on $[a, b]$ for $t_n \to 0$. This proves the assertion of the theorem. $\square$

8.2 Proofs of the results in section 4

Proof of Theorem 4.2:

The assertion of the theorem follows from the Hadamard differentiability of the functional T tangentially to $\mathbf{C}^2[\bar{\mathbb{R}}]$ as shown in section 8.1, together with the functional delta method according to theorem 3 in [25]. $\square$

Proof of Theorem 4.3:

A functional delta method based on quadratic Hadamard differentiability as defined in Definition 3.3 can be proved along the lines of the proof of theorem 3 in [25]. Thus, the assertion of the theorem follows together with Theorem 3.4. $\square$

8.3 Proofs of the results in section 5

Proof of Theorem 5.1:

Under the assumptions of the theorem the map $\tilde{T}$ is quadratic Hadamard differentiable at $(\tilde{F}, \tilde{G})$. The assertion of the theorem follows then from a functional delta method for the bootstrap of quadratic Hadamard differentiable functionals which can be stated as follows.

Suppose the map $T : \mathbf{V} \longrightarrow \mathbb{R}$ is measurable and quadratic Hadamard differentiable at F. Let $n, m \in \mathbb{N}$ with $n, m \to \infty$ and $m = o(n)$. Assume further that there are two sequences $\{F_n\}$ and $\{F_m^*\}$ of random elements in $\mathbf{V}$, with

$$\begin{aligned} n^{1/2}(F_n - F) &\overset{\mathcal{D}}{\Longrightarrow} \mathbb{X}, \qquad n \to \infty, \\ m^{1/2}(F_m^* - F_n) &\overset{\mathcal{D}}{\Longrightarrow} \mathbb{X}, \qquad a.s.,\ n, m \to \infty, \end{aligned}$$

where '$a.s.$' stands for 'almost surely, given F_n'. Let $\mathcal{L}(X)$ denote the distribution of a random element $X \in \mathbf{V}$, and $\mathcal{L}^*(X)$ be the conditional distribution of X, given F_n. We write ρ_P for the

Prohorov metric for probability measures. Then we have for $n, m \to \infty$,

$$\rho_P\Big(\mathcal{L}^*[m(T(F_m^*) - T(F_n))], \mathcal{L}[T_F^{(2)}(\mathbb{X})]\Big) \xrightarrow{P} 0. \tag{8.11}$$

We follow the pattern of the proof of theorem 5 in [25]. The theorem of Skorohod, Dudley und Wichura (cf. [48], Corollary 2.3.1) yields a sequence $F_n' \overset{\mathcal{D}}{=} F_n$ with $n^{1/2}(F_n' - F) \xrightarrow{\|\cdot\|_\infty} \mathbb{X}'$ $a.s.$, $n \to \infty$, where $\mathbb{X}' \overset{\mathcal{D}}{=} \mathbb{X}$. For the bootstrap sample or F_m^*, respectively, we get

$$m^{1/2}(F_m^* - F_n') \overset{\mathcal{D}}{\Longrightarrow} \mathbb{X} \quad a.s.,\ n, m \to \infty.$$

A second application of the theorem of Skorohod, Dudley und Wichura permits the construction of a sequence $F_m^{*\prime} \overset{\mathcal{D}}{=} F_m^*$ for the given sequence F_n', with $m^{1/2}(F_m^{*\prime} - F_n') \xrightarrow{\|\cdot\|_\infty} \mathbb{X}^*$ $a.s.,\ n, m \to \infty$, where again we have $\mathbb{X}^* \overset{\mathcal{D}}{=} \mathbb{X}$. Now, since we have chosen $m = o(n)$,

$$\begin{aligned} m^{1/2}(F_m^{*\prime} - F) &= m^{1/2}(F_m^{*\prime} - F_n') + m^{1/2}(F_n' - F) \\ &= m^{1/2}(F_m^{*\prime} - F_n') + \sqrt{\frac{m}{n}}\, n^{1/2}(F_n' - F) \xrightarrow{\|\cdot\|_\infty} \mathbb{X}^* \quad a.s.,\ n, m \to \infty. \end{aligned}$$

Using the quadratic Hadamard differentiability of the functional T, we obtain

$$\begin{aligned} m\,(T(F_m^{*\prime}) - T(F_n')) &= m\,(T(F_m^{*\prime}) - T(F)) - \frac{m}{n}\, n\,(T(F_n') - T(F)) \\ &= T_F^{(2)}(\mathbb{X}^*) + o_P^*(1) \qquad a.s., \quad n, m \to \infty. \end{aligned}$$

For a fixed F_n' we have from $F_m^{*\prime} \overset{\mathcal{D}}{=} F_m^*$ the equality in distribution

$$m\,(T(F_m^{*\prime}) - T(F_n')) \overset{\mathcal{D}}{=} m\,(T(F_m^*) - T(F_n'))\,,$$

such that

$$m\,(T(F_m^*) - T(F_n')) \overset{\mathcal{D}}{\Longrightarrow} T_F^{(2)}(\mathbb{X}) \quad a.s., \quad n, m \to \infty.$$

Thus, with $n, m \to \infty$ we get

$$\rho_P\Big(\mathcal{L}^*[m(T(F_m^*) - T(F_n'))], \mathcal{L}[T_F^{(2)}(\mathbb{X})]\Big) \longrightarrow 0 \quad a.s.$$

The left-hand side is a measurable function of $F_n' \overset{\mathcal{D}}{=} F_n$, thus we obtain the weak consistency (8.11) of the bootstrap as required. □

Proof of Theorem 5.2:

The assertion of the theorem follows from the Theorem 3.1 and the functional delta method for the bootstrap method for Hadamard differentiable functionals according to theorem 5 in [25]. □

Acknowledgements

The authors are indebted to J.-J. Ren for pointing out some references. Support of the Deutsche Forschungsgemeinschaft (TR 471/1, Mu 1230/8-1) is gratefully acknowledged. The authors would like to thank two referees for helpful suggestions leading to an improved version of this manuscript.

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Table 1: Test of H_Δ for $\mathcal{F}_{Leh}$: $\Delta_0^2 = 1$, $\tilde{d}^2 = 1$

True functions F and G	$m = n$	Bootstrap Method	$a = 0.05,\ b = 0.95$		$a = 0.10,\ b = 0.90$	
			α		α	
			0.05	0.10	0.05	0.10
(a)	50	PC	0.023	0.056	0.033	0.067
		BC$_a$	0.071	0.126	0.054	0.109
	100	PC	0.027	0.068	0.035	0.067
$F(t) = 1 - e^{-0.5t}$,		BC$_a$	0.062	0.103	0.045	0.096
$G(t) = 1 - e^{-1.5(t-\delta)}$, $\delta > 0$	200	PC	0.032	0.070	0.023	0.053
		BC$_a$	0.053	0.096	0.038	0.082
(b)	50	PC	0.022	0.047	0.047	0.103
		BC$_a$	0.036	0.063	0.058	0.120
	100	PC	0.030	0.062	0.055	0.093
$F(t) = 1 - e^{-0.5t}$,		BC$_a$	0.045	0.086	0.056	0.106
$G(t) = 1 - e^{-1.5t^{\theta_2}}$, $\theta_2 > 1$	200	PC	0.016	0.042	0.054	0.112
		BC$_a$	0.030	0.059	0.067	0.124
(c)	50	PC	0.048	0.080	0.018	0.030
		BC$_a$	0.116	0.153	0.043	0.077
	100	PC	0.037	0.065	0.008	0.022
$F(t) = 1 - e^{-0.5t}$,		BC$_a$	0.082	0.126	0.042	0.094
$G(t) = 1 - e^{-1.5t^{\theta_2}}$, $\theta_2 < 1$	200	PC	0.033	0.075	0.013	0.028
		BC$_a$	0.080	0.157	0.055	0.093

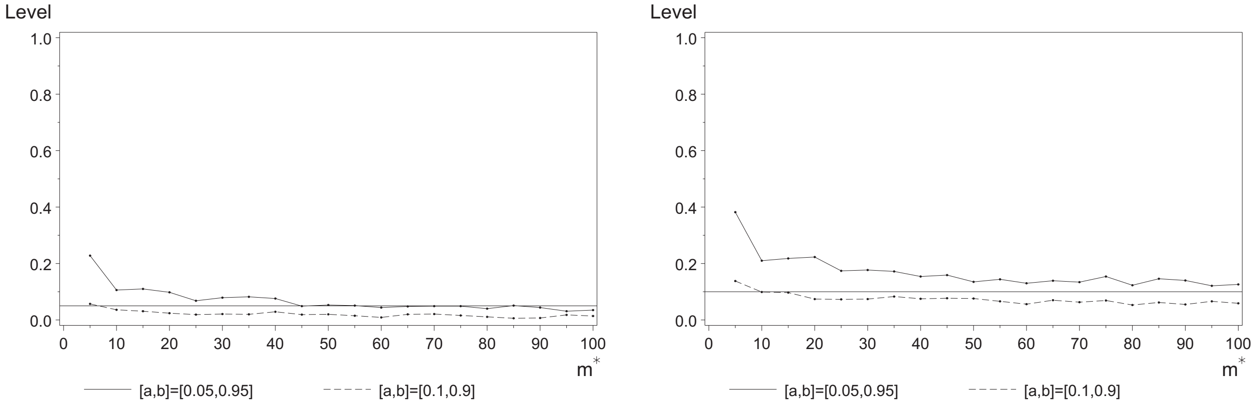

Figure 1: Test of H_0 for $\mathcal{F}_{Leh}$: $F = W(0.5, 1.2)$, $G = W(1.5, 1.2)$, $m = 100$

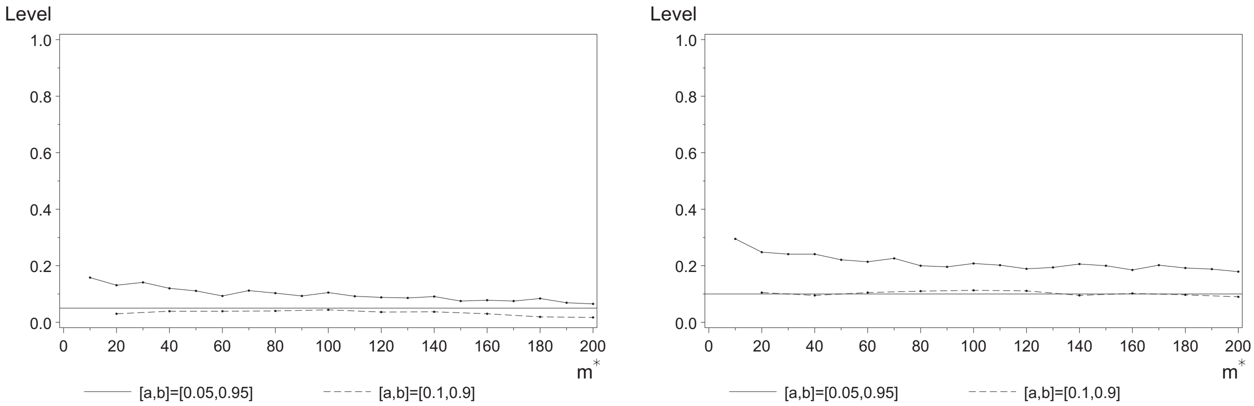

Figure 2: Test of H_0 for $\mathcal{F}_{Leh}$: $F = W(0.5, 1.2)$, $G = W(1.5, 1.2)$, $m = 200$

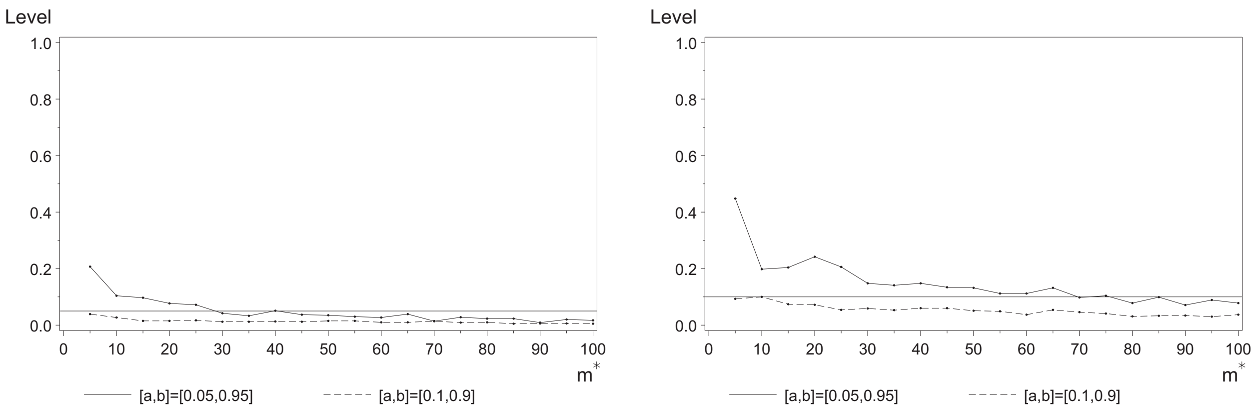

Figure 3: Test of H_0 for $\mathcal{F}_{Leh}$: $F = W(0.5, 0.6)$, $G = W(1.5, 0.6)$, $m = 100$

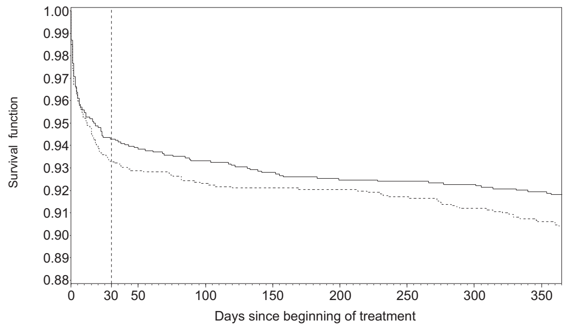

Figure 4: Estimated survival functions for saruplase (—) and streptokinase (– –) from the COMPASS trial.

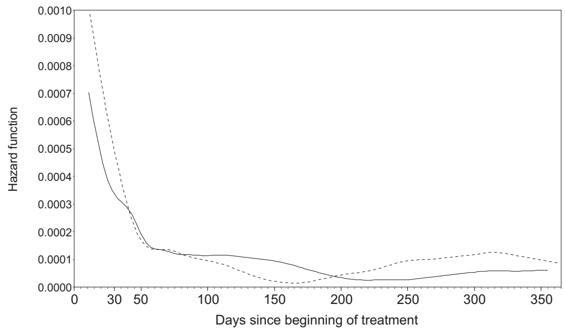

Figure 5: Estimated hazard functions for saruplase (—) and streptokinase (– –) from the COMPASS trial (bandwidth=55).

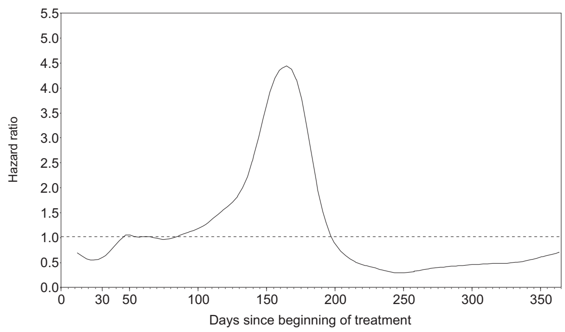

Figure 6: Estimated hazard ratio curve from the COMPASS trial. The dashed line marks the estimated constant hazard ratio ($\hat{\delta}_{hr} = 1.02$) obtained from the ph model.

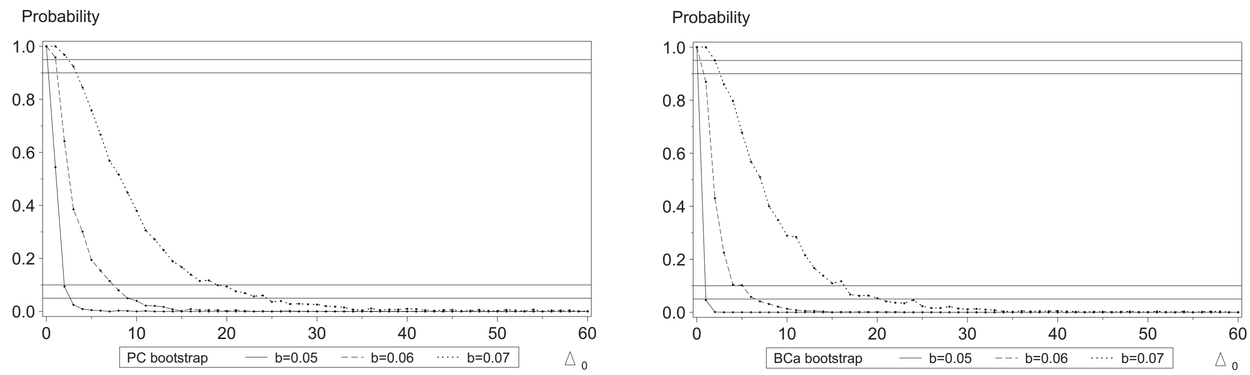

Figure 7: P-value curves for PC and BC$_a$tests of the acceleration model for the COMPASS data (a=0.00).

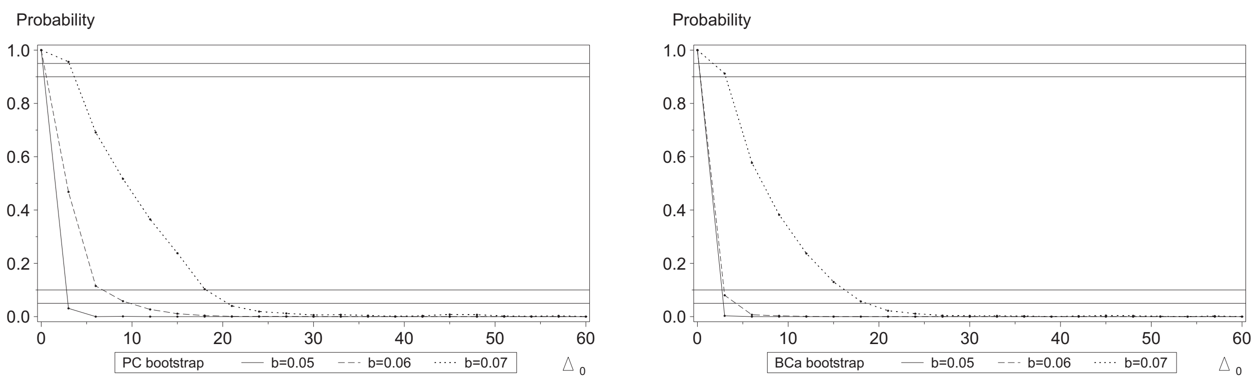

Figure 8: P-value curves for PC and BC$_a$tests of the ph model for the COMPASS data (a=0.00).