Efficient and Robust Estimation of $\tau$-year Risk Prediction Models Leveraging Time Varying Intermediate Outcomes

Yu Zheng*, Tian Lu†, Tianxi Cai*

* Department of Biostatistics, Harvard School of Public Health, Boston, MA 02115
† Department of Biomedical Data Science, Stanford University, Palo Alto, CA 94305

Supplementary Material

This supplementary material includes proof for the proposed method (Part 1) and R code for simulation studies (Part 2).

Part 1: Proof

Throughout, we let $B = E(I(T_i^\dagger > t_s)\Psi_i^\otimes 2 \dot{g}(\gamma_{r|t_s}^T \Psi_i))$, $L_i = J^{-1}X_i^\otimes 2 \dot{g}(\gamma_{r|t_s}^T \Psi_i)I(T_i^\dagger > t_s)$,

$J = E(X_i^\otimes 2 \dot{g}(\beta^T X_i))$, $U_i^X = X_i\{Y_{ri} - g(\beta^T X_i)\}$, $F_{1i} = J^{-1}X_i\{Y_{ri} - g(\beta^T X_i)\}$,

$A = E(\Phi_i^\otimes 2 \dot{g}(\theta^T \Phi_i))$, $U_i^\Phi = \Phi_i\{Y_{ri} - g(\theta_{t_s}^T \Phi_i)\}$, $F_{2i} = J^{-1}X_i\{Y_{ri} - g(\theta_{t_s}^T \Phi_i)\}$,

$\Psi_i = \Psi_i\{Y_{ri} - g(\gamma_{r|t_s}^T \Psi_i)\}$, $F_{3i} = J^{-1}X_i(Y_{ri} - g(\gamma_{r|t_s}^T \Psi_i))$.

For any a vector $a$, $a^\otimes 2 = aa^T$. We use $\approx$ to denote equivalence up to $o_p(1)$.
A Consistency of $\hat{\beta}$ obtained with S at a single visit $t_s$

Under a mild condition that there does not exist a $\beta$ such that $P(\beta^T X_1 > \beta^T X_2 | T^1_1 \leq t \leq T^2_1) = 1$, using a similar argument given by Tian et al. (2007), we can show that $U_0(\beta) = 0$ has a unique solution. To show $\hat{\beta}$ converges to $\bar{\beta}$ in probability, from Newey and McFadden (1994), it suffices to show that

$$\sup_{\beta} |\hat{U}_n(\beta) - U_0(\beta)| = o_p(1).$$

To this end, we recall that

$$\hat{U}_n(\beta) \equiv n^{-1} \sum_{i=1}^{n} X_i \{\hat{Y}^T_{t_s} - g(\beta^T X_i)\} = 0,$$

with

$$\hat{Y}^T_{t_s} = g(\hat{\theta}^T t_s \Phi) + \hat{\omega} t_s g(\hat{\gamma}^T \tau_{|t_s} \Psi).$$

We first establish convergence properties for $\hat{\theta}_{t_s}$ and $\hat{\gamma}_{t_s}$. Using similar arguments as given in Uno et al. (2007) for the convergence of $\hat{\beta}$ to $\bar{\beta}$ and the fact that $\max(\lambda_1, \lambda_2) = o(n^{-1/2})$, we may show that $\sup_{\theta} |\hat{Q}_n(\theta) - Q_0(\theta)| + \sup_{\gamma} |\hat{D}_n(\gamma) - D_0(\gamma)| \to 0$ in probability, where

$$Q_0(\theta) = E[\Phi_i(Y_{t_s,i} - g(\theta^T \Phi_i))], \quad \text{and} \quad D_0(\gamma) = E[I(T^1_{t_s} > t_s) \Psi_i(Y_i - g(\gamma^T \Psi_i))].$$

This, together with the fact that $Q_0(\theta) = 0$ and $D_0(\gamma) = 0$ respectively have unique solutions at $\bar{\theta}_{t_s}$ and $\bar{\gamma}_{t_s}$, implies that $\hat{\theta}_{t_s} \to \bar{\theta}_{t_s}$ and $\hat{\gamma}_{t_s} \to \bar{\gamma}_{t_s}$ in probability.

Next, let $U^*_n(\beta) = n^{-1} \sum_{i=1}^{n} X_i \{Y^T_{t_s} - g(\beta^T X_i)\}$ and

$$Y^T_{t_s} = g(\hat{\theta}^T t_s \Phi) + \hat{\omega} t_s g(\hat{\gamma}^T \tau_{|t_s} \Psi).$$

The consistency of $\hat{\theta}_{t_s}$ and $\hat{\gamma}_{t_s}$ together with the uniform consistency of $\hat{G}(\cdot)$ implies that $\sup_{\beta} |U^*_n(\beta) - \hat{U}_n(\beta)| \to 0$ in probability. This, coupled with the uniform law of large numbers (Pollard 1990), implies that $\sup_{\beta} |\hat{U}_n(\beta) - E\{U^*_n(\beta)\}| \to 0$ in probability. It is not difficult to
see that $E(U_n^*(\beta) = U_0(\beta)$ since

$$\begin{align*}
U_0(\beta) - E(U_n^*(\beta)) &= E[X_i(Y_{i,t} + I(T_i^1 > t_s)Y_{i,t} - g(\beta^T X_i))] \\
&= E[X_i \{g(\theta_{i,s}^T \Phi_i) + \omega_{i,s} \phi(\gamma_i \Psi_i) - g(\beta^T X_i)\}]
\end{align*}$$

$$\begin{align*}
&= E[X_i \{Y_{i,s} - g(\theta_{i,s}^T \Phi_i)\}] + \left[E[X_i(Y_{i,t} | T_i^1 > t_s) - E[X_i(g(\gamma_i \Psi_i) | T_i^1 > t_s)] \right] P(T_i^1 > t_s) \\
&= E[X_i \{Y_{i,s} - g(\theta_{i,s}^T \Phi_i)\}] + E[X_i(Y_{i,t} - g(\gamma_i \Psi_i)) | T_i > t_s] P(T_i^1 > t_s)
\end{align*}$$

The last equality holds because $E(X_i Y_{i,t} | T_i^1 > t_s) = E(X_i Y_{i,t} | T_i > t_s)$ due to the independence between $C_i$ and $(X_i, T_i^1)$. Both terms in the above quantity are 0 because $Q_0(\tilde{\theta}_s) = \mathbf{D}_0(\gamma) = 0$ and $X$ is part of $\Phi(X)$ and $\Phi(Z)$. Therefore, $\sup_\beta | \hat{U}_n(\beta) - U_0(\beta) | \to 0$ in probability and hence $\hat{\beta} \to \tilde{\beta}$ in probability.

B Asymptotic Distribution of $\hat{\beta}$ Obtained with $S$ measured at $t_s$

Uno et al. (2007) has shown that:

$$\begin{align*}
\sqrt{n}(\hat{\beta} - \beta) &\approx n^{-1/2} \sum_{i=1}^{n} \int_0^\tau \psi(s) dE\{U_i^X I(T_i^1 \wedge \tau \leq s)\} \\
&= n^{-1/2} \sum_{i=1}^{n} \int_0^\tau \psi(s) dE\{U_i^X I(T_i^1 \leq s)\} + \psi(\tau) E\{U_i^X I(T_i^1 > \tau)\}
\end{align*}$$

where $\psi(s) = \int_0^s \frac{dM_{ci}(u)}{\pi(u)}$, $\pi(u) = Pr(T_i > u)$, $M_{ci}(u) = I(T_i \leq u, \delta_i = 0) - \int_0^u I(T_i > v)d\Lambda_c(v)$ and $\Lambda_c(.)$ is the cumulative hazard function of $C_i$. It can be further shown that

$$\begin{align*}
\sqrt{n}(\hat{\beta} - \beta) &\approx n^{-1/2} \sum_{i=1}^{n} \int_0^\tau \psi(s) dE\{U_i^X I(T_i^1 \leq s)\} + \psi(\tau) E\{U_i^X I(T_i^1 > \tau)\} \\
&\approx n^{-1/2} \sum_{i=1}^{n} \int_0^\tau E\{U_i^X I(T_i^1 \leq s)\} dM_{ci}(s) \frac{dM_{ci}(s)}{\pi(s)}
\end{align*}$$

Similarly, it can be shown that

$$\begin{align*}
\sqrt{n}(\hat{\theta}_{i,s} - \tilde{\theta}_{i,s}) &\approx n^{-1/2} \sum_{i=1}^{n} \int_0^{t_s} E\{U_i^\Phi I(T_i^1 > s)\} \frac{dM_{ci}(s)}{\pi(s)}
\end{align*}$$

and

$$\begin{align*}
\sqrt{n}(\hat{\gamma}_{i,s} - \tilde{\gamma}_{i,s}) &\approx n^{-1/2} \sum_{i=1}^{n} \int_0^{t_s} E\{U_i^\Phi I(T_i^1 > s)\} \frac{dM_{ci}(s)}{\pi(s)}
\end{align*}$$

B.1
Here, \( \text{[B.2]} \) is true because \( I(T_i > t_s)w_{ri} = I(T_i^+ > t_s)w_{ri} \).

Now, from a Taylor series expansion of \( \hat{U}_n(\cdot) \) and a law of large numbers,

\[
\sqrt{n}(\hat{\beta} - \beta) \approx \mathbb{J}^{-1} n^{-\frac{1}{2}} \sum_{i=1}^{n} X_i \left[ \{g(\tilde{\theta}_{t_s} \Phi) - g(\tilde{\theta}_{t_s} \Phi_i)\} + \hat{\omega}_{t_i} \{g(\hat{\gamma}_{r|t_s} \Psi) - g(\hat{\gamma}_{r|t_s} \Psi_i)\} \right] \\
+ (\hat{\omega}_{t_i} - \omega_{t_i}) g(\hat{\gamma}_{r|t_s} \Psi_i) + Y_{r|t_i}^T - g(\hat{\beta}^T X_i) \\
\approx \mathbb{J}^{-1} n^{-\frac{1}{2}} \sum_{i=1}^{n} X_i \Phi_i^T g(\tilde{\theta}_{t_s} \Phi) \sqrt{n}(\hat{\theta}_{t_s} - \tilde{\theta}_{t_s}) + \mathbb{J}^{-1} n^{-\frac{1}{2}} \sum_{i=1}^{n} \omega_{t_i} X_i \Phi_i^T g(\hat{\gamma}_{r|t_s} \Psi) \sqrt{n}(\hat{\gamma}_{r|t_s} - \gamma_{r|t_s}) \\
+ \mathbb{J}^{-1} n^{-\frac{1}{2}} \sum_{i=1}^{n} \omega_{t_i} X_i g(\hat{\gamma}_{r|t_s} \Psi) n^{-\frac{1}{2}} \sum_{t_s}^n \psi_i(t_s) + \mathbb{J}^{-1} n^{-\frac{1}{2}} \sum_{i=1}^{n} X_i \{Y_{r|t_i}^T - g(\hat{\beta}^T X_i)\} \\
\approx \mathbb{J}^{-1} \sqrt{n}(\hat{\theta}_{t_s} - \tilde{\theta}_{t_s}) + \mathbb{J}^{-1} \mathbb{L} \sqrt{n}(\hat{\gamma}_{r|t_s} - \gamma_{r|t_s}) + n^{-\frac{1}{2}} \sum_{i=1}^{n} \left[ E(L_i) \psi_i(t_s) + \mathbb{J}^{-1} X_i \{Y_{r|t_i}^T - g(\hat{\beta}^T X_i)\} \right],
\]

where \( \mathbb{K} = E\{X_i \Phi_i^T g(\hat{\theta}_{t_s} \Phi)\} \), and \( \mathbb{L} = E\{I(T_i^+ > t_s)X_i \Phi_i^T g(\hat{\gamma}_{r|t_s} \Psi)\} \). Following from the expansions of \( \hat{\theta} \) and \( \hat{\gamma} \) given in \( \text{[B.1]} \) and \( \text{[B.2]} \), we have

\[
\sqrt{n}(\hat{\beta} - \beta) \approx n^{-\frac{1}{2}} \sum_{i=1}^{n} w_{t_i} \mathbb{J}^{-1} \mathbb{K} \mathbb{A}^{-1} U_i^\Phi + n^{-\frac{1}{2}} \sum_{i=1}^{n} I(T_i > t_s) w_{r|t_i} \mathbb{J}^{-1} \mathbb{L} \mathbb{B}^{-1} U_i^\Phi \\
+ n^{-\frac{1}{2}} \sum_{i=1}^{n} \left[ E(L_i) \psi_i(t_s) + \mathbb{J}^{-1} X_i \{Y_{r|t_i}^T - g(\hat{\beta}^T X_i)\} \right] \\
+ n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_0^{t_s} E\{\mathbb{J}^{-1} \mathbb{K} \mathbb{A}^{-1} U_i^\Phi I(T_i^+ > s)\} \frac{dM_{ci}(s)}{\pi(s)} \\
+ n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_t^{\infty} E\{\mathbb{J}^{-1} \mathbb{L} \mathbb{B}^{-1} U_i^\Phi I(T_i^+ > s)\} \frac{dM_{ci}(s)}{\pi(s)}
\]

To further simplify, we note that for \( j = 1, \ldots, p \),

\[
[\mathbb{K} \mathbb{A}^{-1}]_{jj} = E\{X_j \Phi_i^T g(\hat{\theta}_{t_s} \Phi)\} E[\Phi \mathbb{A}^{-1} \Phi]^{-1} = \argmin_{\alpha} E[g(\hat{\theta}_{t_s} \Phi)(X_j - \alpha^T \Phi)^2].
\]

Since each \( X_j \) is an element of \( \Phi(X) \), \( \min_{\alpha} E[g(\hat{\theta}_{t_s} \Phi)(X_j - \alpha^T \Phi(X))^2] = 0 \). Thus we have

\[
X_i = \mathbb{K} \mathbb{A}^{-1} \Phi_i, \quad \text{and} \quad \mathbb{J}^{-1} \mathbb{K} \mathbb{A}^{-1} U_i^\Phi = F_{21},
\]
Similarly, 

\[ [LB^{-1}]_j = E[I(T^4 > t_s) X_j \Psi^T \hat{g}(\gamma_r^{(t_s)} \Psi)] E[I(T^4 > t_s) \Psi^{\delta^2} \hat{g}(\gamma_r^{(t_s)} \Psi)]^{-1} \]

\[ = \arg\min_\alpha E[\hat{g}(\hat{\theta}_r \Psi(X)) \{X_j - \alpha^T \Psi(X)\}^2], \quad \text{for } j = 1, \ldots, p. \]

\[ X_j = LB^{-1} \Psi_j, \quad \text{and} \quad J^{-1} LB^{-1} U_{ij}^\Psi = F_{3i}. \]

The above equation can be written as:

\[ \sqrt{n}(\hat{\beta} - \bar{\beta}) \approx n^{-1/2} \sum_{i=1}^n \left[ w_{t_s} F_{2i} + I(T_i^4 > t_s) w_{r_s} F_{3i} + E(L_i) \psi_i(t_s) + \int J^{-1} LB^{-1} U_{ij}^\Psi \{Y_{ij}^\Psi - g(\bar{\beta}^T X_j)\} \right] \]

\[ \approx n^{-1/2} \sum_{i=1}^n \left[ F_{2i} + \int_{0}^{t_s} E(L_i) \frac{dM_{ci}(s)}{\pi(s)} + \left\{ \frac{I(C_i > t_s)}{G(t_s)} - 1 \right\} L_i \right] \]

\[ + (w_{t_s} - 1) F_{2i} + \int_{0}^{t_s} E[F_{2i} I(T_i^4 > s)] \frac{dM_{ci}(s)}{\pi(s)} \]

\[ + (w_{r_s} - 1) I(T_i > t_s) F_{3i} + \int_{t_s}^{t} E[F_{3i} I(T_i^4 > s)] \frac{dM_{ci}(s)}{\pi(s)} \]

Note that

\[ (w_{t_s} - 1) F_{2i} = \left\{ \frac{I(T_i \leq t_s)}{G(t_i)} + \frac{I(T_i > t_s)}{G(t_s)} - 1 \right\} F_{2i} \]

\[ = \left\{ \frac{I(T_i \leq t_s)}{G(t_i)} - \frac{I(T_i \leq t_s)(1 - \delta_i)}{G(t_i)} + \frac{1}{G(t_s)} - \frac{I(T_i \leq t_s)}{G(t_s)} - 1 \right\} F_{2i} \]

\[ = \left\{ - \int_{0}^{t_s} \frac{dI(T_i \leq s)(1 - \delta_i)}{G(s)} + \frac{1}{G(t_s)} - 1 + \left\{ \frac{1}{G(t_i)} - \frac{1}{G(t_s)} \right\} I(T_i \leq t_s) \right\} F_{ii} \]

\[ = \left\{ - \int_{0}^{t_s} \frac{dI(T_i \leq s)(1 - \delta_i)}{G(s)} + \int_{0}^{t_s} \frac{1}{G(s)} - \int_{0}^{t_s} I(T_i \leq s) \frac{1}{G(s)} \right\} F_{2i} \]

\[ = - \int_{0}^{t_s} F_{2i} \frac{S(s) dm_{ci}(s)}{\pi(s)} \]

and similarly, \( (w_{r_s} - 1) I(T_i^4 > t_s) F_{3i} = - \int_{t_s}^{t} I(T_i^4 > s) F_{3i} \frac{dM_{ci}(s)}{\pi(s)} \). Together with the fact that

\[ \left\{ \frac{I(C_i > t_s)}{G(t_s)} - 1 \right\} L_i = (w_{t_s} - 1) L_i = - \int_{0}^{t_s} L_i \frac{S(s) dm_{ci}(s)}{\pi(s)} \]
we have

\[ n^{\frac{1}{2}} (\hat{\beta} - \beta) \approx n^{-\frac{1}{2}} \sum_{i=1}^{n} \left( F_{1i} + \int_{0}^{t_s} \left[ E(L_i) - (L_i + F_{2i} - E(F_{2i}|T_i^\dagger > s)) S(s) \right] \frac{dM_{ci}(s)}{\pi(s)} - \int_{t_s}^{\tau} \{ F_{3i} - E(F_{3i}|T_i^\dagger > s) \} S(s) \frac{dM_{ci}(s)}{\pi(s)} \right) \]

\[ = n^{-\frac{1}{2}} \sum_{i=1}^{n} \left( F_{2i} - \int_{0}^{t_s} (F_{2i} + L_i - E(F_{2i} + L_i|T_i^\dagger > s)) S(s) \frac{dM_{ci}(s)}{\pi(s)} - \int_{t_s}^{\tau} \{ F_{3i} - E(F_{3i}|T_i^\dagger > s) \} S(s) \frac{dM_{ci}(s)}{\pi(s)} \right). \]

By the Central Limit Theory, we have \( n^{\frac{1}{2}} (\hat{\beta} - \beta) \to \mathcal{N}(0, \Sigma_{ls}) \) where

\[ \Sigma_{ls} = \text{var}(F_{1i}) + \int_{0}^{t_s} \text{var}(F_{2i} + L_i|T_i^\dagger > s) \frac{S(s)^2 d\Lambda_c(s)}{\pi(s)} + \int_{t_s}^{\tau} \text{var}(F_{3i}|T_i^\dagger > s) \frac{S(s)^2 d\Lambda_c(s)}{\pi(s)} \]
Part 2: Simulation Code in R

The following code is for low dimension setting. For the setting with moderate number of co-
variates, the code is very similar except for changing the code for generating $T_i$, $S_i$, $Z_i$ based
on the formula in Section 3.2.

The code for the functions Est.Surv.C.FUN and PTB.Surv.C.FUN can be requested for down-
loading from the author (ezheng@sdac.harvard.edu).

```
library(glmpath);library(glmnet);library(survival) # The following code is used to simulate
data, generate estimators and resampling for inference, and find the optimal linear combination
of estimators; # The code for the analysis specific functions is provided following the program;
t0=0.8; # this is the $\tau$
allts=c(0.05,0.1,0.15,0.2); # these are the $t_k$'s
n.beta=4; # length of $\beta$
nts=length(allts); # number of time points for intermediate outcome
nn=500; # sample size
Tc=12; Ct=0.5; # Rare events/heavy censoring setting
# Tc=6; Ct=1; # Moderate events/censoring setting
set.seed(seed) # setting seed from 1 to 500 for the 500 runs
# The following code is to simulate datasets.
```
\[ Z_i = \text{mvrnorm}(n, \text{rep}(0, 3), \text{matrix}(c(1, 0.3, 0.3, 0.3, 1, 0.3, 0.3, 0.3, 0.3, 0.3, 1, 0.3, 0.3, 0.3, 0.3, 0.3, 0.3, 0.3, 0.3, 0.3, 0.3, 0.3, 0.3, 0.3, 0.3, 0.3, 0.3, 0.3, 0.3), 3, 3)) \]

\[ \text{ginv.logit} = \text{function}(pp) \log(pp/(1-pp)) \]

\[ \text{uni} = \text{ginv.logit}(\text{runif}(n)) \]

\[ T_i = \exp(Z_i \% \% c(0.5, 0.5, 0.5) + 0.5 \cdot Z_i[, 1]^2 + Z_i[, 2]^2 + 0.5 \cdot Z_i[, 3]^2 - 3 + \text{uni} \cdot T_c) \]

\[ S_i = \text{matrix}(, \text{ncol} = \text{length(allts)}, \text{nrow} = \text{length}(T_i)) \]

for (i in 1:length(allts)) {
    tsi = allts[i] # let tsi = allts[4] for constant correlation
    \[ S[i, i] = \text{uni} + 0.1 \cdot (Z[i, 1] + Z[i, 2]) + \text{rnorm}(n, \text{mean} = 0, \text{sd} = 1)/(10 \cdot tsi^1.5); \]
}

\[ X_i = \text{pmin}(T_i, C_i); \text{Deltai} = 1*(T_i != C_i); \]

\[ \text{mydata} = \text{cbind}(T_i, X_i, \text{Deltai}, S_i, Z_i) \]

\[ \text{Pdelta} = \text{mean}((1-\text{mydata[,3]})*(\text{mydata[,2]>t0})) \# \text{censor rate}; \]

\[ \text{Pevent} = \text{mean}((\text{mydata[,2]>t0})*\text{mydata[,3]}) \# \text{event rate} \]

\[ \text{PScensor} = \text{CorSlogT} = \text{NULL} \]

for (aa in 1:nts) {
    ts0 = allts[aa]
    \[ S_i = \text{mydata[,3+aa]} \]
    \[ \text{PScensor} = \text{c}(\text{PScensor}, \text{mean}(\text{mydata[,2]>ts0})) \]
    \[ \text{CorSlogT} = \text{c}(\text{CorSlogT}, \text{cor}(S_i, \text{log}(\text{mydata[,1]))}) \]
}

##### censor intermediate covariate;
```r
mydata[mydata[,2][allts[aa],3+aa]=NA
}

# The following code is to generate different estimators for \( \beta \).
# beta.all includes the estimator from non-censored data, IPW_{KM}, IPW_{Cox,X}, AIPW_{KM},
# AUG_{KM,X} and AUG_{KM,Z} in the manuscript.

Modelfit = Est.Surv.C.FUN(mydata,lambda=NULL,nknot=3,tsi=allts,
AIPW=1,CoxT=F,NSselection="ridge",selection="none"))

beta.all=c(Modelfit$beta);

# The following code is to do resampling for the estimators;

PTB.Surv=PTB.Surv.C.FUN(mydata,n.ptb=500,nknot=3,tsi=allts,NSselection="ridge",
AIPW=1,ipwcox=1,CoxT=F, selection="none")

PTBipw=PTB.Surv$betaIPW; PTBipwcox.x=PTB.Surv$bhatIPWcox.x

PTBAIPWkm.x=PTB.Surv$bhatAIPWkm.x; PTBts=PTB.Surv$beta.ts

# The following code used to generate the optimal linear combination of the estimators;

# comb.a is AUG_{CMB,Z} in the manuscript;

# comb.x is AUG_{CMB,X} in the manuscript;

comb_a=comb_sd_a=comb_x=comb_sd_x=comb_xs=comb_sd_xs=NULL

inv.beta=Modelfit$beta[-c(1,3,4),]
```
for (i in 1:n.beta){

    Y=PTBipw[,i]

    PTBtsi=PTBts[,seq(i,ncol(PTBts),by=n.beta)]

    XS=matrix(Y,ncol=ncol(PTBtsi),nrow=length(Y))-PTBtsi

    X.x=XS[,seq(1,ncol(XS),by=2)]

    newXS=inv.beta[,i]

    newx=newXS[c(1,seq(2,length(newXS),by=2))]

    lassoModel.XS=try(cv.glmnet(XS,y=Y,alpha=1))

    lassoModel.x=try(cv.glmnet(X.x,y=Y,alpha=1))

    beta_a=coef(lassoModel.XS,s="lambda.min")

    comb_a=c(comb_a,t(newXS[-1])%*%beta_a[-1]+newXS[1]*(1-sum(beta_a[-1])))

    comb_sd_a=c(comb_sd_a,sd(Y-XS%*%beta_a[-1]))

    beta_x=coef(lassoModel.x,s="lambda.min")

    comb_x=c(comb_x,t(newx[-1])%*%beta_x[-1]+newx[1]*(1-sum(beta_x[-1])))

    comb_sd_x=c(comb_sd_x,sd(Y-X.x%*%beta_x[-1]))

}

######################################################################## End Code ################################################################