

## COMPUTING THE EFFICIENT SCORE IN SEMI-PARAMETRIC PROBLEMS

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*Abstract:* An approach to organizing the calculation of the efficient score for a finite dimensional parameter of interest in the presence of an infinite dimensional nuisance parameter is presented. The approach involves choosing a set of submodels for the nuisance parameter. The condition that the scores for the submodels be orthogonal to the efficient score takes the form of an equation whose solution appears in a representation of the efficient score. The approach is illustrated with several examples.

*Key words and phrases:* Case-control, censoring, interval censored data, missing covariates, projection, tangent space.

### 1. Introduction

Computing the efficient score in a semiparametric problem can allow comparison of the variance of available estimators to the semi-parametric variance bound, aid in the development of efficient or improved estimating equations, and aid in the calculation of standard errors for estimators based on estimating equations. Bickel, Klaassen, Ritov and Wellner (1993) describe three approaches to finding the efficient score in the presence of an infinite dimensional nuisance parameter. They are via guessing a candidate estimator, via solving the orthogonality equations, and via inversion of the information operator. See also Newey (1990), Pfanzagl (1990) or Stein (1956), for example, or the references given there. When a candidate estimator is not readily guessed, it may not be immediately obvious how to approach the orthogonality equations or the information operator, and the efficient score is arrived at through a combination of ingenuity and intuition. The purpose of this paper is to present a systematic approach that can be helpful in organizing the derivation of the orthogonality equations.

Begin with some notation and definitions. Consider a model described by a parameter of interest,  $\beta$ , and nuisance parameters,  $\alpha$ . Let  $Y$  denote observed data and let  $f$  denote its density, so that the parameterization may be expressed as

$$(\alpha, \beta) \longrightarrow f_{\alpha, \beta}(Y). \quad (1)$$

Let  $S_\beta$  denote the score for the parameter of interest, the derivative of the log-likelihood with respect to  $\beta$ ,  $S_\beta = \frac{d}{d\beta} \log f_{\alpha,\beta}(Y)$ . A submodel for the nuisance parameter is a mapping of the form  $\eta \rightarrow \alpha_\eta$ . Scores for submodels of the nuisance parameters take the form  $\frac{d}{d\eta} \log f_{\alpha_\eta,\beta}(Y) \Big|_{\alpha_\eta=\alpha}$ . The efficient score for  $\beta$  is the difference between the score for  $\beta$  and the score for a particular submodel of the nuisance parameters. The particular submodel is the one with the property that the difference is uncorrelated with the scores for all submodels of the nuisance parameters. That is, the efficient score is

$$S_\beta - \frac{d}{d\eta} \log f_{\alpha_\eta,\beta}(Y) \Big|_{\alpha_\eta=\alpha},$$

for a submodel with the property that

$$E \left\{ \left( S_\beta - \frac{d}{d\eta} \log f_{\alpha_\eta,\beta}(Y) \Big|_{\alpha_\eta=\alpha} \right) S \right\} = 0 \quad (2)$$

for all scores  $S$  for submodels of the nuisance parameters. The equations (2) are the orthogonality equations.

To motivate the approach developed here, it is helpful to first consider the orthogonality equations for the case of finite dimensional nuisance parameters. Let  $S_\alpha$  denote the gradient of the log likelihood with respect to  $\alpha$ ,  $S_\alpha = \nabla_\alpha \log f_{\alpha,\beta}(Y)$ . Then, scores for submodels of the nuisance parameters are linear combinations of the components of  $S_\alpha$ ,  $\frac{d}{d\eta} \log f_{\alpha_\eta,\beta}(Y) \Big|_{\alpha_\eta=\alpha} = \varphi^T S_\alpha$ , where the row vector of coefficients,  $\varphi^T$ , is  $\varphi = \frac{d\alpha}{d\eta} \Big|_{\alpha_\eta=\alpha}$ . It follows that the efficient score for  $\beta$  is the difference between  $S_\beta$  and the particular linear combination of the components of  $S_\alpha$  with the property that the difference is uncorrelated with  $S_\alpha$ . That is, the efficient score is given by

$$S_\beta - \varphi^{*T} S_\alpha. \quad (3)$$

where the coefficients of the linear combination,  $\varphi^*$ , are defined implicitly by the orthogonality equations,

$$E \left\{ \left( S_\beta - \varphi^{*T} S_\alpha \right) S_\alpha^T \right\} = 0. \quad (4)$$

These equations take the form of a matrix equation in  $\varphi^*$  with as many dimensions as there are in the nuisance parameter,

$$\left( E S_\alpha S_\alpha^T \right) \varphi^* = E S_\alpha S_\beta. \quad (5)$$

With finite dimensional nuisance parameters, using the components of  $S_\alpha$  as a basis for the space of scores for submodels for the nuisance parameters

leads to the tractable formulation of the orthogonality equations, (4). When the nuisance parameter is not finite dimensional, a tractable formulation of the orthogonality equations is not always immediately obvious. Here, an infinite dimensional analogue to using the components of  $S_\alpha$  as a basis is developed in order to arrive at a tractable approach to organizing the derivation of the orthogonality equations when  $\alpha$  is infinite dimensional.

In the next section, the approach to formulating the orthogonality equations when the nuisance parameter is infinite dimensional is presented. The presentation is introduced through a simple example. In the third section, the approach is applied to some examples. Efficiency calculations for some of the examples are well known, and so allow comparisons between the heuristic presented here and other approaches to computing the efficient score.

## 2. The Orthogonality Equations

The approach presented here is to start with parameterization in the same form as (1) and then form an analogue of the tractable representation of the orthogonality equations, (4). To form the analogue, the components of  $S_\alpha$  in (4) are replaced by scores for a subset of submodels of the nuisance parameter. The submodels in the set are chosen so that their scores span the space of all scores for the nuisance parameter. The resulting formulation of the orthogonality equations leads to an integral equation analogue of (5). Correspondingly, the efficient score is not expressed as the difference between  $S_\beta$  and a finite dimensional linear combination of the components of  $S_\alpha$ . Instead, the finite dimensional linear combination is replaced by an infinite dimensional linear combination of the scores for the set of submodels.

To motivate the approach to forming the analogue to (4), it is useful to consider a simple example of a semi-parametric regression problem. Suppose that the data are a sample of triplets,  $(X_i, T_i, W_i)$ ,  $i = 1, \dots, n$ , where the  $W_i$  are outcomes and the  $(X_i, T_i)$  are covariates. Suppose that the outcomes may be expressed in terms of the covariates and independent and identically distributed error terms  $\epsilon_i$  by  $W_i = \alpha(T_i) + X_i\beta + \epsilon_i$ . Suppose that the joint distribution of the  $(X_i, T_i)$  pairs are unspecified, and suppose that the error terms are independent of the  $(X_i, T_i)$  pairs. For convenience, suppose that the distribution of the  $\epsilon_i$  are specified as standard normal. The score for  $\beta$  is

$$\begin{aligned} S_\beta &= \frac{d}{d\beta} \log \prod_{i=1}^n (2\pi)^{-1/2} \exp(-(W_i - X_i\beta - \alpha(T_i))^2/2) \\ &= \sum_{i=1}^n (W_i - X_i\beta - \alpha(T_i)) X_i. \end{aligned}$$

(Here, the joint distribution of the  $(X_i, T_i)$  pairs is conditioned out of the likelihood, as they are ancillary for  $\alpha$  and  $\beta$ .) Similarly, scores for submodels of the nuisance parameter  $\alpha$  take the form

$$\begin{aligned} & \frac{d}{d\eta} \log \prod_{i=1}^n (2\pi)^{-1/2} \exp\left(-\frac{1}{2}(W_i - X_i\beta - \alpha_\eta(T_i))^2/2\right) \\ &= \sum_{i=1}^n (W_i - X_i\beta - \alpha(T_i)) \varphi(T_i), \end{aligned}$$

where  $\varphi$  corresponds to the derivative of  $\alpha_\eta$  with respect to  $\eta$ ,  $\varphi(t) = \left. \frac{d}{d\eta} \alpha_\eta(t) \right|_{\alpha_\eta = \alpha}$ . The efficient score is therefore given by  $S_\beta - \sum_{i=1}^n [W_i - X_i\beta - \alpha(T_i)] \varphi^*(T_i)$ , where  $\varphi^*$  solves the orthogonality equations:

$$\text{for all } \varphi, \quad E \left\{ \left( S_\beta - \sum_{i=1}^n [W_i - X_i\beta - \alpha(T_i)] \varphi^*(T_i) \right) \sum_{i=1}^n [W_i - X_i\beta - \alpha(T_i)] \varphi(T_i) \right\} = 0.$$

These equations are similar to the equations (4) derived for finite dimensional nuisance parameters: the function  $\varphi^*$  and the functions  $\varphi$  in these equations play the role of the vectors  $\varphi^{*T}$  and  $\varphi$  in equation (4). In these equations, however,  $\varphi^*$  and  $\varphi$  are indexed by the range of the nuisance function  $\alpha$ , while in (4),  $\phi^*$  and  $\varphi$  are indexed by the dimensions of the finite dimensional vector of nuisance parameters  $\alpha$ . In the infinite dimensional case, as in the finite dimensional case, to compute the efficient score it suffices to find  $\varphi^*$ .

The correspondence between the dimensions of the vector  $\alpha$  in the finite dimensional case and the range of the function  $\alpha$  in this semi-parametric regression example suggests an approach to organizing the calculation of  $\varphi^*$ . In the finite dimensional case, the components of  $S_\alpha$  were used as a basis for the space of scores for the nuisance parameters. The components of  $S_\alpha$  are the scores for the submodels in which all but one component of the nuisance parameters are fixed. Analogues to these submodels in the semi-parametric regression example are submodels in which  $\alpha$  is fixed except at one value of its range. That is, the analogues are submodels of the form

$$\eta \longrightarrow \alpha + \eta \delta^{t^*}(t), \quad (6)$$

where  $\delta^{t^*}(t) = 1_{\{t \in (t^*, t^* + dt)\}}/dt$  is the Dirac  $\delta$  function at  $t^*$ . The score for such a submodel is  $\sum_{i=1}^n [W_i - X_i\beta - \alpha(T_i)] \delta^{t^*}(t)$ . Substituting these scores into the orthogonality equations results in an analogue to (4),

$$E \left\{ \left( S_\beta - \sum_{i=1}^n [W_i - X_i\beta - \alpha(T_i)] \varphi^*(T_i) \right) \sum_{i=1}^n [W_i - X_i\beta - \alpha(T_i)] \delta^{t^*}(t) \right\} = 0. \quad (7)$$

Formally evaluating the left hand side of (7) results in

$$\begin{aligned} & \sum_{i=1}^n \int f_T(t) dt E \left\{ [W_i - X_i\beta - \alpha(T_i)]^2 (X_i - \varphi^*(t)) \delta^{t^*}(t) \mid T_i = t \right\} \\ &= \sum_{i=1}^n \int f_T(t) dt \delta^{t^*}(t) \cdot (E \{X_i \mid T_i = t^*\} - \varphi^*(t^*)) \\ &= n f_T(t^*) (E \{X_i \mid T_i = t^*\} - \varphi^*(t^*)), \end{aligned}$$

where  $f_T$  is the marginal density of the  $T_i$ . Setting the left hand side to zero reveals that  $\varphi^*(t) = E \{X_i \mid T_i = t\}$ . Strategies for achieving this bound, and discussions of smoothness conditions may be found, for example, in Chen (1988), Chen (1995) and Schick (1993).

Finding the efficient score in the example was made tractable by using the scores for the subset of submodels, (6), when formulating the orthogonality equations. A generalization of the approach is now described.

Suppose that the possible values of the nuisance parameter may be identified with a space of functions. Let  $\mathcal{X}$  denote the range of the functions and let  $\Psi$  denote the mapping that takes functions to values of the nuisance parameter. The mapping  $\Psi$  need not be one-to-one. It is convenient, and there is no loss of generality, to suppose that the function that is identically zero is mapped to the true value of  $\alpha$ . For each element,  $\xi$ , in the range of the function,  $\mathcal{X}$ , denote the Dirac function at  $\xi$  by  $\delta^\xi(x) = 1_{\{x \in (\xi, \xi+dx)\}}/dx$ . Let  $S^\xi$  denote the score for the submodel traced by the image under  $\Psi$  of  $\eta\delta^\xi$ , as  $\eta$  varies,

$$S^\xi = \left. \frac{d}{d\eta} \log f_{\Psi(\eta\delta^\xi), \beta}(Y) \right|_{\eta=0}.$$

In a variety of settings, the  $S^\xi$  span the space of scores for submodels of the nuisance parameters in the sense that for any submodel,  $\eta \rightarrow \Psi(g_\eta)$ , the score for the submodel can be expressed as a linear combination of the  $S^\xi$ ,

$$\left. \frac{d}{d\eta} \log f_{\Psi(g_\eta), \beta}(Y) \right|_{g_\eta=0} = \int_{\mathcal{X}} \frac{d}{d\eta} g_\eta(\xi) S^\xi d\xi.$$

In such settings, the efficient score for  $\beta$  is

$$S_\beta - \int_{\mathcal{X}} \varphi^*(x) S^x dx, \tag{8}$$

where  $\varphi^*$  is defined by the orthogonality equations,

$$\text{for all } \xi, \quad E \left\{ \left( S_\beta - \int_{\mathcal{X}} \varphi^*(x) S^x dx \right) S^\xi \right\} = 0. \tag{9}$$

The orthogonality equations, (9), will generally take the form of an integral equation for  $\varphi^*$ .

In some situations, natural choices for  $\Psi$  and  $\mathcal{X}$  will not be evident. This may especially be the case for models involving constraints. In such cases, the complexities in the structure of the tangent space induced by the constraints are faced through the choice of the parameterization. In some settings, natural choices for  $\Psi$  and  $\mathcal{X}$  will lead to over-parameterization of the nuisances. In these situations, the integral equation will not have a unique solution. Nevertheless, all the solutions to the integral equation when substituted into (8) will result in the same efficient score. In many situations, different choices of  $\Psi$  and  $\mathcal{X}$ , corresponding to different parameterizations for the nuisance parameter, are available. A particular choice of parameterization may lead to simpler computations.

The general approach presented here parallels the calculations in settings where the nuisance is finite dimensional in the same way as in the case of the example. The set  $\mathcal{X}$  is an infinite dimensional analogue of the indices of components of a finite dimensional vector of parameters,  $\alpha$ . The submodels  $\eta \rightarrow f_{\Psi(\eta\delta^x),\beta}$  correspond to the submodels in finite dimensional settings that vary one component of  $\alpha$ , while holding the other components fixed, and the scores  $S^\xi$  correspond to the components of the gradient of the log likelihood with respect to  $\alpha$ . The function  $x \rightarrow \varphi^*(x)$  in (8) is an analogue of the finite dimensional vector  $\varphi^*$  in (3). Solving the integral equation that results from evaluating (9) corresponds to inverting the matrix in  $ES_\alpha S_\alpha^T$  that results from evaluating (4).

This section concludes with a brief description of parallels between the approach developed here and the approach based on information operators. The mapping

$$\dot{\mathbf{i}} : \frac{d}{d\eta}g_\eta \rightarrow \int_{\mathcal{X}} \frac{d}{d\eta}g_\eta(\xi)S^\xi d\xi$$

is a score operator. The equation (9) is a representation of the normal equations in terms of the basis for the nuisance tangent space formed by the images of the Dirac functions. That is, the normal equations are that for  $\xi \in \mathcal{X}$ ,  $\langle S_\beta - \dot{\mathbf{i}}\varphi^*, \dot{\mathbf{i}}\delta^\xi \rangle = 0$ , instead of the more familiar form,  $\dot{\mathbf{i}}^T S_\beta = \dot{\mathbf{i}}^T \dot{\mathbf{i}}\varphi^*$ . Solving the integral equation that results from evaluating (9) corresponds to inverting the information operator  $\dot{\mathbf{i}}^T \dot{\mathbf{i}}$ . See, for example, Begun, Hall, Huang and Wellner (1983), Van der Vaart (1991), Groeneboom and Wellner (1992, p.27), or Bickel, Klaassen, Ritov and Wellner (1993, p.79).

### 3. Examples

In this section, several examples are outlined. In each example, a representation of the parameter space in the form of (1) is proposed, and a choice of  $\mathcal{X}$  and

$\Phi$  is presented. In many cases, the parameter space is represented in terms of an exponential tilt of the true distribution (or a tilt modified to respect constraints). Then, efficient score in the form of (8) and the orthogonality equations in the form (9) are found.

**3.1. Median of a symmetric distribution**

Suppose that  $T_i, i = 1, \dots, n$ , are independent and identically distributed random variables with symmetric density  $g$ . Let  $\beta$  denote the parameter of interest, the median of  $g$ , and let  $\alpha(t)$  denote the nuisance,  $g(t - \beta)$ . The likelihood is  $\prod_{i=1}^n \alpha(T_i - \beta)$ .

Let  $\mathcal{X}$  be  $[0, \infty)$  and define  $\Psi$  by

$$\Psi(\zeta)(t) = \alpha(t)\exp\{\zeta(|t|)\} / 2 \int_0^\infty \alpha(u)\exp\{\zeta(|u|)\}du .$$

Then,

$$S^x = \sum_{i=1}^n \left[ \frac{1_{\{|T_i - \beta| \in (x, x+dx)\}}}{dx} - 2\alpha(x) \right],$$

so that the efficient score, (8), is

$$\sum_{i=1}^n \left[ \frac{\alpha'(T_i - \beta)}{\alpha(T_i - \beta)} - \left( \varphi^*(|T_i - \beta|) - 2 \int_0^\infty \varphi^*(u)\alpha(u)du \right) \right];$$

the orthogonality equations, (9), are

$$\text{for all } x, \quad n2\alpha(x) \left\{ \varphi^*(x) - 2 \int_0^\infty \varphi^*(u)\alpha(u)du \right\} = 0,$$

from which it follows that  $\varphi^*$  is constant so that the efficient score for  $\beta$  is

$$\sum_{i=1}^n \frac{\alpha'(T_i - \beta)}{\alpha(T_i - \beta)}.$$

This example is also treated in, for example, Stein (1956), Ibragimov and Has'minskii (1981) and Bickel, Klaassen, Ritov and Wellner (1993).

**3.2. Mean of an arbitrary distribution**

Suppose that  $T_i, i = 1, \dots, n$ , are independent and identically distributed random variables with density  $g$ . Let  $\beta$  denote the parameter of interest, the expectation of the  $T_i$ , and let  $\alpha(t)$  denote the nuisance,  $g(t + \beta)$ . The likelihood is  $\prod_{i=1}^n \alpha(T_i - \beta)$ .

Let  $\mathcal{X}$  be the reals and define  $\Psi$  by  $\Psi(h)(t) = \alpha(t + \mu(h))\exp\{h(t + \mu(h)) - \psi(h)\}$ , where  $\psi$  is defined by  $\exp(\psi(h)) = \log \int \alpha(s)\exp\{h(s)\} ds$  and  $\mu$  is defined

by  $\mu(h) = \int \alpha(s) \exp \{h(s) - \psi(h)\} s ds$ . The term  $\mu(h)$  is necessary so that the expectation of  $T$  under  $f_{\beta, \psi(h)}$  is  $\beta$ . Then

$$S^x = \sum_{i=1}^n \left\{ \frac{\alpha'(T_i - \beta)}{\alpha(T_i - \beta)} \alpha(x) x + \frac{1_{\{T_i - \beta \in (x, x+dx)\}}}{dx} - \alpha(x) \right\},$$

so that the efficient score, (8), is

$$\sum_{i=1}^n \left\{ \frac{\alpha'(T_i - \beta)}{\alpha(T_i - \beta)} (-1 - E[(T_i - \beta)\varphi^*(T_i - \beta)]) - \varphi^*(T_i - \beta) + E[\varphi^*(T_i - \beta)] \right\}$$

the orthogonality equations (9) are: for all  $x$ ,

$$\begin{aligned} n\alpha(x)x \left\{ E \left[ \frac{\alpha'(T_i - \beta)}{\alpha(T_i - \beta)} \right]^2 (-1 - E[\varphi^*(T_i - \beta)(T_i - \beta)]) - E \left[ \frac{\alpha'(T_i - \beta)}{\alpha(T_i - \beta)} \varphi^*(T_i - \beta) \right] \right\} \\ + n\alpha(x) \left\{ \left[ \frac{\alpha'(x)}{\alpha(x)} \right] (-1 - E[\varphi^*(T_i - \beta)(T_i - \beta)]) - \varphi^*(x) + E[\varphi^*(T_i - \beta)] \right\} = 0, \end{aligned}$$

from which it follows that

$$\varphi^*(t) = \frac{\alpha'(t)}{\alpha(t)} - \frac{t - \beta}{\text{Var}(T_i)} + c,$$

for arbitrary  $c$ , so that the efficient score for  $\beta$  is, with finite  $\text{Var}(T_i)$ ,  $\sum_{i=1}^n \frac{T_i - \beta}{\text{Var}(T_i)}$ . This example is also treated in, for example, Newey (1990) and Ibragimov and Has'minskii (1981).

### 3.3. Cumulative hazard from censored data

Suppose that  $(T_i, C_i)$ ,  $i = 1, \dots, n$ , are independent identically distributed pairs of independent random variables. Let  $\lambda$  denote the hazard function of the  $T_i$ . Suppose that the distribution of the  $C_i$  is completely unspecified. Let  $\beta$  denote the parameter of interest, the cumulative hazard,  $\beta = \int_{-\infty}^t \lambda(s) ds$ , and define the nuisance parameter  $\alpha$  by  $\alpha(s) = \lambda(s)\beta^{-1_{\{s \leq t\}}}$ . Then,  $\lambda(s) = \alpha(s)\beta$  for  $s \leq t$  and is  $\alpha(s)$  for  $s \geq t$ , where  $\alpha(s)$  is arbitrary except that  $\int_{-\infty}^t \alpha(s) = 1$ . The  $T_i$  are failure times, the  $C_i$  are censoring indicators, the  $Z_i$  are covariates, and the failure times given the covariates are assumed to follow a proportional hazards model. The  $C_i$  are ancillary and the conditional likelihood given the  $C_i$  is

$$\prod_{i=1}^n \exp \left( - \int_{-\infty}^{\min(T_i, C_i)} \alpha(s) ds \beta^{1_{\{s \leq t\}}} \right) \left( \alpha(\min(T_i, C_i)) \beta^{1_{\{s \leq t\}}} \right)^{1_{\{T_i \leq C_i\}}}.$$



Let  $\mathcal{X}$  be the reals and define  $\Psi$  by  $\Psi(g)(s) = \lambda(s)\exp(g(s) - \psi(g)1_{\{s \leq t\}})$ , where  $\psi$  is defined by  $\exp\{\psi(g)\} = \int_{-\infty}^t \lambda(s)\exp(g(s))ds$ . Suppose that only the  $\min(C_i, T_i)$  and  $1_{\{T_i \leq C_i\}}$  are available. Then,

$$S^x = \sum_{i=1}^n \int_{-\infty}^{\infty} Y_i(s)(dN_i(s) - \lambda(s)ds) \left( \frac{1_{\{s \in (x, x+dx)\}}}{dx} - 1_{\{s \leq t\}} 1_{\{x \leq t\}} \frac{\lambda(x)}{\beta} \right)$$

where  $Y_i(s) = 1_{\{\min(T_i, C_i) \geq s\}}$  and  $N_i(s) = (1 - Y_i(s)) 1_{\{T_i \leq C_i\}}$ , so that the efficient score, (8), is

$$\sum_{i=1}^n \int_{-\infty}^{\infty} Y_i(s) (dN_i(s) - \lambda(s)ds) \left( -\frac{1_{\{s \leq t\}}}{\beta} - \varphi^*(s) + 1_{\{s \leq t\}} \frac{\int_{-\infty}^t \varphi^*(u)\lambda(u)du}{\beta} \right);$$

the orthogonality equations, (9), are

$$\begin{aligned} &\text{for all } x, n\lambda(x)EY_i(x) \left( \frac{-1_{\{x \leq t\}}}{\beta} - \varphi^*(x) + 1_{\{x \leq t\}} \frac{\int_{-\infty}^t \varphi^*(u)\lambda(u)du}{\beta} \right) \\ &\quad - n\lambda(x) \int_{-\infty}^{\infty} EY_i(s)\lambda(s)ds \left( -\frac{1_{\{s \leq t\}}}{\beta} - \varphi^*(s) + 1_{\{s \leq t\}} \frac{\int_{-\infty}^t \varphi^*(u)\lambda(u)du}{\beta} \right) = 0, \end{aligned}$$

from which it follows that

$$\varphi^*(x) = \left( \frac{\tau}{EY_i(x)} + c \right) 1_{\{x \leq t\}}, \quad \text{where } \tau = \beta^{-1} \int_{-\infty}^t \frac{\lambda(x)}{EY_i(x)} dx$$

for arbitrary  $c$ , so that the efficient score for  $\beta$  is

$$\sum_{i=1}^n \int_{-\infty}^t Y_i(s) (dN_i(s) - \lambda(s)ds) \left( -\frac{1}{\beta} - \left\{ \frac{\tau}{EY_i(s)} - 1 \right\} \right).$$

Derivations of the this and similar results may be found in, for example, Breslow and Crowley (1974), Gill (1983) and Andersen, Borgan, Gill and Keiding (1993).

### 3.4. Proportional hazards

Suppose that  $(T_i, C_i, Z_i)$ ,  $i = 1, \dots, n$ , are independent identically distributed triplets of random variables. Suppose that the  $T_i$  are conditionally independent of the  $C_i$  given the  $Z_i$ . Suppose that the joint distribution of the  $(C_i, Z_i)$  pairs is completely unspecified and that only the  $\min(C_i, T_i)$ , the  $1_{\{T_i \leq C_i\}}$  and the  $Z_i$  are available. Suppose that there is an unspecified non-negative function  $\alpha$  and a parameter of interest  $\beta$  such that the hazard function of the  $T_i$  at  $t$ , given that  $Z_i = z$ , is of the form  $\alpha(t)\exp(\beta z)$ . The conditional likelihood given the censoring variables is

$$\prod_{i=1}^n \exp \left( - \int_{-\infty}^{\min(T_i, C_i)} \alpha(s) ds \exp(\beta Z_i) \right) (\alpha(\min(T_i, C_i)) \exp(\beta Z_i))^{1_{\{T_i \leq C_i\}}} .$$

Let  $\mathcal{X}$  be the reals and let  $\Psi$  be defined by  $\Psi(g)(t) = \alpha(t)\exp\{g(t)\}$ . Then

$$S^x = \sum_{i=1}^n \int_{-\infty}^{\infty} Y_i(s) (dN_i(s) - \alpha(s)\exp(Z_i\beta)ds) \frac{1_{\{s \in (x, x+dx)\}}}{dx}$$

where the  $Y_i(s)$  and the  $N_i(s)$  are as in the preceding example, so that the efficient score, (8), is

$$\sum_{i=1}^n \int_{-\infty}^{\infty} Y_i(s) (dN_i(s) - \alpha(s)\exp(Z_i\beta)ds) (Z_i - \varphi^*(s)),$$

and the orthogonality equations, (9), are

$$\text{for all } x, \quad nEY_i(x)\alpha(x)\exp(Z_i\beta)(Z_i - \varphi^*(x)) = 0.$$

It follows that

$$\varphi^*(x) = \frac{EY_i(x)\exp(Z_i\beta)Z_i}{EY_i(x)\exp(Z_i\beta)}.$$

Similar derivations may be found in Bickel, Klaassen, Ritov and Wellner (1993) and Andersen and Gill (1982). See also, for example, Tsiatis (1981) and Breslow (1974).

### 3.5. Missing covariates

Let  $\mathcal{D} = \{1, \dots, D\}$  denote a set of stratum indicators and suppose that  $(X_{i,d}, Y_{i,d}), i = 1, \dots, n_d, d \in \mathcal{D}$ , are independent pairs of covariates and outcome pairs. Denote the marginal density of  $X_{i,d}$ , the nuisance parameter, by  $\alpha(x, d)$  and denote the conditional density of  $Y_{i,d}$  given  $X_{i,d}$  by  $f_\beta(y|x)$ , assumed known up to the finite dimensional parameter of interest  $\beta$ . Let  $Y_{j,d}, j = n_d + 1, n_d + 2, \dots, n_d + m_d, d \in \mathcal{D}$ , be independent outcomes with density  $\int \alpha(x, d)f_\beta(y|x)dx$ . The  $Y_{i,d}, i = n_d + 1, \dots, n_d + m_d$ , have missing covariates. The likelihood is

$$\prod_{d \in \mathcal{D}} \left( \prod_{i=1}^{n_d} \alpha(X_i, d) f_\beta(Y_i|X_i) \prod_{i=n_d+1}^{m_d} \int \alpha(x, d) f_\beta(Y_i|x) dx \right).$$

Let  $\mathcal{X}$  be the cross product of the support of the  $X_{i,d}$  and  $\mathcal{D}$ , and define  $\Psi$  by  $\Psi(g)(s, d) = \alpha(s, d)\exp(g(x, d) - \psi(g, d))$ , where

$$\exp(\psi(g, d)) = \int \alpha(x, d)\exp(g(x, d)) dx.$$

Then

$$S^{x,d} = \sum_{i=1}^{n_d} \left( \frac{1_{\{X_{i,d} \in (x, x+dx)\}}}{dx} - \alpha(x, d) \right) + \sum_{j=n_d+1}^{n_d+m_d} \left( \frac{\alpha(x, d)f_\beta(Y_{j,d}|x)}{\int \alpha(s, d)f_\beta(Y_{j,d}|s)ds} - \alpha(x, d) \right)$$

so that the efficient score, (8), is

$$\sum_{d \in \mathcal{D}} \sum_{i=1}^{n_d} \left( s_{\beta}(Y_{i,d}|X_{i,d}) - \varphi^*(X_{i,d}, d) - \int \alpha(x, d) \varphi^*(x, d) dx \right) + \sum_{d \in \mathcal{D}} \sum_{j=n_d+1}^{m_d} \frac{\int \alpha(x, d) f_{\beta}(Y_{j,d}|x) (s_{\beta}(Y_{j,d}|x) - \varphi^*(x, d) - \int \alpha(s, d) \varphi^*(s, d) ds) dx}{\int \alpha(u, d) f_{\beta}(Y_{j,d}|u) du},$$

where  $s_{\beta}(y|x) = \frac{d}{d\beta} \log f_{\beta}(y|x)$ ; the orthogonality equations, (9), are

$$\text{for all } x, d, \quad \alpha(x, d) \left( n_d \varphi^*(x) - m_d \int K(x, s, d) \varphi^*(s) ds \right) = \nu(x, d), \quad (10)$$

where

$$K(x, s, d) = \int \alpha(u, d) \int f_{\beta}(y|u) \frac{f(y|s) \alpha(s, d) f(y|x) ds}{(\int \alpha(v, d) f_{\beta}(y|v) dv)^2} dy du$$

and

$$\nu(x, d) = \alpha(x, d) \int \alpha(u, d) \int f_{\beta}(y|u) \frac{f(y|s) \alpha(s, d) f(y|x) s(y|s) ds}{(\int \alpha(v, d) f_{\beta}(y|v) dv)^2} dy du.$$

The equation (10) takes the form of a Fredholm type II integral equation for  $\varphi^*$ . In general, there is not an explicit solution to the integral equation, but approximate solutions may be found. Derivations of the efficient score for this and related problems may be found in, for example, Robins, Rotnitzky and Zhao (1995), Cosslett (1981) and Chamberlain (1987).

### 3.6. Regression with interval censored data

Let failure times  $T_i$ ,  $i = 1, \dots, n$ , satisfy  $T_i = Z_i \beta + \epsilon_i$ , where the  $\epsilon_i$  are independent and independent of the  $Z_i$  with unspecified marginal density  $\alpha$ , the  $Z_i$  are real valued, and  $\beta$  is a real valued parameter of interest. Let  $n_i$  denote numbers of examination times and let  $X_i = (X_{i,1}, \dots, X_{i,n_i})$  denote the ordered sequence of examination times. For convenience, define  $X_{i,0} = -\infty$ , and  $X_{i,n_i+1} = \infty$ . Let  $X_{i,L}$  be the last of the  $i$ th subjects examination times preceding  $T_i$ , and let  $X_{i,U}$  be the first examination time following  $T_i$ . Suppose that only the  $X_{i,L}$ ,  $X_{i,U}$ ,  $Z_i$  and triplets are available. The failure times  $T_i$ , given the covariates  $Z_i$  follow an accelerated failure time model. The failure times are not observed, however, as they are only known to lie between the immediately preceding and following examination times. The likelihood is

$$\prod_{i=1}^n (F(X_{i,U} - Z_i \beta) - F(X_{i,L} - Z_i \beta)),$$

where  $F$  is the distribution function corresponding to  $\alpha$ ,  $F(x) = \int_{-\infty}^x \alpha(u)du$ .

Let  $\mathcal{X}$  be the reals, and define  $\Psi$  by  $\Psi(g)(e) = \alpha(e) \exp(g(e) - \psi(g))$  where  $\psi$  is defined by  $\exp(\psi(g)) = \int \alpha(e) \exp(g(e))de$ . Then,

$$S^x = \sum_{i=1}^n \frac{1_{\{x \in (X_{i,U} - Z_i\beta, X_{i,L} - Z_i\beta)\}}}{F(X_{i,U} - Z_i\beta) - F(X_{i,L} - Z_i\beta)},$$

so that (8) is

$$\sum_{i=1}^n \frac{(\alpha(X_{i,U} - Z_i\beta) - \alpha(X_{i,L} - Z_i\beta)) Z_i}{F(X_{i,U} - Z_i\beta) - F(X_{i,L} - Z_i\beta)} - \frac{\int_{X_{i,U} - Z_i\beta}^{X_{i,L} - Z_i\beta} \alpha(u) \varphi^*(u) du}{F(X_{i,U} - Z_i\beta) - F(X_{i,L} - Z_i\beta)}.$$

In this expression, the appearance of  $\varphi^*$  in the integral suggests that it may be convenient to parameterize the nuisance and to define the score operator in terms of the function  $\mu(t) = \int_{-\infty}^t \alpha(u) \varphi^*(u) du$ , so that

$$S^x = \sum_{i=1}^n \frac{1_{\{x=X_{i,U}-Z_i\beta\}}/dx - 1_{\{x=X_{i,L}-Z_i\beta\}}/dx}{F(X_{i,U} - Z_i\beta) - F(X_{i,L} - Z_i\beta)}$$

and the efficient score, (8), is

$$\sum_{i=1}^n \frac{(\alpha(X_{i,U} - Z_i\beta) - \alpha(X_{i,L} - Z_i\beta)) Z_i}{F(X_{i,U} - Z_i\beta) - F(X_{i,L} - Z_i\beta)} - \frac{\mu(X_{i,U} - Z_i\beta) - \mu(X_{i,L} - Z_i\beta)}{F(X_{i,U} - Z_i\beta) - F(X_{i,L} - Z_i\beta)}.$$

The orthogonality equations, (9), take the form of the type II Fredholm equation for  $\mu$ ,

$$\begin{aligned} n \frac{P\{X_{i,U}-Z_i\beta=x\}}{dx} E \left\{ \frac{(\alpha(x)-\alpha(X_{i,L}-Z_i\beta))Z_i}{(F(x)-F(X_{i,L}-Z_i\beta))^2} - \frac{\mu(x)-\mu(X_{i,L}-Z_i\beta)}{(F(x)-F(X_{i,L}-Z_i\beta))^2} \middle| X_{i,U}-Z_i\beta=x \right\} \\ - n \frac{P\{X_{i,L}-Z_i\beta=x\}}{dx} E \left\{ \frac{(\alpha(X_{i,U}-Z_i\beta)-\alpha(x))Z_i}{(F(X_{i,U}-Z_i\beta)-F(x))^2} - \frac{\mu(X_{i,U}-Z_i\beta)-\mu(x)}{(F(X_{i,U}-Z_i\beta)-F(x))^2} \middle| X_{i,L}-Z_i\beta=x \right\}. \end{aligned}$$

This does not have an explicit solution but approximate solutions may be found. Similar calculations appear in Rabinowitz, Tsiatis and Aragon (1995).

### 3.7. Logistic regression from case-control data with independent covariates

Let  $X_1$  and  $X_2$  be independent random variables with unspecified marginal densities  $\alpha_1$  and  $\alpha_2$  respectively, and let  $Y$  be Bernoulli with conditional expectation given  $X_1$  and  $X_2$  equal to  $\pi(X_1, X_2; \beta)$ , where  $\beta$  is a finite dimensional parameter of interest and  $\pi$  is known. Let  $(X_{1,i}, X_{2,i}, Y_i)$ ,  $i = 1, \dots, n$ , be drawn from the conditional distribution of  $(X_1, X_2, Y)$  given  $Y = 1$ , and let

$(X_{1,i}, X_{2,i}, Y_i)$ ,  $i = n + 1, \dots, n + m$ , be drawn from the conditional distribution of  $(X_1, X_2, Y)$  given  $Y = 0$ . The likelihood is

$$\prod_{i=1}^n \frac{\alpha_1(X_{1,i})\alpha_2(X_{2,i})\pi(X_{1,i}, X_{2,i}, 1)}{\int \int \alpha_1(x_1)\alpha_2(x_2)\pi(x_1, x_2, 1)} \prod_{i=1}^{n+m} \frac{\alpha_1(X_{1,i})\alpha_2(X_{2,i})\pi(X_{1,i}, X_{2,i}, 0)}{\int \int \alpha_1(x_1)\alpha_2(x_2)\pi(x_1, x_2, 0)}.$$

Let  $\mathcal{X}$  be the cross product of the ranges of  $X_1$  and  $X_2$ , assumed disjoint without loss of generality, and define  $\Psi$  by

$$\Psi_1(\zeta_1, \zeta_2)(x_1) = \frac{\alpha_1(t) \exp \{ \zeta_1(x_1) \}}{\int \alpha_1(u_1) \exp \{ \zeta_1(u_1) \} du_1},$$

$$\Psi_2(\zeta_1, \zeta_2)(x_2) = \frac{\alpha_2(t) \exp \{ \zeta_2(x_2) \}}{\int \alpha_2(u_2) \exp \{ \zeta_2(u_2) \} du_2}.$$

Then, for  $x_1$  in the range of  $X_1$ ,

$$S^{x_1} = \sum_{i=1}^{n+m} \left[ \frac{1_{\{X_{1,i} \in (x_1, x_1+dx_1)\}}}{dx_1} - \frac{\int \alpha_1(x_1)\alpha_2(x_2)\pi(x_1, x_2; \beta)^{Y_i} \{1 - \pi(x_1, x_2; \beta)\}^{1-Y_i} dx_2}{\int \int \alpha_1(u_1)\alpha_2(u_2)\pi(u_1, u_2; \beta)^{Y_i} \{1 - \pi(u_1, u_2; \beta)\}^{1-Y_i} du_1 du_2} \right],$$

and for  $x_2$  in the range of  $X_2$ ,

$$S^{x_2} = \sum_{i=1}^{n+m} \left[ \frac{1_{\{X_{2,i} \in (x_2, x_2+dx_2)\}}}{dx_2} - \frac{\int \alpha_1(x_1)\alpha_2(x_2)\pi(x_1, x_2; \beta)^{Y_i} \{1 - \pi(x_1, x_2; \beta)\}^{1-Y_i} dx_1}{\int \int \alpha_1(u_1)\alpha_2(u_2)\pi(u_1, u_2; \beta)^{Y_i} \{1 - \pi(u_1, u_2; \beta)\}^{1-Y_i} du_1 du_2} \right].$$

Then the residual from the projection of the  $j$ th component of the score for  $\beta$ , is

$$\sum_{i=1}^{n+m} \left( \frac{\{Y_i - \pi(X_{1,i}, X_{2,i}; \beta)\} \frac{d}{d\beta_j} \pi(X_{1,i}, X_{2,i}; \beta)}{\pi(X_{1,i}, X_{2,i}; \beta) - \pi^2(X_{1,i}, X_{2,i}; \beta)} - \varphi^*_1(X_{1,i}) - \varphi^*_2(X_{2,i}) \right. \\ \left. - \int \int \left[ \frac{\{Y_i - \pi(x_1, x_2; \beta)\} \frac{d}{d\beta_j} \pi(x_1, x_2; \beta)}{\pi(x_1, x_2; \beta) - \pi^2(x_1, x_2; \beta)} - \varphi^*_1(x_1) - \varphi^*_2(x_2) \right] \mu(x_1, x_2, Y_i) dx_1 dx_2 \right),$$

where

$$\mu(x_1, x_2, y) = \frac{\alpha_1(x_1)\alpha_2(x_2)\pi(x_1, x_2; \beta)^y \{1 - \pi(x_1, x_2; \beta)\}^{1-y}}{\int \int \alpha_1(u_1)\alpha_2(u_2)\pi(u_1, u_2; \beta)^y \{1 - \pi(u_1, u_2; \beta)\}^{1-y} du_1 du_2};$$

the orthogonality equations, (9), may be written as the pair of Fredholm type II integral equations, for all  $x_1$

$$m \int \left[ \frac{\{0 - \pi(x_1, x_2; \beta)\} \frac{d}{d\beta_j} \pi(x_1, x_2; \beta)}{\pi(x_1, x_2; \beta) - \pi^2(x_1, x_2; \beta)} - \varphi^*_1(x_1) - \varphi^*_2(x_2) \right] \mu(x_1, x_2, 0) dx_2 \\ + n \int \left[ \frac{\{1 - \pi(x_1, x_2; \beta)\} \frac{d}{d\beta_j} \pi(x_1, x_2; \beta)}{\pi(x_1, x_2; \beta) - \pi^2(x_1, x_2; \beta)} - \varphi^*_1(x_1) - \varphi^*_2(x_2) \right] \mu(x_1, x_2, 1) dx_2,$$

and for all  $x_2$

$$\begin{aligned}
 & m \int \left[ \frac{\{0 - \pi(x_1, x_2; \beta)\} \frac{d}{d\beta_j} \pi(x_1, x_2; \beta)}{\pi(x_1, x_2; \beta) - \pi^2(x_1, x_2; \beta)} - \varphi^*_1(x_1) - \varphi^*_2(x_2) \right] \mu(x_1, x_2, 0) dx_1 \\
 & + n \int \left[ \frac{\{1 - \pi(x_1, x_2; \beta)\} \frac{d}{d\beta_j} \pi(x_1, x_2; \beta)}{\pi(x_1, x_2; \beta) - \pi^2(x_1, x_2; \beta)} - \varphi^*_1(x_1) - \varphi^*_2(x_2) \right] \mu(x_1, x_2, 1) dx_1.
 \end{aligned}$$

It may be of interest to note that, when  $\pi$  is a nontrivial function of both  $x_1$  and  $x_2$ , the efficient score is not equivalent to the score that is obtained through the prospective likelihood described in Prentice and Pyke (1979).

### 3.8. Current status and complete data

Let  $T$  denote a failure time and let  $C$  denote a censoring time. Suppose that  $C$  and  $T$  are independent. Denote the distribution function of  $T$  by  $F$ , supposed unspecified. Denote the distribution function of  $C$  by  $G$ . Let  $Y$  be the indicator that  $T$  is less than  $C$ . Let  $\beta$  denote the parameter of interest,  $F(t)$ , and define the nuisance parameter  $\alpha$  by

$$\alpha(s)ds = \begin{cases} dF(s)/\beta & \text{if } s \leq t, \\ dF(s)/(1 - \beta) & \text{if } s > t. \end{cases}$$

Let  $T_i, i = 1, \dots, n$ , be independent and identically distributed according to the distribution of  $T$ , and let  $(C_j, Y_j), j = 1, \dots, m$ , be independent and identically distributed according to the joint distribution of  $C$  and  $Y$ . The likelihood is

$$\begin{aligned}
 & \prod_{i=1}^n \alpha(T_i) (1/\beta)^{1_{\{T_i \leq t\}}} (1/(1 - \beta))^{1_{\{T_i > t\}}} \prod_{j=1}^m \left( \alpha(s) (1/\beta)^{1_{\{s \leq t\}}} (1/(1 - \beta))^{1_{\{s > t\}}} \right)^{Y_j} \\
 & \times \left( 1 - \alpha(s) (1/\beta)^{1_{\{s \leq t\}}} (1/(1 - \beta))^{1_{\{s > t\}}} \right)^{1 - Y_j}.
 \end{aligned}$$

Let  $\mathcal{X}$  be  $[0, \infty)$  and define  $\Psi$  by

$$\Psi(\zeta)(s) = \begin{cases} \alpha(s) \exp\{\zeta(s)\} / \int_0^t \alpha(u) \exp\{\zeta(u)\} du. & \text{if } s \leq t, \\ \alpha(s) \exp\{\zeta(s)\} / \int_t^\infty \alpha(u) \exp\{\zeta(u)\} du. & \text{if } s > t. \end{cases}$$

Then,

$$S^x = \begin{cases} \left( \sum_{i=1}^n \left[ \frac{1_{\{T_i \in (x, x+dx)\}}}{dx} - \alpha(x) 1_{\{T_i \leq t\}} \right] + \sum_{j=1}^m \frac{Y_j - F(A_j)}{F(A_j) - F^2(A_j)} \alpha(x) (F(t) 1_{\{x \leq A_j \leq t\}} - F(A_j) 1_{\{A_j \leq t\}}) \right) & \text{if } x \leq t, \\ \left( \sum_{i=1}^n \left[ \frac{1_{\{T_i \in (x, x+dx)\}}}{dx} - \alpha(x) 1_{\{T_i \leq t\}} \right] + \sum_{j=1}^m \frac{Y_j - F(A_j)}{F(A_j) - F^2(A_j)} \alpha(x) (\{F(A_j) - F(t)\} 1_{\{t \leq A_j \leq x\}} - \{1 - F(A_j)\} 1_{\{A_j > x\}}) \right) & \text{if } x > t, \end{cases}$$

so that the efficient score, (8), is

$$\sum_{i=1}^n \frac{1_{\{T_i \leq t\}} - \beta}{\beta(1 - \beta)} + \sum_{j=1}^m \frac{Y_j - F(A_j)}{F(A_j)\{1 - F(A_j)\}} \frac{F(A_j \wedge t)\{1 - F(A_j \vee t)\}}{\beta(1 - \beta)}$$

$$+ \sum_{i=1}^n \varphi^{**}(T_i) + \sum_{j=1}^m \frac{Y_j - F(A_j)}{F(A_j)\{1 - F(A_j)\}} \int_{-\infty}^{A_j} \varphi^{**}(s)f(s)ds,$$

where

$$\varphi^{**}(s) = \varphi^*(s) - 1_{\{s \leq t\}} \int_{-\infty}^t \varphi^*(u)\alpha(u)du - 1_{\{s > t\}} \int_t^{\infty} \varphi^*(u)\alpha(u)du.$$

The orthogonality equations (9) are

$$f(x)b(x) = f(x)\varphi^{**}(x) - f(x) \int_{-\infty}^{\infty} \varphi^{**}(s)K(x, ds),$$

where

$$b(x) = \begin{cases} \int_{-\infty}^t dG(a) \left( \frac{1_{\{x \leq a\}} - \frac{F(a)}{F(t)}}{F(t)\{1 - F(a)\}} \right) & \text{if } x \leq t, \\ - \int_t^{\infty} dG(a) \left( \frac{1_{\{x > a\}} - \frac{1 - F(a)}{1 - F(t)}}{F(a)\{1 - F(t)\}} \right) & \text{if } x > t, \end{cases}$$

and

$$K(x, ds) = \begin{cases} f(s)ds 1_{\{s \leq t\}} \int_s^t dG(a) \left( \frac{1_{\{x \leq a\}} - \frac{F(a)}{F(t)}}{F(a)\{1 - F(a)\}} \right) & \text{if } x \leq t, \\ f(s)ds 1_{\{s > t\}} \int_t^s dG(a) \left( \frac{1_{\{x > a\}} - \frac{1 - F(a)}{1 - F(t)}}{F(a)\{1 - F(a)\}} \right) & \text{if } x > t. \end{cases}$$

This problem is treated in Bagiella (1997).

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