

Additional File 1:

A comparative study of augmented inverse propensity weighted estimators using outcome-adaptive lasso and other penalized regression methods

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1. Appendix: Description and results of numerical experiments

1.1 Notation

Let Y be the outcome variable of interest, and let Z be the treatment variable, where $Z = 1$ corresponds to the treatment group and $Z = 0$ corresponds to the control group. Let $Y(1)$ and $Y(0)$ denote the potential outcomes under treatment and control, respectively. Define X_j ($j = 1, 2, \dots, p$) as the j -th covariate, and let \mathbf{X} be a p -dimensional vector of covariates observed prior to Z . In the potential outcome framework, we assume the stable unit treatment value assumption (SUTVA) and consistency, implying the outcome Y is whichever potential outcome aligns with the actual treatment (i.e., $Y = ZY(1) + (1 - Z)Y(0)$).

For each participant i ($= 1, 2, \dots, n$) in an observational study, uppercase letters (e.g., Y_i, Z_i, \mathbf{X}_i) denote random variables, while the corresponding lowercase letters (e.g., y_i, z_i, \mathbf{x}_i) denote their realized values. The set of random variables $\{Y_i, Z_i, \mathbf{X}_i\}$ is assumed to be independently and identically distributed.

We introduce the partition of a covariate index set based on its relationship with the outcome and treatment:

1. \mathcal{C} (confounders): variables related to both the outcome and the treatment.
2. \mathcal{P} (outcome predictors): variables related only to the outcome.
3. \mathcal{I} (instrumental variables): variables related only to the treatment.
4. \mathcal{S} (spurious variables): variables related to neither the outcome nor the treatment.

The outcome-oriented covariate selection targets the variables related to the outcome, namely $j \in \mathcal{C} \cup \mathcal{P}$.

We focus on the popular measure of treatment effect (Witte and Didelez 2018), the average treatment effect (ATE) defined as $\theta = E[Y(1)] - E[Y(0)]$.

1.2 Penalized regression methods

We used lasso and OAL for parameter estimation in the PS model assuming a logistic regression. Additionally, we used lasso, elastic net, SCAD, adaptive lasso, adaptive elastic net, LSP, and MCP for parameter estimation in the outcome models assuming a linear regression. Table 1 summarizes the ATE estimators used in the numerical experiments, along with the methods used to estimate the parameters in the PS and outcome models. The AIPW estimators using the OAL for the PS model are classified as AIPW-OCSvP. We used IPW-OAL and gComp-AdL as reference values, each relying solely on either the PS model or the outcome models. We used AIPW-Targ, which relies on the outcome-oriented covariates $j \in \mathcal{C} \cup \mathcal{P}$, as a target of AIPW-OCSvP.

Under the logistic model for the PS, the OAL estimates $\hat{\alpha}(OAL)$ are obtained by solving

$$\hat{\boldsymbol{\alpha}}(OAL) = \underset{\boldsymbol{\alpha}}{\operatorname{argmin}} \left[\sum_{i=1}^n \{-z_i(\mathbf{x}_i^T \boldsymbol{\alpha}) + \log(1 + \exp(\mathbf{x}_i^T \boldsymbol{\alpha}))\} + \lambda \sum_{j=1}^d \hat{\omega}_j |\alpha_j| \right],$$

where $\hat{\omega}_j = |\tilde{\beta}_j|^{-\gamma}$ with $\gamma > 1$, and $\tilde{\beta}_j$ is the ordinary least squares estimate for X_j obtained from a linear regression of Y on Z and \mathbf{X} . OAL is a straightforward variant of the ordinary adaptive lasso that incorporates information from the outcome model when computing the weights and thus can be implemented using existing statistical packages such as the *glmnet* package in R.

The lasso was implemented using the `cv.glmnet` function of *glmnet* package in R with default arguments. OAL was implemented using the `cv.glmnet` function to select hyperparameters, following the method outlined by Shortreed and Ertefaie [24]. Adaptive lasso (AdL) for outcome models was implemented by the `cv.glmnet` function with the penalty factors of $|\hat{\boldsymbol{\beta}}(\text{ols})|^{-1}$, where $\hat{\boldsymbol{\beta}}(\text{ols})$ was the ordinary least squares estimate obtained from the same outcome regression model. Elastic net (EN) was implemented by the `cv.glmnet` function using the elastic net mixing parameter $\alpha = 0.5$. Notably, the value of α of 0 or 1 corresponds to the ridge or lasso penalty, respectively. Adaptive elastic net (AEN) was implemented on the `aenet` function of *msaenet* package in R using the elastic net mixing parameter $\alpha = \{0.2, 0.4, \dots, 0.8\}$. SCAD and MCP were implemented using the `cv.ncvreg` function of the *ncvreg* package in R, with default arguments. LSP was implemented by iterating adaptive lasso updates: we started with an initial weights $\hat{w}_j^{(0)} = 1$ for all j and updated the weights $\hat{\mathbf{w}}^{(l+1)} = 1/(|\hat{\boldsymbol{\beta}}^{(l)}| + 0.0001)$, repeating up to $l_{\max} = 4$ [30]. We selected the hyperparameters for each penalized covariate selection method by 10-fold cross-validation with default loss functions, except in the case of OAL.

Table 1. The ATE estimators used in the analysis of a clinical trial example and numerical experiments.

Estimator name	ATE estimator	Variable selection method for PS model	Variable selection method for outcome model
naive	Difference in means	-	-
IPW-OAL	IPW	OAL	-
gComp-AdL	g-computation	-	adaptive lasso
AIPW-Targ	AIPW	$x_j j \in \mathcal{C} \cup \mathcal{P}$	$x_j j \in \mathcal{C} \cup \mathcal{P}$
AIPW-Las-Las	AIPW	lasso	lasso
AIPW-OAL-Las	AIPW	OAL	lasso
AIPW-OAL-EN	AIPW	OAL	elastic net
AIPW-OAL-AdL	AIPW	OAL	adaptive lasso

AIPW-OAL-AEN	AIPW	OAL	adaptive elastic net
AIPW-OAL-SCAD	AIPW	OAL	SCAD
AIPW-OAL-LSP	AIPW	OAL	log-sum penalty
AIPW-OAL-MCP	AIPW	OAL	MCP
AIPW-Farrell*	AIPW	lasso	lasso

* The estimator proposed by Farrell² uses lasso only to select covariates to be adjusted for and then fits unpenalized PS and outcome models with the selected covariates for the AIPW estimator.

1.3 Setup of numerical experiments

Suppose that each participant i has a covariate vector \mathbf{X}_i , which is independently and identically distributed from a p -dimensional multivariate normal distribution with mean vector $\boldsymbol{\mu} = \mathbf{0}$, every variance equal to 1, and every correlation coefficient ρ . The binary treatment variable Z_i and the continuous outcome variable Y_i are generated as follows:

$$\text{logit}\{\Pr(Z_i = 1|\mathbf{X}_i)\} = \sum_{j=1}^p \alpha_j X_{ij}, Y_i = 0.5Z_i + \sum_{j=1}^p \beta_j X_{ij} + \epsilon_i,$$

where ϵ_i is an error term denoting an independently and identically distributed random variable from a standard normal distribution. To evaluate the performance under strong and weak confounding, we specify $\boldsymbol{\alpha}$ and $\boldsymbol{\beta}$ as follows:

Strong confounding: $\boldsymbol{\alpha} = \{1, 1, 0, 0, 1, 1, 0, \dots, 0\}$, $\boldsymbol{\beta} = \{0.6, 0.6, 0.6, 0.6, 0, 0, 0, \dots, 0\}$,

Weak confounding: $\boldsymbol{\alpha} = \{0.4, 0.4, 0, 0, 1, 1, 0, \dots, 0\}$, $\boldsymbol{\beta} = \{0.2, 0.2, 0.6, 0.6, 0, 0, 0, \dots, 0\}$.

Under weak confounding, identifying the true confounders is more difficult than under strong confounding. In all scenarios, $\mathcal{C} = \{1, 2\}$, $\mathcal{P} = \{3, 4\}$, $\mathcal{I} = \{5, 6\}$, and $\mathcal{S} = \{7, \dots, p\}$.

To examine model mis-specification, we introduce the transformed variables $\mathbf{U} = \{3X_1/(1 + \exp X_2), 5 \sin X_2, X_3^3/3, 5 \sin X_4, (X_5 + X_6)/\sqrt{2}, 5 \sin X_6, X_7, \dots, X_p\}$. As an example, we used \mathbf{U} to generate the treatment variable instead of \mathbf{X} and \mathbf{X} to generate the outcome variable in the scenario where the PS model was mis-specified but the outcome models were correctly specified. The transformed variable \mathbf{U} is unobservable; therefore, the PS and outcome regression models always include \mathbf{X} as exploratory variables, even when composing the AIPW-Targ estimator.

To assess performance under binary covariates, we used the transformed covariates \mathbf{X}_{binary} to evaluate the performance under binary covariates. $X_{binary,j}$ is set to 1 if $X_j > 0$; otherwise, $X_{binary,j}$ is set to -1. All covariates are standardized via Z-score normalization prior to performing penalized regression.

We consider $(n, p) \in \{(200, 80), (500, 200), (1000, 400)\}$ for the sample size (n) and number of covariates (p). We investigated three correlation levels $\rho \in \{0, 0.2, 0.5\}$ in the scenarios where both PS and outcome models can be correctly specified while we used one correlation level $\rho = 0$ in the other scenarios. Each condition was replicated 1000 times.

1.4 Results under strong confounding scenarios

Figures A.1 to A.6 graphically present the ATE estimates of each method for 1000 simulations under strong confounding. The dashed line indicates the true ATE of 0.5. The white circles represent the mean values of 1000 ATE estimates. The naive estimates are excluded from the figures because they significantly differed from the other estimates. The boxes for AIPW-OCSvP with the oracle property for the PS and outcome models are highlighted in gray.

Tables A.1 to A.6 present the bias, standard error, and root-mean-squared error for the ATE estimators under strong confounding. Values exceeding 10^8 or falling below -10^8 are displayed with a hyphen.

$n = 200, p = 80$ (strong confounding, continuous covariates)

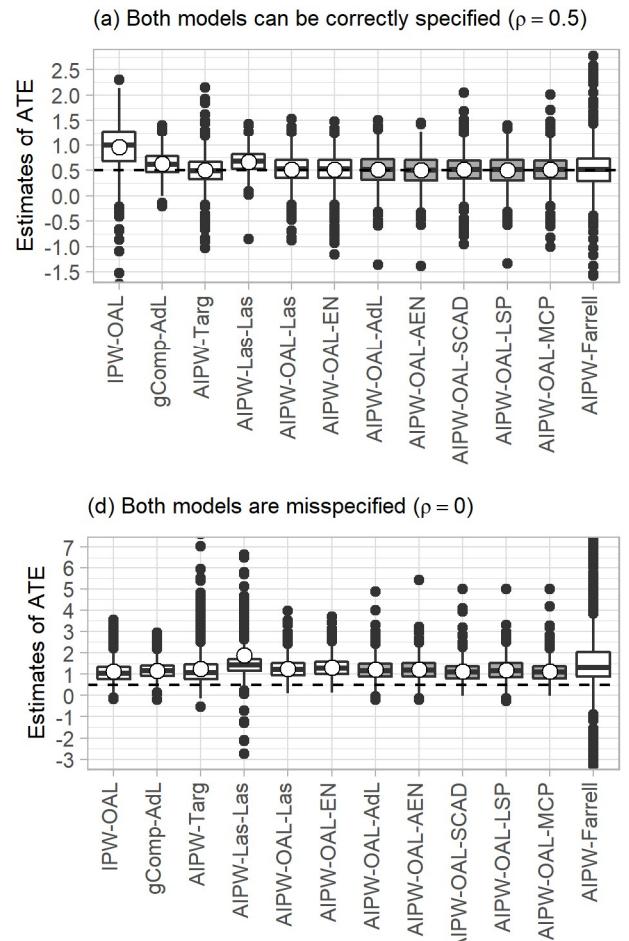
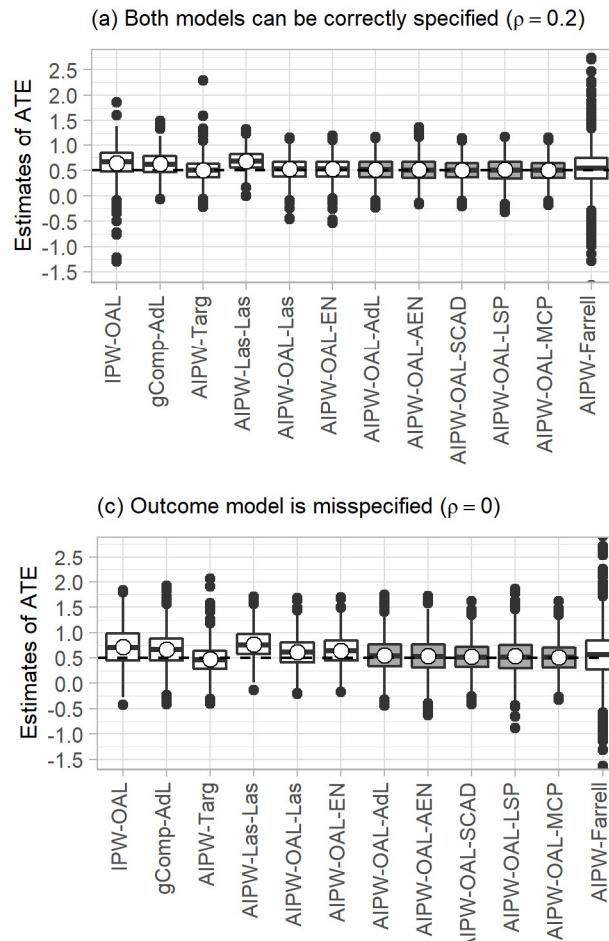
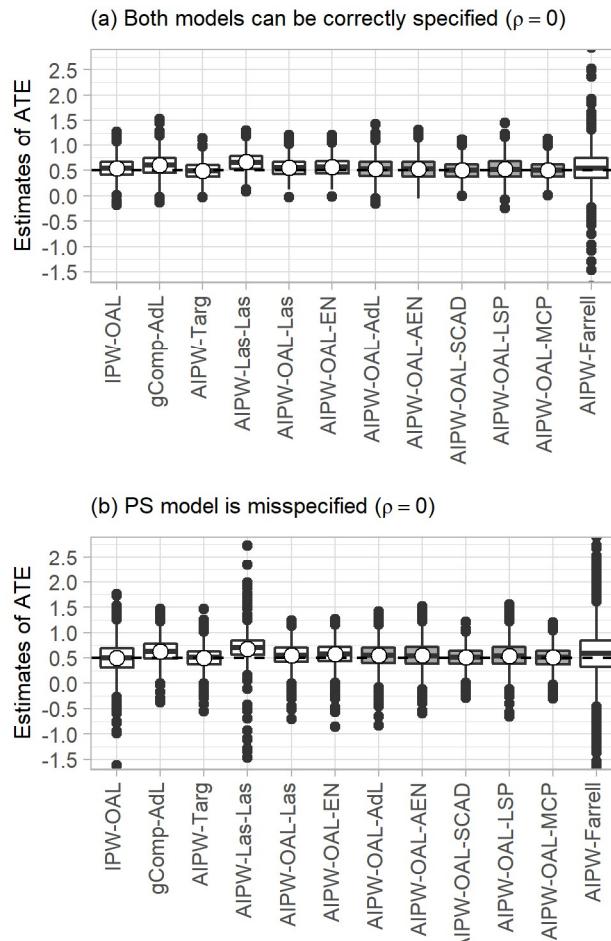


Figure A.1. Box plots of 1000 estimates for the average treatment effect (ATE) with continuous covariates and $(n, p) = (200, 80)$ under strong confounding. The vertical axis range is different only in the bottom-right plot (d).

Table A.1. Bias, standard error (SE), and root-mean-squared error (RMSE) for the ATE estimators with continuous covariates and $(n, p) = (200, 80)$ under strong confounding. (a), (b), (c), and (d) represent the scenarios where both PS and outcome models can be correctly specified, PS model is misspecified, the outcome model is misspecified, and both PS and outcome models are misspecified, respectively. Values exceeding 10^8 or falling below -10^8 are displayed with a hyphen.

$n = 200, p = 80$ (strong confounding, binary covariates)

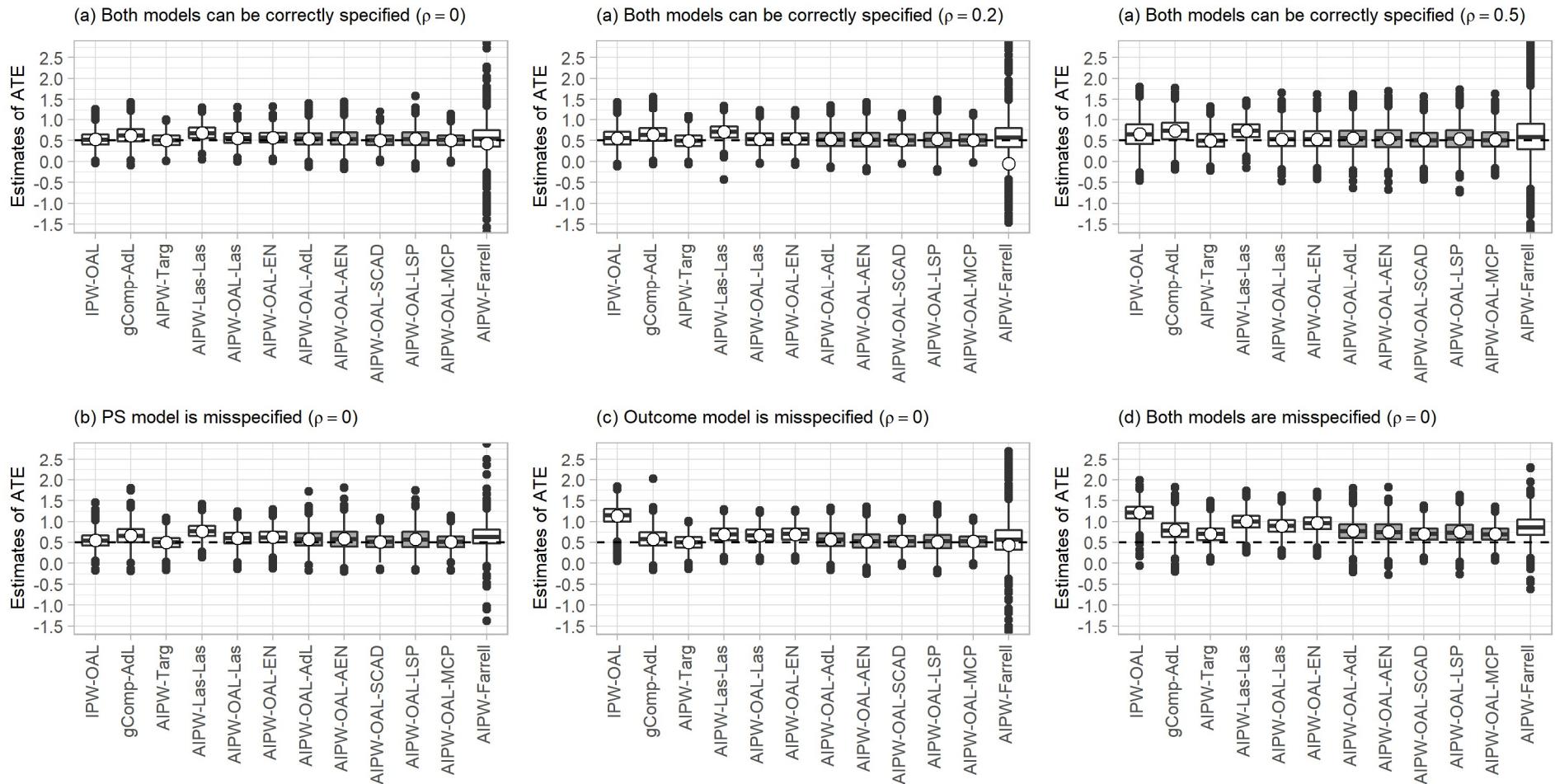


Figure A.2. Box plots of 1000 estimates for the average treatment effect (ATE) with binary covariates and $(n, p) = (200, 80)$ under strong confounding.

Table A.2. Bias, standard error (SE), and root-mean-squared error (RMSE) for the ATE estimators with binary covariates and $(n, p) = (200, 80)$ under strong confounding. (a), (b), (c), and (d) represent the scenarios where both PS and outcome models can be correctly specified, PS model is misspecified, the outcome model is misspecified, and both PS and outcome models are misspecified, respectively. Values exceeding 10^8 or falling below -10^8 are displayed with a hyphen.

	(a) $\rho = 0$			(a) $\rho = 0.2$			(a) $\rho = 0.5$			(b) $\rho = 0$			(c) $\rho = 0$			(d) $\rho = 0$		
	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE
naive	0.754	0.215	0.784	1.321	0.230	1.341	2.154	0.229	2.167	0.793	0.208	0.820	2.156	0.518	2.217	2.576	0.521	2.628
IPW-OAL	0.023	0.192	0.193	0.055	0.228	0.235	0.149	0.345	0.376	0.047	0.201	0.207	0.633	0.238	0.676	0.703	0.223	0.738
gComp-AdL	0.123	0.220	0.252	0.147	0.242	0.284	0.227	0.306	0.381	0.165	0.256	0.305	0.078	0.227	0.240	0.297	0.263	0.396
AIPW-Targ	-0.002	0.166	0.166	-0.005	0.191	0.191	-0.006	0.236	0.236	-0.004	0.167	0.167	-0.002	0.193	0.193	0.199	0.201	0.283
AIPW-Las-Las	0.174	0.182	0.252	0.204	0.203	0.288	0.234	0.243	0.337	0.271	0.189	0.330	0.190	0.204	0.278	0.501	0.220	0.547
AIPW-OAL-Las	0.052	0.182	0.190	0.030	0.206	0.209	0.030	0.278	0.280	0.102	0.194	0.219	0.165	0.194	0.255	0.395	0.214	0.449
AIPW-OAL-EN	0.067	0.183	0.195	0.038	0.205	0.209	0.033	0.277	0.279	0.127	0.195	0.233	0.193	0.199	0.277	0.463	0.222	0.513
AIPW-OAL-AdL	0.041	0.215	0.219	0.025	0.237	0.238	0.049	0.319	0.322	0.080	0.246	0.259	0.063	0.222	0.230	0.278	0.262	0.382
AIPW-OAL-AEN	0.043	0.230	0.234	0.026	0.249	0.250	0.044	0.327	0.330	0.084	0.270	0.283	0.028	0.236	0.237	0.257	0.280	0.380
AIPW-OAL-SCAD	0.006	0.179	0.179	0.005	0.203	0.203	0.012	0.277	0.277	0.015	0.184	0.185	0.022	0.193	0.194	0.203	0.207	0.289
AIPW-OAL-LSP	0.039	0.236	0.239	0.022	0.258	0.259	0.041	0.338	0.340	0.072	0.276	0.285	0.018	0.236	0.236	0.250	0.280	0.375
AIPW-OAL-MCP	0.006	0.179	0.179	0.005	0.203	0.203	0.013	0.275	0.276	0.013	0.182	0.183	0.020	0.193	0.194	0.199	0.205	0.286
AIPW-Farrell	-0.072	2.957	2.958	-0.557	17.071	17.080	-	-	-	-	-	-	-0.058	2.368	2.369	-	-	-

$n = 500, p = 200$ (strong confounding, continuous covariates)

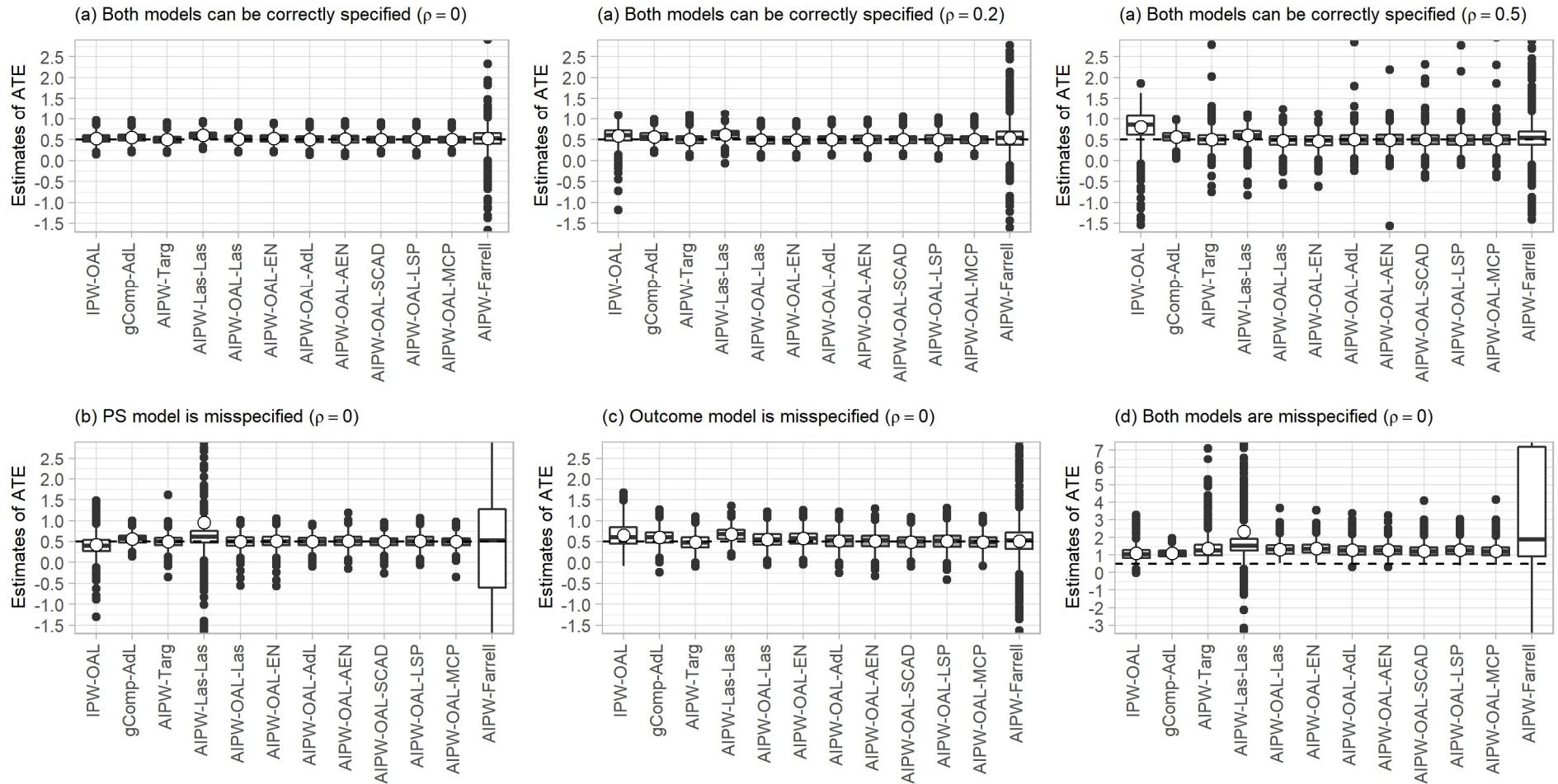


Figure A.3. Box plots of 1000 estimates for the average treatment effect (ATE) with continuous covariates and $(n, p) = (500, 200)$ under strong confounding. The vertical axis range is different only in the bottom-right plot (d).

Table A.3. Bias, standard error (SE), and root-mean-squared error (RMSE) for the ATE estimators with continuous covariates and $(n, p) = (500, 200)$ under strong confounding. (a), (b), (c), and (d) represent the scenarios where both PS and outcome models can be correctly specified, PS model is misspecified, the outcome model is misspecified, and both PS and outcome models are misspecified, respectively. Values exceeding 10^8 or falling below -10^8 are displayed with a hyphen.

	(a) $\rho = 0$			(a) $\rho = 0.2$			(a) $\rho = 0.5$			(b) $\rho = 0$			(c) $\rho = 0$			(d) $\rho = 0$		
	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE
naive	0.731	0.134	0.743	1.498	0.145	1.505	2.379	0.155	2.384	0.734	0.137	0.747	1.685	0.273	1.707	2.191	0.276	2.208
IPW-OAL	0.024	0.117	0.119	0.092	0.212	0.231	0.304	0.442	0.537	-0.080	0.296	0.307	0.158	0.302	0.340	0.598	0.460	0.754
gComp-AdL	0.051	0.109	0.120	0.065	0.123	0.139	0.067	0.137	0.153	0.058	0.122	0.135	0.097	0.178	0.203	0.584	0.239	0.631
AIPW-Targ	-0.002	0.103	0.103	0.003	0.133	0.133	0.008	0.248	0.248	-0.003	0.145	0.145	-0.018	0.179	0.180	0.873	0.645	1.086
AIPW-Las-Las	0.101	0.105	0.146	0.119	0.126	0.173	0.106	0.161	0.193	0.456	13.334	13.342	0.172	0.168	0.241	1.840	6.053	6.326
AIPW-OAL-Las	0.020	0.105	0.107	-0.010	0.132	0.132	-0.026	0.181	0.183	-0.003	0.155	0.155	0.051	0.184	0.191	0.818	0.347	0.889
AIPW-OAL-EN	0.029	0.105	0.109	-0.015	0.132	0.133	-0.035	0.181	0.184	0.007	0.160	0.160	0.072	0.185	0.199	0.857	0.339	0.922
AIPW-OAL-AdL	0.006	0.109	0.109	0.001	0.133	0.133	-0.003	0.192	0.192	0.001	0.141	0.141	0.015	0.188	0.188	0.764	0.357	0.843
AIPW-OAL-AEN	0.010	0.120	0.120	0.003	0.143	0.143	-0.004	0.196	0.196	0.014	0.153	0.154	0.016	0.195	0.196	0.775	0.358	0.854
AIPW-OAL-SCAD	-0.002	0.103	0.103	0.004	0.131	0.131	0.007	0.193	0.193	-0.003	0.131	0.131	-0.010	0.172	0.173	0.716	0.364	0.804
AIPW-OAL-LSP	0.006	0.120	0.120	0.002	0.147	0.147	-0.001	0.199	0.199	0.009	0.153	0.153	0.009	0.198	0.198	0.765	0.355	0.844
AIPW-OAL-MCP	-0.002	0.103	0.103	0.004	0.131	0.131	0.009	0.202	0.202	-0.003	0.130	0.130	-0.012	0.173	0.173	0.716	0.368	0.805
AIPW-Farrell	0.027	0.432	0.433	0.039	0.540	0.542	-	-	-	-	-	-	0.013	0.641	0.641	-	-	-

$n = 500, p = 200$ (strong confounding, binary covariates)

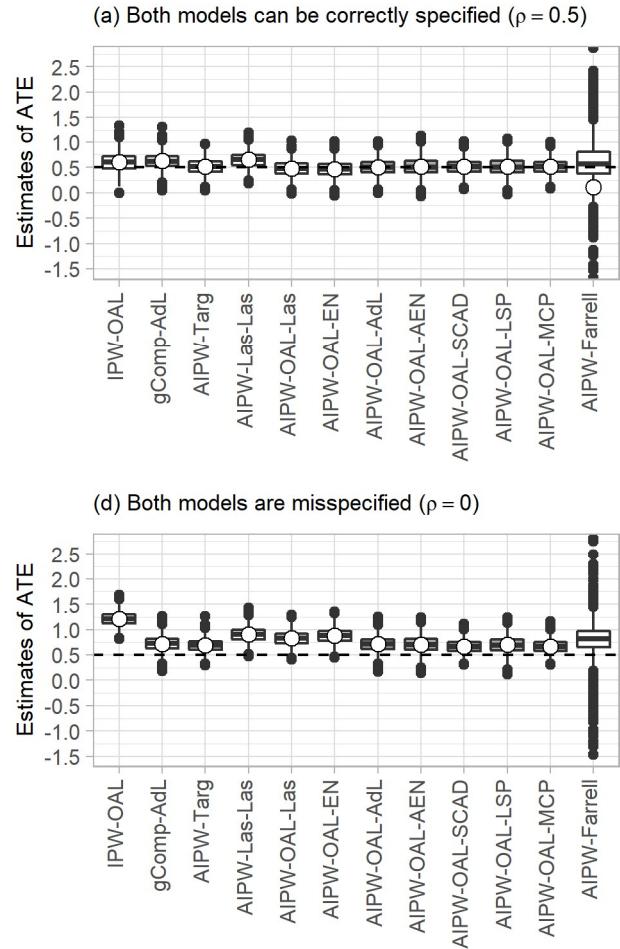
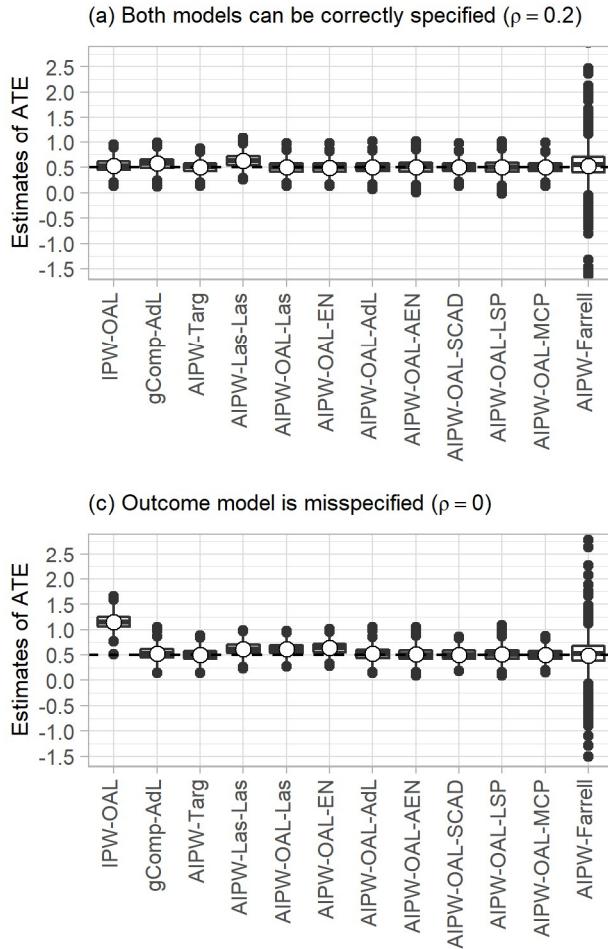
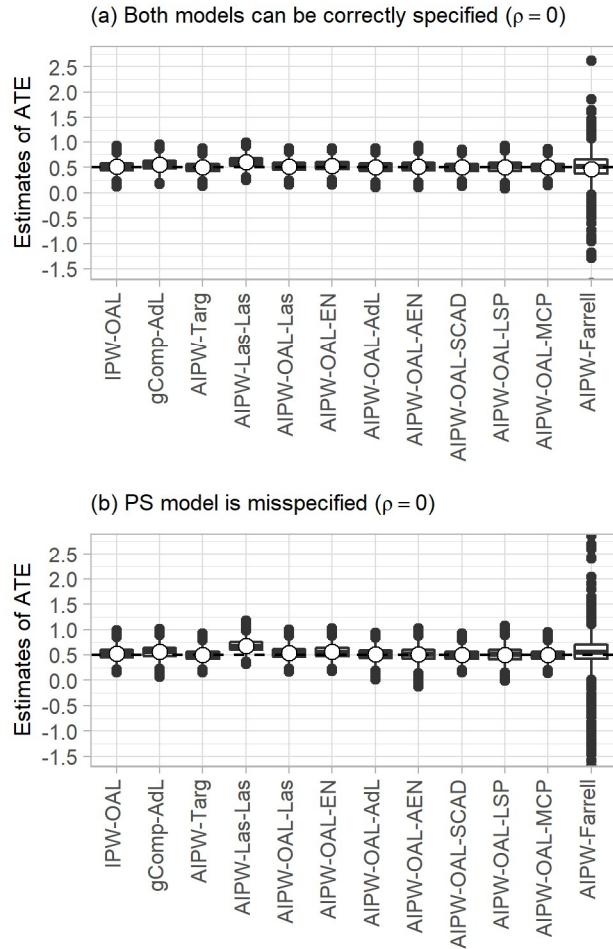


Figure A.4. Box plots of 1000 estimates for the average treatment effect (ATE) with binary covariates and $(n, p) = (500, 200)$ under strong confounding.

Table A.4. Bias, standard error (SE), and root-mean-squared error (RMSE) for the ATE estimators with binary covariates and $(n, p) = (500, 200)$ under strong confounding. (a), (b), (c), and (d) represent the scenarios where both PS and outcome models can be correctly specified, PS model is misspecified, the outcome model is misspecified, and both PS and outcome models are misspecified, respectively. Values exceeding 10^8 or falling below -10^8 are displayed with a hyphen.

	(a) $\rho = 0$			(a) $\rho = 0.2$			(a) $\rho = 0.5$			(b) $\rho = 0$			(c) $\rho = 0$			(d) $\rho = 0$		
	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE
naive	0.749	0.136	0.761	1.322	0.142	1.329	2.150	0.144	2.155	0.785	0.139	0.797	2.136	0.346	2.164	2.549	0.339	2.571
IPW-OAL	0.011	0.106	0.106	0.033	0.124	0.128	0.099	0.185	0.210	0.027	0.113	0.116	0.650	0.133	0.664	0.704	0.137	0.717
gComp-AdL	0.053	0.116	0.127	0.072	0.127	0.146	0.123	0.151	0.195	0.063	0.131	0.145	0.029	0.125	0.129	0.220	0.149	0.266
AIPW-Targ	0.000	0.104	0.104	0.004	0.115	0.115	0.011	0.143	0.143	-0.006	0.108	0.108	0.001	0.120	0.120	0.187	0.129	0.227
AIPW-Las-Las	0.105	0.110	0.152	0.130	0.124	0.180	0.151	0.150	0.213	0.172	0.118	0.209	0.114	0.124	0.169	0.402	0.141	0.426
AIPW-OAL-Las	0.020	0.104	0.106	-0.003	0.117	0.117	-0.023	0.150	0.151	0.038	0.115	0.121	0.115	0.116	0.164	0.325	0.134	0.351
AIPW-OAL-EN	0.029	0.105	0.109	-0.004	0.117	0.117	-0.031	0.151	0.154	0.056	0.117	0.130	0.135	0.117	0.178	0.377	0.139	0.401
AIPW-OAL-AdL	0.006	0.112	0.112	0.001	0.123	0.123	0.001	0.154	0.154	0.011	0.127	0.128	0.023	0.125	0.127	0.212	0.149	0.259
AIPW-OAL-AEN	0.011	0.124	0.124	0.005	0.135	0.135	0.012	0.166	0.167	0.011	0.146	0.147	0.007	0.131	0.131	0.206	0.165	0.264
AIPW-OAL-SCAD	0.000	0.104	0.104	0.004	0.115	0.115	0.010	0.144	0.144	-0.005	0.109	0.109	0.003	0.115	0.115	0.165	0.121	0.205
AIPW-OAL-LSP	0.006	0.127	0.127	0.002	0.137	0.137	0.009	0.167	0.167	0.005	0.145	0.145	0.006	0.133	0.133	0.198	0.169	0.261
AIPW-OAL-MCP	0.000	0.104	0.104	0.004	0.115	0.115	0.012	0.144	0.144	-0.005	0.109	0.109	0.002	0.115	0.115	0.165	0.122	0.205
AIPW-Farrell	-0.032	0.933	0.933	0.030	1.339	1.339	-0.388	33.013	33.015	-	-	-	-0.012	1.243	1.243	-	-	-

$n = 1000, p = 400$ (strong confounding, continuous covariates)

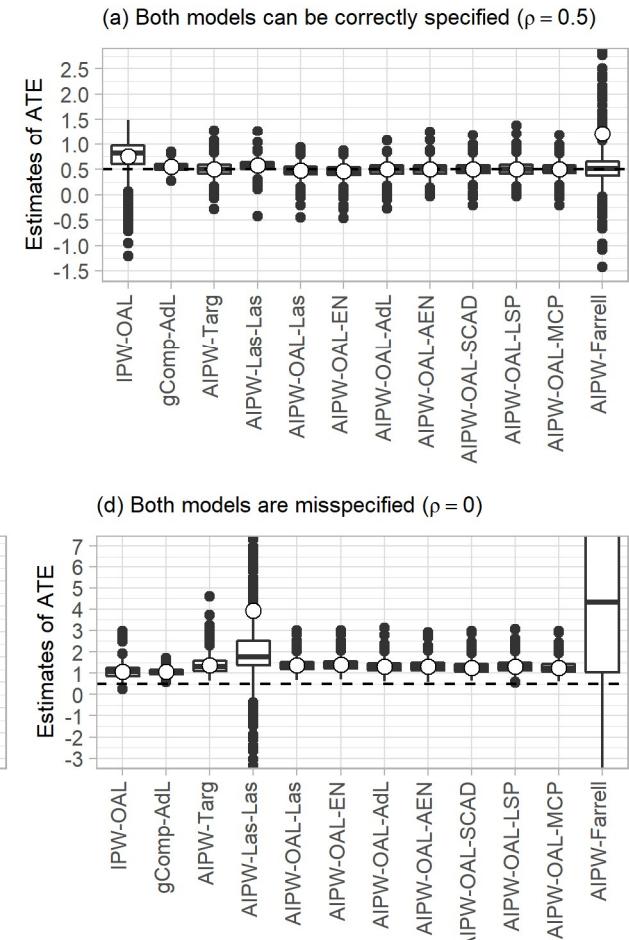
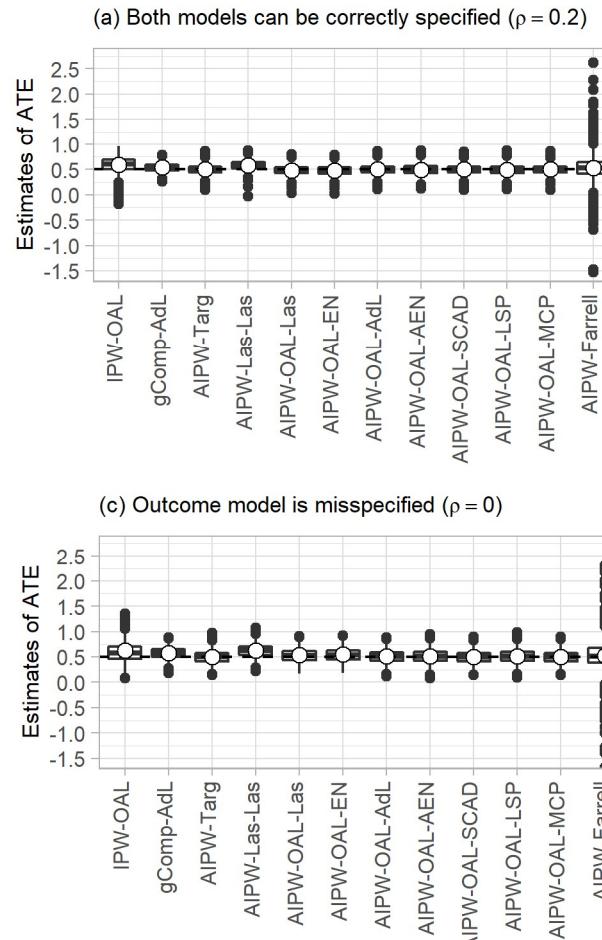
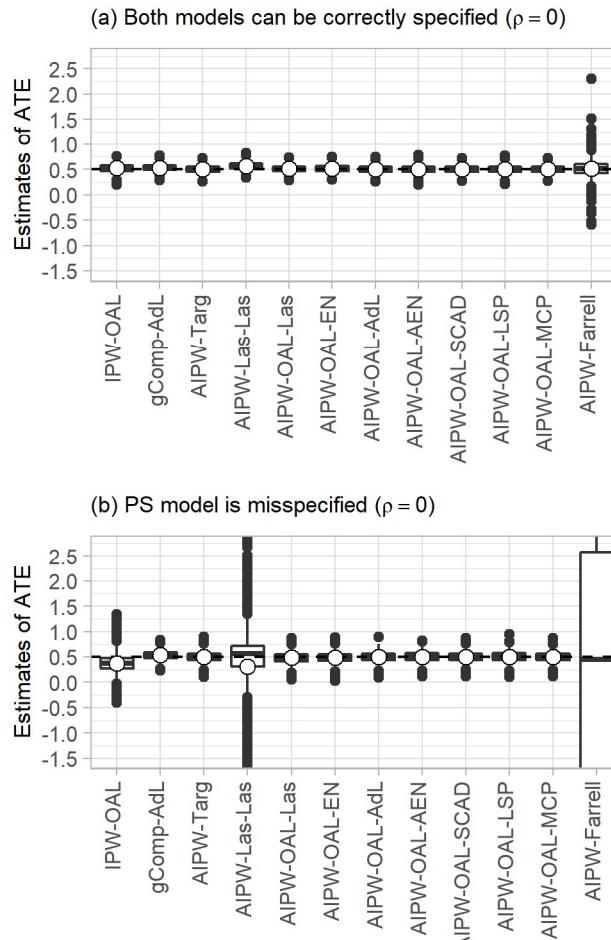


Figure A.5. Box plots of 1000 estimates for the average treatment effect (ATE) with continuous covariates and $(n, p) = (1000, 400)$ under strong confounding. The vertical axis range is different only in the bottom-right plot (d).

Table A.5. Bias, standard error (SE), and root-mean-squared error (RMSE) for the ATE estimators with continuous covariates and $(n, p) = (1000, 400)$ under strong confounding. (a), (b), (c), and (d) represent the scenarios where both PS and outcome models can be correctly specified, PS model is misspecified, the outcome model is misspecified, and both PS and outcome models are misspecified, respectively. Values exceeding 10^8 or falling below -10^8 are displayed with a hyphen.

	(a) $\rho = 0$			(a) $\rho = 0.2$			(a) $\rho = 0.5$			(b) $\rho = 0$			(c) $\rho = 0$			(d) $\rho = 0$		
	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE
naive	0.728	0.097	0.734	1.503	0.105	1.506	2.385	0.112	2.387	0.737	0.097	0.744	1.685	0.201	1.697	2.196	0.196	2.205
IPW-OAL	0.024	0.080	0.084	0.087	0.157	0.179	0.260	0.342	0.429	-0.124	0.203	0.238	0.124	0.240	0.270	0.565	0.342	0.661
gComp-AdL	0.030	0.071	0.077	0.038	0.083	0.091	0.048	0.089	0.101	0.032	0.079	0.085	0.074	0.110	0.133	0.552	0.168	0.577
AIPW-Targ	0.001	0.071	0.071	-0.001	0.092	0.092	0.005	0.139	0.139	0.001	0.096	0.096	-0.006	0.125	0.125	0.880	0.427	0.978
AIPW-Las-Las	0.068	0.076	0.102	0.079	0.094	0.123	0.075	0.118	0.140	-0.196	4.784	4.788	0.125	0.121	0.174	3.448	25.144	25.379
AIPW-OAL-Las	0.012	0.071	0.072	-0.017	0.095	0.096	-0.029	0.135	0.138	-0.016	0.102	0.103	0.032	0.130	0.134	0.854	0.277	0.897
AIPW-OAL-EN	0.017	0.072	0.074	-0.024	0.095	0.098	-0.039	0.136	0.141	-0.012	0.105	0.106	0.045	0.130	0.138	0.887	0.271	0.927
AIPW-OAL-AdL	0.003	0.073	0.073	-0.003	0.093	0.093	-0.002	0.130	0.130	-0.003	0.097	0.097	0.009	0.124	0.125	0.804	0.283	0.852
AIPW-OAL-AEN	0.005	0.080	0.081	-0.004	0.098	0.098	0.000	0.131	0.131	0.005	0.104	0.104	0.013	0.132	0.133	0.816	0.281	0.863
AIPW-OAL-SCAD	0.001	0.070	0.070	-0.001	0.092	0.092	0.005	0.132	0.132	0.001	0.092	0.092	-0.003	0.123	0.123	0.760	0.288	0.812
AIPW-OAL-LSP	0.003	0.081	0.081	-0.005	0.099	0.099	0.001	0.134	0.134	0.001	0.105	0.105	0.010	0.130	0.130	0.812	0.284	0.860
AIPW-OAL-MCP	0.001	0.071	0.071	-0.001	0.091	0.091	0.004	0.133	0.133	0.001	0.092	0.092	-0.003	0.123	0.123	0.759	0.291	0.812
AIPW-Farrell	0.012	0.243	0.244	0.027	0.377	0.378	0.718	20.051	20.064	-	-	-	0.021	0.416	0.416	-	-	-

$n = 1000, p = 400$ (strong confounding, binary covariates)

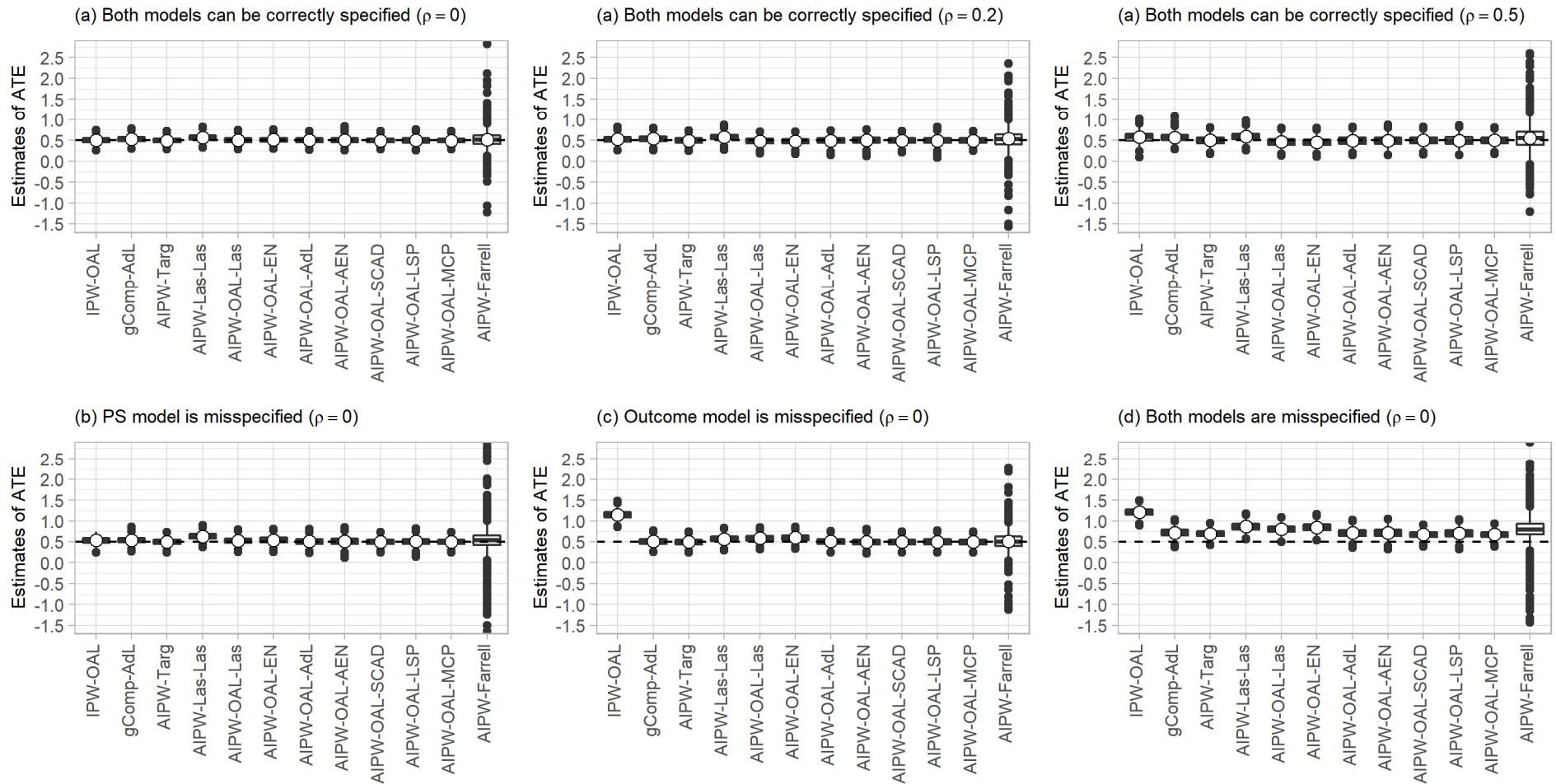


Figure A.6. Box plots of 1000 estimates for the average treatment effect (ATE) with binary covariates and $(n, p) = (1000, 400)$ under strong confounding.

Table A.6. Bias, standard error (SE), and root-mean-squared error (RMSE) for the ATE estimators with binary covariates and $(n, p) = (1000, 400)$ under strong confounding. (a), (b), (c), and (d) represent the scenarios where both PS and outcome models can be correctly specified, PS model is misspecified, the outcome model is misspecified, and both PS and outcome models are misspecified, respectively. Values exceeding 10^8 or falling below -10^8 are displayed with a hyphen.

	(a) $\rho = 0$			(a) $\rho = 0.2$			(a) $\rho = 0.5$			(b) $\rho = 0$			(c) $\rho = 0$			(d) $\rho = 0$		
	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE
naive	0.746	0.095	0.752	1.318	0.100	1.322	2.153	0.101	2.155	0.790	0.094	0.796	2.139	0.244	2.153	2.565	0.230	2.576
IPW-OAL	0.007	0.075	0.075	0.024	0.086	0.090	0.076	0.126	0.147	0.032	0.078	0.085	0.649	0.094	0.655	0.711	0.096	0.718
gComp-AdL	0.026	0.075	0.080	0.037	0.081	0.089	0.071	0.101	0.123	0.038	0.080	0.089	0.010	0.082	0.083	0.217	0.101	0.239
AIPW-Targ	-0.004	0.073	0.073	-0.006	0.080	0.080	0.000	0.103	0.103	0.000	0.076	0.076	-0.004	0.083	0.083	0.192	0.089	0.211
AIPW-Las-Las	0.066	0.078	0.102	0.078	0.088	0.118	0.093	0.110	0.144	0.132	0.079	0.154	0.069	0.089	0.112	0.366	0.098	0.379
AIPW-OAL-Las	0.006	0.073	0.073	-0.018	0.081	0.083	-0.039	0.104	0.111	0.027	0.079	0.084	0.082	0.079	0.114	0.304	0.094	0.318
AIPW-OAL-EN	0.012	0.073	0.074	-0.022	0.081	0.084	-0.050	0.105	0.116	0.041	0.081	0.091	0.097	0.079	0.125	0.347	0.096	0.360
AIPW-OAL-AdL	-0.002	0.075	0.075	-0.006	0.083	0.083	-0.009	0.106	0.106	0.008	0.082	0.083	0.007	0.082	0.082	0.212	0.101	0.235
AIPW-OAL-AEN	0.001	0.081	0.081	-0.004	0.092	0.092	-0.007	0.113	0.113	0.010	0.098	0.098	-0.001	0.086	0.086	0.217	0.112	0.244
AIPW-OAL-SCAD	-0.004	0.073	0.073	-0.006	0.080	0.080	0.000	0.102	0.102	0.000	0.076	0.076	-0.004	0.078	0.078	0.171	0.083	0.190
AIPW-OAL-LSP	-0.001	0.080	0.080	-0.005	0.092	0.092	-0.005	0.113	0.113	0.006	0.097	0.097	0.001	0.086	0.086	0.204	0.112	0.233
AIPW-OAL-MCP	-0.004	0.073	0.073	-0.006	0.079	0.080	0.001	0.102	0.102	0.000	0.076	0.076	-0.004	0.078	0.078	0.172	0.084	0.191
AIPW-Farrell	0.018	0.302	0.303	0.037	0.336	0.338	0.055	0.590	0.592	-	-	-	0.007	0.330	0.330	-	-	-

1.5 Results under weak confounding scenarios

Figures A.7 to A.12 graphically present the ATE estimates of each method for 1000 simulations under strong confounding. The dashed line indicates the true ATE of 0.5. The white circles represent the mean values of 1000 ATE estimates. The naive estimates are excluded from the figures because they significantly differed from the other estimates. The boxes for AIPW-OCSvP with the oracle property for the PS and outcome models are highlighted in gray.

Tables A.7 to A.12 present the bias, standard error, and root-mean-squared error for the ATE estimators under strong confounding. Values exceeding 10^8 or falling below -10^8 are displayed with a hyphen.

$n = 200, p = 80$ (weak confounding, continuous covariates)

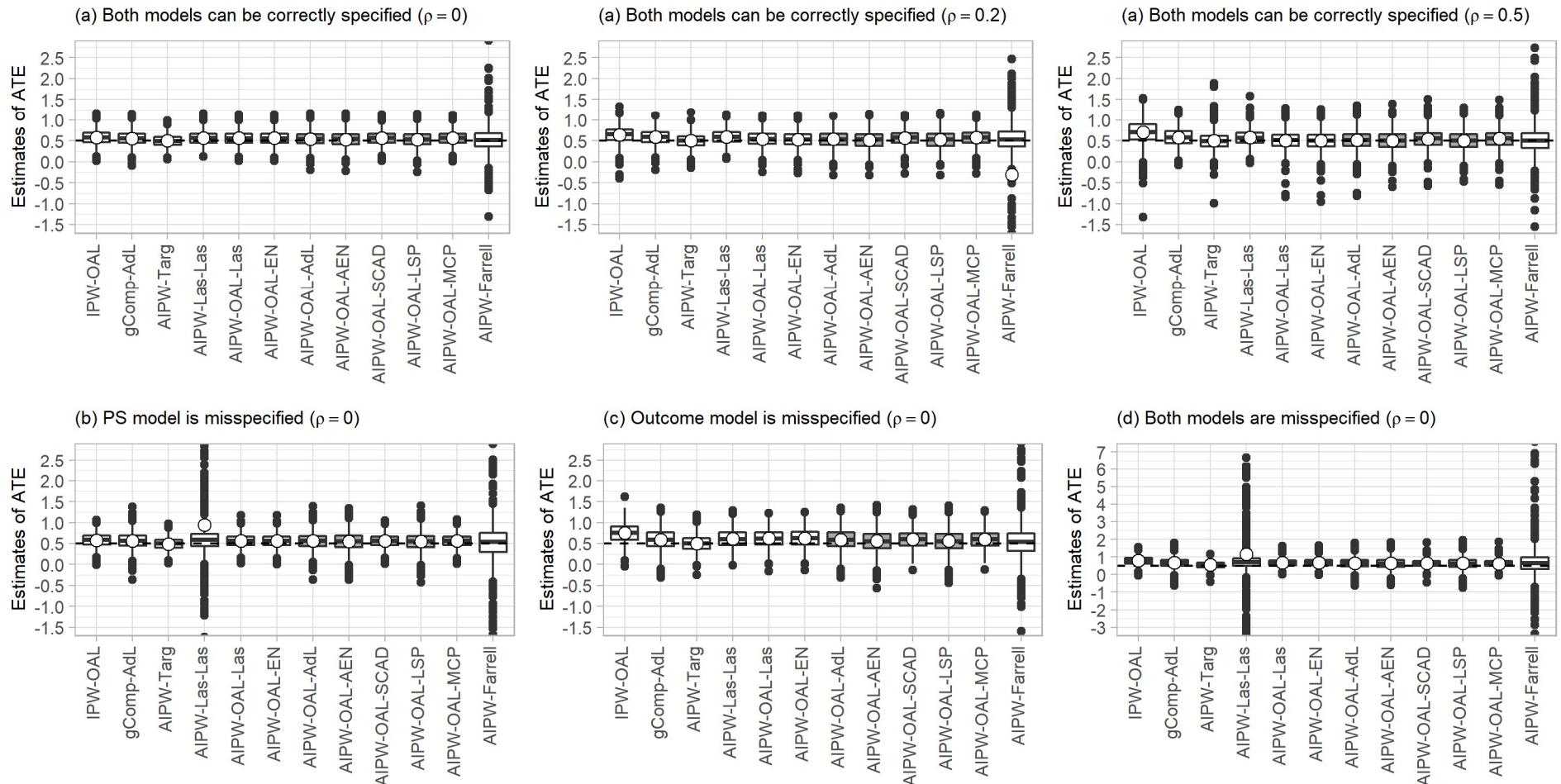


Figure A.7. Box plots of 1000 estimates for the average treatment effect (ATE) with continuous covariates and $(n, p) = (200, 80)$ under weak confounding. The vertical axis range is different only in the bottom-right plot (d).

Table A.7. Bias, standard error (SE), and root-mean-squared error (RMSE) for the ATE estimators with continuous covariates and $(n, p) = (200, 80)$ under weak confounding. (a), (b), (c), and (d) represent the scenarios where both PS and outcome models can be correctly specified, PS model is misspecified, the outcome model is misspecified, and both PS and outcome models are misspecified, respectively. Values exceeding 10^8 or falling below -10^8 are displayed with a hyphen.

$n = 200, p = 80$ (weak confounding, binary covariates)

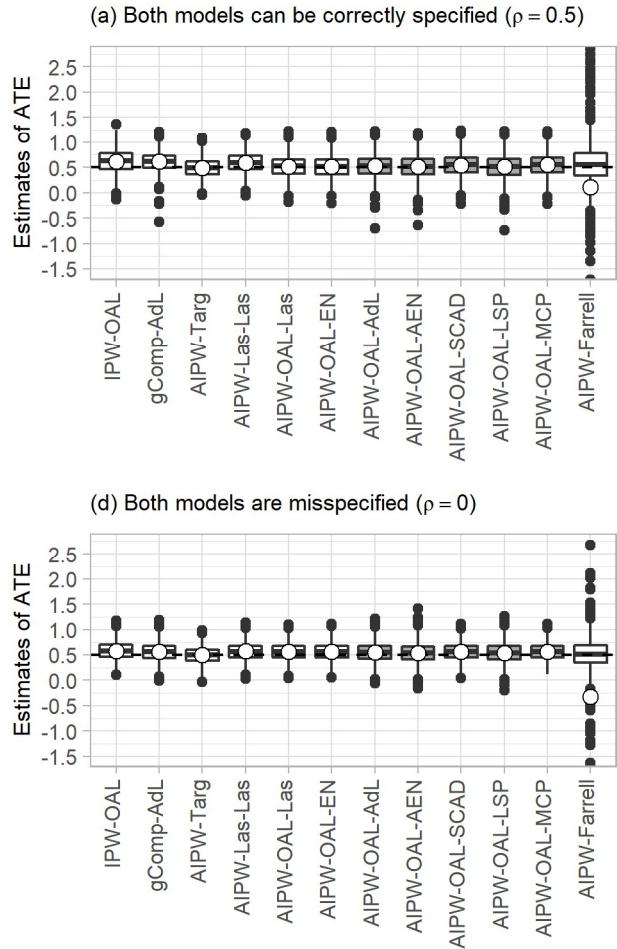
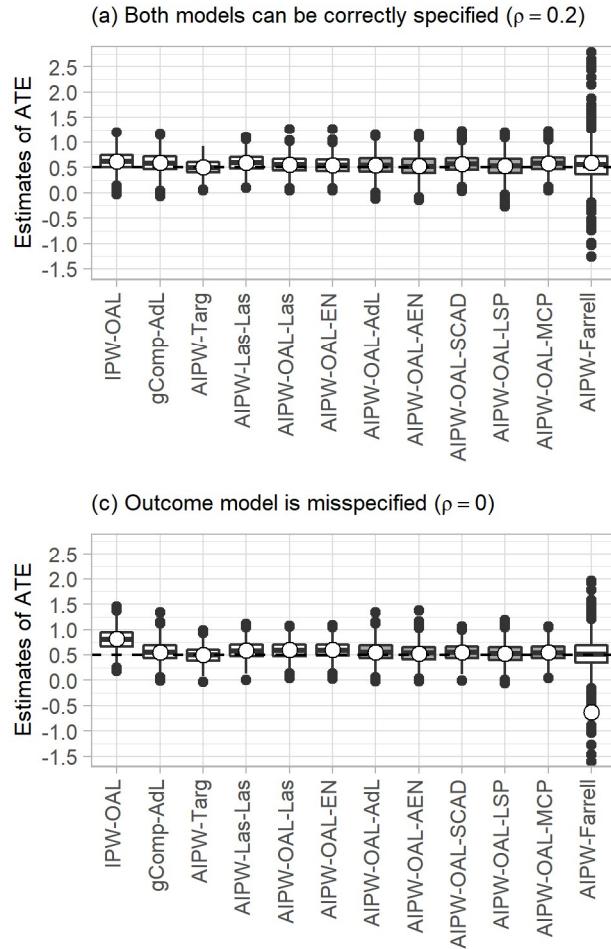
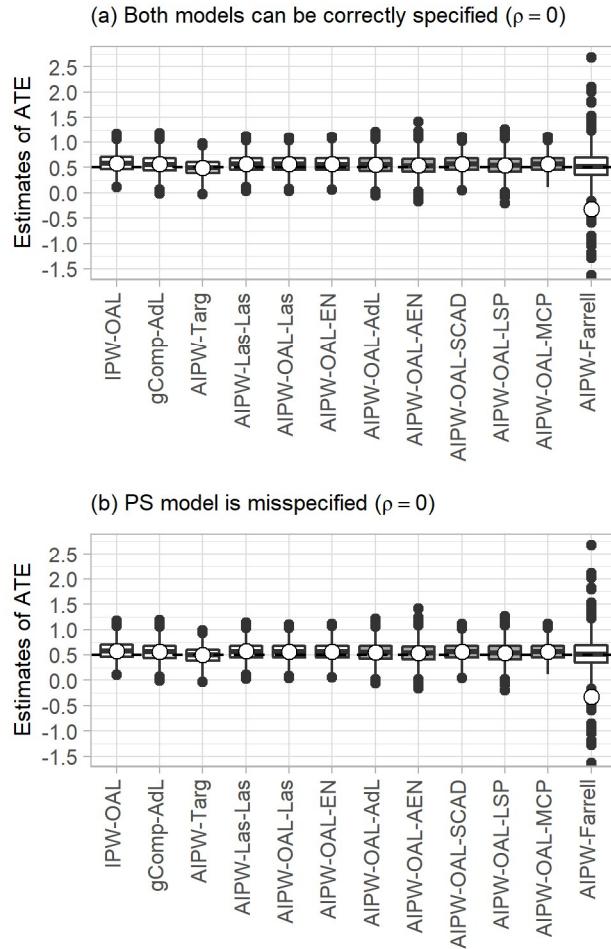


Figure A.8. Box plots of 1000 estimates for the average treatment effect (ATE) with binary covariates and $(n, p) = (200, 80)$ under weak confounding.

Table A.8. Bias, standard error (SE), and root-mean-squared error (RMSE) for the ATE estimators with binary covariates and $(n, p) = (200, 80)$ under weak confounding. (a), (b), (c), and (d) represent the scenarios where both PS and outcome models can be correctly specified, PS model is misspecified, the outcome model is misspecified, and both PS and outcome models are misspecified, respectively. Values exceeding 10^8 or falling below -10^8 are displayed with a hyphen.

	(a) $\rho = 0$			(a) $\rho = 0.2$			(a) $\rho = 0.5$			(b) $\rho = 0$			(c) $\rho = 0$			(d) $\rho = 0$		
	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE
naive	0.110	0.193	0.222	0.485	0.202	0.525	1.061	0.196	1.079	0.110	0.193	0.222	0.326	0.408	0.522	0.110	0.193	0.222
IPW-OAL	0.080	0.168	0.186	0.121	0.189	0.225	0.119	0.235	0.263	0.080	0.168	0.186	0.312	0.204	0.373	0.080	0.168	0.186
gComp-AdL	0.061	0.185	0.195	0.086	0.193	0.212	0.112	0.204	0.233	0.061	0.185	0.195	0.056	0.190	0.198	0.061	0.185	0.195
AIPW-Targ	-0.005	0.150	0.150	-0.002	0.158	0.158	-0.008	0.175	0.176	-0.005	0.150	0.150	-0.005	0.151	0.151	-0.005	0.150	0.150
AIPW-Las-Las	0.070	0.166	0.180	0.094	0.176	0.200	0.091	0.193	0.213	0.070	0.166	0.180	0.085	0.168	0.188	0.070	0.166	0.180
AIPW-OAL-Las	0.064	0.165	0.177	0.051	0.178	0.185	0.021	0.209	0.210	0.064	0.165	0.177	0.096	0.161	0.188	0.064	0.165	0.177
AIPW-OAL-EN	0.063	0.165	0.176	0.042	0.176	0.181	0.011	0.207	0.207	0.063	0.165	0.176	0.098	0.163	0.190	0.063	0.165	0.176
AIPW-OAL-AdL	0.051	0.189	0.196	0.042	0.200	0.204	0.023	0.226	0.227	0.051	0.189	0.196	0.055	0.190	0.198	0.051	0.189	0.196
AIPW-OAL-AEN	0.037	0.203	0.207	0.025	0.211	0.213	0.014	0.236	0.236	0.037	0.203	0.207	0.029	0.198	0.200	0.037	0.203	0.207
AIPW-OAL-SCAD	0.063	0.165	0.176	0.071	0.180	0.194	0.045	0.211	0.216	0.063	0.165	0.176	0.052	0.159	0.167	0.063	0.165	0.176
AIPW-OAL-LSP	0.039	0.204	0.208	0.026	0.217	0.218	0.012	0.245	0.245	0.039	0.204	0.208	0.030	0.200	0.202	0.039	0.204	0.208
AIPW-OAL-MCP	0.063	0.165	0.177	0.077	0.180	0.195	0.052	0.213	0.219	0.063	0.165	0.177	0.050	0.160	0.168	0.063	0.165	0.177
AIPW-Farrell	-0.823	25.845	25.858	0.096	1.912	1.914	-0.393	36.593	36.595	-0.823	25.845	25.858	-1.126	35.279	35.297	-0.823	25.845	25.858

$n = 500, p = 200$ (weak confounding, continuous covariates)

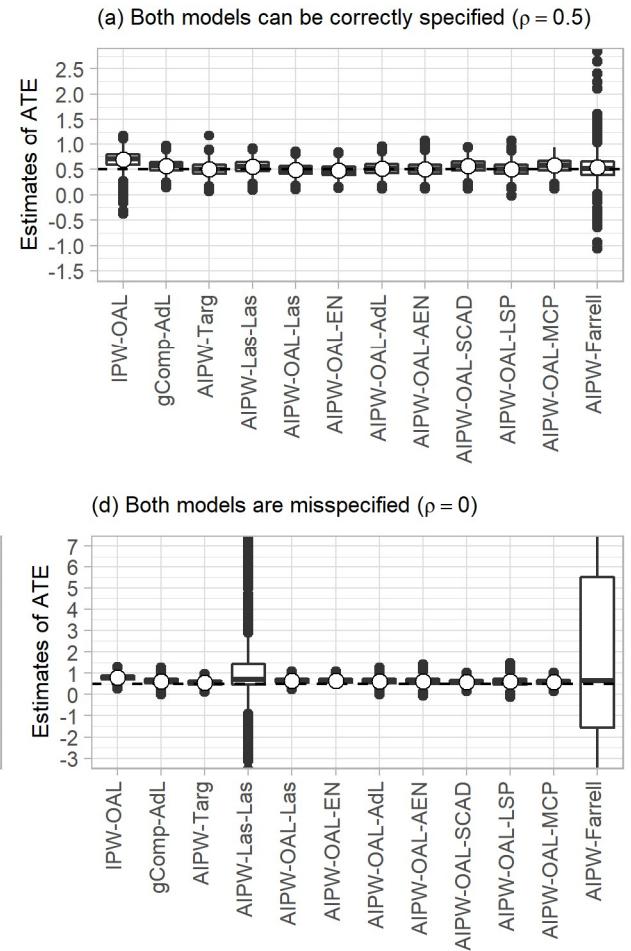
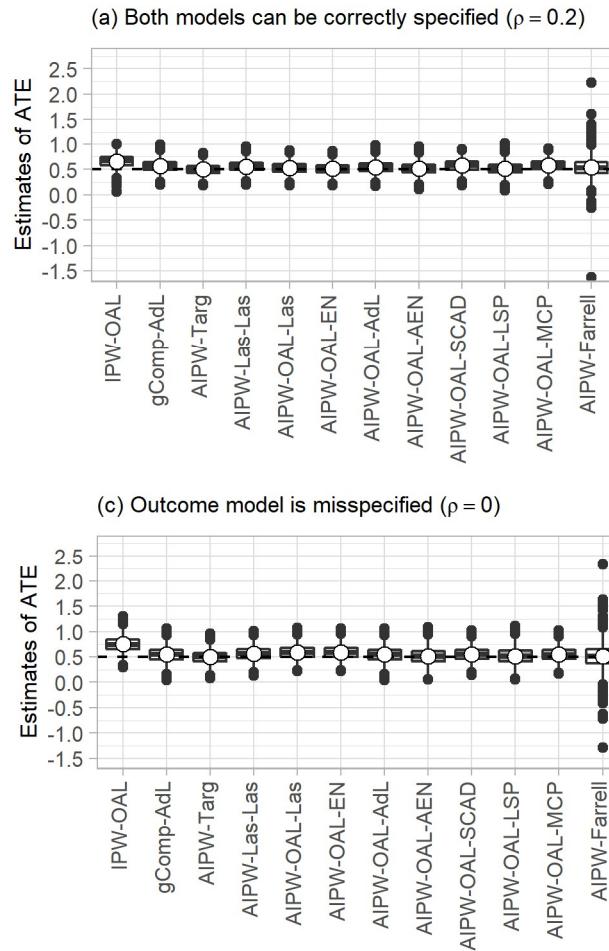
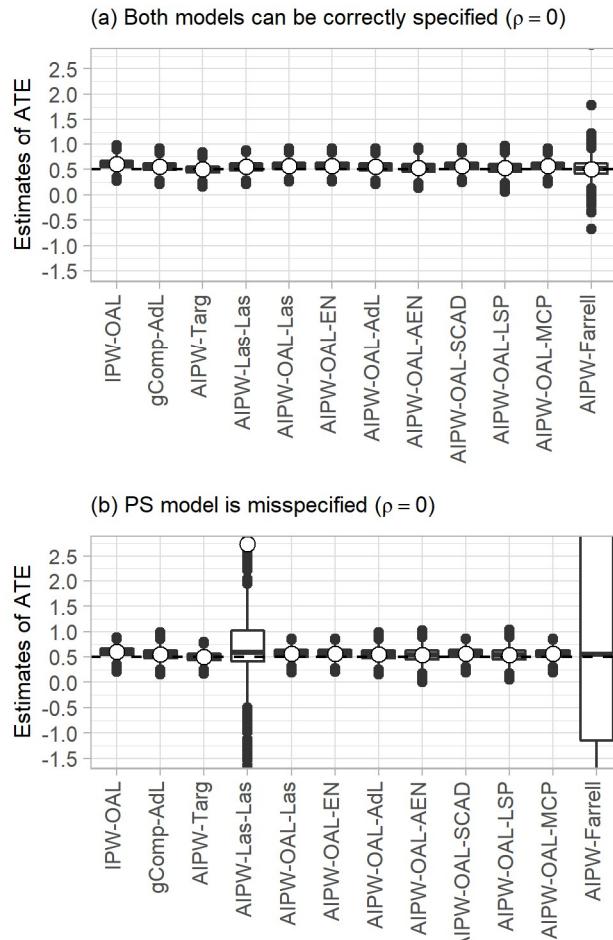


Figure A.9. Box plots of 1000 estimates for the average treatment effect (ATE) with continuous covariates and $(n, p) = (500, 200)$ under weak confounding. The vertical axis range is different only in the bottom-right plot (d).

Table A.9. Bias, standard error (SE), and root-mean-squared error (RMSE) for the ATE estimators with continuous covariates and $(n, p) = (500, 200)$ under weak confounding. (a), (b), (c), and (d) represent the scenarios where both PS and outcome models can be correctly specified, PS model is misspecified, the outcome model is misspecified, and both PS and outcome models are misspecified, respectively. Values exceeding 10^8 or falling below -10^8 are displayed with a hyphen.

	(a) $\rho = 0$			(a) $\rho = 0.2$			(a) $\rho = 0.5$			(b) $\rho = 0$			(c) $\rho = 0$			(d) $\rho = 0$		
	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE
naive	0.113	0.122	0.166	0.645	0.127	0.657	1.303	0.132	1.309	0.105	0.122	0.161	0.253	0.226	0.340	0.304	0.225	0.378
IPW-OAL	0.103	0.101	0.144	0.155	0.128	0.201	0.186	0.176	0.256	0.098	0.098	0.138	0.249	0.155	0.293	0.296	0.149	0.332
gComp-AdL	0.052	0.104	0.117	0.067	0.112	0.131	0.064	0.122	0.138	0.055	0.117	0.129	0.051	0.143	0.152	0.118	0.155	0.195
AIPW-Targ	0.000	0.094	0.094	-0.002	0.099	0.099	0.003	0.126	0.126	0.003	0.092	0.092	-0.005	0.132	0.132	0.051	0.123	0.133
AIPW-Las-Las	0.050	0.101	0.113	0.059	0.110	0.125	0.056	0.127	0.139	2.241	142.220	142.238	0.065	0.142	0.156	-5.012	192.469	192.534
AIPW-OAL-Las	0.063	0.098	0.117	0.027	0.107	0.111	-0.010	0.124	0.125	0.066	0.099	0.119	0.090	0.134	0.161	0.144	0.132	0.196
AIPW-OAL-EN	0.063	0.099	0.117	0.013	0.106	0.107	-0.028	0.125	0.128	0.067	0.099	0.120	0.093	0.134	0.163	0.152	0.134	0.203
AIPW-OAL-AdL	0.049	0.106	0.116	0.039	0.116	0.122	0.016	0.128	0.129	0.054	0.118	0.129	0.050	0.143	0.152	0.117	0.156	0.195
AIPW-OAL-AEN	0.028	0.116	0.120	0.014	0.127	0.127	0.008	0.139	0.139	0.038	0.142	0.147	0.017	0.157	0.158	0.104	0.185	0.212
AIPW-OAL-SCAD	0.066	0.100	0.119	0.073	0.114	0.135	0.064	0.130	0.145	0.067	0.098	0.119	0.049	0.134	0.143	0.091	0.128	0.157
AIPW-OAL-LSP	0.028	0.116	0.120	0.016	0.125	0.126	0.008	0.139	0.139	0.037	0.144	0.148	0.016	0.158	0.159	0.099	0.188	0.212
AIPW-OAL-MCP	0.062	0.100	0.118	0.076	0.116	0.138	0.074	0.134	0.153	0.063	0.098	0.116	0.046	0.134	0.142	0.086	0.128	0.154
AIPW-Farrell	0.009	0.243	0.243	0.036	0.227	0.229	0.039	0.472	0.474	-	-	-	0.008	0.302	0.302	-	-	-

$n = 500, p = 200$ (weak confounding, binary covariates)

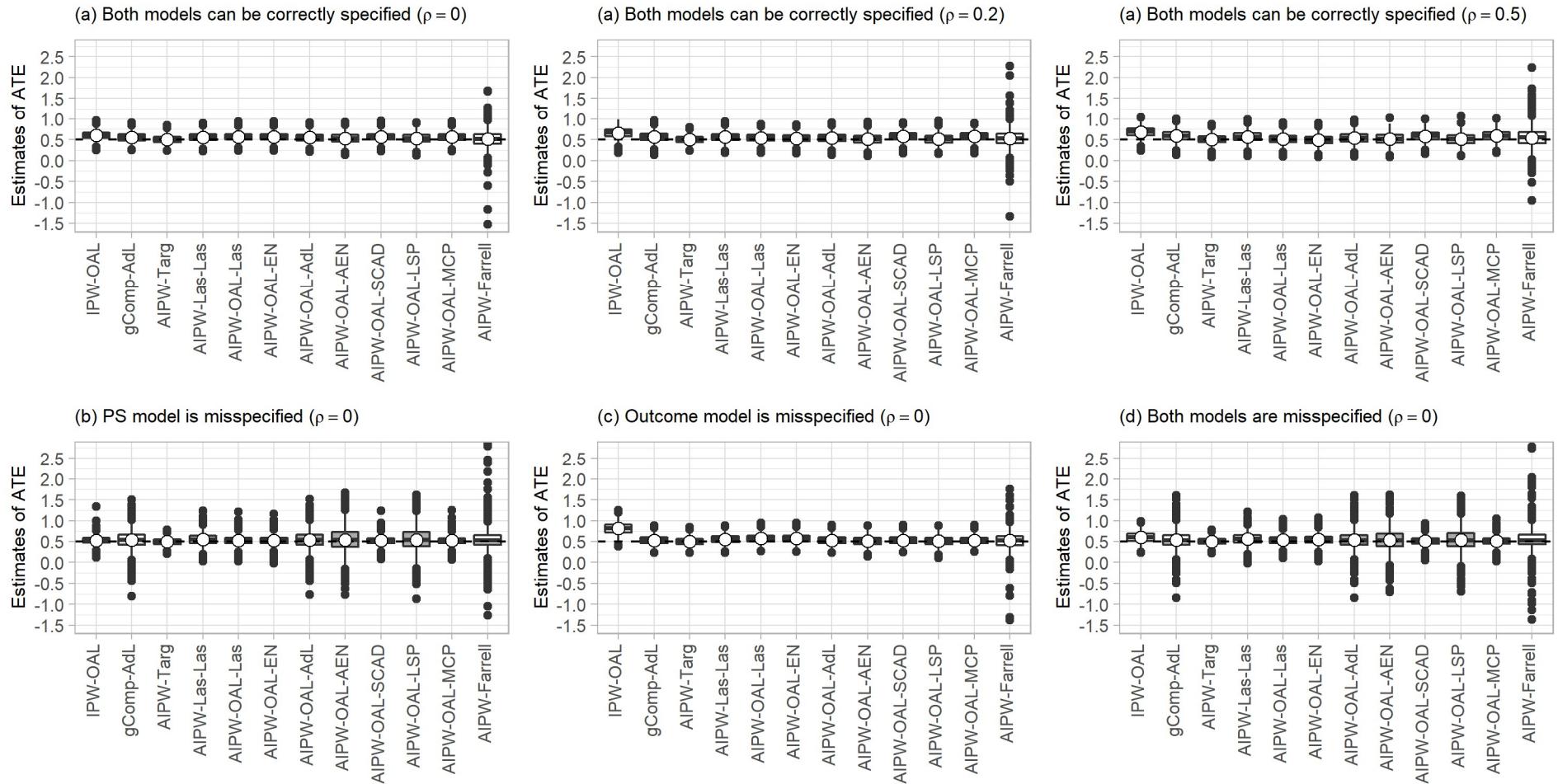


Figure A.10. Box plots of 1000 estimates for the average treatment effect (ATE) with binary covariates and $(n, p) = (500, 200)$ under weak confounding.

Table A.10. Bias, standard error (SE), and root-mean-squared error (RMSE) for the ATE estimators with binary covariates and $(n, p) = (500, 200)$ under weak confounding. (a), (b), (c), and (d) represent the scenarios where both PS and outcome models can be correctly specified, PS model is misspecified, the outcome model is misspecified, and both PS and outcome models are misspecified, respectively. Values exceeding 10^8 or falling below -10^8 are displayed with a hyphen.

	(a) $\rho = 0$			(a) $\rho = 0.2$			(a) $\rho = 0.5$			(b) $\rho = 0$			(c) $\rho = 0$			(d) $\rho = 0$		
	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE
naive	0.112	0.123	0.167	0.488	0.124	0.504	1.062	0.127	1.070	0.027	0.121	0.124	0.318	0.269	0.416	0.100	0.262	0.280
IPW-OAL	0.101	0.100	0.142	0.152	0.120	0.193	0.178	0.136	0.224	0.030	0.100	0.105	0.310	0.132	0.337	0.099	0.127	0.161
gComp-AdL	0.051	0.109	0.120	0.064	0.113	0.129	0.091	0.124	0.154	0.043	0.248	0.252	0.030	0.107	0.111	0.035	0.249	0.251
AIPW-Targ	0.000	0.094	0.094	0.000	0.098	0.098	0.003	0.109	0.109	-0.002	0.090	0.090	0.000	0.094	0.094	0.003	0.091	0.091
AIPW-Las-Las	0.052	0.103	0.116	0.061	0.109	0.125	0.068	0.125	0.142	0.052	0.142	0.151	0.054	0.104	0.117	0.067	0.146	0.160
AIPW-OAL-Las	0.063	0.098	0.117	0.044	0.106	0.115	0.011	0.116	0.116	0.028	0.118	0.121	0.070	0.098	0.120	0.036	0.116	0.122
AIPW-OAL-EN	0.062	0.098	0.116	0.032	0.105	0.110	-0.008	0.116	0.116	0.030	0.119	0.123	0.072	0.098	0.122	0.046	0.124	0.132
AIPW-OAL-AdL	0.048	0.110	0.120	0.042	0.115	0.122	0.034	0.127	0.132	0.044	0.249	0.253	0.030	0.107	0.111	0.035	0.249	0.251
AIPW-OAL-AEN	0.027	0.122	0.124	0.013	0.125	0.125	0.019	0.135	0.137	0.043	0.330	0.333	0.011	0.114	0.115	0.034	0.302	0.304
AIPW-OAL-SCAD	0.066	0.099	0.119	0.077	0.111	0.136	0.080	0.126	0.149	0.023	0.109	0.111	0.031	0.097	0.101	0.010	0.104	0.104
AIPW-OAL-LSP	0.029	0.121	0.125	0.014	0.125	0.126	0.016	0.137	0.137	0.042	0.327	0.330	0.012	0.116	0.116	0.033	0.314	0.315
AIPW-OAL-MCP	0.063	0.100	0.118	0.077	0.112	0.136	0.086	0.129	0.155	0.020	0.108	0.110	0.025	0.097	0.100	0.009	0.106	0.106
AIPW-Farrell	0.016	0.203	0.203	0.033	0.225	0.227	0.046	0.298	0.302	-	-	-	0.019	0.209	0.210	-	-	-

$n = 1000, p = 400$ (weak confounding, continuous covariates)

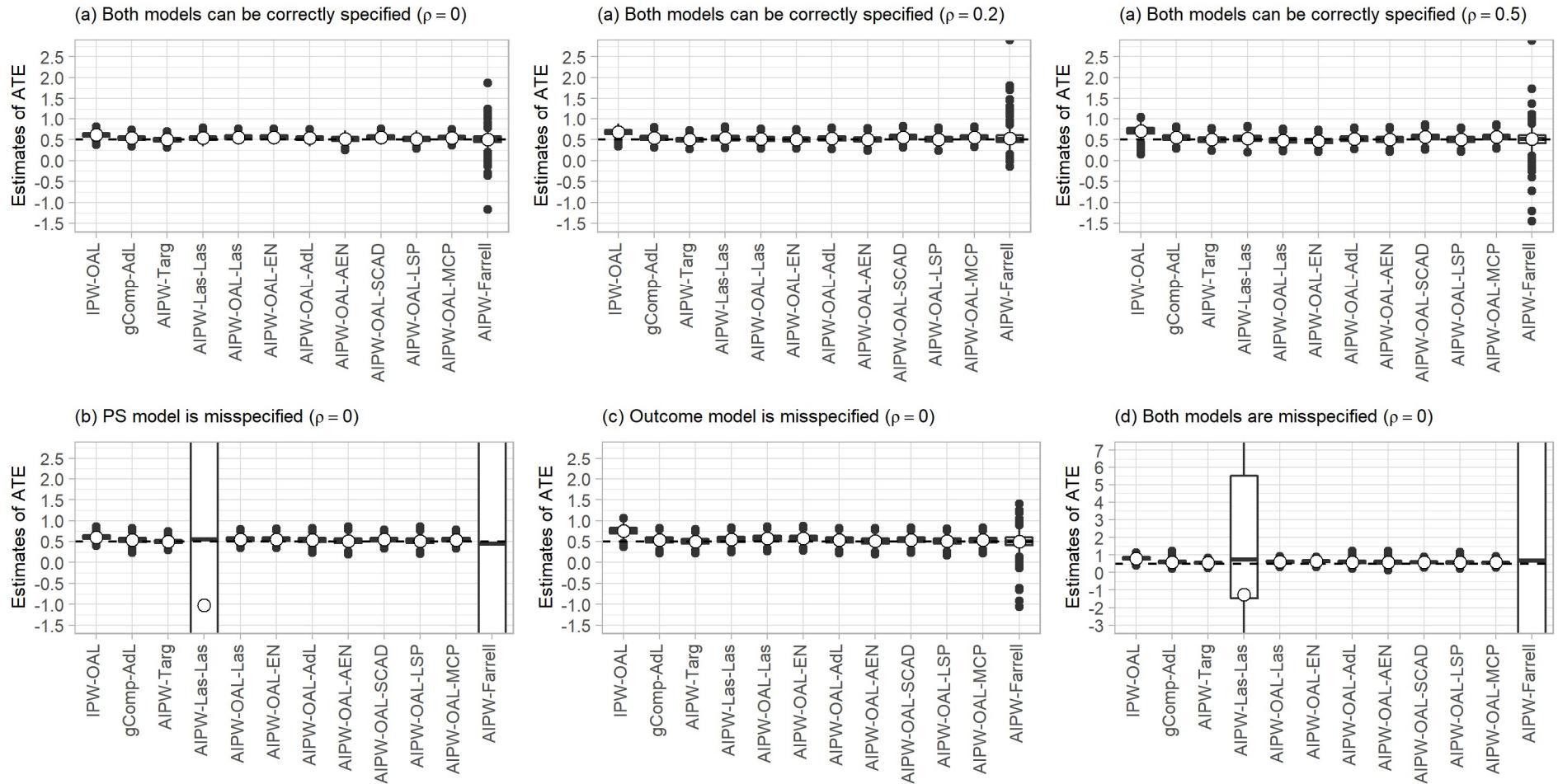


Figure A.11. Box plots of 1000 estimates for the average treatment effect (ATE) with continuous covariates and $(n, p) = (1000, 400)$ under weak confounding. The vertical axis range is different only in the bottom-right plot (d).

Table A.11. Bias, standard error (SE), and root-mean-squared error (RMSE) for the ATE estimators with continuous covariates and $(n, p) = (1000, 400)$ under weak confounding. (a), (b), (c), and (d) represent the scenarios where both PS and outcome models can be correctly specified, PS model is misspecified, the outcome model is misspecified, and both PS and outcome models are misspecified, respectively. Values exceeding 10^8 or falling below -10^8 are displayed with a hyphen.

	(a) $\rho = 0$			(a) $\rho = 0.2$			(a) $\rho = 0.5$			(b) $\rho = 0$			(c) $\rho = 0$			(d) $\rho = 0$		
	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE
naive	0.114	0.085	0.142	0.651	0.092	0.657	1.304	0.094	1.307	0.103	0.082	0.132	0.262	0.156	0.305	0.309	0.154	0.345
IPW-OAL	0.112	0.068	0.131	0.180	0.089	0.201	0.207	0.115	0.237	0.102	0.068	0.123	0.255	0.108	0.276	0.299	0.114	0.320
gComp-AdL	0.035	0.070	0.079	0.044	0.079	0.090	0.049	0.084	0.097	0.036	0.075	0.083	0.037	0.092	0.100	0.094	0.108	0.143
AIPW-Targ	0.002	0.065	0.065	-0.004	0.071	0.071	-0.002	0.088	0.088	0.000	0.066	0.066	0.002	0.087	0.087	0.052	0.092	0.106
AIPW-Las-Las	0.034	0.072	0.080	0.037	0.079	0.087	0.034	0.094	0.100	-1.519	96.111	96.123	0.048	0.095	0.107	-1.765	136.825	136.837
AIPW-OAL-Las	0.055	0.066	0.086	0.021	0.074	0.077	-0.017	0.084	0.085	0.052	0.067	0.085	0.078	0.089	0.118	0.125	0.096	0.157
AIPW-OAL-EN	0.055	0.066	0.086	0.007	0.074	0.074	-0.037	0.083	0.091	0.053	0.067	0.085	0.081	0.090	0.121	0.132	0.097	0.163
AIPW-OAL-AdL	0.035	0.070	0.078	0.031	0.079	0.085	0.020	0.088	0.090	0.036	0.075	0.083	0.037	0.093	0.100	0.094	0.108	0.143
AIPW-OAL-AEN	0.014	0.078	0.080	0.005	0.083	0.083	0.006	0.093	0.093	0.018	0.091	0.093	0.014	0.100	0.101	0.087	0.127	0.154
AIPW-OAL-SCAD	0.052	0.068	0.085	0.058	0.079	0.098	0.060	0.092	0.110	0.048	0.068	0.083	0.038	0.089	0.097	0.073	0.094	0.119
AIPW-OAL-LSP	0.014	0.076	0.077	0.004	0.083	0.083	0.006	0.093	0.093	0.017	0.090	0.092	0.013	0.101	0.102	0.086	0.124	0.151
AIPW-OAL-MCP	0.044	0.067	0.080	0.052	0.078	0.094	0.062	0.093	0.112	0.039	0.068	0.078	0.032	0.089	0.095	0.068	0.094	0.116
AIPW-Farrell	0.007	0.150	0.151	0.034	0.196	0.199	0.009	0.229	0.230	-	-	-	0.005	0.181	0.181	-	-	-

$n = 1000, p = 400$ (weak confounding, binary covariates)

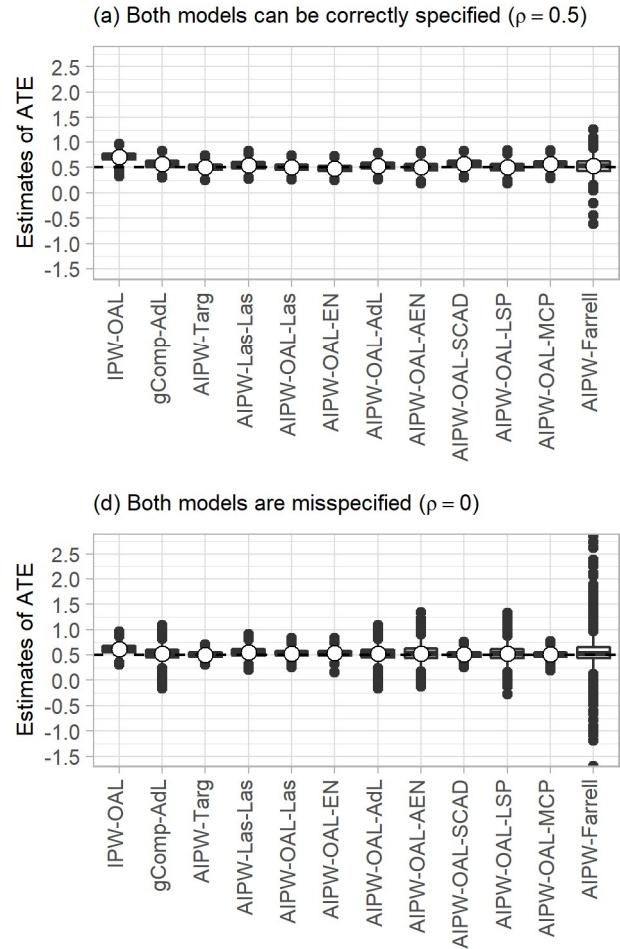
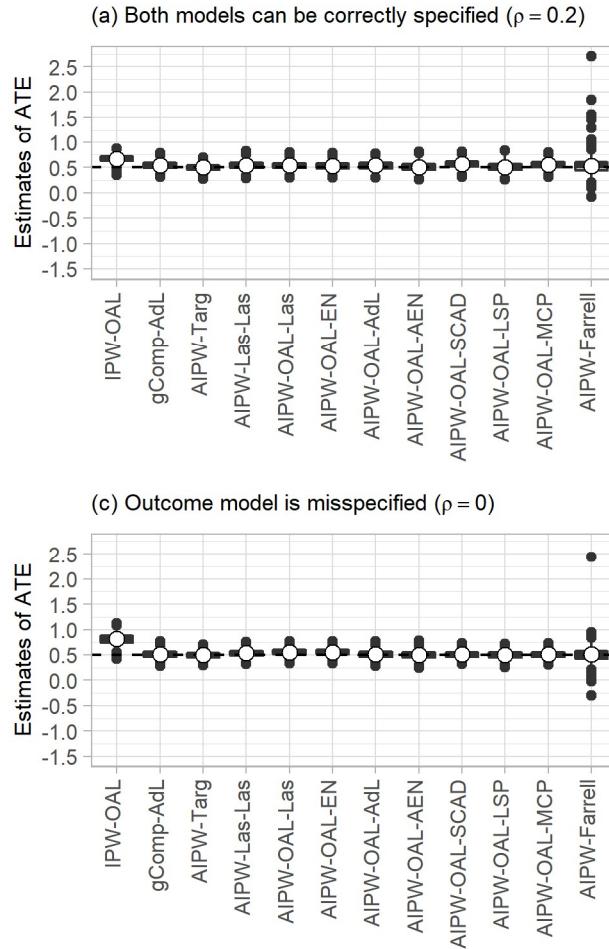
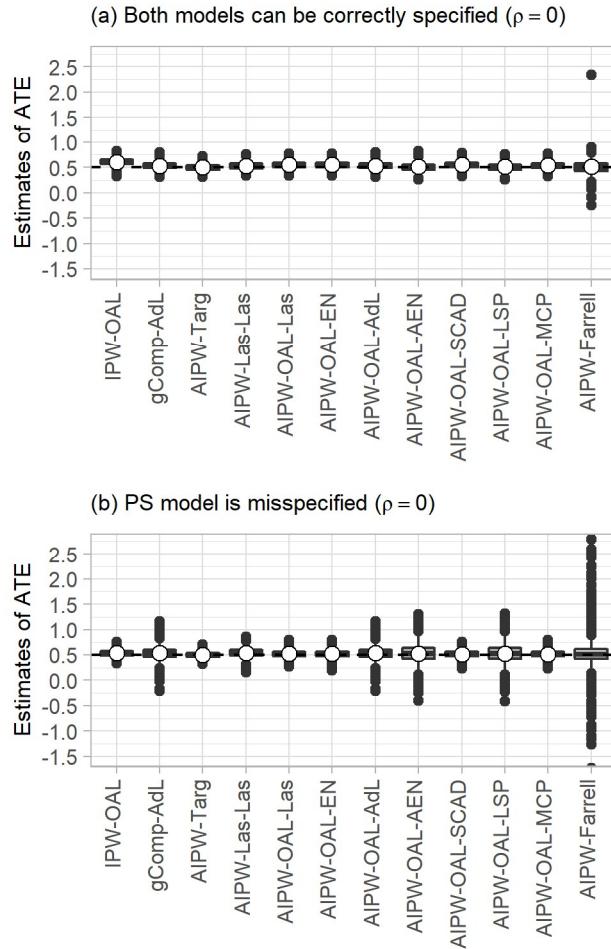


Figure A.12. Box plots of 1000 estimates for the average treatment effect (ATE) with binary covariates and $(n, p) = (1000, 400)$ under weak confounding.

Table A.12. Bias, standard error (SE), and root-mean-squared error (RMSE) for the ATE estimators with binary covariates and $(n, p) = (1000, 400)$ under weak confounding. (a), (b), (c), and (d) represent the scenarios where both PS and outcome models can be correctly specified, PS model is misspecified, the outcome model is misspecified, and both PS and outcome models are misspecified, respectively. Values exceeding 10^8 or falling below -10^8 are displayed with a hyphen.

	(a) $\rho = 0$			(a) $\rho = 0.2$			(a) $\rho = 0.5$			(b) $\rho = 0$			(c) $\rho = 0$			(d) $\rho = 0$		
	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE
naive	0.109	0.085	0.139	0.490	0.092	0.498	1.064	0.089	1.068	0.030	0.084	0.089	0.321	0.183	0.370	0.110	0.183	0.214
IPW-OAL	0.109	0.068	0.128	0.172	0.080	0.190	0.203	0.104	0.228	0.032	0.066	0.074	0.311	0.101	0.327	0.109	0.093	0.143
gComp-AdL	0.032	0.072	0.079	0.044	0.077	0.088	0.067	0.086	0.110	0.032	0.144	0.147	0.013	0.070	0.072	0.023	0.139	0.141
AIPW-Targ	-0.001	0.065	0.065	-0.003	0.068	0.068	-0.002	0.075	0.075	0.000	0.062	0.062	-0.001	0.065	0.065	0.004	0.062	0.062
AIPW-Las-Las	0.032	0.072	0.079	0.040	0.080	0.089	0.040	0.088	0.097	0.040	0.091	0.100	0.032	0.073	0.079	0.054	0.094	0.108
AIPW-OAL-Las	0.052	0.066	0.084	0.036	0.073	0.081	-0.001	0.080	0.080	0.020	0.068	0.071	0.052	0.067	0.085	0.027	0.071	0.076
AIPW-OAL-EN	0.053	0.066	0.085	0.025	0.072	0.077	-0.022	0.079	0.082	0.021	0.070	0.073	0.055	0.067	0.087	0.034	0.075	0.083
AIPW-OAL-AdL	0.032	0.072	0.079	0.035	0.078	0.085	0.034	0.089	0.095	0.032	0.144	0.147	0.013	0.070	0.072	0.023	0.139	0.141
AIPW-OAL-AEN	0.010	0.080	0.080	0.009	0.088	0.088	0.007	0.093	0.094	0.028	0.198	0.200	0.001	0.073	0.073	0.026	0.173	0.175
AIPW-OAL-SCAD	0.049	0.068	0.084	0.061	0.075	0.097	0.066	0.090	0.111	0.016	0.066	0.068	0.011	0.067	0.068	0.007	0.066	0.067
AIPW-OAL-LSP	0.010	0.079	0.079	0.009	0.085	0.086	0.005	0.091	0.092	0.025	0.199	0.200	0.000	0.074	0.074	0.022	0.178	0.180
AIPW-OAL-MCP	0.041	0.068	0.079	0.051	0.074	0.090	0.063	0.089	0.109	0.013	0.066	0.067	0.008	0.066	0.067	0.006	0.065	0.066
AIPW-Farrell	0.009	0.178	0.178	0.032	0.158	0.161	0.025	0.151	0.153	-	-	-	0.010	0.216	0.216	-	-	-

References

1. Shortreed SM and Ertefaie A. Outcome-adaptive lasso: Variable selection for causal inference. *Biometrics* 2017; **73**: 1111–1122.
2. Farrell M. Robust inference on average treatment effects with possibly more covariates than observations. *Journal of Econometrics* 2015; **189**, 1–23.