

**S3 File.** Code, outcome parameters, and graphical information for the penalized regression using the elastic net via the R packages glmnet and selectiveInference.

```
# create matrix from x variables (predictors) and standardize
x_matrix_tmp <- data.frame(data1$age, data1$v_cn_diff, data1$telo, data1$coke_yrs, data1$alc_yrs)
# subset the dataframe
x_matrix <- data.matrix(x_matrix_tmp) # convert subsetted data frame to matrix
xdata.z <- scale(x_matrix, center=T, scale=T)

# create vector for y variable (dti, dependent) and standardize
y_vector <- as.vector(data1$rd_coke)
ydata.z <- scale(y_vector, center=T, scale=T)

# run elastic net (lasso/ridge special case anchors) with LOOCV as per Finch and Finch article
glmnet1.cv <- cv.glmnet(xdata.z,ydata.z, standardize = FALSE, type.measure="mse", nfolds=22)

# obtain lambda with min MSE
glmnet1.cv$lambda.min
[1] 0.01899326

# obtain coefficients from model with optimal lambda value
coef(glmnet1.cv,s = "lambda.min")

      1
(Intercept)      -8.245236e-16
data1.age         3.754791e-01
data1.et_diff     3.279492e-01
data1.telo        -3.307578e-01
data1.coke_yrs    6.068837e-01
data1.alc_yrs     7.078269e-02

# obtain r-squared from best fitted model
r2 <- glmnet1.cv$glmnet.fit$dev.ratio[which(glmnet1.cv$glmnet.fit$lambda == glmnet1.cv$lambda.min)]
r2
[1] 0.78524

# examine relationship between coefficient values and model fit (as R-squared)
glmnet2.z <- glmnet(xdata.z,ydata.z,alpha=1, standardize=FALSE, nlambda=100)
plot(glmnet2.z, xvar="dev", label=TRUE, ylab=c("Regression Coefficient"), xlab=c("R Squared"))
```

```
# use selectiveinference package for covariance test estimate
# of the null hypothesis = no relationship with the dependent variable

lasso.sigma <- estimateSigma(xdata.z,ydata.z, intercept=FALSE, standardize=FALSE)
lasso.beta <- coef(glmnet2.z, glmnet1.cv$lambda.min )[-1]
lasso.inference <- fixedLassoInf(xdata.z,ydata.z, lasso.beta, glmnet1.cv$lambda.min, sigma=lasso.sigma$sigmahat)
```

```
Call:
fixedLassoInf(x = xdata.z, y = ydata.z, beta = lasso.beta, lambda = glmnet1.cv$lambda.min,
  sigma = lasso.sigma$sigmahat)
```

Standard deviation of noise (specified or estimated) sigma = 0.546

Testing results at lambda = 0.019, with alpha = 0.100

Var	Coef	Z-score	P-value	LowCI	UpCI	LowTailArea	UpTailArea
1	0.375	2.862	0.004	0.148	0.595	0.048	0.050
2	0.327	2.453	0.014	0.088	0.547	0.049	0.049
3	-0.330	-2.363	0.047	-0.560	-0.004	0.049	0.049
4	0.606	3.884	0.000	0.352	1.048	0.050	0.049
5	0.075	0.540	0.592	-0.721	0.280	0.050	0.049

Var labels: 1. data1.age 2. data1.et\_diff 3. data1.telo 4. data1.coke\_yrs 5. data1.alc\_yrs

```
sink() # write output
```

```
# examine fit parameters (variance) across the range of lambda from glmnet fit
> print(glmnet1.cv$glmnet.fit)
```

```
Call: glmnet(x = xdata.z, y = ydata.z, standardize = FALSE)
```

	Df	%Dev	Lambda
[1,]	0	0.00000	0.698600
[2,]	1	0.09095	0.636600
[3,]	1	0.16650	0.580000
[4,]	1	0.22920	0.528500
[5,]	1	0.28120	0.481500
[6,]	1	0.32440	0.438800
[7,]	1	0.36030	0.399800
[8,]	1	0.39010	0.364300

[9,] 2 0.42360 0.331900  
[10,] 2 0.45490 0.302400  
[11,] 2 0.48090 0.275600  
[12,] 2 0.50250 0.251100  
[13,] 3 0.52200 0.228800  
[14,] 4 0.56220 0.208500  
[15,] 4 0.59970 0.189900  
[16,] 4 0.63080 0.173100  
[17,] 4 0.65670 0.157700  
[18,] 4 0.67810 0.143700  
[19,] 4 0.69600 0.130900  
[20,] 4 0.71080 0.119300  
[21,] 4 0.72300 0.108700  
[22,] 4 0.73320 0.099030  
[23,] 4 0.74170 0.090230  
[24,] 4 0.74870 0.082220  
[25,] 5 0.75520 0.074910  
[26,] 5 0.76060 0.068260  
[27,] 5 0.76510 0.062190  
[28,] 5 0.76890 0.056670  
[29,] 5 0.77200 0.051630  
[30,] 5 0.77460 0.047050  
[31,] 5 0.77670 0.042870  
[32,] 5 0.77850 0.039060  
[33,] 5 0.78000 0.035590  
[34,] 5 0.78120 0.032430  
[35,] 5 0.78220 0.029550  
[36,] 5 0.78310 0.026920  
[37,] 5 0.78380 0.024530  
[38,] 5 0.78440 0.022350  
[39,] 5 0.78480 0.020370  
[40,] 5 0.78520 0.018560  
[41,] 5 0.78560 0.016910  
[42,] 5 0.78590 0.015410  
[43,] 5 0.78610 0.014040  
[44,] 5 0.78630 0.012790  
[45,] 5 0.78640 0.011650  
[46,] 5 0.78660 0.010620  
[47,] 5 0.78670 0.009675  
[48,] 5 0.78680 0.008816  
[49,] 5 0.78680 0.008033

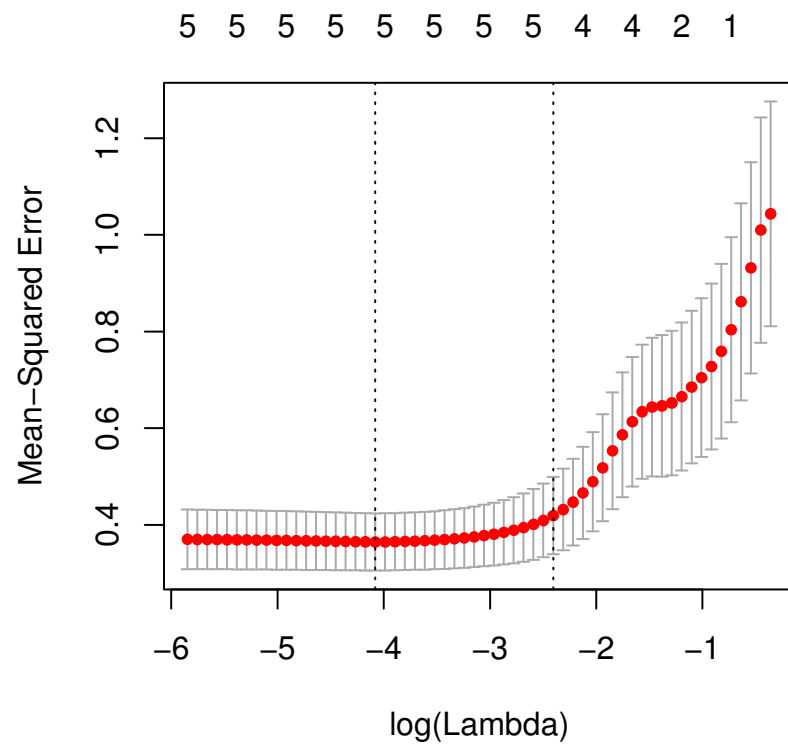
```
[50,] 5 0.78690 0.007319
[51,] 5 0.78700 0.006669
[52,] 5 0.78700 0.006076
[53,] 5 0.78700 0.005537
[54,] 5 0.78710 0.005045
[55,] 5 0.78710 0.004597
[56,] 5 0.78710 0.004188
[57,] 5 0.78710 0.003816
[58,] 5 0.78710 0.003477
[59,] 5 0.78710 0.003168
[60,] 5 0.78720 0.002887
[61,] 5 0.78720 0.002630
[62,] 5 0.78720 0.002397
```

```
glmnet1.cv$lambda.min # obtain lambda with min MSE
[1] 0.0190806
```

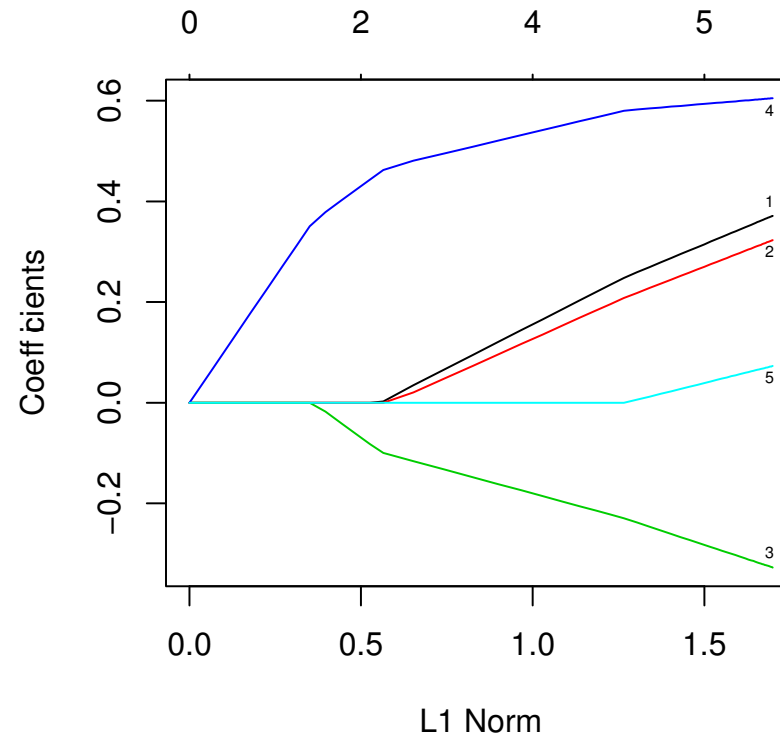
```
> # obtain r-squared from best fitted model
> r2 <- glmnet1.cv$glmnet.fit$dev.ratio[which(glmnet1.cv$glmnet.fit$lambda == glmnet1.cv$lambda.min)]
> r2
[1] 0.7852
```

```
> RMSE <- sqrt(glmnet1.cv$lambda.min)
> RMSE
[1] 0.130031
```

```
> plot(glmnet1.cv)
```

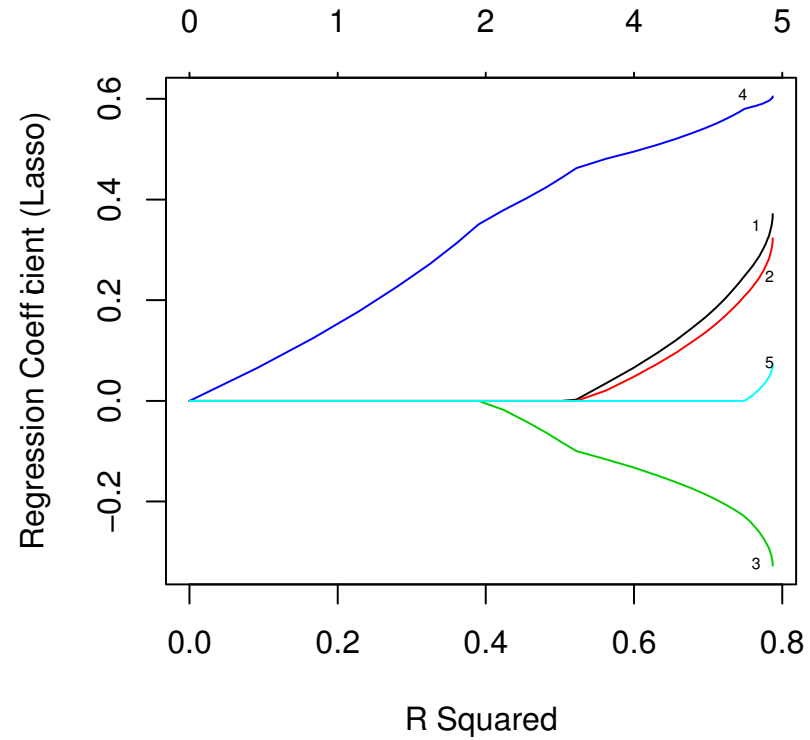


```
> plot(glmnet1.cv$glmnet.fit, xdata.z = "dev", label = TRUE)
```



1. Age
2. Anti-saccade (drift rate difference: cocaine vs. non-drug)
3. Telomere length
4. Years of cocaine use
5. Years of alcohol use

```
> plot(glmnet2.z, xvar="dev", label=TRUE, ylab=c("Regression Coefficient (Lasso)"), xlab=c("R Squared"))
```



1. Age
2. Anti-saccade (drift rate difference: cocaine vs. non-drug)
3. Telomere length
4. Years of cocaine use
5. Years of alcohol use