Supplementary Materials for "Causal inference with multiple concurrent medications: a comparison of methods and an application in multidrug-resistant tuberculosis"

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1. Brief Overview of the Data Generation Mechanisms along with their R code

This section gives a brief introduction to the Data Generation Scenarios as mentioned in **Section 3.1**.

Data Generation Scenario 1: We generate 12 independent baseline covariates represented by X_1,..., X_{12} which follow a standard uniform distribution. We then generate 4 medications represented by A^1,..., A^4 using the baseline covariates and sample them from a multinomial bernoulli distribution. We also have a positive pairwise correlation of 0.15 between A^1 and A^2 and a 0.25 correlation between A^3 and A^4. None of the other treatments were correlated otherwise. This sampling was performed using the *rmvbin* function in the package *bindata*. The outcome variable Y was generated using a logistic model using the baseline covariates and the medications, which includes first order interactions between (X_i,X_j), (X_i,A^j) and (A^i,A^j). The R code for the generation of this data is as follows:

```
library(bindata)
n <- 500
set.seed(2010)
#Covariate Generation
X_1 <- runif(n,0,1)
X_2 <- runif(n,0,1)
X_3 <- runif(n,0,1)
X_4 <- runif(n,0,1)
X_5 <- runif(n,0,1)
X_6 <- runif(n,0,1)
X_7 <- runif(n,0,1)
X_8 <- runif(n,0,1)
X_9 <- runif(n,0,1)
X_10 <- runif(n,0,1)
X_11 <- runif(n,0,1)
X_12 <- runif(n,0,1)

#Medication Generation
pA_1 <- plogis(0.7*X_1 - 0.87*X_3 + X_5 + X_7 + 0.8*X_2 - 1.6*X_4)
pA_2 <- plogis(0.9*X_1 - 0.66*X_3 + 0.8*X_5 + X_7 - 0.8*X_6)
pA_3 <- plogis(1.4*X_1 - 0.45*X_3 + 0.4*X_5 - X_7 - X_8)
pA_4 <- plogis(1.8*X_1 - 0.95*X_3 - 0.1*X_5 - X_7 - X_12)

m <- diag(4)
m[1,2] <- 0.15
m[2,1] <- 0.15
m[4,3] <- 0.25
m[3,4] <- 0.25
```

```r
#Considering positive binary correlations between A_1, A_2 as 0.15 and A_3, A_4 as 0.25
A <- matrix(nrow=n,ncol=4)
for (i in 1:n){
  prob <- c(pA_1[i],pA_2[i],pA_3[i],pA_4[i])
  A[i,] <- rmvbin(1, margprob = prob, bincorr = m)
}

#Separating the array obtained above into separate medications
Gap <- as.data.frame(A)
A_1 <- Gap[,1]
A_2 <- Gap[,2]
A_3 <- Gap[,3]
A_4 <- Gap[,4]

#Generating the outcome model
pY <- plogis(-1.8 + 1.2*X_1*A_3 + 2.15*X_3*A_1 - 0.5*X_5*X_9 + 3.89*X_7*X_1
             + X_10*A_2 - 1.5*X_11*A_4 + 4.2*(1-A_1)*A_3 + 15*(1-A_2)*A_4)
Y <- rbinom(n, 1, prob=pY)
```

Data Generation Scenario II: We generate 14 independent baseline covariates represented by X_1,. . . , X_{14} which follow a standard uniform distribution or a standard normal distribution. We then generate 8 medications represented by A^1,. . . , A^8 using the baseline covariates and sample them from a multinomial bernoulli distribution. We also have a positive pairwise correlation of 0.15 between A^1 and A^2, a 0.25 correlation between A^3 and A^4, a 0.15 correlation between A^5 and A^6 and a 0.25 correlation between A^7 and A^8. None of the other treatments were correlated otherwise. This sampling was again performed using the *rmvbin* function in the package *bindata*. The outcome variable Y was generated using a logistic model using the baseline covariates and the medications, which also includes first order interactions and second order interactions. The R code for the generation of this data is as follows:

```r
set.seed(2100)
#Covariate Generation
n <- 500
X_1 <- runif(n,0,1)
X_2 <- runif(n,0,1)
X_3 <- runif(n,0,1)
X_4 <- runif(n,0,1)
X_5 <- runif(n,0,1)
X_6 <- runif(n,0,1)
X_7 <- runif(n,0,1)
X_8 <- runif(n,0,1)
X_9 <- rnorm(n,0,1)
X_10 <- runif(n,0,1)
X_11 <- runif(n,0,1)
X_12 <- rnorm(n,0,1)
X_13 <- runif(n,0,1)
X_14 <- runif(n,0,1)

#Medication Generation
pA_1 <- plogis(0.5*X_1 + 2.3*X_2 + 0.74*X_3 - 1.8*X_4)
```

```r
pA_2 <- plogis(0.4*X_1 + 2.5*X_2 + 0.87*X_3 - 1.5*X_5)
pA_3 <- plogis(0.8*X_1 - 0.4*X_2 + 0.34*X_3 + 0.8*X_6)
pA_4 <- plogis(0.7*X_1 - 0.65*X_2 + 0.55*X_3 + 1.1*X_7)
pA_5 <- plogis(1.9*X_1 - 0.33*X_2 + 1.67*X_3 - 0.6*X_8)
pA_6 <- plogis(1.5*X_1 - 0.53*X_2 + 1.88*X_3 - 0.3*X_9)
pA_7 <- plogis(-0.85*X_1 + 1.35*X_2 - 0.99*X_3 + 1.4*X_7)
pA_8 <- plogis(-0.65*X_1 + 1.03*X_2 - 0.875*X_3 + 1.1*X_6)

m <- diag(4)
m[1,2] <- 0.15
m[2,1] <- 0.15
m[4,3] <- 0.25
m[3,4] <- 0.25

#Considering positive binary correlations between A_1, A_2 as 0.15 and A_3, A_4 as 0.25
A <- matrix(nrow=n,ncol=4)
for (i in 1:n){
  prob <- c(pA_1[i],pA_2[i],pA_3[i],pA_4[i])
  A[i,] <- rmvbin(1, margprob = prob, bincorr = m)
}

#Considering positive binary correlations between A_5, A_6 as 0.15 and A_7, A_8 as 0.25
B <- matrix(nrow=n,ncol=4)
for (i in 1:n){
  prob <- c(pA_5[i],pA_6[i],pA_7[i],pA_8[i])
  B[i,] <- rmvbin(1, margprob = prob, bincorr = m)
}

#Separating the array obtained above into separate medications
Gap <- as.data.frame(A)
A_1 <- Gap[,1]
A_2 <- Gap[,2]
A_3 <- Gap[,3]
A_4 <- Gap[,4]

Gap <- as.data.frame(B)
A_5 <- Gap[,1]
A_6 <- Gap[,2]
A_7 <- Gap[,3]
A_8 <- Gap[,4]

#Generating the outcome model
pY <- plogis(-1.3 + 0.8*X_1 + 0.89*X_2*A_2 + 1.5*X_11*A_8 - 1.8*X_13
             + 0.9*X_14*A_1*A_8 + 0.4*A_1*A_2*A_5 + 7.2*(1-A_2)*X_9*X_12
             - 15*(1-A_7)*A_6 - 12*X_9*(1-A_7) - X_10*(1-A_8)*(1-A_7)
             + 5*(1-A_8)*(1-A_1) + 5*(1-A_1)*X_12*X_14)
Y <- rbinom(n, 1, prob=pY)
```

2. Comparison of methods with a large number of possible regimens

We generated 1,000 datasets of sample size $n = 500$, using Data Generation Scenario 2. In our simulation data, out of the 256 possible regimens, roughly 150 different regimens occurred in each dataset. Some of these regimens were only followed by several subjects, making the corresponding GPSs difficult to estimate. In order to speed up the computation of the multi-class classification, one might consider removing the observations with the most sparsely observed regimens in order to fit the model. It is expected that this should not affect the prediction of the probabilities of the most prevalent regimens as they represent a very small part of the overall regimen probability space.

To investigate this, we considered three different approaches. The first approach took the entire dataset and classified for all of the regimens observed in the model. We then created a new dataset containing 80% of the original regimens in the data, by removing the subjects with the least occurring 20% of regimens. This new subsetted data became the basis for obtaining the model for SVMs and Softmax Regression. The fitted model was then used to compute the GPS for regimen 1 for all n individuals in the dataset. The final simulation was carried out by performing the modeling after removal of the 30% of the least occurring regimens in the original dataset and carrying out the same method as explained above.

Table 1 displays the simulation results for this case (using the same statistical methods described in Section 3.3 of the manuscript). Without subsetting, only TMLE was nearly unbiased when implemented with all GPS methods though PSA(I) had low bias when implemented with GBMs. The results obtained after removing the rarest 20% and 30% were consistent with the full sample results for all methods. The computational times taken by SVMs on a local laptop computer when removing 0%, 20% and 30% of the original regimens were 5, 3, and 2 seconds, respectively. Similarly, the runtimes taken by Softmax regression for the same three datasets were 412, 234, and 202 seconds, respectively. The GBMs implemented in the `twang` package estimate the probability of every regimen separately versus all others. Therefore, removing the observations with rare regimens would not help the estimation speed or accuracy. The runtime results suggest that this subsetting approach can greatly reduce computational time for SVMs and Softmax regression without affecting the statistical results.

Table 1: Monte Carlo means and standard errors for different causal estimators that utilize the generalized propensity score. Data with a sample size of $n = 500$ were drawn from Data Generation Scenario 2 and 1,000 replicates were used. The true value for regimen 1 is $\mathbb{E}(Y^1) = 0.55$. SVM: Support Vector Machine; GBM: Generalized Boosted Model; IPTW: Inverse Probability of Treatment Weighting; PSA: Propensity Score Adjustment; TMLE: Targeted Maximum Likelihood Estimation. Outcome regression models were fit by (I) regimen and (II) treatments as main terms covariates. Q_n *corr* indicates whether the outcome model includes the true treatment-treatment interactions.

Class Truncation %		0	20	30
Median n observations removed		0	30	45
	Q_n *corr*	*Reg* 1	*Reg* 1	*Reg* 1
SVM				
IPTW	N/A	0.58(0.08)	0.58(0.08)	0.58(0.08)
PSA(I)	Y	0.57(0.08)	0.57(0.08)	0.57(0.08)
PSA(II)	N	0.45(0.05)	0.45(0.05)	0.45(0.05)
TMLE(I)	Y	0.55(0.11)	0.54(0.11)	0.55(0.11)
TMLE(II)	N	0.56(0.08)	0.55(0.09)	0.55(0.09)
Softmax Regression				
IPTW	N/A	0.55(0.13)	0.55(0.13)	0.56(0.13)
PSA(I)	Y	0.57(0.08)	0.57(0.08)	0.57(0.08)
PSA(II)	N	0.44(0.05)	0.44(0.05)	0.45(0.05)
TMLE(I)	Y	0.55(0.11)	0.55(0.11)	0.55(0.11)
TMLE(II)	N	0.55(0.12)	0.55(0.12)	0.55(0.12)
GBM				
IPTW	N/A	0.57(0.09)	—	—
PSA(I)	Y	0.56(0.12)	—	—
PSA(II)	N	0.42(0.05)	—	—
TMLE(I)	Y	0.54(0.11)	—	—
TMLE(II)	N	0.55(0.09)	—	—

3. Summary statistics for the support of the regimens in the simulation studies

This section presents the tables for summary statistics and the plots for the supports for regimens 1 and 2 for simulation study I and regimen 1 for simulation study II, where simulation study I refers to the simulation study presented in Section 3 of the paper and simulation study II refers to the simulation study presented in Section 2 of the supplementary material. We define the "support" of a regimen to be the number of patients exposed to that regimen in the dataset.

Table 2: Summary Statistics for support for regimen 1 and regimen 2 for simulation study I.

	$n = 500$		$n = 1000$	
	Reg 1	*Reg* 2	*Reg* 1	*Reg* 2
Minimum	68.00	29.00	147.00	74.00
1^{st} Quantile	87.00	46.00	177.00	94.00
Median	92.00	51.00	185.00	101.00
Mean	92.48	51.04	184.90	100.90
3^{rd} Quantile	98.00	56.00	193.00	107.00
Maximum	122.00	75.00	226.00	131.00

Table 3: Summary Statistics for support for regimen 1 for simulation study II with $n = 500$.

	Reg 1
Minimum	16.00
1^{st} Quantile	33.00
Median	37.00
Mean	36.75
3^{rd} Quantile	41.00
Maximum	55.00

Figure 1: Histogram for the support of the top 2 regimens for Simulation Study I for $n = 500$.

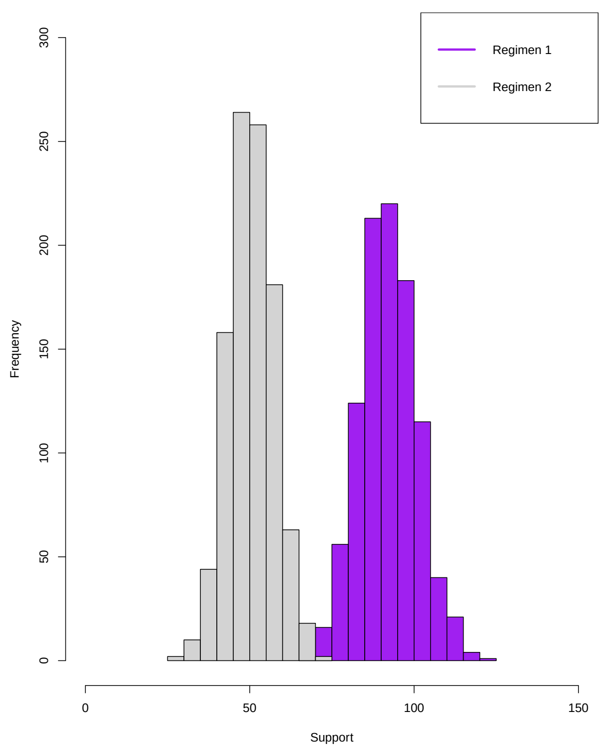


Figure 2: Histogram for the support of the top 2 regimens for Simulation Study I for $n = 1000$.

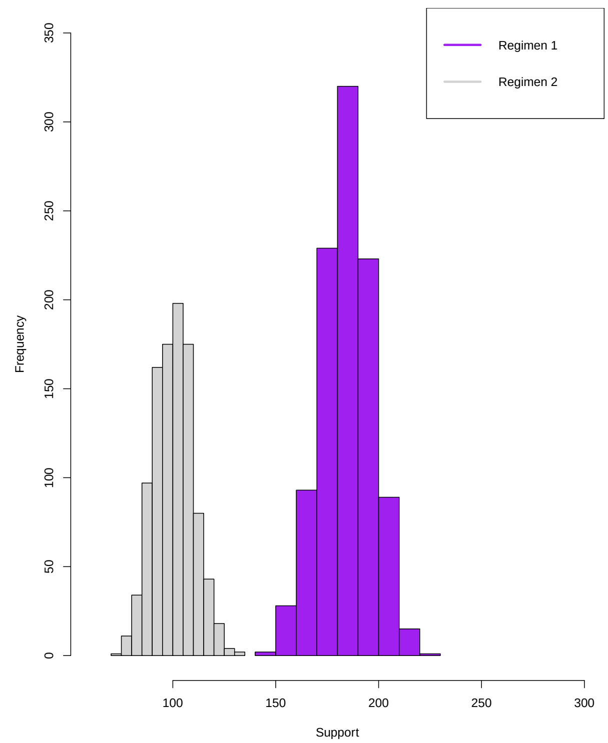
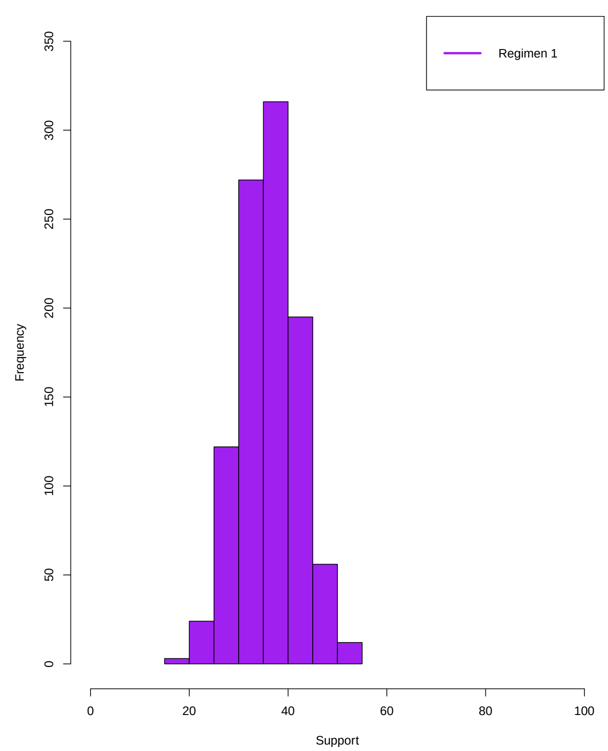


Figure 3: Histogram for the support of Regimen 1 for Simulation Study II for $n = 500$.



4. Summary Statistics for the weights obtained by the different estimating methods

This section contains the summary statistics of the weights obtained by SVM, Softmax Regression and GBM over 50 datasets for the regimens in simulation study I.

Table 4: Summary Statistics for the weights obtained by the different estimating methods for regimen 1 for simulation study I over 50 datasets with $n = 1000$.

	SVM	**Softmax Regression**	**GBM**
Minimum	2.66	1.39	1.12
1^{st} Quantile	4.44	4.04	4.35
Median	5.37	6.19	6.23
Mean	6.11	8.38	7.20
3^{rd} Quantile	6.97	10.08	8.88
Maximum	39.30	229.67	106.49

Table 5: Summary Statistics for the weights obtained by the different estimating methods for regimen 2 for simulation study I over 50 datasets with $n = 1000$.

	SVM	**Softmax Regression**	**GBM**
Minimum	3.09	1.44	1.05
1^{st} Quantile	7.80	6.87	8.25
Median	11.08	12.99	13.73
Mean	13.11	23.98	17.06
3^{rd} Quantile	16.27	26.93	21.33
Maximum	96.00	1163.50	544.76

5. Summary for the Generalized Propensity Scores for the MDR-TB Data

This section contains the summary of the truncated and the untruncated GPS obtained for the MDR-TB data using the different machine learning methods explained in **Section 2.2**. The GPS of the regimens are given by pi1 to pi10, where pi1 denotes GPS for Regimen 1 in our study and pi10 denotes the GPS for Regimen 10 in the study as mentioned in **Section 4**. The summary contains the following values:

- **Min.**: Minimum value of the GPS for the regimen in the sample study
- **1st Qu.**: Value of the first quantile of the GPS for the regimen in the sample study
- **Median**: Median value of the GPS for the regimen in the sample study
- **Mean**: Mean value of the GPS for the regimen in the sample study
- **3rd Qu.**: Value of the third quantile of the GPS for the regimen in the sample study
- **Max.**: Maximum value of the GPS for the regimen in the sample study

summary(Algorithm_Untruncated) denotes the summary of the untruncated GPS obtained using Algorithm whereas **summary(Algorithm_Truncated)** denotes the summary of the truncated GPS (20% truncation) obtained using Algorithm as mentioned in **Section 4**.

```r
summary(SVM_Untruncated)
```

```
##       pi1                 pi2                 pi3
##  Min.   :0.0000844   Min.   :0.0001795   Min.   :0.0000585
##  1st Qu.:0.0003483   1st Qu.:0.0008688   1st Qu.:0.0007783
##  Median :0.0007693   Median :0.0016455   Median :0.0031000
##  Mean   :0.1568600   Mean   :0.0376882   Mean   :0.0280186
##  3rd Qu.:0.0084027   3rd Qu.:0.0056493   3rd Qu.:0.0157749
##  Max.   :0.6704224   Max.   :0.1603302   Max.   :0.1602677
##       pi4                 pi5                 pi6
##  Min.   :0.0000540   Min.   :0.0000441   Min.   :0.0004766
##  1st Qu.:0.0005957   1st Qu.:0.0006334   1st Qu.:0.0020562
##  Median :0.0029060   Median :0.0014290   Median :0.0053386
##  Mean   :0.0283911   Mean   :0.0207455   Mean   :0.0294543
##  3rd Qu.:0.0282561   3rd Qu.:0.0025562   3rd Qu.:0.0256537
##  Max.   :0.3174220   Max.   :0.1382175   Max.   :0.2802544
##       pi7                 pi8                 pi9
##  Min.   :0.0001285   Min.   :0.0002740   Min.   :0.0000968
##  1st Qu.:0.0005905   1st Qu.:0.0005881   1st Qu.:0.0009952
##  Median :0.0012020   Median :0.0011180   Median :0.0026187
##  Mean   :0.0180373   Mean   :0.0159779   Mean   :0.0156337
##  3rd Qu.:0.0049643   3rd Qu.:0.0019540   3rd Qu.:0.0054387
##  Max.   :0.0815344   Max.   :0.1821654   Max.   :0.1104928
##       pi10
##  Min.   :0.0002061
##  1st Qu.:0.0006178
##  Median :0.0008883
##  Mean   :0.0133153
##  3rd Qu.:0.0323348
##  Max.   :0.0620212
```

```r
summary(Softmax_Untruncated)
```

```
##       pi1                pi2                pi3
##  Min.   :0.001606   Min.   :0.001009   Min.   :0.0009516
##  1st Qu.:0.017372   1st Qu.:0.007144   1st Qu.:0.0085008
```

```
##  Median :0.067361   Median :0.021264   Median :0.0225757
##  Mean   :0.143315   Mean   :0.039558   Mean   :0.0366144
##  3rd Qu.:0.192485   3rd Qu.:0.055097   3rd Qu.:0.0490858
##  Max.   :0.673014   Max.   :0.177946   Max.   :0.1515242
##       pi4                pi5                 pi6
##  Min.   :0.001242   Min.   :0.0006062   Min.   :0.003809
##  1st Qu.:0.005267   1st Qu.:0.0053993   1st Qu.:0.011288
##  Median :0.013764   Median :0.0150462   Median :0.018037
##  Mean   :0.032116   Mean   :0.0272295   Mean   :0.025229
##  3rd Qu.:0.029981   3rd Qu.:0.0373691   3rd Qu.:0.031908
##  Max.   :0.298142   Max.   :0.1224405   Max.   :0.146441
##       pi7                 pi8                 pi9
##  Min.   :0.0008831   Min.   :0.0006065   Min.   :0.0006481
##  1st Qu.:0.0041477   1st Qu.:0.0061504   1st Qu.:0.0046522
##  Median :0.0123683   Median :0.0129524   Median :0.0124783
##  Mean   :0.0193383   Mean   :0.0212144   Mean   :0.0219139
##  3rd Qu.:0.0276799   3rd Qu.:0.0239001   3rd Qu.:0.0314892
##  Max.   :0.0876790   Max.   :0.1267092   Max.   :0.0955858
##       pi10
##  Min.   :0.0004913
##  1st Qu.:0.0048800
##  Median :0.0114627
##  Mean   :0.0162796
##  3rd Qu.:0.0284771
##  Max.   :0.0625170
```

```r
summary(GBM_Untruncated)
```

```
##       pi1                pi2                 pi3
##  Min.   :0.002027   Min.   :0.0007163   Min.   :0.007166
##  1st Qu.:0.003807   1st Qu.:0.0009530   1st Qu.:0.007206
##  Median :0.006176   Median :0.0019908   Median :0.008290
##  Mean   :0.168206   Mean   :0.0404401   Mean   :0.029222
##  3rd Qu.:0.010221   3rd Qu.:0.0041522   3rd Qu.:0.010328
##  Max.   :0.764830   Max.   :0.3301783   Max.   :0.179817
##       pi4                 pi5                 pi6
##  Min.   :0.0000014   Min.   :0.0000003   Min.   :0.007889
##  1st Qu.:0.0000777   1st Qu.:0.0000354   1st Qu.:0.012612
##  Median :0.0004492   Median :0.0003447   Median :0.013787
##  Mean   :0.0263304   Mean   :0.0232197   Mean   :0.022999
##  3rd Qu.:0.0167375   3rd Qu.:0.0005962   3rd Qu.:0.016079
##  Max.   :0.9999966   Max.   :0.3551773   Max.   :0.307409
##       pi7                 pi8                pi9
##  Min.   :0.0009184   Min.   :0.008467   Min.   :0.0000007
##  1st Qu.:0.0011354   1st Qu.:0.009411   1st Qu.:0.0000590
##  Median :0.0020279   Median :0.009560   Median :0.0004007
##  Mean   :0.0197763   Mean   :0.017003   Mean   :0.0167759
##  3rd Qu.:0.0038864   3rd Qu.:0.011996   3rd Qu.:0.0027138
##  Max.   :0.1147831   Max.   :0.053754   Max.   :0.9586112
##       pi10
##  Min.   :0.0000003
##  1st Qu.:0.0000269
##  Median :0.0000887
##  Mean   :0.0152205
##  3rd Qu.:0.0221909
```

```
##  Max.   :0.3435316
```

```r
summary(SVM_Truncated)
```

```
##       pi1                 pi2                 pi3           
##  Min.   :0.0002831   Min.   :0.0007573   Min.   :0.0002799  
##  1st Qu.:0.0003483   1st Qu.:0.0008688   1st Qu.:0.0007783  
##  Median :0.0007693   Median :0.0016455   Median :0.0031000  
##  Mean   :0.1568845   Mean   :0.0377691   Mean   :0.0280471  
##  3rd Qu.:0.0084027   3rd Qu.:0.0056493   3rd Qu.:0.0157749  
##  Max.   :0.6704224   Max.   :0.1603302   Max.   :0.1602677  
##       pi4                 pi5                 pi6          
##  Min.   :0.0003056   Min.   :0.0001582   Min.   :0.001543  
##  1st Qu.:0.0005957   1st Qu.:0.0006334   1st Qu.:0.002056  
##  Median :0.0029060   Median :0.0014290   Median :0.005339  
##  Mean   :0.0284244   Mean   :0.0207595   Mean   :0.029564  
##  3rd Qu.:0.0282561   3rd Qu.:0.0025562   3rd Qu.:0.025654  
##  Max.   :0.3174220   Max.   :0.1382175   Max.   :0.280254  
##       pi7                 pi8                 pi9           
##  Min.   :0.0004759   Min.   :0.0005308   Min.   :0.0003049  
##  1st Qu.:0.0005905   1st Qu.:0.0005881   1st Qu.:0.0009952  
##  Median :0.0012020   Median :0.0011180   Median :0.0026187  
##  Mean   :0.0180826   Mean   :0.0159963   Mean   :0.0156600  
##  3rd Qu.:0.0049643   3rd Qu.:0.0019540   3rd Qu.:0.0054387  
##  Max.   :0.0815344   Max.   :0.1821654   Max.   :0.1104928  
##       pi10          
##  Min.   :0.0005180  
##  1st Qu.:0.0006178  
##  Median :0.0008883  
##  Mean   :0.0133594  
##  3rd Qu.:0.0323348  
##  Max.   :0.0620212
```

```r
summary(Softmax_Truncated)
```

```
##       pi1               pi2                pi3          
##  Min.   :0.01423   Min.   :0.005934   Min.   :0.006702  
##  1st Qu.:0.01737   1st Qu.:0.007144   1st Qu.:0.008501  
##  Median :0.06736   Median :0.021264   Median :0.022576  
##  Mean   :0.14408   Mean   :0.039938   Mean   :0.037119  
##  3rd Qu.:0.19248   3rd Qu.:0.055097   3rd Qu.:0.049086  
##  Max.   :0.67301   Max.   :0.177946   Max.   :0.151524  
##       pi4                pi5                pi6         
##  Min.   :0.004416   Min.   :0.004763   Min.   :0.01005  
##  1st Qu.:0.005267   1st Qu.:0.005399   1st Qu.:0.01129  
##  Median :0.013764   Median :0.015046   Median :0.01804  
##  Mean   :0.032373   Mean   :0.027548   Mean   :0.02563  
##  3rd Qu.:0.029981   3rd Qu.:0.037369   3rd Qu.:0.03191  
##  Max.   :0.298142   Max.   :0.122440   Max.   :0.14644  
##       pi7                pi8                pi9          
##  Min.   :0.003598   Min.   :0.005216   Min.   :0.004309  
##  1st Qu.:0.004148   1st Qu.:0.006150   1st Qu.:0.004652  
##  Median :0.012368   Median :0.012952   Median :0.012478  
##  Mean   :0.019558   Mean   :0.021613   Mean   :0.022207  
##  3rd Qu.:0.027680   3rd Qu.:0.023900   3rd Qu.:0.031489
```

```
## Max.   :0.087679   Max.   :0.126709   Max.   :0.095586
##      pi10
## Min.   :0.003998
## 1st Qu.:0.004880
## Median :0.011463
## Mean   :0.016521
## 3rd Qu.:0.028477
## Max.   :0.062517
```

```r
summary(GBM_Truncated)
```

```
##      pi1                 pi2                  pi3
## Min.   :0.003807   Min.   :0.0009182   Min.   :0.007206
## 1st Qu.:0.003807   1st Qu.:0.0009530   1st Qu.:0.007206
## Median :0.006176   Median :0.0019908   Median :0.008290
## Mean   :0.168406   Mean   :0.0404581   Mean   :0.029225
## 3rd Qu.:0.010221   3rd Qu.:0.0041522   3rd Qu.:0.010328
## Max.   :0.764830   Max.   :0.3301783   Max.   :0.179817
##      pi4                  pi5                  pi6
## Min.   :0.0000389   Min.   :0.0000300   Min.   :0.01138
## 1st Qu.:0.0000777   1st Qu.:0.0000354   1st Qu.:0.01261
## Median :0.0004492   Median :0.0003447   Median :0.01379
## Mean   :0.0263347   Mean   :0.0232217   Mean   :0.02349
## 3rd Qu.:0.0167375   3rd Qu.:0.0005962   3rd Qu.:0.01608
## Max.   :0.9999966   Max.   :0.3551773   Max.   :0.30741
##      pi7                 pi8                  pi9
## Min.   :0.001127   Min.   :0.009411   Min.   :0.0000432
## 1st Qu.:0.001135   1st Qu.:0.009411   1st Qu.:0.0000590
## Median :0.002028   Median :0.009560   Median :0.0004007
## Mean   :0.019807   Mean   :0.017013   Mean   :0.0167803
## 3rd Qu.:0.003886   3rd Qu.:0.011996   3rd Qu.:0.0027138
## Max.   :0.114783   Max.   :0.053754   Max.   :0.9586112
##      pi10
## Min.   :0.0000189
## 1st Qu.:0.0000269
## Median :0.0000887
## Mean   :0.0152223
## 3rd Qu.:0.0221909
## Max.   :0.3435316
```

6. Tables for the Probability estimates of treatment success of the truncated GPS(20% truncation) as mentioned in Section 4 for MDR-TB data

In a sensitivity analysis, 20% truncation was used to remove the smallest values of the Generalized Propensity Score for the top 10 available regimens. The point estimates of $\mathbb{E}(Y^r)$ and the confidence intervals for the top 10 regimens are presented in Table 6 and 7. The GPS truncation resulted in at most small changes in the point estimates as opposed to the results obtained without the truncation of GPS and had similar conclusions to it.

Table 6: Estimates of the probability of treatment success along with the confidence intervals under regimens 1-5 for the MDR-TB application in Section 4 after 20% truncation of the GPS. SVM: Support Vector Machine; GBM: Generalized Boosted Model; IPTW: Inverse Probability of Treatment Weighting; PSA: Propensity Score Adjustment; TMLE: Targeted Maximum Likelihood Estimation. Outcome regression models were fit by (I) regimen and (II) treatments as main terms covariates.

Regimen	1 OFX-KM- Z-EMB- ETH	2 OFX-KM- Z- ETH-CS	3 OFX-KM- PTO- CS-PAS	4 Z-EMB- RBT	5 OFX-SM- PTO- CS-PAS
SVM					
IPTW	0.47	0.71	0.59	0.27	0.31
	(0.44,0.49)	(0.62,0.80)	(0.47,0.70)	(0.10,0.44)	(0.17,0.46)
PSA(I)	0.44	0.68	0.64	0.32	0.55
PSA(II)	0.66	0.69	0.64	0.42	0.68
TMLE(I)	0.61	0.78	0.64	0.54	0.31
	(0.60,0.61)	(0.76,0.80)	(0.63,0.65)	(0.52,0.56)	(0.28,0.34)
TMLE(II)	0.49	0.69	0.60	0.34	0.37
	(0.48,0.50)	(0.67,0.71)	(0.58,0.63)	(0.29,0.38)	(0.33,0.41)
Softmax Regression					
IPTW	0.46	0.65	0.56	0.27	0.37
	(0.43,0.49)	(0.59,0.70)	(0.49,0.64)	(0.18,0.36)	(0.29,0.44)
PSA(I)	0.38	0.64	0.55	0.22	0.45
PSA(II)	0.56	0.65	0.59	0.36	0.62
TMLE(I)	0.61	0.69	0.61	0.56	0.37
	(0.60,0.63)	(0.67,0.71)	(0.58,0.63)	(0.53,0.59)	(0.35,0.39)
TMLE(II)	0.48	0.64	0.59	0.26	0.45
	(0.47,0.50)	(0.62,0.67)	(0.57,0.62)	(0.22,0.30)	(0.42,0.48)
GBM					
IPTW	0.55	0.80	0.59	0.25	0.27
	(0.39,0.72)	(0.65,0.96)	(0.47,0.70)	(0.11,0.40)	(0.02,0.52)
PSA(I)	0.43	0.68	0.63	0.35	0.55
PSA(II)	0.65	0.68	0.64	0.37	0.66
TMLE(I)	0.63	0.84	0.60	0.54	0.27
	(0.58,0.68)	(0.79,0.87)	(0.54,0.67)	(0.52,0.56)	(0.23,0.31)
TMLE(II)	0.55	0.77	0.57	0.34	0.30
	(0.50,0.60)	(0.72,0.81)	(0.50,0.64)	(0.29,0.38)	(0.24,0.36)

Table 7: Estimates of the probability of treatment success along with the confidence intervals under regimens 6-10 for the MDR-TB application in Section 4 after 20% truncation of the GPS. SVM: Support Vector Machine; GBM: Generalized Boosted Model; IPTW: Inverse Probability of Treatment Weighting; PSA: Propensity Score Adjustment; TMLE: Targeted Maximum Likelihood Estimation. Outcome regression models were fit by (I) regimen and (II) treatments as main terms covariates.

Regimen	6 None	7 OFX-KM- Z- ETH	8 OFX-CM- Z- ETH-CS-PAS	9 OFX- PTO- CS-PAS	10 OFX-KM- Z-EMB- ETH-CS
SVM					
IPTW	0.19	0.56	0.67	0.57	0.56
	(0.08,0.31)	(0.49,0.64)	(0.55,0.80)	(0.37,0.76)	(0.48,0.65)
PSA(I)	0.29	0.59	0.61	0.56	0.57
PSA(II)	0.38	0.63	0.61	0.58	0.67
TMLE(I)	0.21	0.58	0.66	0.62	0.60
	(0.18,0.23)	(0.56,0.60)	(0.65,0.67)	(0.58,0.66)	(0.58,0.62)
TMLE(II)	0.24	0.58	0.60	0.58	0.57
	(0.21,0.27)	(0.56,0.60)	(0.58,0.62)	(0.53,0.62)	(0.54,0.60)
Softmax Regression					
IPTW	0.31	0.56	0.69	0.45	0.56
	(0.24,0.38)	(0.48,0.64)	(0.61,0.78)	(0.35,0.54)	(0.48,0.65)
PSA(I)	0.37	0.55	0.57	0.46	0.54
PSA(II)	0.38	0.56	0.59	0.50	0.65
TMLE(I)	0.25	0.56	0.69	0.56	0.59
	(0.22,0.28)	(0.53,0.60)	(0.67,0.71)	(0.53,0.58)	(0.56,0.63)
TMLE(II)	0.36	0.56	0.62	0.49	0.56
	(0.30,0.41)	(0.53,0.60)	(0.60,0.64)	(0.47,0.52)	(0.52,0.61)
GBM					
IPTW	0.24	0.68	0.75	0.56	0.55
	(0.17,0.32)	(0.42,0.94)	(0.66,0.83)	(0.25,0.86)	(0.45,0.65)
PSA(I)	0.38	0.60	0.60	0.54	0.57
PSA(II)	0.40	0.63	0.60	0.52	0.65
TMLE(I)	0.25	0.67	0.73	0.62	0.59
	(0.22,0.28)	(0.62,0.73)	(0.70,0.77)	(0.56,0.67)	(0.57,0.61)
TMLE(II)	0.26	0.65	0.67	0.58	0.55
	(0.22,0.31)	(0.60,0.70)	(0.63,0.71)	(0.52,0.64)	(0.52,0.58)