Web-based Supplementary Materials for "Treatment Decisions Based on Scalar and Functional Baseline Covariates" by Adam Ciarleglio, Eva Petkova, R. Todd Ogden, and Thaddeus Tarpey.

Web Appendix A: Correspondence with A-learning.

Consider the loss function given by equation (4) in Section 2.2:

$$L_{n,\phi}(\boldsymbol{\beta}, \boldsymbol{b}_1, \ldots, \boldsymbol{b}_q) = \frac{1}{n}\sum_{i=1}^{n}\left[Y_i - \phi(\boldsymbol{Z}_i, \boldsymbol{X}_i) - \left(\tilde{\boldsymbol{Z}}_i^{\intercal}\boldsymbol{\beta} + \sum_{\ell=1}^{q}\boldsymbol{X}_{\ell i}\boldsymbol{b}_\ell\right)\{A_i - \pi(\boldsymbol{Z}_i, \boldsymbol{X}_i)\}\right]^2. \tag{1}$$

If we let $\boldsymbol{\zeta} = (\boldsymbol{\beta}^{\intercal}, \boldsymbol{b}_1^{\intercal}, \ldots, \boldsymbol{b}_q^{\intercal})^{\intercal}$ and $\boldsymbol{H}_i = (\tilde{\boldsymbol{Z}}_i^{\intercal}, \boldsymbol{X}_{1i}^{\intercal}, \ldots, \boldsymbol{X}_{qi}^{\intercal})$ then we can write (1) as

$$L_n(\boldsymbol{\zeta}) = \frac{1}{n}\sum_{i=1}^{n}\left[Y_i - \phi(\boldsymbol{Z}_i, \boldsymbol{X}_i) - \boldsymbol{H}_i\boldsymbol{\zeta}\{A_i - \pi(\boldsymbol{Z}_i, \boldsymbol{X}_i)\}\right]^2.$$

Taking the derivative with respect to $\boldsymbol{\zeta}$ yields

$$\frac{\partial}{\partial\boldsymbol{\zeta}}L_n(\boldsymbol{\zeta}) = -\frac{2}{n}\sum_{i=1}^{n}\left[Y_i - \phi(\boldsymbol{Z}_i, \boldsymbol{X}_i) - \boldsymbol{H}_i\boldsymbol{\zeta}\{A_i - \pi(\boldsymbol{Z}_i, \boldsymbol{X}_i)\}\right]\boldsymbol{H}_i^{\intercal}\{A_i - \pi(\boldsymbol{Z}_i, \boldsymbol{X}_i)\},$$

and solving the set of estimating equations $\frac{\partial}{\partial\boldsymbol{\zeta}}L_n(\boldsymbol{\zeta}) = 0$ for $\boldsymbol{\zeta}$ is equivalent to solving the estimating equations that are solved in the context of A-learning.

Web Appendix B: Brief Discussion on Confidence Intervals for the Difference in Mean Outcomes Under Competing Regimes

Let g and g_1 be two competing rules for assigning treatment. Furthermore, let $V_g = E\{Y^*(g)\}$ and $V_{g_1} = E\{Y^*(g_1)\}$ be the expected values of the response of interest using treatment allocation procedures g and g_1 respectively and let $I = V_g - V_{g_1}$. Since larger values of the response are preferable, if $I > 0$ then allocation procedure g is considered to be superior to g_1 whereas if $I \leq 0$ then g is equivalent or inferior to g_1. We are interested in constructing a confidence interval for I and employ a bootstrap procedure that is outlined below.

Let V_g be the mean response for those who follow the treatment assignment depending on the baseline scalar and functional covariates. The estimate of this value, $\hat{V}_g$, is computed from the sample by taking the average response for those subjects who actually received the optimal treatment prescribed by regime g. Let V_1 be the mean response for those who take treatment 1. The estimate of this value, $\hat{V}_1$, is computed from the sample simply by taking the average response for those subjects who received treatment 1. To obtain a $(1-\alpha)100\%$ confidence interval for $I = V_g - V_1$ the following bootstrap procedure is employed:

1. Draw B bootstrap samples with replacement from the original data.

2. For each bootstrap sample b in $\{1, \ldots, B\}$, obtain an estimate for the treatment regime g, which we refer to as $\hat{g}^{(b)}$, and compute $\hat{I}^{(b)} = \hat{V}_{\hat{g}^{(b)}} - \hat{V}_1^{(b)}$ where $\hat{V}_{\hat{g}^{(b)}}$ and $\hat{V}_1^{(b)}$ are the estimated mean responses under $\hat{g}^{(b)}$ and treatment 1 respectively in the bth bootstrap sample.

3. From $\hat{I}^{(1)}, \ldots, \hat{I}^{(B)}$, compute the $\alpha/2$th and $(1-\alpha/2)$th percentiles to construct a $(1-\alpha)100\%$ confidence interval for I.

One reviewer pointed out that standard methods for inference, including the bootstrap, may be invalid. Several investigators have developed approaches for handling the challenges associated with conducting inference in such a setting including Robins (2004); Chakraborty *et al.* (2009); Laber *et al.* (2014), and van der Laan and Luedtke (2014). However, none have specifically investigated settings in which the estimated regime depends on functional covariates. In Web Appendix C below, we apply the bootstrap procedure outlined above to our simulated data from Section 3 of the paper and show that the coverage of the constructed confidence intervals is acceptable for the settings that we consider.

Web Appendix C: Additional Results from Numerical Investigations

Estimation Accuracy for Scalar Contrast Parameters

Tables 1 - 6 show the Monte-Carlo mean β (se) values for the scalar parameters in the contrast in each setting for each scenario.

Table 1: Scenario 1: Monte-Carlo mean (se) for scalar contrast parameter estimates.

True Values	ϕ_1				ϕ_2			
	$n = 600$	$n = 300$	$n = 150$	$n = 75$	$n = 600$	$n = 300$	$n = 150$	$n = 75$
$\beta_0 = -0.65$	-0.65 (0.29)	-0.59 (0.42)	-0.56 (0.57)	-0.46 (0.80)	-0.52 (0.57)	-0.50 (0.85)	-0.46 (1.21)	-0.44 (1.80)
$\beta_1 = 0.65$	0.65 (0.04)	0.65 (0.07)	0.64 (0.10)	0.64 (0.15)	0.64 (0.13)	0.64 (0.19)	0.62 (0.28)	0.67 (0.40)
$\beta_2 = -0.65$	-0.65 (0.05)	-0.65 (0.07)	-0.64 (0.11)	-0.64 (0.16)	-0.65 (0.14)	-0.66 (0.20)	-0.66 (0.29)	-0.69 (0.39)

Table 2: Scenario 2: Monte-Carlo mean (se) for scalar contrast parameter estimates.

True Values	ϕ_1				ϕ_2			
	$n = 600$	$n = 300$	$n = 150$	$n = 75$	$n = 600$	$n = 300$	$n = 150$	$n = 75$
$\beta_0 = -0.65$	-0.64 (0.29)	-0.58 (0.39)	-0.54 (0.54)	-0.44 (0.71)	-0.54 (0.41)	-0.49 (0.56)	-0.44 (0.76)	-0.36 (1.09)
$\beta_1 = 0.65$	0.66 (0.07)	0.66 (0.10)	0.65 (0.15)	0.65 (0.21)	0.65 (0.10)	0.65 (0.14)	0.64 (0.20)	0.67 (0.26)
$\beta_2 = -0.65$	-0.66 (0.07)	-0.66 (0.10)	-0.65 (0.15)	-0.66 (0.21)	-0.66 (0.10)	-0.66 (0.13)	-0.66 (0.20)	-0.68 (0.27)

Table 3: Scenario 3: Monte-Carlo mean (se) for scalar contrast parameter estimates.

True Values	ϕ_1				ϕ_2			
	$n = 600$	$n = 300$	$n = 150$	$n = 75$	$n = 600$	$n = 300$	$n = 150$	$n = 75$
$\beta_0 = -0.65$	-0.67 (0.24)	-0.62 (0.34)	-0.56 (0.47)	-0.50 (0.65)	-0.54 (0.43)	-0.50 (0.61)	-0.46 (0.84)	-0.43 (1.24)
$\beta_1 = 0.65$	0.65 (0.05)	0.64 (0.07)	0.64 (0.10)	0.64 (0.15)	0.64 (0.09)	0.64 (0.12)	0.63 (0.19)	0.66 (0.27)
$\beta_2 = -0.65$	-0.65 (0.05)	-0.65 (0.07)	-0.64 (0.10)	-0.64 (0.15)	-0.65 (0.09)	-0.65 (0.13)	-0.65 (0.20)	-0.67 (0.27)

Table 4: Scenario 4: Monte-Carlo mean (se) for scalar contrast parameter estimates.

True Values	ϕ_1				ϕ_2			
	$n = 600$		$n = 300$		$n = 600$		$n = 300$	
$\beta_0 = -0.65$	-0.66	(0.74)	-0.59	(1.08)	-0.69	(1.60)	-0.62	(2.33)
$\beta_1 = 0.65$	0.65	(0.05)	0.65	(0.08)	0.64	(0.13)	0.64	(0.19)
$\beta_2 = -0.65$	-0.65	(0.06)	-0.65	(0.09)	-0.65	(0.15)	-0.66	(0.21)
$\beta_3 = 0$	0.00	(0.05)	0.00	(0.08)	-0.01	(0.13)	0.00	(0.19)
$\beta_4 = 0$	0.00	(0.06)	0.00	(0.09)	0.02	(0.13)	0.02	(0.19)
$\beta_5 = 0$	0.00	(0.06)	-0.01	(0.09)	0.01	(0.13)	-0.01	(0.21)
$\beta_6 = 0$	0.00	(0.06)	0.00	(0.09)	-0.01	(0.12)	0.00	(0.20)
$\beta_7 = 0$	0.00	(0.05)	0.00	(0.08)	0.00	(0.11)	0.01	(0.18)
$\beta_8 = 0$	0.01	(0.06)	0.01	(0.09)	0.00	(0.13)	0.00	(0.20)
$\beta_9 = 0$	0.00	(0.06)	0.00	(0.09)	-0.01	(0.13)	0.00	(0.20)
$\beta_{10} = 0$	0.00	(0.06)	0.00	(0.09)	0.01	(0.14)	0.00	(0.20)
$\beta_{11} = 0$	0.00	(0.06)	0.01	(0.09)	-0.01	(0.14)	0.00	(0.20)
$\beta_{12} = 0$	0.00	(0.06)	0.01	(0.08)	0.01	(0.13)	0.01	(0.20)
$\beta_{13} = 0$	0.00	(0.05)	-0.01	(0.09)	-0.01	(0.13)	-0.02	(0.19)
$\beta_{14} = 0$	0.01	(0.06)	0.00	(0.09)	0.01	(0.14)	0.01	(0.19)
$\beta_{15} = 0$	0.00	(0.05)	0.00	(0.07)	0.00	(0.12)	0.01	(0.17)

Table 5: Scenario 5: Monte-Carlo mean (se) for scalar contrast parameter estimates.

True Values	ϕ_1				ϕ_2			
	$n = 600$		$n = 300$		$n = 600$		$n = 300$	
$\beta_0 = -0.65$	-0.63	(0.73)	-0.60	(1.03)	-0.60	(1.05)	-0.51	(1.56)
$\beta_1 = 0.65$	0.66	(0.07)	0.66	(0.11)	0.65	(0.10)	0.65	(0.14)
$\beta_2 = -0.65$	-0.65	(0.07)	-0.66	(0.11)	-0.65	(0.10)	-0.66	(0.14)
$\beta_3 = 0$	0.00	(0.06)	0.00	(0.08)	-0.01	(0.08)	-0.01	(0.12)
$\beta_4 = 0$	0.00	(0.06)	0.00	(0.09)	0.01	(0.09)	0.01	(0.12)
$\beta_5 = 0$	0.00	(0.06)	-0.01	(0.09)	0.00	(0.09)	-0.01	(0.13)
$\beta_6 = 0$	0.00	(0.06)	0.00	(0.09)	0.00	(0.09)	0.00	(0.13)
$\beta_7 = 0$	0.00	(0.05)	0.00	(0.08)	0.00	(0.08)	0.00	(0.12)
$\beta_8 = 0$	0.01	(0.06)	0.01	(0.09)	0.00	(0.08)	0.01	(0.13)
$\beta_9 = 0$	-0.01	(0.06)	-0.01	(0.09)	-0.01	(0.09)	-0.01	(0.13)
$\beta_{10} = 0$	0.00	(0.06)	0.00	(0.08)	0.01	(0.09)	0.00	(0.13)
$\beta_{11} = 0$	0.00	(0.06)	0.00	(0.09)	-0.01	(0.09)	-0.01	(0.13)
$\beta_{12} = 0$	0.00	(0.06)	0.01	(0.09)	0.01	(0.08)	0.01	(0.13)
$\beta_{13} = 0$	0.00	(0.06)	0.00	(0.09)	-0.01	(0.08)	-0.02	(0.11)
$\beta_{14} = 0$	0.01	(0.06)	0.00	(0.08)	0.01	(0.08)	0.01	(0.12)
$\beta_{15} = 0$	0.00	(0.05)	0.00	(0.07)	0.00	(0.08)	0.00	(0.11)

Table 6: Scenario 6: Monte-Carlo mean (se) for scalar contrast parameter estimates.

True Values	ϕ_1		ϕ_2	
	$n = 600$	$n = 300$	$n = 600$	$n = 300$
$\beta_0 = -0.65$	-0.67 (0.59)	-0.59 (0.89)	-0.62 (1.10)	-0.51 (1.58)
$\beta_1 = 0.65$	0.65 (0.05)	0.64 (0.07)	0.64 (0.09)	0.64 (0.13)
$\beta_2 = -0.65$	-0.65 (0.06)	-0.65 (0.08)	-0.65 (0.10)	-0.66 (0.14)
$\beta_3 = 0$	0.00 (0.04)	0.00 (0.07)	-0.01 (0.09)	0.00 (0.13)
$\beta_4 = 0$	0.00 (0.04)	0.00 (0.07)	0.01 (0.09)	0.02 (0.13)
$\beta_5 = 0$	0.00 (0.05)	-0.01 (0.08)	0.00 (0.09)	-0.01 (0.14)
$\beta_6 = 0$	0.00 (0.05)	0.00 (0.07)	-0.01 (0.09)	-0.00 (0.14)
$\beta_7 = 0$	0.00 (0.05)	0.00 (0.07)	0.00 (0.08)	0.00 (0.12)
$\beta_8 = 0$	0.00 (0.05)	0.01 (0.07)	0.00 (0.09)	0.00 (0.14)
$\beta_9 = 0$	0.00 (0.05)	0.00 (0.07)	0.00 (0.09)	0.00 (0.13)
$\beta_{10} = 0$	0.00 (0.05)	0.00 (0.07)	0.01 (0.09)	0.00 (0.13)
$\beta_{11} = 0$	0.00 (0.05)	0.01 (0.07)	-0.01 (0.09)	0.00 (0.14)
$\beta_{12} = 0$	0.00 (0.05)	0.00 (0.07)	0.01 (0.09)	0.01 (0.14)
$\beta_{13} = 0$	0.00 (0.04)	0.00 (0.07)	-0.01 (0.09)	-0.02 (0.13)
$\beta_{14} = 0$	0.00 (0.05)	0.00 (0.07)	0.01 (0.10)	0.01 (0.14)
$\beta_{15} = 0$	0.00 (0.04)	0.00 (0.06)	0.00 (0.08)	0.01 (0.12)

Estimation Accuracy of Functional Contrast Parameters

Figure 1 provides information on estimation accuracy of the functional contrast parameters $\{\omega_1, \omega_2\}$ for Scenarios 1 - 3 and $\{\omega_1, \ldots, \omega_{15}\}$ for Scenarios 4 - 6. For ease of comparison, we present box plots of the log IMSE values for each coefficient function for each setting for each scenario.

Bootstrap Confidence Intervals

Below we show results of applying the bootstrap resampling approach discussed in Web Appendix B to our simulated data. We applied this resampling procedure to 250 data sets from Scenarios 1 - 3 for sample sizes 75, 150, 300, and 600, using ϕ_1 as the working model for h_0. Let g correspond to the treatment decision model that includes the scalar and functional covariates being assessed in the numerical investigations.

We used $B = 500$ bootstrap samples to obtain confidence intervals for I_1, the average

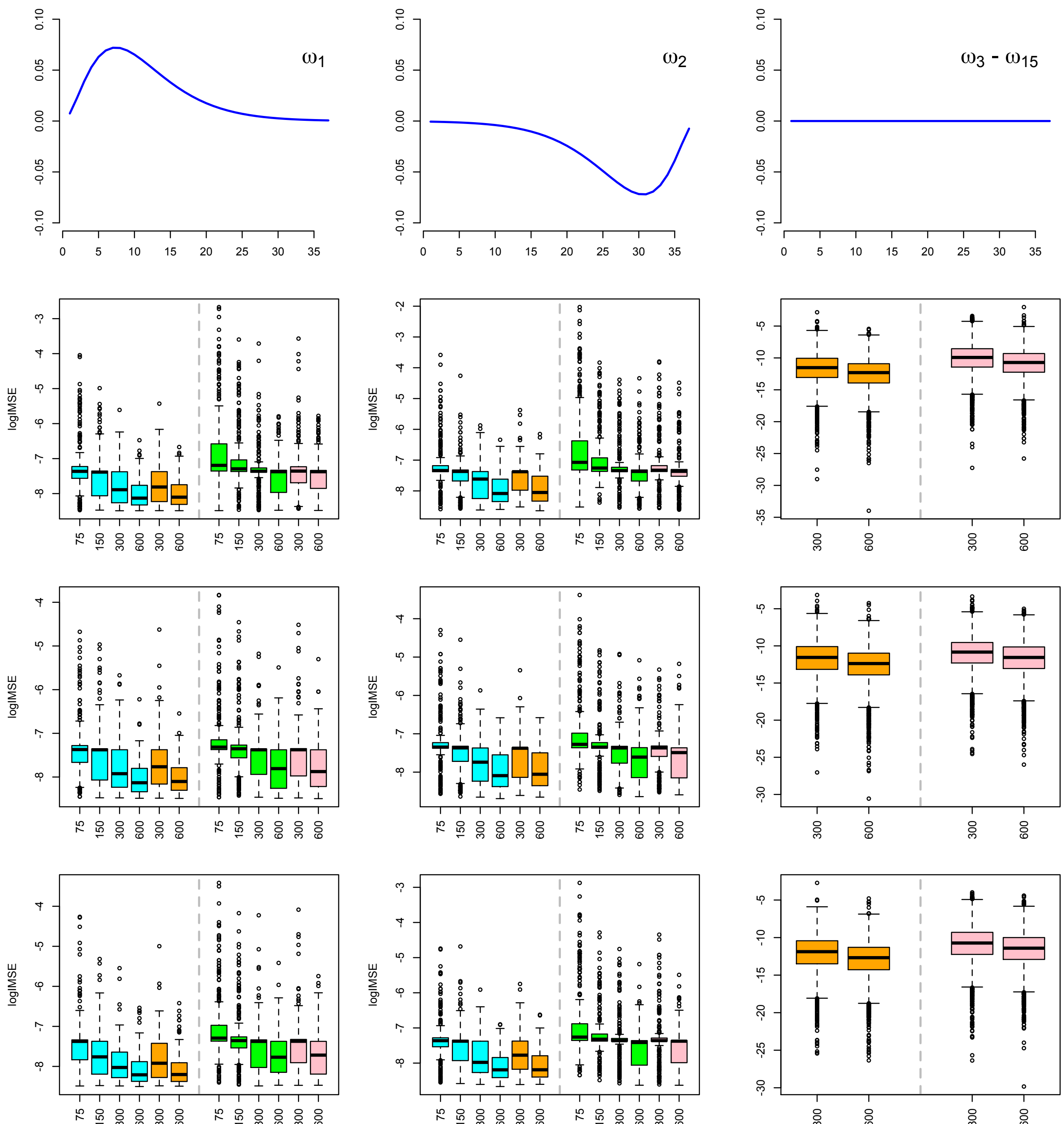

Figure 1: **First Row**: true contrast coefficient functions. **Second Row**: log IMSE values from Scenarios 1 (cyan) and 4 (orange) using ϕ_1 and Scenarios 1 (green) and 4 (pink) using ϕ_2 for each coefficient function directly above in top row. **Third Row**: log IMSE values from Scenarios 2 (cyan) and 5 (orange) using ϕ_1 and Scenarios 2 (green) and 5 (pink) using ϕ_2 for each coefficient function directly above in top row. **Fourth Row**: log IMSE values from Scenarios 3 (cyan) and 6 (orange) using ϕ_1 and Scenarios 3 (green) and 6 (pink) using ϕ_2 for each coefficient function directly above in top row.

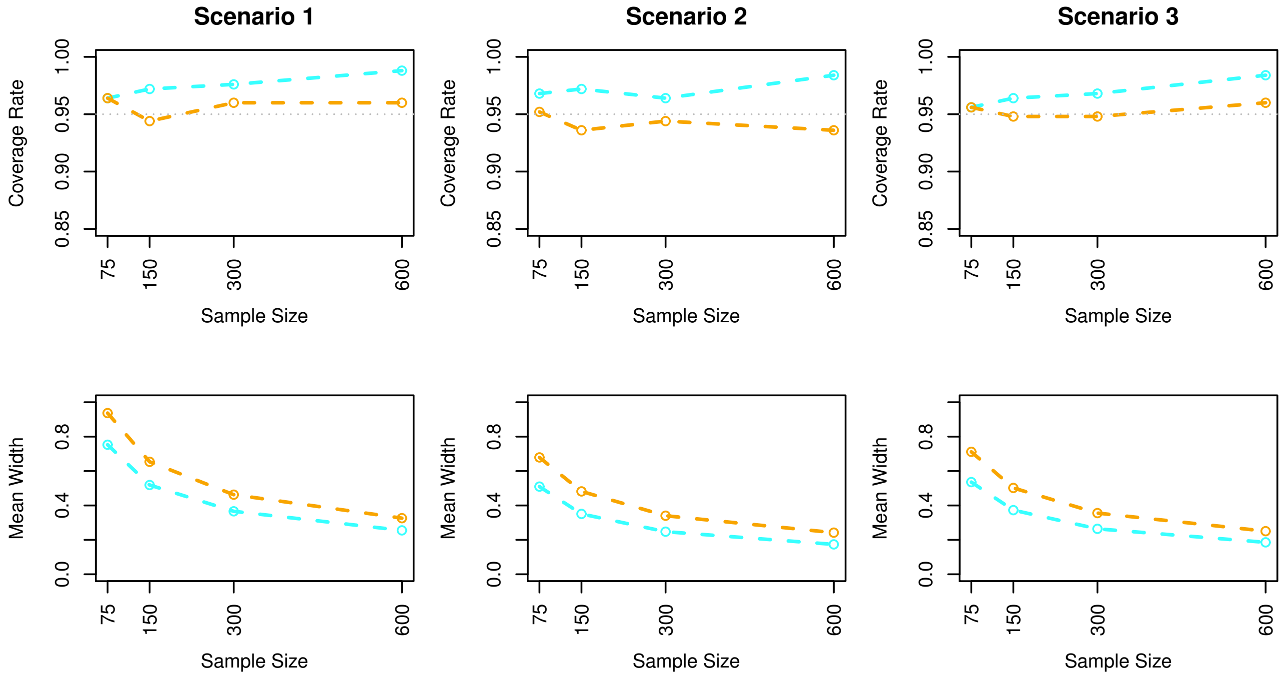

Figure 2: **First Row**: Coverage rate of bootstrap confidence intervals for mean improvements I_0 (cyan) and I_1 (orange) for Scenarios 1 - 3 and at different sample sizes. **Second Row**: Corresponding mean interval widths.

improvement in using g rather than treatment 1 for all subjects, and for I_0, the average improvement in using g rather than treatment 0 for all subjects. In all scenarios, we note that use of the true optimal treatment over treatment 1 yields an average improvement of about 0.50 while use of the true optimal treatment over treatment 0 yields an average improvement of about 0.38.

The coverage rates and mean widths of the 95% bootstrap confidence intervals for the improvement values in each setting and for different sample sizes are shown in top and bottom panels of Figure 2 respectively. For our simulated data, the typical bootstrap confidence interval appears to perform satisfactorily with respect to coverage and width.

Table 7: Average time (sd) in seconds to estimate the treatment regime based on 10 fits.

		n			
Scenario	ϕ	75	150	300	600
1	ϕ_1	1.254 (0.025)	1.399 (0.027)	1.760 (0.049)	2.526 (0.063)
	ϕ_2	0.608 (0.012)	0.677 (0.014)	0.871 (0.048)	1.227 (0.041)
2	ϕ_1	1.264 (0.033)	1.395 (0.027)	1.709 (0.020)	2.483 (0.044)
	ϕ_2	0.622 (0.027)	0.677 (0.012)	0.839 (0.033)	1.202 (0.039)
3	ϕ_1	1.273 (0.030)	1.412 (0.023)	1.751 (0.026)	2.520 (0.043)
	ϕ_2	0.604 (0.018)	0.684 (0.016)	0.832 (0.011)	1.210 (0.029)
4	ϕ_1	-	-	33.294 (6.542)	39.859 (3.555)
	ϕ_2	-	-	8.805 (0.412)	12.207 (0.365)
5	ϕ_1	-	-	30.489 (4.687)	45.356 (6.448)
	ϕ_2	-	-	8.437 (0.442)	12.563 (0.537)
6	ϕ_1	-	-	30.488 (2.112)	42.877 (3.276)
	ϕ_2	-	-	8.726 (0.328)	12.515 (0.464)

Web Appendix D: Computational Considerations

For each combination of scenario, working baseline function, and sample size considered in the numerical investigations of Section 3, we computed the time to estimate the treatment regime using our proposed method on 10 data sets. All computing was done on an Apple iMac desktop with a 3.4 GHz Intel Core i7 processor using R version 3.0.3. Table 7 shows the average time to fit and standard deviation in seconds over the 10 data sets in each setting.

References

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