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Technical Report on the Cancer Survival Query System

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References

1.0 Introduction

This technical report includes information on the Cancer Survival Query System, and provides technical details and tables supplemental to those provided in Feuer EJ, Lee M, Mariotto AB, Cronin KA, Scoppa S, Penson DF, Hachey M, Cynkin L, Carter GA, Campbell D, Percy-Laurry A, Zou Z, Schrag D, Hankey BF. The Cancer Survival Query System: Making survival estimates from the Surveillance, Epidemiology, and End Results program more timely and relevant for recently diagnosed patients. Cancer. 2012 May 8. [Epub ahead of print]).

This report was updated on October 15, 2012. Errors were found in Figure 2 and Table 4 of the manuscript which are included in Section 6 of this report. All tables and figures in Section 6 have been corrected and updated.

This technical report includes development of the Profile Method based on relative survival as opposed to using cause of death as was done in the manuscript (Section 2), technical details of inference for cause-specific crude cumulative mortality for discrete time intervals are described along with the Cox model for grouped survival data (Section 3), a description of the development of the colorectal cancer nomogram (Section 4), all of the Cox regression tables used in the computation of net cancer-specific survival rates for the prostate cancer (Section 5.1) and colorectal cancer (Section 5.2) nomograms, and all of the tables and figures associated with the validation of the prostate (Section 6.1) and colorectal cancer (Section 6.2) nomograms.

2.0 The Profile Method Based on Relative Survival

Parallel methodology to that in the manuscript for the extension of Cronin and Feuer[1] to the profile method using relative survival in the calculation of crude cause-specific mortality is presented here. Equations 5 from the manuscript for G_{cM}, the cumulative crude cancer-specific

mortality, and equation 6 for G_{oM}, the crude cumulative crude other cause mortality, can be rewritten using relative and observed survival as

$$\bar{G}_{cM} = \sum_{x=1}^{M}\left(\prod_{i=1}^{x-1}\hat{P}_i\right)\left[(1-\bar{R}_x) - \frac{1}{2}(1-\bar{R}_x)(1-\bar{E}_x)\right] \quad (1)$$

$$\bar{G}_{oM} = \sum_{x=1}^{M}\left(\prod_{i=1}^{x-1}\hat{P}_i\right)\left[(1-\bar{E}_x) - \frac{1}{2}(1-\bar{R}_x)(1-\bar{E}_x)\right] \quad (2)$$

where $\hat{P}_i$ is the life table estimate of the observed survival rate in interval *i*, $\bar{E}_i$ is the expected survival rate in interval *i* for the patient group as obtained from US Life Tables based on the age, race, sex, and calendar year of diagnosis mix of the group, and $\bar{R}_i = \frac{\hat{P}_i}{\bar{E}_i}$ is the estimated relative survival rate in interval *i* . Equations (1) and (2) have been previously presented in Cronin and Feuer.[1]

Next we extend Cronin and Feuer[1] to the case of a specific cancer patient *j* with characteristics z_j which influence net cancer-specific survival, and characteristics w_j which influence net other cause survival. Generally z_j and w_j will have some factors in common (e.g. age). Equations (1) and (2) can be re-written as

$$\bar{G}_{cM}(z_j, w_j) = \sum_{x=1}^{M}\left(\prod_{i=1}^{x-1}\left(\bar{R}_i(z_j)\,\bar{E}_i(w_j)\right)\right)\left[\left(1-\bar{R}_x(z_j) - \frac{1}{2}\left(1-\bar{R}_x(z_j)\right)\left(1-\bar{E}_x(w_j)\right)\right)\right] \quad (3)$$

$$\bar{G}_{oM}(z_j, w_j) = \sum_{x=1}^{M}\left(\prod_{i=1}^{x-1}\left(\bar{R}_i(z_j)\,\bar{E}_i(w_j)\right)\right)\left[\left(1-\bar{E}_x(w_j)\right) - \frac{1}{2}\left(1-\bar{R}_x(z_j)\right)\left(1-\bar{E}_x(w_j)\right)\right] \quad (4)$$

Note that $\hat{P}_i$ is partitioned under independence into components associated with net cancer-specific and net other cause survival. In this formulation $\bar{R}_i(z_j) = \frac{\hat{P}_i(\mathrm{z_j})}{E_i(\mathrm{z_j})}$ can be estimated using various formulations such as those proposed in Haukulinen[2] or Dickman et al.[3]

In calculating $\bar{R}_i(z_j), z_j$ includes the characteristics of the cancer that define the cohort from which observed survival, i.e., $\hat{P}_i(\mathrm{z_j})$, will be obtained for patient *j*. The demographic variables included in z_j provide for calculating $\bar{E}_i(\mathrm{z_j})$, the expected survival for patient *j* obtained from US Life-tables. As was the case when using cause of death, $\bar{E}_i(w_j)$ can be estimated from a rich range of independent alternative data sources.

3.0 Estimation of crude cumulative mortality for an individual patient

In this section, we present technical details, which are not covered in Subsection 2.2.1 of the manuscript, for estimation of crude cumulative mortality for discrete time intervals for an individual with specific covariates. In addition, we describe the Cox model for grouped survival data.

3.1 Inference for grouped survival data

Prentice and Gloeckler[7] proposed the grouped data version of the proportional hazards model for estimation of the relative risk parameter. Here we briefly describe their methods.

Suppose that failure times are grouped into m disjoint intervals such as $[t_0, t_1)$, $[t_1, t_2)$, $\cdots$, $[t_{m-1}, t_m)$, where $t_0 = 0$, $t_m = \infty$. Let Z be a $p \times 1$ vector of covariates. Given $Z = z$, a likelihood function can be written as

$$\begin{aligned} L &= \prod_{i=1}^{m} \left[\prod_{l \in D_i} \{S(t_{i-1} \mid z_l) - S(t_i \mid z_l)\} \prod_{l \in C_i} S(t_i \mid z_l) \right] \\ &= \prod_{i=1}^{m} \left[\prod_{l \in D_i} \left\{ 1 - \frac{S(t_i \mid z_l)}{S(t_{i-1} \mid z_l)} \right\} \prod_{l \in R_i - D_i} \frac{S(t_i \mid z_l)}{S(t_{i-1} \mid z_l)} \right], \end{aligned}$$

where $S(t \mid z) = \Pr(T > t \mid Z = z)$ is the survival function for the underlying failure time T conditional on $Z = z$, D_i is the set of individuals failing in $[t_{i-1}, t_i)$, C_i is the set of individuals censored in $[t_{i-1}, t_i)$, and R_i is the risk set at time t_{i-1}.

Under the proportional hazards model, the survival function given $Z = z$ is given by

$$S(t \mid z) = S_0(t)^{\exp(\beta^T z)},$$

where $S_0(t) = \exp\{-\int_0^t \lambda_0(u)du\}$, $\lambda_0(t)$ is a baseline hazard function and β is a $p \times 1$ parameter vector. Let $\alpha_i = S_0(t_i)/S_0(t_{i-1}) = \exp \left\{ -\int_{t_{i-1}}^{t_i} \lambda_0(u)du \right\}$ and $\gamma_i = \log\{-\log(\alpha_i)\}$. Then

$$1 - \frac{S(t_i \mid z_l)}{S(t_{i-1} \mid z_l)} = 1 - \exp\left\{ -\exp(\gamma_i + z_l^T \beta) \right\}.$$

Note that $1 - \{S(t_i \mid z_l)/S(t_{i-1} \mid z_l)\}$ is the hazard of failure in the ith interval $[t_{i-1}, t_i)$ for an individual with covariate z_l and it is modeled by a complementary log-log link function. The likelihood function can be rewritten as

$$L = \prod_{i=1}^{m} \left[\prod_{l \in D_i} \left\{1 - \exp\left\{-\exp(\gamma_i + z_l^T \beta)\right\}\right\} \prod_{l \in R_i - D_i} \exp\left\{-\exp(\gamma_i + z_l^T \beta)\right\} \right]. \tag{5}$$

The parameters $\gamma_1, \ldots, \gamma_m$ and $\beta = (\beta_1, \ldots, \beta_p)$ can be estimated by using an iterative method such as a Newton-Raphson algorithm. The variance-covariance matrix of the maximum likelihood estimates (MLEs) is obtained by the inverse of the observed information matrix evaluated at the MLEs. The survival function at time t_k is estimated by

$$\hat{S}(t_k \mid z) = \prod_{i=1}^{k-1} \exp\left\{-\exp(\hat{\gamma}_i + z^T \hat{\beta})\right\}.$$

For details, see Prentice and Gloeckler[7].

3.2 Inference for grouped competing risks data

Suppose that there are two competing risks, death from cancer and death from other causes, and failure times are grouped into m disjoint intervals such as $[t_0, t_1)$, $[t_1, t_2)$, $\cdots$, $[t_{m-1}, t_m)$, where $t_0 = 0$, $t_m = \infty$. We assume that competing risks are acting independently as in Cronin and Feuer[1] to use two data sources for estimation of crude cumulative mortality from cancer and from other causes. Let Z be a $p \times 1$ vector of covariates that influences net cancer-specific survival and W be a $q \times 1$ vector of covariates that influences net other cause survival. Z and W will have some same covariates such as demographic characteristics.

Extending Cronin and Feuer[1] and using cause of death information[5], crude cumulative mortality from cancer and from other causes by interval M for an individual with specific covariates $Z = z_j$ and $W = w_j$ can be defined by

$$G_{cM}(z_j, w_j) = \sum_{x=1}^{M} g_{cx}^j \quad \text{and} \quad G_{oM}(z_j, w_j) = \sum_{x=1}^{M} g_{ox}^j, \tag{6}$$

where

$$g_{cx}^j = \left\{ \prod_{i=1}^{x-1} S_i(z_j) E_i(w_j) \right\} \left\{ (1 - S_x(z_j)) - \frac{1}{2}(1 - S_x(z_j))(1 - E_x(w_j)) \right\},$$

$$g_{ox}^{j} = \left\{ \prod_{i=1}^{x-1} S_i(z_j) E_i(w_j) \right\} \left\{ (1 - E_x(w_j)) - \frac{1}{2}(1 - S_x(z_j))(1 - E_x(w_j)) \right\},$$

$S_i(z_j)$ is net cancer-specific survival in the ith interval conditioned on surviving until the beginning of the interval for an individual with covariates z_j, and $E_i(w_j)$ is net other cause survival in the ith interval conditioned on surviving until the beginning of the interval for an individual with covariates w_j.

3.2.1 Fixed net other cause survival

We use the grouped data version of the proportional hazards model proposed by Prentice and Gloeckler [7] for estimation of net cancer-specific survival $S_i(z_j)$. Using notations given in Section 3.1, net cancer-specific survival $S_i(z_j)$ can be expressed by

$$S_i(z_j) = \frac{S(t_i \mid z_j)}{S(t_{i-1} \mid z_j)} = \exp\left\{ -\exp(\gamma_i + z_j^T \beta) \right\}.$$

Under the proportional hazards model, the crude cumulative mortality from cancer and from other causes $G_{cM}(z_j, w_j)$ and $G_{oM}(z_j, w_j)$ in (6) are given by

$$G_{cM}(z_j, w_j) = \sum_{x=1}^{M} g_{cx}^{j} \quad \text{and} \quad G_{oM}(z_j, w_j) = \sum_{x=1}^{M} g_{ox}^{j}, \tag{7}$$

where

$$g_{cx}^{j} = \left[\prod_{i=1}^{x-1} \exp\left\{ -\exp(\gamma_i + z_j^T \beta) \right\} E_i(w_j) \right] \left[\frac{1}{2} \left\{ 1 - \exp\left(-\exp(\gamma_x + z_j^T \beta) \right) \right\} (1 + E_x(w_j)) \right]$$

and

$$g_{co}^{j} = \left[\prod_{i=1}^{x-1} \exp\left\{ -\exp(\gamma_i + z_j^T \beta) \right\} E_i(w_j) \right] \left[\frac{1}{2} (1 - E_x(w_j)) \left\{ 1 + \exp\left(-\exp(\gamma_x + z_j^T \beta) \right) \right\} \right].$$

The MLEs $\hat{\gamma}_1, \ldots, \hat{\gamma}_m$ and $\hat{\beta} = (\hat{\beta}_1, \ldots, \hat{\beta}_p)$ can be obtained by maximizing the likelihood function in (5) treating failure times with death from other causes as censored. Net other cause survival $E_i(w_j)$ can be estimated from the US life table. Details of estimating net other cause survival are given in Subsection 2.2.2 of the manuscript. The crude cumulative

mortalities $G_{cM}(z_j, w_j)$ and $G_{oM}(z_j, w_j)$ in (7) are estimated by

$$\hat{G}_{cM}(z_j, w_j) = \sum_{x=1}^{M} \hat{g}_{cx}^j \quad \text{and} \quad \hat{G}_{co}(z_j, w_j) = \sum_{x=1}^{M} \hat{g}_{co}^j,$$

where

$$\hat{g}_{cx}^j = \left[\prod_{i=1}^{x-1} \exp\left\{-\exp(\hat{\gamma}_i + z_j^T\hat{\beta})\right\} \bar{E}_i(w_j)\right] \left[\frac{1}{2}\left\{1 - \exp\left(-\exp(\hat{\gamma}_x + z_j^T\hat{\beta})\right)\right\}\left(1 + \bar{E}_x(w_j)\right)\right]$$

and

$$\hat{g}_{co}^j = \left[\prod_{i=1}^{x-1} \exp\left\{-\exp(\hat{\gamma}_i + z_j^T\hat{\beta})\right\} \bar{E}_i(w_j)\right] \left[\frac{1}{2}\left(1 - \bar{E}_x(w_j)\right)\left\{1 + \exp\left(-\exp(\hat{\gamma}_x + z_j^T\hat{\beta})\right)\right\}\right].$$

To derive variance estimation of $\hat{G}_{cM}(z_j, w_j)$ and $\hat{G}_{oM}(z_j, w_j)$, we consider $\bar{E}_i(w_j)$ to be fixed as in Cronin and Feuer[1]. By the delta method, the variance of $\hat{G}_{cM}(z_j, w_j)$ can be estimated by

$$\widehat{\text{var}}(\hat{G}_{cM}(z_j, w_j)) = \hat{g}_c^j \hat{A}_1 \hat{H}^{-1} (\hat{g}_c^j \hat{A}_1)^T,$$

where

$$\hat{g}_c^j = \left(\hat{g}_{c1}^j, \hat{g}_{c2}^j, \cdots, \hat{g}_{cM}^j\right),$$

$$\hat{A}_1 = \begin{bmatrix} \frac{\partial \log g_{c1}^j}{\partial \gamma_1} & 0 & 0 & 0 & 0 & \cdots & 0 & \frac{\partial \log g_{c1}^j}{\partial \beta_1} & \cdots & \frac{\partial \log g_{c1}^j}{\partial \beta_p} \\ \frac{\partial \log g_{c2}^j}{\partial \gamma_1} & \frac{\partial \log g_{c2}^j}{\partial \gamma_2} & 0 & 0 & 0 & \cdots & 0 & \frac{\partial \log g_{c2}^j}{\partial \beta_1} & \cdots & \frac{\partial \log g_{c2}^j}{\partial \beta_p} \\ \frac{\partial \log g_{c3}^j}{\partial \gamma_1} & \frac{\partial \log g_{c3}^j}{\partial \gamma_2} & \frac{\partial \log g_{c3}^j}{\partial \gamma_3} & 0 & 0 & \cdots & 0 & \frac{\partial \log g_{c3}^j}{\partial \beta_1} & \cdots & \frac{\partial \log g_{c3}^j}{\partial \beta_p} \\ \frac{\partial \log g_{c4}^j}{\partial \gamma_1} & \frac{\partial \log g_{c4}^j}{\partial \gamma_2} & \frac{\partial \log g_{c4}^j}{\partial \gamma_3} & \frac{\partial \log g_{c4}^j}{\partial \gamma_4} & 0 & \cdots & 0 & \frac{\partial \log g_{c4}^j}{\partial \beta_1} & \cdots & \frac{\partial \log g_{c4}^j}{\partial \beta_p} \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \\ \frac{\partial \log g_{cM}^j}{\partial \gamma_1} & \frac{\partial \log g_{cM}^j}{\partial \gamma_2} & \frac{\partial \log g_{cM}^j}{\partial \gamma_3} & \frac{\partial \log g_{cM}^j}{\partial \gamma_4} & \frac{\partial \log g_{cM}^j}{\partial \gamma_5} & \cdots & \frac{\partial \log g_{cM}^j}{\partial \gamma_m} & \frac{\partial \log g_{cM}^j}{\partial \beta_1} & \cdots & \frac{\partial \log g_{cM}^j}{\partial \beta_p} \end{bmatrix}_{\substack{\gamma = \hat{\gamma} \\ \beta = \hat{\beta}}},$$

and $\hat{H}^{-1}$ is the inverse of the observed information matrix evaluated at the MLEs $\hat{\gamma}_1, \ldots, \hat{\gamma}_m$, $\hat{\beta} = (\hat{\beta}_1, \ldots, \hat{\beta}_p)$, that is, the covariance matrix of the MLEs. In the same way, the variance estimate of $\hat{G}_{oM}(z_j, w_j)$ is given by

$$\widehat{\text{var}}(\hat{G}_{oM}(z_j, w_j)) = \hat{g}_o^j \hat{A}_2 \hat{H}^{-1} (\hat{g}_o^j \hat{A}_2)^T,$$

where

$$\hat{g}_o^j = \left(\hat{g}_{o1}^j, \hat{g}_{o2}^j, \cdots, \hat{g}_{oM}^j\right)$$

and

$$\hat{A}_2 = \begin{bmatrix} \frac{\partial \log g_{o1}^j}{\partial \gamma_1} & 0 & 0 & 0 & 0 & \cdots & 0 & \frac{\partial \log g_{o1}^j}{\partial \beta_1} & \cdots & \frac{\partial \log g_{o1}^j}{\partial \beta_p} \\ \frac{\partial \log g_{o2}^j}{\partial \gamma_1} & \frac{\partial \log g_{o2}^j}{\partial \gamma_2} & 0 & 0 & 0 & \cdots & 0 & \frac{\partial \log g_{o2}^j}{\partial \beta_1} & \cdots & \frac{\partial \log g_{o2}^j}{\partial \beta_p} \\ \frac{\partial \log g_{o3}^j}{\partial \gamma_1} & \frac{\partial \log g_{o3}^j}{\partial \gamma_2} & \frac{\partial \log g_{o3}^j}{\partial \gamma_3} & 0 & 0 & \cdots & 0 & \frac{\partial \log g_{o3}^j}{\partial \beta_1} & \cdots & \frac{\partial \log g_{o3}^j}{\partial \beta_p} \\ \frac{\partial \log g_{o4}^j}{\partial \gamma_1} & \frac{\partial \log g_{o4}^j}{\partial \gamma_2} & \frac{\partial \log g_{o4}^j}{\partial \gamma_3} & \frac{\partial \log g_{o4}^j}{\partial \gamma_4} & 0 & \cdots & 0 & \frac{\partial \log g_{o4}^j}{\partial \beta_1} & \cdots & \frac{\partial \log g_{o4}^j}{\partial \beta_p} \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \\ \frac{\partial \log g_{oM}^j}{\partial \gamma_1} & \frac{\partial \log g_{oM}^j}{\partial \gamma_2} & \frac{\partial \log g_{oM}^j}{\partial \gamma_3} & \frac{\partial \log g_{oM}^j}{\partial \gamma_4} & \frac{\partial \log g_{oM}^j}{\partial \gamma_5} & \cdots & \frac{\partial \log g_{oM}^j}{\partial \gamma_m} & \frac{\partial \log g_{oM}^j}{\partial \beta_1} & \cdots & \frac{\partial \log g_{oM}^j}{\partial \beta_p} \end{bmatrix}_{\substack{\gamma = \hat{\gamma} \\ \beta = \hat{\beta}}}.$$

3.2.2 Applying grouped survival methods to estimation of net other cause survival

In Subsection 3.2.1, we used Prentice and Gloeckler's[7] method to estimation of net cancer-specific survival only. But we can use the method to estimate net other cause survival $E_i(w_j)$ as well as net cancer-specific survival $S_i(z_j)$. Net cancer-specific survival and net other cause survival can be expressed by

$$S_i(z_j) = \exp\left\{-\exp(\gamma_{1i} + z_j^T \beta_1)\right\} \quad \text{and} \quad E_i(w_j) = \exp\left\{-\exp(\gamma_{2i} + w_j^T \beta_2)\right\}, \quad i = 1, \ldots, m,$$

where $\gamma_{11}, \ldots, \gamma_{1m}$, $\beta_1 = (\beta_{11}, \ldots, \beta_{1p})$, $\gamma_{21}, \ldots, \gamma_{2m}$ and $\beta_2 = (\beta_{21}, \ldots, \beta_{2q})$ are the parameters for death from cancer and from other causes under the Cox model for grouped survival data. The crude cumulative mortality from cancer and from other causes $G_{cM}(z_j, w_j)$ and $G_{oM}(z_j, w_j)$ in (6) are given by

$$G_{cM}(z_j, w_j) = \sum_{x=1}^{M} g_{cx}^j \quad \text{and} \quad G_{oM}(z_j, w_j) = \sum_{x=1}^{M} g_{ox}^j, \tag{8}$$

where

$$\begin{aligned} g_{cx}^j &= \left[\prod_{i=1}^{x-1} \exp\left\{-\exp(\gamma_{1i} + z_j^T \beta_1)\right\} \exp\left\{-\exp(\gamma_{2i} + w_j^T \beta_2)\right\}\right] \\ &\quad \times \left[\frac{1}{2}\left\{1 - \exp\left(-\exp(\gamma_{1x} + z_j^T \beta_1)\right)\right\}\left(1 + \exp\left\{-\exp(\gamma_{2x} + w_j^T \beta_2)\right\}\right)\right] \end{aligned}$$

and

$$
\begin{aligned}
g_{co}^{j} &= \left[\prod_{i=1}^{x-1} \exp\left\{-\exp(\gamma_{1i} + z_j^T\beta_1)\right\} \exp\left\{-\exp(\gamma_{2i} + w_j^T\beta_2)\right\}\right] \\
&\quad \times \left[\frac{1}{2}\left(1 - \exp\left\{-\exp(\gamma_{2x} + w_j^T\beta_2)\right\}\right)\left\{1 + \exp\left(-\exp(\gamma_{1x} + z_j^T\beta_1)\right)\right\}\right].
\end{aligned}
$$

The parameters $\gamma_{11}, \ldots, \gamma_{1m}$ and $\beta_1 = (\beta_{11}, \ldots, \beta_{1p})$ can be obtained by maximizing the likelihood function in (5) treating failure times with death from other causes as censored. In a similar way, we can obtain the MLEs of the parameters $\gamma_{21}, \ldots, \gamma_{2m}$ and $\beta_2 = (\beta_{21}, \ldots, \beta_{2q})$. The crude cumulative mortalities $G_{cM}(z_j, w_j)$ and $G_{oM}(z_j, w_j)$ are estimated by

$$
\hat{G}_{cM}(z_j, w_j) = \sum_{x=1}^{M} \hat{g}_{cx}^{j} \quad \text{and} \quad \hat{G}_{co}(z_j, w_j) = \sum_{x=1}^{M} \hat{g}_{co}^{j},
$$

where

$$
\begin{aligned}
\hat{g}_{cx}^{j} &= \left[\prod_{i=1}^{x-1} \exp\left\{-\exp(\hat{\gamma}_{1i} + z_j^T\hat{\beta}_1)\right\} \exp\left\{-\exp(\hat{\gamma}_{2i} + w_j^T\hat{\beta}_2)\right\}\right] \\
&\quad \times \left[\frac{1}{2}\left\{1 - \exp\left(-\exp(\hat{\gamma}_{1x} + z_j^T\hat{\beta}_1)\right)\right\}\left(1 + \exp\left\{-\exp(\hat{\gamma}_{2x} + w_j^T\hat{\beta}_2)\right\}\right)\right]
\end{aligned}
$$

and

$$
\begin{aligned}
\hat{g}_{co}^{j} &= \left[\prod_{i=1}^{x-1} \exp\left\{-\exp(\hat{\gamma}_{1i} + z_j^T\hat{\beta}_1)\right\} \exp\left\{-\exp(\hat{\gamma}_{2i} + w_j^T\hat{\beta}_2)\right\}\right] \\
&\quad \times \left[\frac{1}{2}\left(1 - \exp\left\{-\exp(\hat{\gamma}_{2x} + w_j^T\hat{\beta}_2)\right\}\right)\left\{1 + \exp\left(-\exp(\hat{\gamma}_{1x} + z_j^T\hat{\beta}_1)\right)\right\}\right].
\end{aligned}
$$

By the delta method, the variance of $\hat{G}_{cM}(z_j, w_j)$ can be estimated by

$$
\widehat{\mathrm{var}}(\hat{G}_{cM}(z_j, w_j)) = \hat{g}_c^j \begin{bmatrix} \hat{A}_1 & \hat{B}_1 \end{bmatrix} \hat{H}^{-1} \left(\hat{g}_c^j \begin{bmatrix} \hat{A}_1 & \hat{B}_1 \end{bmatrix}\right)^T,
$$

where

$$
\hat{g}_c^j = \left(\hat{g}_{c1}^j, \hat{g}_{c2}^j, \cdots, \hat{g}_{cM}^j\right),
$$

$$\hat{A}_1 = \left[\begin{array}{cccccccccc}
\frac{\partial \log g^j_{c1}}{\partial \gamma_{11}} & 0 & 0 & 0 & 0 & \cdots & 0 & \frac{\partial \log g^j_{c1}}{\partial \beta_{11}} & \cdots & \frac{\partial \log g^j_{c1}}{\partial \beta_{1p}} \\
\frac{\partial \log g^j_{c2}}{\partial \gamma_{11}} & \frac{\partial \log g^j_{c2}}{\partial \gamma_{12}} & 0 & 0 & 0 & \cdots & 0 & \frac{\partial \log g^j_{c2}}{\partial \beta_{11}} & \cdots & \frac{\partial \log g^j_{c2}}{\partial \beta_{1p}} \\
\frac{\partial \log g^j_{c3}}{\partial \gamma_{11}} & \frac{\partial \log g^j_{c3}}{\partial \gamma_{12}} & \frac{\partial \log g^j_{c3}}{\partial \gamma_{13}} & 0 & 0 & \cdots & 0 & \frac{\partial \log g^j_{c3}}{\partial \beta_{11}} & \cdots & \frac{\partial \log g^j_{c3}}{\partial \beta_{1p}} \\
\frac{\partial \log g^j_{c4}}{\partial \gamma_{11}} & \frac{\partial \log g^j_{c4}}{\partial \gamma_{12}} & \frac{\partial \log g^j_{c4}}{\partial \gamma_{13}} & \frac{\partial \log g^j_{c4}}{\partial \gamma_{14}} & 0 & \cdots & 0 & \frac{\partial \log g^j_{c4}}{\partial \beta_{11}} & \cdots & \frac{\partial \log g^j_{c4}}{\partial \beta_{1p}} \\
\vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \\
\frac{\partial \log g^j_{cM}}{\partial \gamma_{11}} & \frac{\partial \log g^j_{cM}}{\partial \gamma_{12}} & \frac{\partial \log g^j_{cM}}{\partial \gamma_{13}} & \frac{\partial \log g^j_{cM}}{\partial \gamma_{14}} & \frac{\partial \log g^j_{cM}}{\partial \gamma_{15}} & \cdots & \frac{\partial \log g^j_{cM}}{\partial \gamma_{1m}} & \frac{\partial \log g^j_{cM}}{\partial \beta_{11}} & \cdots & \frac{\partial \log g^j_{cM}}{\partial \beta_{1p}}
\end{array}\right]_{\substack{\gamma_1 = \hat{\gamma}_1 \\ \beta_1 = \hat{\beta}_1}},$$

and

$$\hat{B}_1 = \left[\begin{array}{cccccccccc}
\frac{\partial \log g^j_{c1}}{\partial \gamma_{21}} & 0 & 0 & 0 & 0 & \cdots & 0 & \frac{\partial \log g^j_{c1}}{\partial \beta_{21}} & \cdots & \frac{\partial \log g^j_{c1}}{\partial \beta_{2q}} \\
\frac{\partial \log g^j_{c2}}{\partial \gamma_{21}} & \frac{\partial \log g^j_{c2}}{\partial \gamma_{22}} & 0 & 0 & 0 & \cdots & 0 & \frac{\partial \log g^j_{c2}}{\partial \beta_{21}} & \cdots & \frac{\partial \log g^j_{c2}}{\partial \beta_{2q}} \\
\frac{\partial \log g^j_{c3}}{\partial \gamma_{21}} & \frac{\partial \log g^j_{c3}}{\partial \gamma_{22}} & \frac{\partial \log g^j_{c3}}{\partial \gamma_{23}} & 0 & 0 & \cdots & 0 & \frac{\partial \log g^j_{c3}}{\partial \beta_{21}} & \cdots & \frac{\partial \log g^j_{c3}}{\partial \beta_{2q}} \\
\frac{\partial \log g^j_{c4}}{\partial \gamma_{21}} & \frac{\partial \log g^j_{c4}}{\partial \gamma_{22}} & \frac{\partial \log g^j_{c4}}{\partial \gamma_{23}} & \frac{\partial \log g^j_{c4}}{\partial \gamma_{24}} & 0 & \cdots & 0 & \frac{\partial \log g^j_{c4}}{\partial \beta_{21}} & \cdots & \frac{\partial \log g^j_{c4}}{\partial \beta_{2q}} \\
\vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \\
\frac{\partial \log g^j_{cM}}{\partial \gamma_{21}} & \frac{\partial \log g^j_{cM}}{\partial \gamma_{22}} & \frac{\partial \log g^j_{cM}}{\partial \gamma_{23}} & \frac{\partial \log g^j_{cM}}{\partial \gamma_{24}} & \frac{\partial \log g^j_{cM}}{\partial \gamma_{25}} & \cdots & \frac{\partial \log g^j_{cM}}{\partial \gamma_{2m}} & \frac{\partial \log g^j_{cM}}{\partial \beta_{21}} & \cdots & \frac{\partial \log g^j_{cM}}{\partial \beta_{2q}}
\end{array}\right]_{\substack{\gamma_2 = \hat{\gamma}_2 \\ \beta_2 = \hat{\beta}_2}},$$

and $\hat{H}^{-1}$ is the inverse of the observed information matrix evaluated at the MLEs $\hat{\gamma}_{11}, \ldots, \hat{\gamma}_{1m}$, $\hat{\beta}_1 = (\hat{\beta}_{11}, \ldots, \hat{\beta}_{1p})$, $\hat{\gamma}_{21}, \ldots, \hat{\gamma}_{2m}$ and $\hat{\beta}_2 = (\hat{\beta}_{21}, \ldots, \hat{\beta}_{2q})$.

The variance estimate of $\hat{G}_{oM}(z_j, w_j)$ is given by

$$\widehat{\mathrm{var}}(\hat{G}_{oM}(z_j, w_j)) = \hat{g}^j_o \left[\begin{array}{cc} \hat{A}_2 & \hat{B}_2 \end{array}\right] \hat{H}^{-1} \left(\hat{g}^j_o \left[\begin{array}{cc} \hat{A}_2 & \hat{B}_2 \end{array}\right]\right)^T,$$

where

$$\hat{g}^j_o = \left(\hat{g}^j_{o1}, \hat{g}^j_{o2}, \cdots, \hat{g}^j_{oM}\right),$$

$$\hat{A}_2 = \left[\begin{array}{cccccccccc}
\frac{\partial \log g^j_{o1}}{\partial \gamma_{11}} & 0 & 0 & 0 & 0 & \cdots & 0 & \frac{\partial \log g^j_{o1}}{\partial \beta_{11}} & \cdots & \frac{\partial \log g^j_{o1}}{\partial \beta_{1p}} \\
\frac{\partial \log g^j_{o2}}{\partial \gamma_{11}} & \frac{\partial \log g^j_{o2}}{\partial \gamma_{12}} & 0 & 0 & 0 & \cdots & 0 & \frac{\partial \log g^j_{o2}}{\partial \beta_{11}} & \cdots & \frac{\partial \log g^j_{o2}}{\partial \beta_{1p}} \\
\frac{\partial \log g^j_{o3}}{\partial \gamma_{11}} & \frac{\partial \log g^j_{o3}}{\partial \gamma_{12}} & \frac{\partial \log g^j_{o3}}{\partial \gamma_{13}} & 0 & 0 & \cdots & 0 & \frac{\partial \log g^j_{o3}}{\partial \beta_{11}} & \cdots & \frac{\partial \log g^j_{o3}}{\partial \beta_{1p}} \\
\frac{\partial \log g^j_{o4}}{\partial \gamma_{11}} & \frac{\partial \log g^j_{o4}}{\partial \gamma_{12}} & \frac{\partial \log g^j_{o4}}{\partial \gamma_{13}} & \frac{\partial \log g^j_{o4}}{\partial \gamma_{14}} & 0 & \cdots & 0 & \frac{\partial \log g^j_{o4}}{\partial \beta_{11}} & \cdots & \frac{\partial \log g^j_{o4}}{\partial \beta_{1p}} \\
\vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \\
\frac{\partial \log g^j_{oM}}{\partial \gamma_{11}} & \frac{\partial \log g^j_{oM}}{\partial \gamma_{12}} & \frac{\partial \log g^j_{oM}}{\partial \gamma_{13}} & \frac{\partial \log g^j_{oM}}{\partial \gamma_{14}} & \frac{\partial \log g^j_{oM}}{\partial \gamma_{15}} & \cdots & \frac{\partial \log g^j_{oM}}{\partial \gamma_{1m}} & \frac{\partial \log g^j_{oM}}{\partial \beta_{11}} & \cdots & \frac{\partial \log g^j_{oM}}{\partial \beta_{1p}}
\end{array}\right]_{\substack{\gamma_1 = \hat{\gamma}_1 \\ \beta_1 = \hat{\beta}_1}},$$

and

$$\hat{B}_2 = \begin{bmatrix} \frac{\partial \log g^j_{o1}}{\partial \gamma_{21}} & 0 & 0 & 0 & 0 & \cdots & 0 & \frac{\partial \log g^j_{o1}}{\partial \beta_{21}} & \cdots & \frac{\partial \log g^j_{o1}}{\partial \beta_{2q}} \\ \frac{\partial \log g^j_{o2}}{\partial \gamma_{21}} & \frac{\partial \log g^j_{o2}}{\partial \gamma_{22}} & 0 & 0 & 0 & \cdots & 0 & \frac{\partial \log g^j_{o2}}{\partial \beta_{21}} & \cdots & \frac{\partial \log g^j_{o2}}{\partial \beta_{2q}} \\ \frac{\partial \log g^j_{o3}}{\partial \gamma_{21}} & \frac{\partial \log g^j_{o3}}{\partial \gamma_{22}} & \frac{\partial \log g^j_{o3}}{\partial \gamma_{23}} & 0 & 0 & \cdots & 0 & \frac{\partial \log g^j_{o3}}{\partial \beta_{21}} & \cdots & \frac{\partial \log g^j_{o3}}{\partial \beta_{2q}} \\ \frac{\partial \log g^j_{o4}}{\partial \gamma_{21}} & \frac{\partial \log g^j_{o4}}{\partial \gamma_{22}} & \frac{\partial \log g^j_{o4}}{\partial \gamma_{23}} & \frac{\partial \log g^j_{o4}}{\partial \gamma_{24}} & 0 & \cdots & 0 & \frac{\partial \log g^j_{o4}}{\partial \beta_{21}} & \cdots & \frac{\partial \log g^j_{o4}}{\partial \beta_{2q}} \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \\ \frac{\partial \log g^j_{oM}}{\partial \gamma_{21}} & \frac{\partial \log g^j_{oM}}{\partial \gamma_{22}} & \frac{\partial \log g^j_{oM}}{\partial \gamma_{23}} & \frac{\partial \log g^j_{oM}}{\partial \gamma_{24}} & \frac{\partial \log g^j_{oM}}{\partial \gamma_{25}} & \cdots & \frac{\partial \log g^j_{oM}}{\partial \gamma_{2m}} & \frac{\partial \log g^j_{oM}}{\partial \beta_{21}} & \cdots & \frac{\partial \log g^j_{oM}}{\partial \beta_{2q}} \end{bmatrix}_{\substack{\gamma_2 = \hat{\gamma}_2 \\ \beta_2 = \hat{\beta}_2}} .$$

4.0 Development of the Colorectal Cancer Nomogram

4.1 Case Selection and Definition of Cause of Death

The survival information to be provided for colorectal cancer is based on patients diagnosed during 1994-2005 with a Behavior Code of 3, i.e. malignant, whose first invasive cancer was in the colon or rectum. This time period was used because of the availability of data to do the desired staging. Other selection criteria included: Histology Code = 8000-8001, 8010, 8020, 8140, 8210-8211, 8220-8221, 8260-8263, 8480-8482, and 8490, and Subsites = Proximal (Cecum, Ascending Colon, Hepatic Flexure, Transverse Colon, Splenic Flexure), Distal (Descending Colon, Sigmoid Colon, Rectosigmoid Junction), and Rectum.[8] Patients were excluded from the survival analysis using similar criteria as for prostate cancer including those under age 40 and ages 95 and older, and the definition of cause of death used in the survival analysis was obtained from the same source as for prostate.[5,9]

4.2 Prognostic Variables

Prognostic variables for colorectal cancer that were available in the SEER database included Stage, Grade, and Subsite, and the demographic variables Age, Race, and Sex. Stage[10] is based on path staging if available and clinical staging otherwise. Information on survival is provided for both surgically and non-surgically treated patients in stage I, whereas stages II and III include only surgically treated patients (only about 11 percent of patients in stages II and III did not have surgery). Grade data were collected according to rules specified in the SEER Code Manual[10] which are based on coding rules for Grade in the ICD-O, Third Edition.[11]

As was done for prostate cancer, Cox regression models were fit for specified stage groups,[7] i.e., Stage 0 (In situ), Stage I (No Surgery), Stage I (Surgery), Stage II (Surgery), Stage III (Surgery), and Stage IV, by Subsite (Proximal, Distal, and Rectum). For Stages II and III, the

two (IIa vs IIb) and three (IIIa vs IIIb vs IIIc) subgroups for stage respectively within these stage groups were included in the models as indicator variables. Age, Race, Year of Diagnosis, and Marital Status were treated the same way as for prostate cancer. Grade was treated as two categories (well and moderately differentiated vs. poor and undifferentiated). Co-morbidity Score was assumed to be linear with its effect for values of 1.00-5.12 set to the effect at a score of 1.00. All variables were evaluated for proportionality graphically.

5.0 Cox Regression Tables

Table 5.1-1 is the strata table for the prostate cancer nomogram (repeated from the manuscript) and Tables 5.1-2 through 5.1-21 are the Cox regression tables used in calculating net cancer-specific survival for that nomogram, and Tables 5.2-1 and 5.2-2 through 5.2-36 are the analogous tables for the colorectal cancer nomogram.

5.1 Strata Table and Cox Regression Tables for Prostate Cancer Nomogram

Number of observations used in prostate cancer analysis

	Pre-Treatment		Pure Clinical	
	With Como	w/o Como	With Como	w/o Como
Loc Inapp	34527	48978	26587	19386
Loc App	49317	56920	38252	21813
Loc Adv	3615	3328	3042	2061
Dist Mets	3960	2901	3871	2733

Pathological	
With Como	w/o Como
11896	43921
6002	18907

Site: Prostate 5.1-2
Group: Pathological without Comorbidity
Stage: Locally Advanced

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	1.0140[2]	--
u	-0.0820	0.0410	0.9213	0.0457
$c_1(u)$	0.1698	0.0887	1.1851	0.0556
$c_2(u)$	-0.6576	0.4629	0.5181	0.1555
Race	--	--	--	--
White	--	--	1.0	--
Black	-0.1902	0.1418	0.8268	0.1798
Other	-0.2594	0.2351	0.7715	0.2698
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.0324	0.1162	1.0329	0.7803
Year of Diagnosis (Linear)	-0.0609	0.0214	0.5441[3]	0.0044
Stage by Gleason Score	--	--	--	--
T3 N0 M0, 2-7 - Reference	--	--	1.0	--
T3 N0 M0, 8-10	1.5199	0.1119	4.5717	
T4 N0 M0, 2-7	0.4539	0.2731	1.5745	0.0965
T4 N0 M0, 8-10	2.4393	0.1759	11.4652	
T1-T3 N1 M0, 2-7	1.6390	0.2084	5.1499	
T4 N1 M0, 2-7	2.5688	0.5077	13.0504	
T1-T3 N1 M0, 8-10	2.2744	0.1549	9.7220	
T4 N1 M0, 8-10	3.1857	0.2228	24.1834	

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 40-65, but because of sparse data, ages 40-50 were set to the value of the effect at age 50.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidity Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-3
Group: Pathological without Comorbidity
Stage: Localized

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0307	0.0149	1.5848[3]	0.0391
Race	--	--	--	--
White	--	--	1.0	--
Black	0.5042	0.1836	1.6557	0.0060
Other	-0.7771	0.5060	0.4598	0.1246
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2723	0.1686	1.3130	0.1062
Year of Diagnosis (Linear)	-0.0439	0.0312	0.6450[3]	0.1595
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.8503	0.1561	2.3403	

[1]Linear model fit for range of ages 40-65, but because of sparse data, ages 40-50 were set to the value of the effect at age 50.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidity Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-4
Group: Pathological with Comorbidity
Stage: Localized

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	18.1273[2]	--
u	-0.1253	0.1532	0.8822	0.4136
$c_1(u)$	0.8157	0.8044	2.2606	0.3106
$c_2(u)$	-1.3138	1.4906	0.2688	0.3781
Race	--	--	--	--
White	--	--	1.0	--
Black	0.2191	0.2808	1.2449	0.4352
Other	-1.1712	0.5963	0.3100	0.0495
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.0367	0.2036	1.0374	0.8569
Year of Diagnosis (Linear)	-0.1228	0.0337	0.2929[3]	0.0003
Comorbidity (Linear)[4]	0.000732	0.000222	1.0011[5]	0.0010
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	1.0736	0.1604	2.9259	

[1]Restricted Cubic Spline with four knots is given by C(u)= $\&beta_1$ u+ $\&theta_1$ c_1 (u)+$\&theta_2$ c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of 1 comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-5
Group: Pathological with Comorbidity
Stage: Locally Advanced

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	7.3030[2]	--
u	0.1264	0.1191	1.1347	0.2886
$c_1(u)$	-0.6447	0.6304	0.5248	0.3065
$c_2(u)$	1.3127	1.1793	3.7161	0.2657
Race	--	--	--	--
White	--	--	1.0	--
Black	0.1947	0.2338	1.2150	0.4049
Other	-0.00879	0.2795	0.9912	0.9749
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1883	0.1544	1.2072	0.2227
Year of Diagnosis (Linear)	-0.0600	0.0266	0.5486[3]	0.0241
Comorbidity (Linear)[4]	0.000240	0.000217	1.0004[5]	0.2700
Stage by Gleason Score	--	--	--	--
T3 N0 M0, 2-7 - Reference	--	--	1.0	--
T3 N0 M0, 8-10	1.1079	0.1454	3.0281	
T4 N0 M0, 2-7	0.3015	0.3487	1.3519	0.3871
T4 N0 M0, 8-10	1.9394	0.2378	6.9544	
T1-T3 N1 M0, 2-7	0.7684	0.3486	2.1563	0.0275
T4 N1 M0, 2-7	2.3843	0.8034	10.8519	0.0030
T1-T3 N1 M0, 8-10	2.1233	0.1993	8.3586	
T4 N1 M0, 8-10	2.7504	0.3207	15.6490	

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of 1 comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-6
Group: Pretreatment Clinical with Comorbidity
Stage: Distant Mets

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	1.9595[2]	--
u	0.0208	0.0161	1.0211	0.1967
$c_1(u)$	-0.00601	0.0538	0.9940	0.9111
$c_2(u)$	0.0643	0.1819	1.0664	0.7238
Race	--	--	--	--
White	--	--	1.0	--
Black	0.0161	0.0645	1.0162	0.8029
Other	-0.3053	0.0878	0.7369	0.0005
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.0623	0.0455	1.0643	0.1710
Year of Diagnosis (Linear)	-0.0215	0.00733	0.8062[3]	0.0033
Comorbidity (Linear)[4]	0.000144	0.000053	1.0002[5]	0.0069
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.6059	0.0506	1.8329	

[1]Restricted Cubic Spline with four knots is given by C(u)= $\&beta_1$ u+ $\&theta_1$ c_1 (u)+$\&theta_2$ c_2 (u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidity Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-7
Group: Pretreatment Clinical without Comorbidity
Stage: Distant Mets

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	-0.0135	0.00438	0.8171[3]	0.0021
Race	--	--	--	--
White	--	--	1.0	--
Black	0.0392	0.0604	1.0399	0.5168
Other	-0.2872	0.1054	0.7504	0.0065
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1137	0.0508	1.1204	0.0251
Year of Diagnosis (Linear)	-0.0252	0.00883	0.7769[3]	0.0043
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.6617	0.0582	1.9380	

[1]Linear model fit for range of ages 40-65.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidity Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-8
Group: Pretreatment Clinical without Comorbidity
Stage: Locally Advanced and Nodal Disease

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	-0.00269	0.00867	0.9604[3]	0.7562
Race	--	--	--	--
White	--	--	1.0	--
Black	-0.00745	0.1130	0.9926	0.9475
Other	-0.0562	0.1952	0.9453	0.7733
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2386	0.0929	1.2694	0.0103
Year of Diagnosis (Linear)	-0.0319	0.0180	0.7266[3]	0.0764
Stage by Gleason Score	--	--	--	--
T3 N0 M0, 2-7 - Reference	--	--	1.0	--
T3 N0 M0, 8-10	1.0665	0.1302	2.9053	
T4 N0 M0, 2-7	0.4722	0.2349	1.6036	0.0444
T4 N0 M0, 8-10	1.8900	0.1535	6.6197	
T1-T3 N1 M0, 2-7	0.9716	0.1602	2.6422	
T1-T3 N1 M0, 8-10	1.4538	0.1442	4.2793	
T4 N1 M0, 2-7	1.6135	0.4232	5.0201	0.0001
T4 N1 M0, 8-10	2.1573	0.2600	8.6481	

[1]Linear model fit for range of ages 40-65, but because of sparse data, ages 40-50 were set to the value of the effect at age 50.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidity Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-9
Group: Pretreatment Clinical with Comorbidity
Stage: Locally Advanced and Nodal

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	3.4454[2]	--
u	-0.0367	0.0351	0.9640	0.2958
$c_1(u)$	0.2099	0.1212	1.2335	0.0834
$c_2(u)$	-0.4269	0.3385	0.6526	0.2073
Race	--	--	--	--
White	--	--	1.0	--
Black	0.1466	0.1139	1.1579	0.1981
Other	-0.6533	0.1772	0.5203	0.0002
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2093	0.0808	1.2329	0.0096
Year of Diagnosis (Linear)	-0.0341	0.0145	0.7109[3]	0.0188
Comorbidity (Linear)[4]	0.000226	0.000093	1.0003[5]	0.0148
Stage by Gleason Score	--	--	--	--
T3 N0 M0, 2-7 - Reference	--	--	1.0	--
T3 N0 M0, 8-10	0.8941	0.1148	2.4452	
T4 N0 M0, 2-7	0.8291	0.1598	2.2912	
T4 N0 M0, 8-10	1.8773	0.1210	6.5355	
T1-T3 N1 M0, 2-7	0.6493	0.1909	1.9142	0.0007
T1-T3 N1 M0, 8-10	1.2751	0.1551	3.5791	
T4 N1 M0, 2-7	1.4019	0.4584	4.0631	0.0022
T4 N1 M0, 8-10	2.4656	0.2349	11.7701	

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2 (u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidity Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-10
Group: Pretreatment Clinical without Comorbidity
Stage: Localized Apparent

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0333	0.00638	1.6477[3]	
Race	--	--	--	--
White	--	--	1.0	--
Black	0.3865	0.0721	1.4718	
Other	-0.3234	0.1562	0.7237	0.0384
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.3545	0.0645	1.4254	
Year of Diagnosis (Linear)	-0.0658	0.0128	0.5181[3]	
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	1.6390	0.0571	5.1501	

[1]Linear model fit for range of ages 40-65, but because of sparse data, ages 40-50 were set to the value of the effect at age 50.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidity Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-11
Group: Pretreatment Clinical with Comorbidity
Stage: Localized Apparent

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	8.8000[2]	--
u	0.0265	0.0229	1.0269	0.2470
$c_1(u)$	0.1646	0.0806	1.1789	0.0412
$c_2(u)$	-0.3177	0.1949	0.7278	0.1031
Race	--	--	--	--
White	--	--	1.0	--
Black	0.2941	0.0621	1.3419	
Other	-0.5825	0.1013	0.5585	
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2480	0.0424	1.2814	
Year of Diagnosis (Linear)	-0.0842	0.00782	0.4310[3]	
Comorbidity (Linear)[4]	0.000237	0.000049	1.0004[5]	
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	1.1593	0.0380	3.1877	

[1]Restricted Cubic Spline with four knots is given by C(u)= &beta$_1$ u+ &theta$_1$ c_1 (u)+&theta$_2$ c_2 (u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidity Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-12
Group: Pretreatment Clinical without Comorbidity
Stage: Localized Inapparent

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0473	0.00996	2.0317[3]	
Race	--	--	--	--
White	--	--	1.0	--
Black	0.2266	0.1139	1.2543	0.0467
Other	-0.4806	0.2632	0.6184	0.0679
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.3890	0.0996	1.4755	
Year of Diagnosis (Linear)	-0.0960	0.0196	0.3828[3]	
Stage by Gleason Score	--	--	--	--
T1a, 2-7 - Reference	--	--	1.0	--
T1a, 8-10	2.8252	0.8371	16.8645	0.0007
T1b, 2-7	1.7266	0.5211	5.6215	0.0009
T1b, 8-10	4.1209	0.4938	61.6117	
T1c, 2-7	0.9719	0.4510	2.6429	0.0312
T1c, 8-10	2.2865	0.4536	9.8401	

[1]Linear model fit for range of ages 40-65, but because of sparse data, ages 40-50 were set to the value of the effect at age 50.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidity Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-13
Group: Pretreatment Clinical with Comorbidity
Stage: Localized Inapparent

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	3.5964[2]	--
u	-0.0121	0.0375	0.9879	0.7464
$c_1(u)$	0.4363	0.1408	1.5470	0.0020
$c_2(u)$	-1.1623	0.3777	0.3128	0.0021
Race	--	--	--	--
White	--	--	1.0	--
Black	0.1269	0.0940	1.1353	0.1769
Other	-0.6197	0.1633	0.5381	0.0001
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.3255	0.0628	1.3847	
Year of Diagnosis (Linear)	-0.0852	0.0118	0.4265[3]	
Comorbidity (Linear)[4]	0.000363	0.000070	1.0005[5]	
Stage by Gleason Score	--	--	--	--
T1a, 2-7 - Reference	--	--	1.0	--
T1a, 8-10	1.8751	0.2497	6.5213	
T1b, 2-7	0.8490	0.1591	2.3373	
T1b, 8-10	2.6085	0.1452	13.5792	
T1c, 2-7	0.5046	0.1291	1.6563	
T1c, 8-10	1.4644	0.1330	4.3248	

[1]Restricted Cubic Spline with four knots is given by C(u)= $\&beta_1$ u+ $\&theta_1$ c_1 (u)+$\&theta_2$ c_2 (u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidity Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-14
Group: Pure Clinical without Comorbidity
Stage: Distant Mets

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	-0.0156	0.00448	0.7913[3]	0.0005
Race	--	--	--	--
White	--	--	1.0	--
Black	0.0336	0.0612	1.0342	0.5827
Other	-0.3070	0.1071	0.7357	0.0041
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1044	0.0515	1.1101	0.0426
Year of Diagnosis (Linear)	-0.0234	0.00899	0.7914[3]	0.0093
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.6078	0.0590	1.8365	

[1]Linear model fit for range of ages 40-65.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidity Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-15
Group: Pure Clinical with Comorbidity
Stage: Distant Mets

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	1.8906[2]	--
u	0.0188	0.0162	1.0189	0.2460
$c_1(u)$	-0.00358	0.0531	0.9964	0.9463
$c_2(u)$	0.0566	0.1772	1.0582	0.7496
Race	--	--	--	--
White	--	--	1.0	--
Black	0.0233	0.0651	1.0236	0.7206
Other	-0.3022	0.0879	0.7392	0.0006
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.0549	0.0459	1.0564	0.2314
Year of Diagnosis (Linear)	-0.0208	0.00741	0.8122[3]	0.0050
Comorbidity (Linear)[4]	0.1324	0.0537	1.2196[5]	0.0136
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.6028	0.0509	1.8272	

[1]Restricted Cubic Spline with four knots is given by C(u)= &beta$_1$ u+ &theta$_1$ c_1 (u)+&theta$_2$ c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94.[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of 1 comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-16
Group: Pure Clinical without Comorbidity
Stage: Locally Advanced

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.00236	0.0114	1.0360[3]	0.8365
Race	--	--	--	--
White	--	--	1.0	--
Black	0.00863	0.1360	1.0087	0.9494
Other	-0.1137	0.2382	0.8926	0.6333
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.3067	0.1139	1.3589	0.0071
Year of Diagnosis (Linear)	-0.0350	0.0230	0.7045[3]	0.1277
Stage by Gleason Score	--	--	--	--
T3 N0 M0, 2-7 - Reference	--	--	1.0	--
T3 N0 M0, 8-10	1.1538	0.1456	3.1703	
T4 N0 M0, 2-7	0.7545	0.2463	2.1266	0.0022
T4 N0 M0, 8-10	1.9109	0.1689	6.7593	
T1-T3 N1 M0, 2-7	0.6631	0.3555	1.9408	0.0622
T1-T3 N1 M0, 8-10	0.9351	0.2550	2.5476	0.0002
T4 N1 M0, 2-7	1.5708	0.5926	4.8106	0.0080
T4 N1 M0, 8-10	2.5996	0.3184	13.4577	

[1]Linear model fit for range of ages 40-65, but because of sparse data, ages 40-50 were set to the value of the effect at age 50.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidity Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-17
Group: Pure Clinical with Comorbidity
Stage: Locally Advanced

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	3.1400[2]	--
u	-0.0557	0.0362	0.9458	0.1238
$c_1(u)$	0.3086	0.1685	1.3615	0.0671
$c_2(u)$	-0.5545	0.4129	0.5743	0.1793
Race	--	--	--	--
White	--	--	1.0	--
Black	0.1983	0.1199	1.2193	0.0982
Other	-0.6416	0.1890	0.5265	0.0007
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2066	0.0865	1.2295	0.0168
Year of Diagnosis (Linear)	-0.0486	0.0156	0.6152[3]	0.0018
Comorbidity (Linear)[4]	0.2347	0.0961	1.4220[5]	0.0146
Stage by Gleason Score	--	--	--	--
T3 N0 M0, 2-7 - Reference	--	--	1.0	--
T3 N0 M0, 8-10	0.9022	0.1191	2.4650	
T4 N0 M0, 2-7	0.8609	0.1650	2.3654	
T4 N0 M0, 8-10	1.8988	0.1249	6.6782	
T1-T3 N1 M0, 2-7	0.5301	0.3060	1.6990	0.0832
T1-T3 N1 M0, 8-10	1.0414	0.2407	2.8331	
T4 N1 M0, 2-7	1.1196	0.5874	3.0636	0.0566
T4 N1 M0, 8-10	2.6755	0.2589	14.5193	

[1]Restricted Cubic Spline with four knots is given by C(u)= $\&beta_1$ u+ $\&theta_1$ c_1 (u)+$\&theta_2$ c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of 1 comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-18
Group: Pure Clinical without Comorbidity
Stage: Localized Apparent

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0171	0.00867	1.2931[3]	0.0482
Race	--	--	--	--
White	--	--	1.0	--
Black	0.3500	0.0875	1.4191	
Other	-0.5467	0.2137	0.5789	0.0105
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.3073	0.0801	1.3598	0.0001
Year of Diagnosis (Linear)	-0.0987	0.0169	0.3726[3]	
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	1.6989	0.0752	5.4678	

[1]Linear model fit for range of ages 40-65, but because of sparse data, ages 40-50 were set to the value of the effect at age 50.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidity Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-19
Group: Pure Clinical with Comorbidity
Stage: Localized Apparent

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	6.0325[2]	--
u	-0.00362	0.0208	0.9964	0.8617
$c_1(u)$	0.1886	0.0770	1.2076	0.0144
$c_2(u)$	-0.3340	0.1903	0.7160	0.0792
Race	--	--	--	--
White	--	--	1.0	--
Black	0.2395	0.0657	1.2706	0.0003
Other	-0.5906	0.1061	0.5540	
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2390	0.0443	1.2700	
Year of Diagnosis (Linear)	-0.0857	0.00827	0.4243[3]	
Comorbidity (Linear)[4]	0.1928	0.0513	1.3355[5]	0.0002
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	1.1609	0.0406	3.1929	

[1]Restricted Cubic Spline with four knots is given by C(u)= &beta$_1$ u+ &theta$_1$ c_1 (u)+&theta$_2$ c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of 1 comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-20
Group: Pure Clinical without Comorbidity
Stage: Localized Inapparent

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0362	0.0138	1.7224[3]	0.0086
Race	--	--	--	--
White	--	--	1.0	--
Black	0.0624	0.1415	1.0644	0.6593
Other	-0.1999	0.2807	0.8188	0.4763
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.4304	0.1201	1.5378	0.0003
Year of Diagnosis (Linear)	-0.1254	0.0254	0.2853[3]	
Stage by Gleason Score	--	--	--	--
T1a, 2-7 - Reference	--	--	1.0	--
T1a, 8-10	3.4859	0.7382	32.6533	
T1b, 2-7	1.7046	0.5079	5.4992	0.0008
T1b, 8-10	4.2506	0.4618	70.1440	
T1c, 2-7	1.1431	0.4181	3.1364	0.0063
T1c, 8-10	2.5623	0.4267	12.9657	

[1]Linear model fit for range of ages 40-65, but because of sparse data, ages 40-50 were set to the value of the effect at age 50.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidity Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Prostate 5.1-21
Group: Pure Clinical with Comorbidity
Stage: Localized Inapparent

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	5.5932[2]	--
u	-0.0197	0.0346	0.9805	0.5684
$c_1(u)$	0.3944	0.1361	1.4835	0.0037
$c_2(u)$	-1.0251	0.3722	0.3587	0.0059
Race	--	--	--	--
White	--	--	1.0	--
Black	0.1032	0.1003	1.1087	0.3037
Other	-0.6851	0.1774	0.5040	0.0001
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.3162	0.0659	1.3719	
Year of Diagnosis (Linear)	-0.0927	0.0125	0.3959[3]	
Comorbidity (Linear)[4]	0.3381	0.0733	1.6605[5]	
Stage by Gleason Score	--	--	--	--
T1a, 2-7 - Reference	--	--	1.0	--
T1a, 8-10	1.9562	0.2556	7.0724	
T1b, 2-7	0.8997	0.1608	2.4588	
T1b, 8-10	2.6659	0.1473	14.3815	
T1c, 2-7	0.5757	0.1314	1.7783	
T1c, 8-10	1.5399	0.1370	4.6643	

[1]Restricted Cubic Spline with four knots is given by C(u)= $\&beta_1$ u+ $\&theta_1$ c_1 (u)+$\&theta_2$ c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1995 where the range is 1995-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of 1 comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

5.2 Strata Table and Cox Regression Tables for Colorectal Cancer Nomogram

Number of observations used in colorectal cancer analysis

	Colorectal	
	With Como	Without Como
Rectal Stage 0	436	460
Rectal Stage 1 (Surgery)	2110	2982
Rectal Stage 1 (No Surgery)	992	923
Rectal Stage 2 (Surgery)	2065	2738
Rectal Stage 3 (Surgery)	2312	3905
Proximal Stage 4	1504	2434
Proximal Stage 0	510	287
Proximal Stage 1 (Surgery)	6055	
Proximal Stage 1 (No Surgery)	311	
Proximal Stage 1 (Surg & No Surg)		3025
Proximal Stage 2 (Surgery)	12265	6608
Proximal Stage 3 (Surgery)	9140	6595
Proximal Stage 4	5464	5259
Distal Stage 0	624	838
Distal Stage 1 (Surgery)	4596	5163
Distal Stage 1 (No Surgery)	722	760
Distal Stage 2 (Surgery)	6788	5965
Distal Stage 3 (Surgery)	5523	7501
Distal Stage 4	3851	5519

Site: Colorectal 5.2-2
Group: Distal Without Comorbidity
Stage: 0

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0696	0.0240	2.8391[3]	0.0037
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2534	0.2851	1.2884	0.3741
Race	--	--	--	--
White	--	--	1.0	--
Black	1.1259	0.3601	3.0829	0.0018
Other	0.2284	0.4179	1.2566	0.5847
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.7832	0.3078	0.4569	0.0109
Year of Diagnosis (Linear)	0.0540	0.0455	1.8120[3]	0.2347
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.9541	0.4152	2.5964	0.0216

[1]Linear model fit for range of ages 40-65.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-3
Group: Distal Without Comorbidity
Stage: I (No Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.00325	0.0217	1.0499[3]	0.8810
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.7958	0.2846	2.2162	0.0052
Race	--	--	--	--
White	--	--	1.0	--
Black	0.3100	0.3534	1.3635	0.3803
Other	-0.6689	0.6493	0.5123	0.3029
Sex	--	--	--	--
Male	--	--	1.0	--
Female	0.1919	0.2817	1.2116	0.4958
Year of Diagnosis (Linear)	0.0476	0.0547	1.6889[3]	0.3838
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	1.1772	0.5279	3.2452	0.0257

[1]Linear model fit for range of ages 40-65.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-4
Group: Distal Without Comorbidity
Stage: I (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0297	0.0140	1.5615[3]	0.0339
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.3544	0.1559	1.4253	0.0231
Race	--	--	--	--
White	--	--	1.0	--
Black	0.7017	0.2140	2.0172	0.0010
Other	-0.1956	0.2798	0.8223	0.4844
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.3672	0.1526	0.6926	0.0161
Year of Diagnosis (Linear)	-0.00522	0.0288	0.9442[3]	0.8560
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.0412	0.2778	1.0421	0.8820

[1]Linear model fit for range of ages 40-65, but because of sparse data, ages 40-50 were set to the value of the effect at age 50.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-5
Group: Distal Without Comorbidity
Stage: II (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0212	0.00635	1.3749[3]	0.0008
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2982	0.0703	1.3475	
Race	--	--	--	--
White	--	--	1.0	--
Black	0.3601	0.0989	1.4335	0.0003
Other	-0.1573	0.1111	0.8545	0.1569
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.1784	0.0683	0.8366	0.0090
Year of Diagnosis (Linear)	-0.0487	0.0121	0.5854[3]	
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.2038	0.0989	1.2261	0.0392
Stage II	--	--	--	--
Stage IIA	--	--	1.0	--
Stage IIB	0.7444	0.0769	2.1052	

[1]Linear model fit for range of ages 40-65, but because of sparse data, ages 40-50 were set to the value of the effect at age 50.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-6
Group: Distal Without Comorbidity
Stage: III (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0116	0.00320	1.1906[3]	0.0003
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2788	0.0461	1.3215	
Race	--	--	--	--
White	--	--	1.0	--
Black	0.2708	0.0692	1.3110	
Other	-0.0229	0.0625	0.9774	0.7146
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.0684	0.0437	0.9339	0.1172
Year of Diagnosis (Linear)	-0.0559	0.00756	0.5404[3]	
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.5307	0.0481	1.7002	
Stage III	--	--	--	--
Stage IIIA	--	--	1.0	--
Stage IIIB	1.0146	0.1006	2.7581	
Stage IIIC	1.5664	0.1014	4.7895	

[1]Linear model fit for range of ages 40-65.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-7
Group: Distal Without Comorbidity
Stage: IV

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.00860	0.00291	1.1377[3]	0.0031
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1759	0.0322	1.1923	
Race	--	--	--	--
White	--	--	1.0	--
Black	0.1866	0.0490	1.2052	0.0001
Other	0.0139	0.0482	1.0140	0.7738
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.0724	0.0308	0.9302	0.0189
Year of Diagnosis (Linear)	-0.0507	0.00462	0.5723[3]	
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.3736	0.0337	1.4529	

[1]Linear model fit for range of ages 40-65, but because of sparse data, ages 40-50 were set to the value of the effect at age 50.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-8
Group: Proximal Without Comorbidity
Stage: 0

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0301	0.0266	1.5695[3]	0.2581
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.8799	0.3476	2.4106	0.0114
Race	--	--	--	--
White	--	--	1.0	--
Black	-0.5826	0.5144	0.5585	0.2575
Other	0.6316	0.4609	1.8806	0.1705
Sex	--	--	--	--
Male	--	--	1.0	--
Female	0.3002	0.3390	1.3501	0.3758
Year of Diagnosis (Linear)	-0.0746	0.0616	0.4403[3]	0.2260
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	2.0515	0.4029	7.7796	

[1]Linear model fit for range of ages 40-65.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-9
Group: Proximal Without Comorbidity
Stage: I (Comb. Surgery and No Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	2.7207[2]	--
u	0.0667	0.0549	1.0690	0.2245
$c_1(u)$	-0.00828	0.0989	0.9918	0.9333
$c_2(u)$	-0.1308	0.5581	0.8774	0.8147
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2911	0.1791	1.3379	0.1041
Race	--	--	--	--
White	--	--	1.0	--
Black	0.7972	0.1894	2.2194	
Other	-0.1935	0.3314	0.8241	0.5594
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.4562	0.1712	0.6337	0.0077
Year of Diagnosis (Linear)	-0.0291	0.0296	0.7265[3]	0.3262
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.8662	0.2204	2.3777	

[1]Restricted Cubic Spline with four knots is given by C(u)= $\&beta_1$ u+ $\&theta_1$ c_1 (u)+$\&theta_2$ c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 40-65.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-10
Group: Proximal Without Comorbidity
Stage: II (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0214	0.00533	1.3785[3]	
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2927	0.0731	1.3400	
Race	--	--	--	--
White	--	--	1.0	--
Black	0.4705	0.0918	1.6008	
Other	-0.2705	0.1505	0.7630	0.0723
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.1672	0.0708	0.8460	0.0182
Year of Diagnosis (Linear)	-0.0272	0.0120	0.7412[3]	0.0229
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.2518	0.0820	1.2863	0.0021
Stage II	--	--	--	--
Stage IIA	--	--	1.0	--
Stage IIB	0.9089	0.0756	2.4815	

[1]Linear model fit for range of ages 40-65.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-11
Group: Proximal Without Comorbidity
Stage: III (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	1.2586[2]	--
u	0.0405	0.0125	1.0413	0.0012
$c_1(u)$	-0.0484	0.0262	0.9528	0.0643
$c_2(u)$	0.2330	0.1423	1.2624	0.1015
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1929	0.0459	1.2127	
Race	--	--	--	--
White	--	--	1.0	--
Black	0.2526	0.0598	1.2874	
Other	0.1050	0.0776	1.1107	0.1762
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.1507	0.0433	0.8601	0.0005
Year of Diagnosis (Linear)	-0.0388	0.00708	0.6523[3]	
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.3914	0.0441	1.4791	
Stage III	--	--	--	--
Stage IIIA	--	--	1.0	--
Stage IIIB	0.7622	0.1321	2.1431	
Stage IIIC	1.5161	0.1320	4.5544	

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 40-65.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-12
Group: Proximal Without Comorbidity
Stage: IV

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.00939	0.00225	1.1512[3]	
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1463	0.0321	1.1575	
Race	--	--	--	--
White	--	--	1.0	--
Black	0.1306	0.0416	1.1395	0.0017
Other	0.0334	0.0595	1.0339	0.5750
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.0278	0.0303	0.9725	0.3578
Year of Diagnosis (Linear)	-0.0462	0.00448	0.6016[3]	
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.4711	0.0307	1.6018	

[1]Linear model fit for range of ages 40-65.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-13
Group: Rectal without Comorbidity
Stage: 0

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0215	0.0234	1.3816[3]	0.3565
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2028	0.2641	1.2248	0.4426
Race	--	--	--	--
White	--	--	1.0	--
Black	0.3148	0.4178	1.3700	0.4512
Other	-1.1629	0.6919	0.3126	0.0928
Sex	--	--	--	--
Male	--	--	1.0	--
Female	0.00671	0.2472	1.0067	0.9783
Year of Diagnosis (Linear)	-0.0177	0.0476	0.8229[3]	0.7098
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.5792	0.4227	1.7846	0.1706

[1]Linear model fit for range of ages 40-65, but because of sparse data, ages 40-50 were set to the value of the effect at age 50.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-14
Group: Rectal Without Comorbidity
Stage: I (No Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0141	0.0136	1.2356[3]	0.3010
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.7587	0.1804	2.1355	
Race	--	--	--	--
White	--	--	1.0	--
Black	0.0576	0.3746	1.0593	0.8777
Other	0.5919	0.2387	1.8073	0.0132
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.0480	0.1813	0.9531	0.7911
Year of Diagnosis (Linear)	0.0604	0.0357	1.9430[3]	0.0908
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.9351	0.2241	2.5474	

[1]Linear model fit for range of ages 40-65.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-15
Group: Rectal Without Comorbidity
Stage: I (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0130	0.0113	1.2145[3]	0.2512
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1744	0.1303	1.1905	0.1808
Race	--	--	--	--
White	--	--	1.0	--
Black	0.9480	0.1969	2.5805	
Other	0.1041	0.1899	1.1097	0.5835
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.1378	0.1239	0.8712	0.2660
Year of Diagnosis (Linear)	0.00365	0.0228	1.0410[3]	0.8729
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.2237	0.1674	1.2507	0.1814

[1]Linear model fit for range of ages 40-65, but because of sparse data, ages 40-50 were set to the value of the effect at age 50.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-16
Group: Rectal Without Comorbidity
Stage: II (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0220	0.00660	1.3914[3]	0.0008
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.3066	0.0917	1.3588	0.0008
Race	--	--	--	--
White	--	--	1.0	--
Black	0.3451	0.1491	1.4121	0.0207
Other	-0.1081	0.1457	0.8976	0.4584
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.0612	0.0924	0.9406	0.5075
Year of Diagnosis (Linear)	-0.0304	0.0162	0.7159[3]	0.0605
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.5018	0.1094	1.6516	
Stage II	--	--	--	--
Stage IIA	--	--	1.0	--
Stage IIB	0.7807	0.1070	2.1831	

[1]Linear model fit for range of ages 40-65.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-17
Group: Rectal Without Comorbidity
Stage: III (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0153	0.00420	1.2580[3]	0.0003
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.0609	0.0639	1.0628	0.3401
Race	--	--	--	--
White	--	--	1.0	--
Black	0.1918	0.1099	1.2115	0.0808
Other	-0.00885	0.0833	0.9912	0.9154
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.1299	0.0597	0.8782	0.0295
Year of Diagnosis (Linear)	-0.0519	0.0101	0.5652[3]	
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.5037	0.0601	1.6548	
Stage III	--	--	--	--
Stage IIIA	--	--	1.0	--
Stage IIIB	1.0052	0.1131	2.7325	
Stage IIIC	1.4373	0.1133	4.2093	

[1]Linear model fit for range of ages 40-65.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-18
Group: Rectal Without Comorbidity
Stage: IV

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Linear)[1]	0.0155	0.00435	1.2623[3]	0.0004
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2016	0.0470	1.2233	
Race	--	--	--	--
White	--	--	1.0	--
Black	0.3140	0.0771	1.3689	
Other	0.1206	0.0692	1.1282	0.0812
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.0713	0.0489	0.9312	0.1454
Year of Diagnosis (Linear)	-0.0552	0.00707	0.5446[3]	
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.3402	0.0497	1.4052	

[1]Linear model fit for range of ages 40-65, but because of sparse data, ages 40-50 were set to the value of the effect at age 50.
[2] Relative Risk is for age 65 relative to age 50.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

Site: Colorectal 5.2-19
Group: Distal With Comorbidity
Stage: 0

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	8.7744[2]	--
u	0.0119	0.1059	1.0120	0.9103
$c_1(u)$	0.1711	0.4116	1.1866	0.6777
$c_2(u)$	-0.2399	1.0310	0.7867	0.8160
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	-0.0413	0.2629	0.9595	0.8752
Race	--	--	--	--
White	--	--	1.0	--
Black	0.3212	0.4854	1.3788	0.5081
Other	0.4717	0.3885	1.6027	0.2248
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.3928	0.2604	0.6752	0.1314
Year of Diagnosis (Linear)	0.0693	0.0407	2.1441[3]	0.0882
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.6280	0.4211	1.8739	0.1358
Comorbidity (Linear)[4]	0.000458	0.000231	1.0007[5]	0.0470

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-20
Group: Distal With Comorbidity
Stage: I (No Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	4.5910[2]	--
u	0.0451	0.0781	1.0461	0.5637
$c_1(u)$	-0.2192	0.3139	0.8031	0.4849
$c_2(u)$	0.7459	0.7186	2.1084	0.2993
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.4196	0.2167	1.5214	0.0528
Race	--	--	--	--
White	--	--	1.0	--
Black	0.1895	0.3249	1.2086	0.5598
Other	-0.0889	0.3970	0.9149	0.8228
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.5125	0.2197	0.5990	0.0196
Year of Diagnosis (Linear)	-0.0224	0.0327	0.7818[3]	0.4942
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	1.0730	0.3370	2.9242	0.0015
Comorbidity (Linear)[4]	0.000488	0.000185	1.0007[5]	0.0083

[1]Restricted Cubic Spline with four knots is given by C(u)= $\&beta_1$ u+ $\&theta_1$ c_1 (u)+$\&theta_2$ c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-21
Group: Distal With Comorbidity
Stage: I (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	5.4443[2]	--
u	0.0841	0.0449	1.0878	0.0609
$c_1(u)$	-0.1194	0.1558	0.8874	0.4432
$c_2(u)$	0.3879	0.4337	1.4739	0.3711
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1754	0.1092	1.1917	0.1083
Race	--	--	--	--
White	--	--	1.0	--
Black	0.00584	0.2209	1.0059	0.9789
Other	-0.4089	0.2245	0.6644	0.0686
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.1837	0.1069	0.8322	0.0857
Year of Diagnosis (Linear)	-0.00603	0.0171	0.9359[3]	0.7244
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.1209	0.1663	1.1285	0.4673
Comorbidity (Linear)[4]	0.000443	0.000102	1.0007[5]	

[1]Restricted Cubic Spline with four knots is given by C(u)= $\&beta_1$ u+ $\&theta_1$ c_1 (u)+$\&theta_2$ c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-22
Group: Distal With Comorbidity
Stage: II (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	3.0379[2]	--
u	0.0483	0.0202	1.0494	0.0171
$c_1(u)$	-0.0256	0.0645	0.9747	0.6911
$c_2(u)$	0.0931	0.1853	1.0976	0.6152
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2420	0.0571	1.2739	
Race	--	--	--	--
White	--	--	1.0	--
Black	0.3222	0.0938	1.3802	0.0006
Other	-0.1069	0.1060	0.8986	0.3131
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.1878	0.0554	0.8288	0.0007
Year of Diagnosis (Linear)	-0.00832	0.00840	0.9125[3]	0.3219
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.2005	0.0758	1.2221	0.0081
Stage II	--	--	--	--
Stage IIA	--	--	1.0	--
Stage IIB	0.7218	0.0587	2.0581	
Comorbidity (Linear)[4]	0.000232	0.000056	1.0003[5]	

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-23
Group: Distal With Comorbidity
Stage: III (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	2.5539[2]	--
u	0.0202	0.0179	1.0204	0.2581
$c_1(u)$	0.0327	0.0682	1.0332	0.6320
$c_2(u)$	-0.0358	0.1782	0.9648	0.8406
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1030	0.0493	1.1084	0.0368
Race	--	--	--	--
White	--	--	1.0	--
Black	0.2665	0.0860	1.3054	0.0019
Other	-0.1494	0.0801	0.8612	0.0621
Sex	--	--	--	--
Male	--	--	1.0	--
Female	0.0274	0.0483	1.0278	0.5700
Year of Diagnosis (Linear)	-0.0249	0.00725	0.7603[3]	0.0006
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.2879	0.0521	1.3337	
Stage III	--	--	--	--
Stage IIIA	--	--	1.0	--
Stage IIIB	1.0050	0.1073	2.7320	
Stage IIIC	1.4963	0.1099	4.4652	
Comorbidity (Linear)[4]	0.000259	0.000051	1.0004[5]	

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.

[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-24
Group: Distal With Comorbidity
Stage: IV

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	2.2352[2]	--
u	0.0338	0.0137	1.0344	0.0139
$c_1(u)$	-0.0705	0.0529	0.9319	0.1827
$c_2(u)$	0.2620	0.1554	1.2996	0.0917
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1723	0.0385	1.1880	
Race	--	--	--	--
White	--	--	1.0	--
Black	-0.0391	0.0672	0.9616	0.5604
Other	-0.1169	0.0693	0.8897	0.0918
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.0536	0.0378	0.9478	0.1569
Year of Diagnosis (Linear)	-0.0271	0.00519	0.7420[3]	
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.3522	0.0399	1.4222	
Comorbidity (Linear)[4]	0.000201	0.000043	1.0003[5]	

[1]Restricted Cubic Spline with four knots is given by C(u)= $\&beta_1$ u+ $\&theta_1$ c_1 (u)+$\&theta_2$ c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-25
Group: Proximal With Comorbidity
Stage: 0

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	6.3089[2]	--
u	-0.0719	0.0968	0.9306	0.4578
$c_1(u)$	0.5236	0.3064	1.6882	0.0875
$c_2(u)$	-1.3848	0.8634	0.2504	0.1087
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1921	0.2663	1.2118	0.4707
Race	--	--	--	--
White	--	--	1.0	--
Black	0.6814	0.3260	1.9766	0.0366
Other	0.9627	0.5225	2.6188	0.0654
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.1236	0.2593	0.8837	0.6334
Year of Diagnosis (Linear)	0.0181	0.0398	1.2207[3]	0.6487
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.7160	0.3161	2.0461	0.0235
Comorbidity (Linear)[4]	0.000733	0.000197	1.0011[5]	0.0002

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-26
Group: Proximal With Comorbidity
Stage: I (No Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	5.6517[2]	--
u	0.0403	0.0596	1.0412	0.4984
$c_1(u)$	0.0786	0.1262	1.0818	0.5336
$c_2(u)$	-0.3305	0.6433	0.7186	0.6074
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.5659	0.2371	1.7610	0.0170
Race	--	--	--	--
White	--	--	1.0	--
Black	0.5954	0.2721	1.8137	0.0287
Other	-0.5747	0.5927	0.5629	0.3322
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.7178	0.2299	0.4878	0.0018
Year of Diagnosis (Linear)	0.0447	0.0309	1.6353[3]	0.1476
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	1.2885	0.2587	3.6272	
Comorbidity (Linear)[4]	0.000102	0.000179	1.0002[5]	0.5674

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-27
Group: Proximal With Comorbidity
Stage: I (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	4.3102[2]	--
u	0.00861	0.0336	1.0087	0.7976
$c_1(u)$	0.1000	0.0883	1.1052	0.2573
$c_2(u)$	-0.1951	0.2895	0.8227	0.5003
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1016	0.0952	1.1070	0.2857
Race	--	--	--	--
White	--	--	1.0	--
Black	0.5655	0.1462	1.7603	0.0001
Other	0.0653	0.2076	1.0674	0.7532
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.2885	0.0925	0.7494	0.0018
Year of Diagnosis (Linear)	-0.0266	0.0143	0.7460[3]	0.0634
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.1543	0.1264	1.1668	0.2224
Comorbidity (Linear)[4]	0.000552	0.000083	1.0008[5]	

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Group: Proximal With Comorbidity
Stage: II (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	3.1805[2]	--
u	0.0418	0.0167	1.0427	0.0120
$c_1(u)$	-0.0457	0.0464	0.9553	0.3244
$c_2(u)$	0.2360	0.1433	1.2661	0.0997
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2474	0.0488	1.2807	
Race	--	--	--	--
White	--	--	1.0	--
Black	0.3167	0.0831	1.3726	0.0001
Other	-0.0225	0.1092	0.9778	0.8369
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.2355	0.0478	0.7902	
Year of Diagnosis (Linear)	-0.0153	0.00705	0.8449[3]	0.0297
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.1715	0.0491	1.1871	0.0005
Stage II	--	--	--	--
Stage IIA	--	--	1.0	--
Stage IIB	0.7196	0.0503	2.0537	
Comorbidity (Linear)[4]	0.000335	0.000043	1.0005[5]	

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-29
Group: Proximal With Comorbidity
Stage: III (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	2.1039[2]	--
u	0.0154	0.0122	1.0155	0.2093
$c_1(u)$	0.0380	0.0423	1.0388	0.3684
$c_2(u)$	-0.0692	0.1160	0.9332	0.5509
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1220	0.0367	1.1297	0.0009
Race	--	--	--	--
White	--	--	1.0	--
Black	0.1974	0.0622	1.2182	0.0015
Other	-0.1758	0.0784	0.8388	0.0249
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.1618	0.0365	0.8506	
Year of Diagnosis (Linear)	-0.0258	0.00522	0.7527[3]	
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.2607	0.0338	1.2978	
Stage III	--	--	--	--
Stage IIIA	--	--	1.0	--
Stage IIIB	0.7081	0.0857	2.0300	
Stage IIIC	1.3303	0.0869	3.7821	
Comorbidity (Linear)[4]	0.000189	0.000036	1.0003[5]	

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.

[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-30
Group: Proximal With Comorbidity
Stage: IV

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	1.6186[2]	--
u	0.00989	0.0105	1.0099	0.3467
$c_1(u)$	0.0346	0.0362	1.0352	0.3389
$c_2(u)$	-0.0899	0.1096	0.9140	0.4120
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.0839	0.0327	1.0875	0.0102
Race	--	--	--	--
White	--	--	1.0	--
Black	-0.0140	0.0548	0.9861	0.7990
Other	-0.0363	0.0705	0.9643	0.6064
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.0225	0.0318	0.9778	0.4795
Year of Diagnosis (Linear)	-0.0221	0.00431	0.7841[3]	
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.3598	0.0301	1.4330	
Comorbidity (Linear)[4]	0.000137	0.000034	1.0002[5]	

[1]Restricted Cubic Spline with four knots is given by C(u)= $\&beta_1$ u+ $\&theta_1$ c_1 (u)+$\&theta_2$ c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-31
Group: Rectal With Comorbidity
Stage: 0

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	5.4103[2]	--
u	-0.1353	0.0880	0.8734	0.1241
$c_1(u)$	0.4962	0.3339	1.6425	0.1372
$c_2(u)$	-0.8611	0.8568	0.4227	0.3149
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.3814	0.2327	1.4643	0.1012
Race	--	--	--	--
White	--	--	1.0	--
Black	0.9790	0.4027	2.6618	0.0151
Other	-0.8621	0.5627	0.4223	0.1255
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.6438	0.2347	0.5253	0.0061
Year of Diagnosis (Linear)	0.0375	0.0350	1.5100[3]	0.2842
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.5288	0.3365	1.6968	0.1162
Comorbidity (Linear)[4]	0.000461	0.000216	1.0007[5]	0.0325

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-32
Group: Rectal With Comorbidity
Stage: I (No Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	3.8209[2]	--
u	-0.0380	0.0494	0.9627	0.4412
$c_1(u)$	0.3161	0.1454	1.3718	0.0297
$c_2(u)$	-0.9563	0.4675	0.3843	0.0408
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2267	0.1509	1.2544	0.1332
Race	--	--	--	--
White	--	--	1.0	--
Black	0.4776	0.2720	1.6123	0.0790
Other	-0.5788	0.3382	0.5606	0.0870
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.2960	0.1468	0.7438	0.0438
Year of Diagnosis (Linear)	0.0193	0.0232	1.2365[3]	0.4048
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.3118	0.2049	1.3658	0.1282
Comorbidity (Linear)[4]	0.000413	0.000134	1.0006[5]	0.0020

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-33
Group: Rectal With Comorbidity
Stage: I (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	4.0803[2]	--
u	0.0470	0.0508	1.0482	0.3541
$c_1(u)$	-0.0244	0.2160	0.9759	0.9102
$c_2(u)$	0.1059	0.4841	1.1117	0.8268
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1484	0.1217	1.1600	0.2228
Race	--	--	--	--
White	--	--	1.0	--
Black	0.3736	0.2823	1.4530	0.1856
Other	0.1877	0.1950	1.2065	0.3356
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.1903	0.1169	0.8267	0.1034
Year of Diagnosis (Linear)	-0.0268	0.0198	0.7446[3]	0.1757
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.4485	0.1549	1.5660	0.0038
Comorbidity (Linear)[4]	0.000472	0.000125	1.0007[5]	0.0002

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-34
Group: Rectal With Comorbidity
Stage: II (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	2.8281[2]	--
u	0.0487	0.0355	1.0499	0.1704
$c_1(u)$	-0.1015	0.1561	0.9035	0.5154
$c_2(u)$	0.2488	0.3245	1.2825	0.4432
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.2565	0.0923	1.2924	0.0055
Race	--	--	--	--
White	--	--	1.0	--
Black	0.2516	0.1831	1.2861	0.1694
Other	-0.3833	0.1926	0.6816	0.0466
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.1785	0.0913	0.8365	0.0506
Year of Diagnosis (Linear)	-0.0337	0.0139	0.6900[3]	0.0154
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.4791	0.1051	1.6146	
Stage II	--	--	--	--
Stage IIA	--	--	1.0	--
Stage IIB	0.9749	0.1052	2.6509	
Comorbidity (Linear)[4]	0.000221	0.000103	1.0003[5]	0.0310

[1]Restricted Cubic Spline with four knots is given by C(u)= &beta$_1$ u+ &theta$_1$ c_1 (u)+&theta$_2$ c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-35
Group: Rectal With Comorbidity
Stage: III (Surgery)

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	2.9366[2]	--
u	-0.00853	0.0273	0.9915	0.7549
$c_1(u)$	0.1243	0.1197	1.1324	0.2990
$c_2(u)$	-0.1773	0.2703	0.8375	0.5117
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.1399	0.0690	1.1501	0.0427
Race	--	--	--	--
White	--	--	1.0	--
Black	0.1998	0.1394	1.2211	0.1519
Other	0.0554	0.1198	1.0570	0.6437
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.1050	0.0674	0.9003	0.1191
Year of Diagnosis (Linear)	-0.0394	0.0106	0.6484[3]	0.0002
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.4325	0.0669	1.5411	
Stage III	--	--	--	--
Stage IIIA	--	--	1.0	--
Stage IIIB	0.5522	0.1052	1.7371	
Stage IIIC	1.0445	0.1076	2.8418	
Comorbidity (Linear)[4]	0.000125	0.000082	1.0002[5]	0.1287

[1]Restricted Cubic Spline with four knots is given by C(u)= β_1 u+ θ_1 c_1 (u)+θ_2 c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.

[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

Site: Colorectal 5.2-36
Group: Rectal With Comorbidity
Stage: IV

Variable	Beta	Std Error of Beta	Relative Risk	Pvalue
Age (Restricted Cubic Spline)[1]	--	--	2.1282[2]	--
u	0.0481	0.0219	1.0493	0.0277
$c_1(u)$	-0.0725	0.0904	0.9300	0.4222
$c_2(u)$	0.1909	0.2603	1.2103	0.4635
Marital Status	--	--	--	--
Married (Reference)	--	--	1.0	--
Single	0.3245	0.0614	1.3834	
Race	--	--	--	--
White	--	--	1.0	--
Black	0.1692	0.1192	1.1844	0.1558
Other	-0.1471	0.1171	0.8632	0.2091
Sex	--	--	--	--
Male	--	--	1.0	--
Female	-0.00224	0.0604	0.9978	0.9705
Year of Diagnosis (Linear)	-0.0115	0.00841	0.8809[3]	0.1703
Gleason Score	--	--	--	--
2-7 - Reference	--	--	1.0	--
8-10	0.3915	0.0617	1.4792	
Comorbidity (Linear)[4]	0.000167	0.000074	1.0003[5]	0.0243

[1]Restricted Cubic Spline with four knots is given by C(u)= $\&beta_1$ u+ $\&theta_1$ c_1 (u)+$\&theta_2$ c_2(u) where c_1 (u) and c_2 (u) are cubic terms, model fit for range of ages 66-94, but because of sparse data, ages 90-94 were set to the value of the effect at age 90.
[2] Relative Risk is for age 90 relative to age 66.
[3] Relative Risk is for year 2005 relative to 1994 where the range is 1994-2005.
[4]Model fit for range of Comorbidity Scores 0-5.125, but because of sparse data, scores of 1.5-5.125 were set to the value of the effect of a score of 1.5. Average contribution to the comorbidity score of one comorbidity was 0.43480.
[5]Relative Risk is for a Comorbidty Score of 1.5 relative to a score of 0 (no comorbidity).

6.0 Validation

The area under the time-dependent ROC curve statistics are presented for prostate cancer in 6.1 and for colorectal cancer in 6.2. Table 6.1-1 shows results for the 10-fold cross-validation where AUC1 is for cancer-specific mortality and AUC2 is for other cause mortality at 1, 3, 5, 7, and 10 years post diagnosis for patients without comorbidity (ages 40-65) and patients with comorbidity (ages 66-94). The calibration plots are given in Figures 6.1-1 through 6.1-6. In the figures, each number and letter stands for the predicted year post diagnosis (1, 3, 5, 7, 10) and quartile group (a, b, c, d). For example, the point '3a' is for the 3-year crude cumulative mortality rate in the first quartile group for the indicated mortality. The plot of the pairs (mean of the predicted crude mortality and the nonparametric estimate of mortality) lie on a 45 degree angle line indicating that the models are good for predicting crude mortality rates. The analogous table and figures are given in section 6.2 for colorectal cancer.

6.1 Validation Table and Figures for Prostate Cancer Nomogram

Age 66+ with Comorbidity Scores

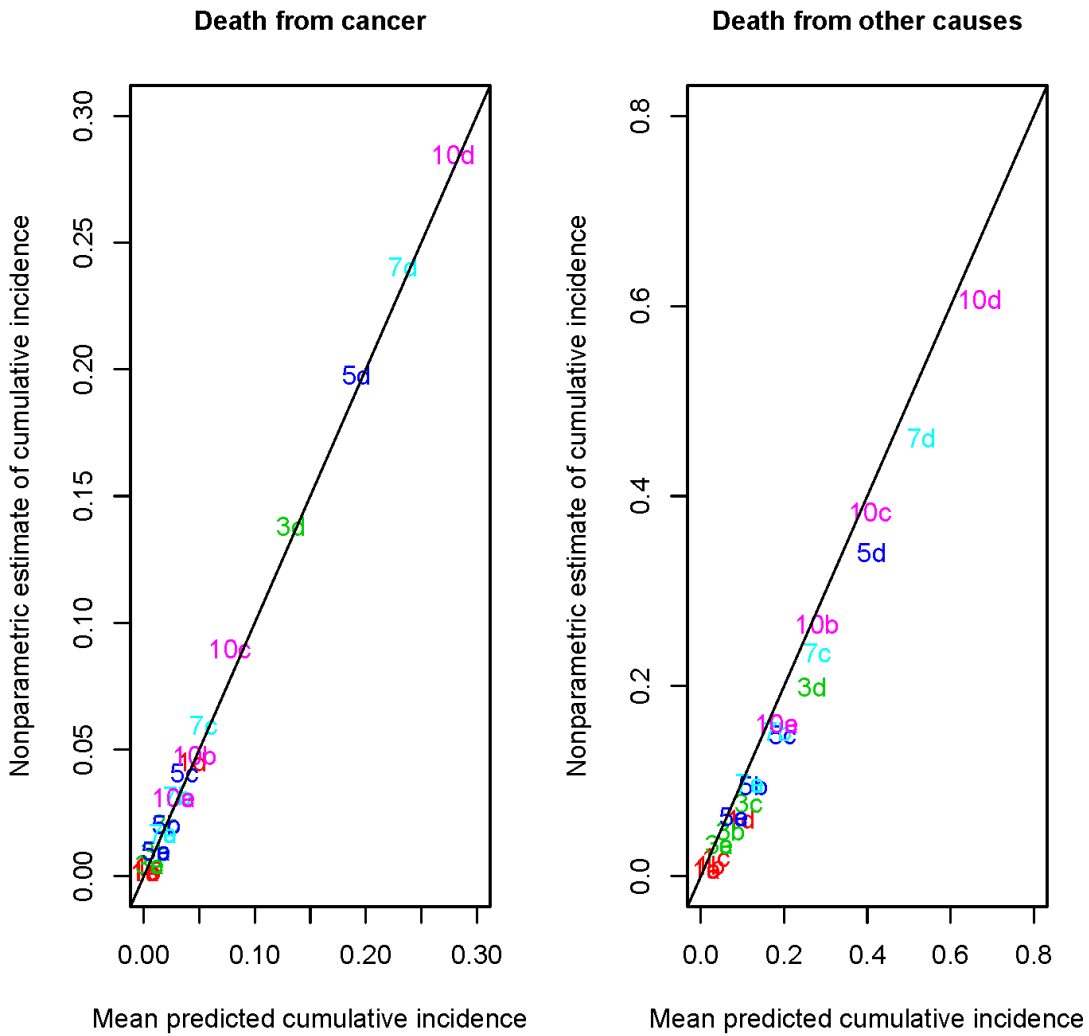
	Pretreatment		Pure Clinical		Pathological	
Year	AUC1	AUC2	AUC1	AUC2	AUC1	AUC2
1-year	0.89	0.75	0.89	0.74	0.61	0.68
3-year	0.87	0.73	0.87	0.71	0.72	0.62
5-year	0.85	0.72	0.84	0.71	0.74	0.62
7year	0.83	0.71	0.83	0.70	0.76	0.61
10-year	0.82	0.69	0.82	0.68	0.76	0.61

Age <66 without Comorbidity Scores

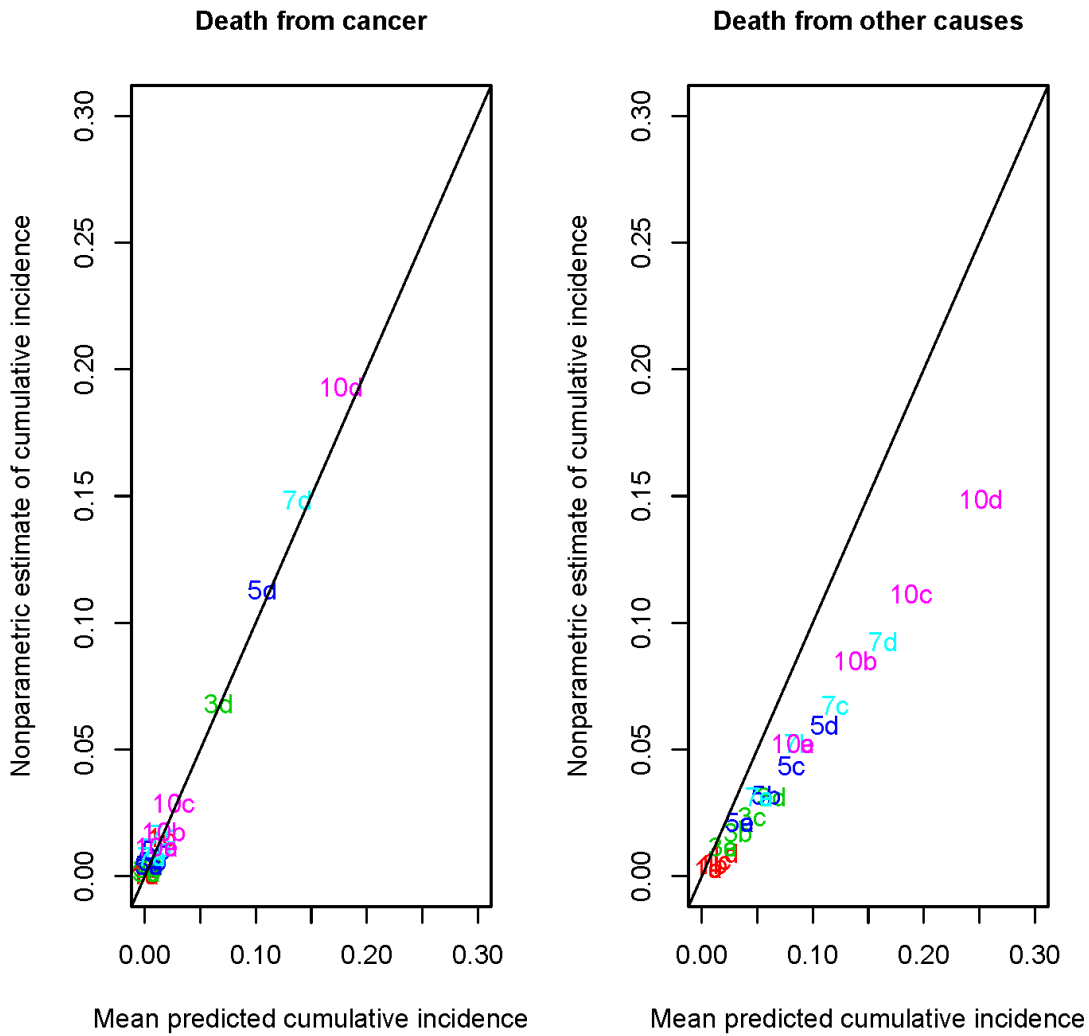
	Pretreatment		Pure Clinical		Pathological	
Year	AUC1	AUC2	AUC1	AUC2	AUC1	AUC2
1-year	0.91	0.63	0.94	0.59	0.59	0.63
3-year	0.92	0.61	0.93	0.58	0.71	0.62
5-year	0.90	0.61	0.91	0.59	0.78	0.62
7year	0.88	0.62	0.90	0.59	0.79	0.62
10-year	0.87	0.62	0.90	0.58	0.79	0.62

For each quartile group based on ordering the predicted cancer mortalities obtained from a 10-fold cross validation for prostate cancer patients, the mean of the predicted cancer mortalities was compared with a nonparametric estimate of crude mortality from cancer developed by Cronin and Feuer, and the agreement was found to be very good. A similar analysis was done for predicted other cause mortalities and again the agreement was good particularly for ages 66+ where comorbidities were included in the models. The figures present graphs by age (<66 and 66+ with comorbidity) and stage and indicate that the survival predictions provided by the Cancer Survival Query System are quite good.

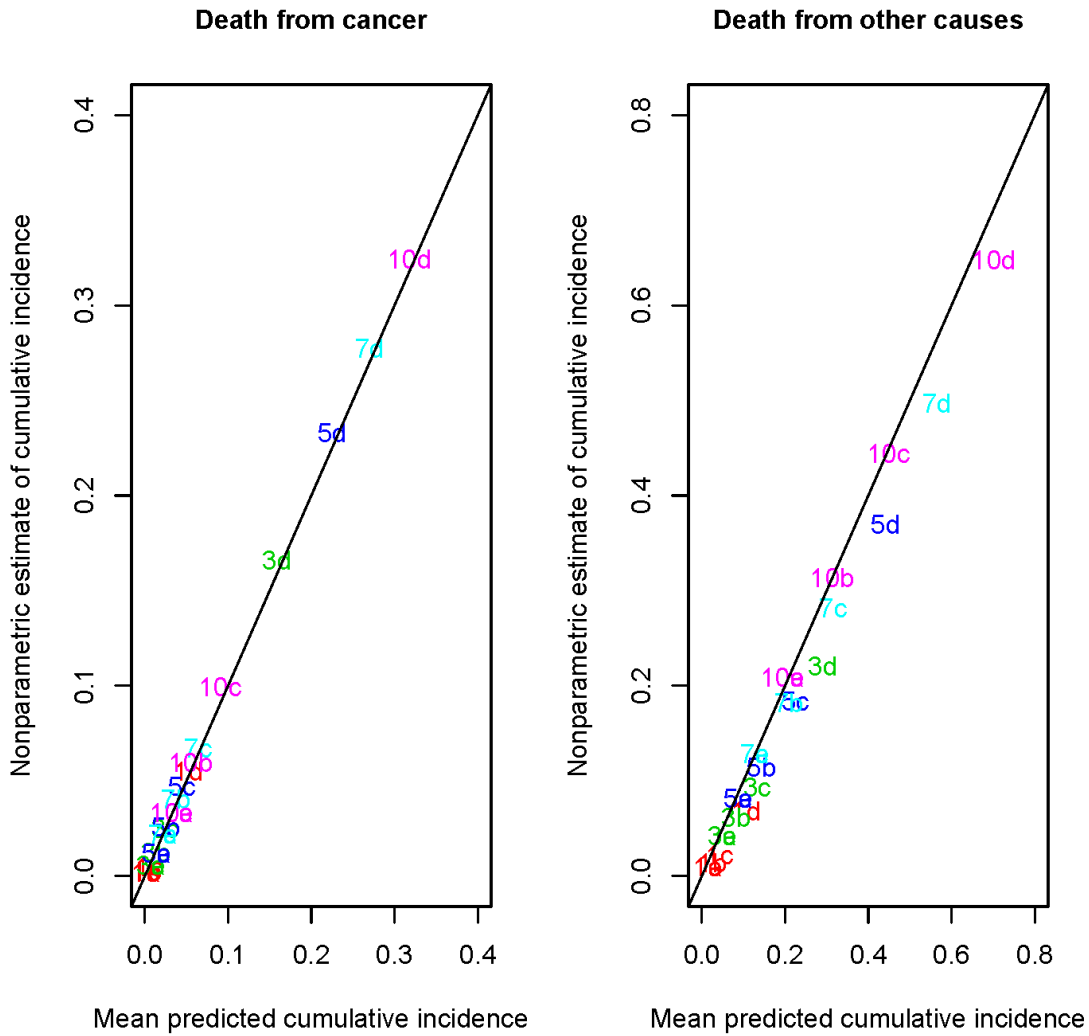
Prostate Pretreatment Ages 66+ With Comorbidity



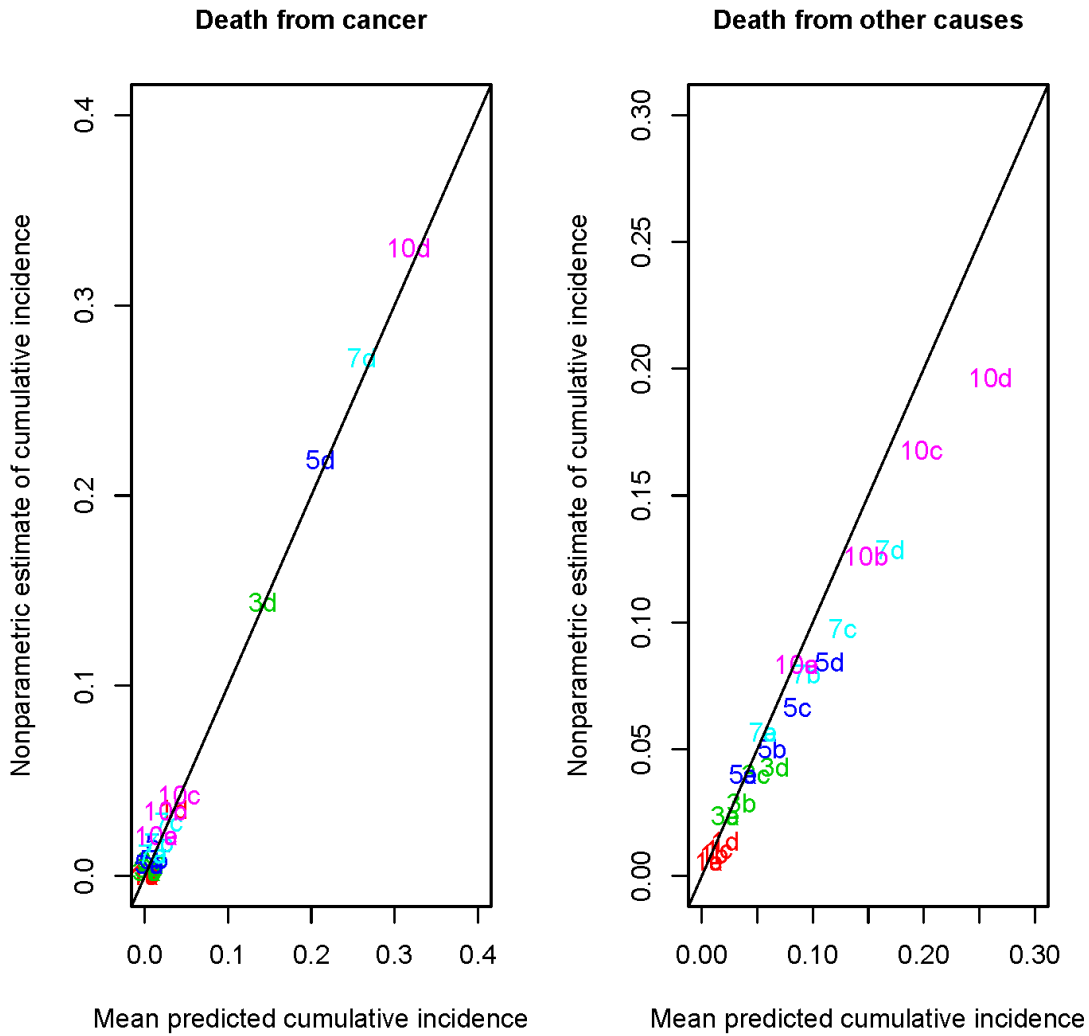
Prostate Pretreatment Ages <66 Without Comorbidity



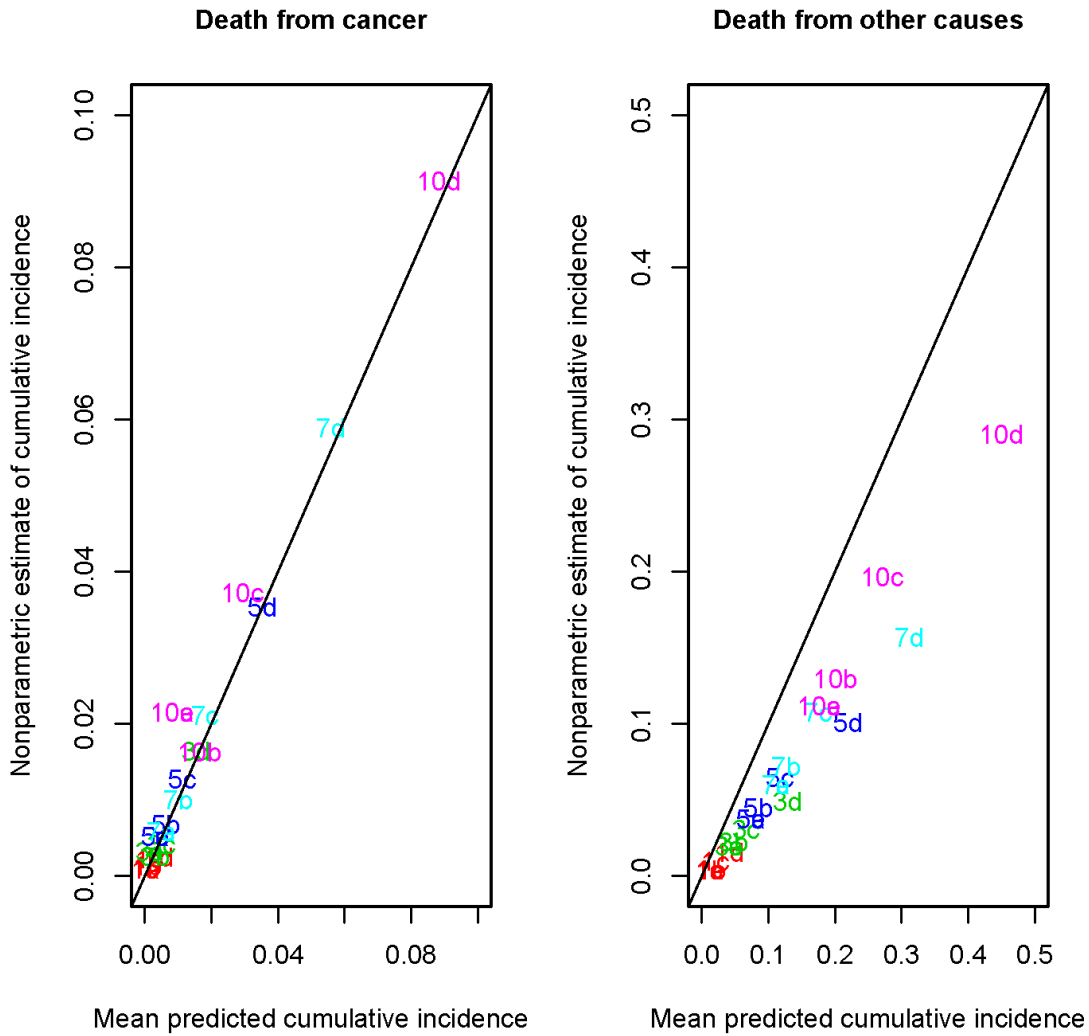
Prostate Pure Clinical Ages 66+ With Comorbidity



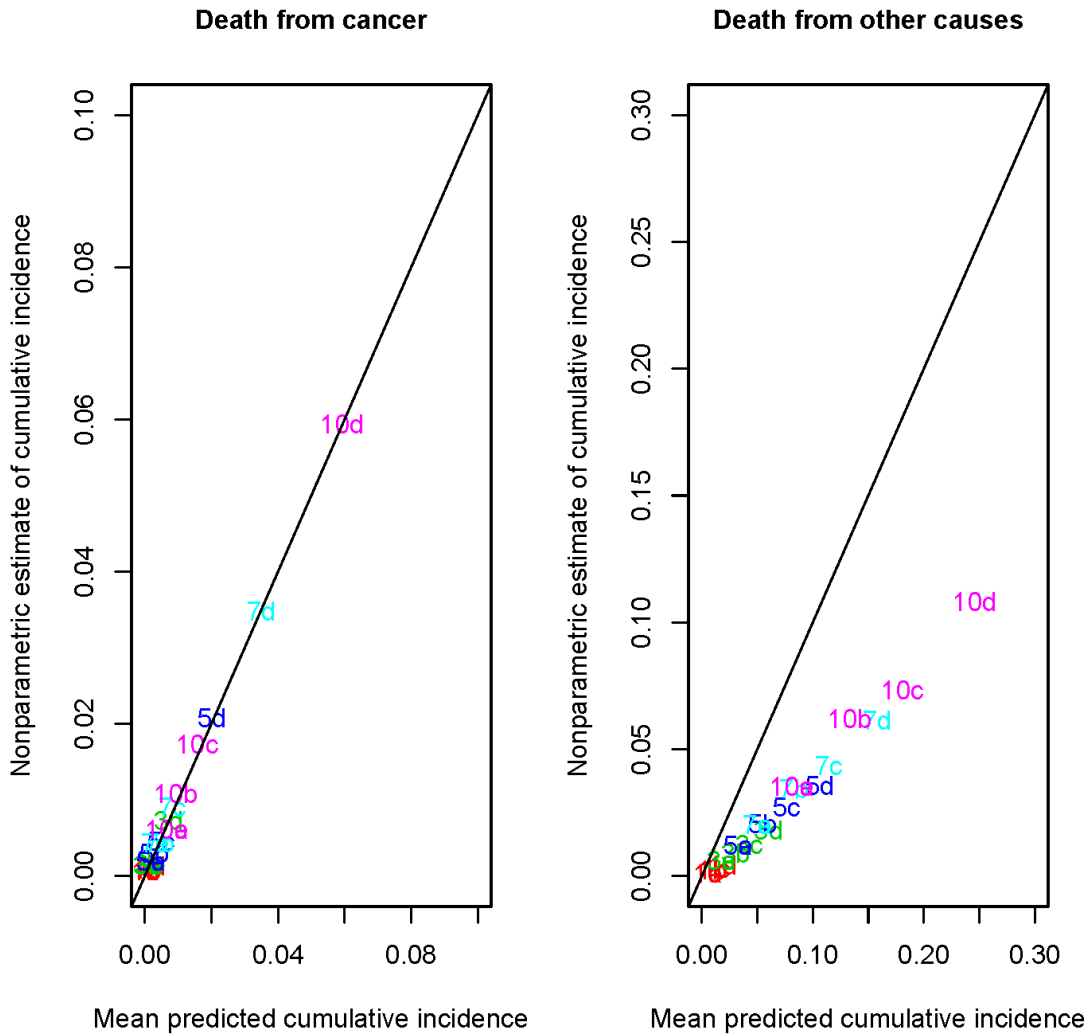
Prostate Pure Clinical Ages <66 Without Comorbidity



Prostate Pathological Ages 66+ With Comorbidity



Prostate Pathological Ages <66 Without Comorbidity



6.2 Validation Table and Figures for Colorectal Cancer Nomogram

Age 66+ with Comorbidity Scores

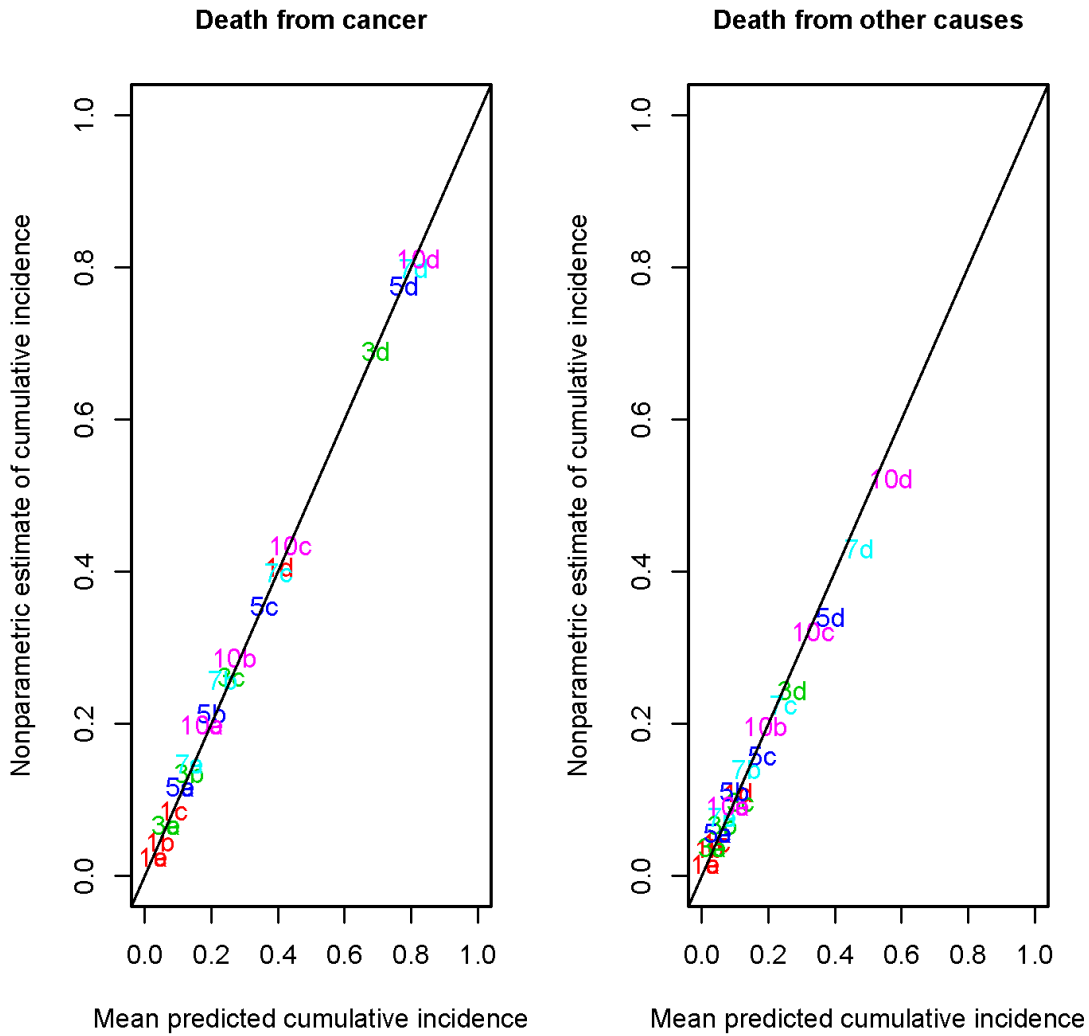
	Rectal		Proximal		Distal	
Year	AUC1	AUC2	AUC1	AUC2	AUC1	AUC2
1-year	0.84	0.71	0.85	0.71	0.85	0.71
3-year	0.83	0.73	0.85	0.72	0.84	0.72
5-year	0.81	0.72	0.84	0.72	0.83	0.73
7year	0.80	0.72	0.83	0.72	0.82	0.73
10-year	0.79	0.71	0.82	0.72	0.81	0.72

Age <66 without Comorbidity Scores

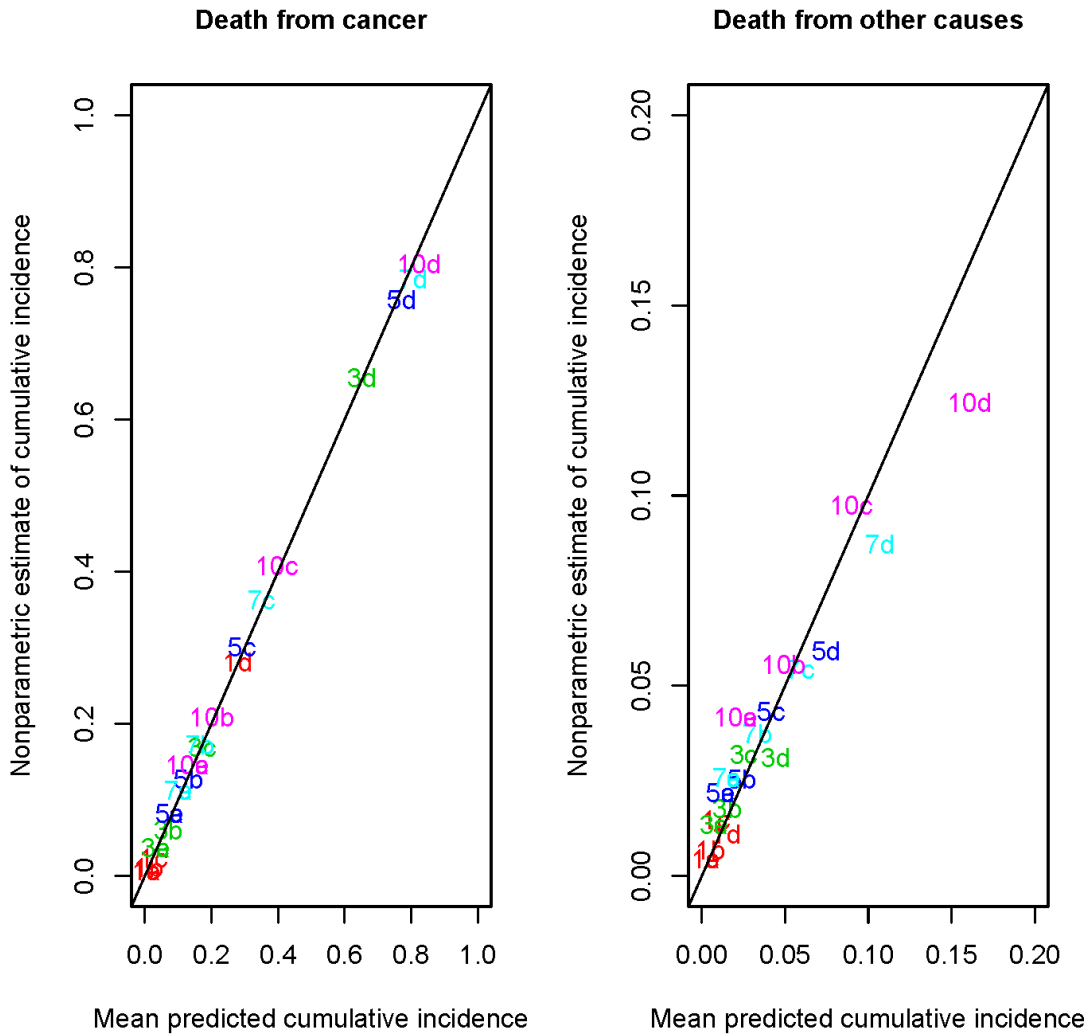
	Rectal		Proximal		Distal	
Year	AUC1	AUC2	AUC1	AUC2	AUC1	AUC2
1-year	0.89	0.60	0.88	0.59	0.88	0.65
3-year	0.87	0.59	0.89	0.59	0.89	0.66
5-year	0.85	0.62	0.88	0.62	0.88	0.65
7year	0.83	0.63	0.88	0.64	0.87	0.66
10-year	0.83	0.62	0.88	0.65	0.87	0.66

For each quartile group based on ordering the predicted cancer mortalities obtained from a 10-fold cross validation for colorectal cancer patients, the mean of the predicted cancer mortalities was compared with a nonparametric estimate of crude mortality from cancer developed by Cronin and Feuer, and the agreement was found to be very good. A similar analysis was done for predicted other cause mortalities and again the agreement was good particularly for ages 66+ where comorbidities were included in the models. The figures present graphs by age (<66 and 66+ with comorbidity) and cancer site and indicate that the survival predictions provided by the Cancer Survival Query System are quite good.

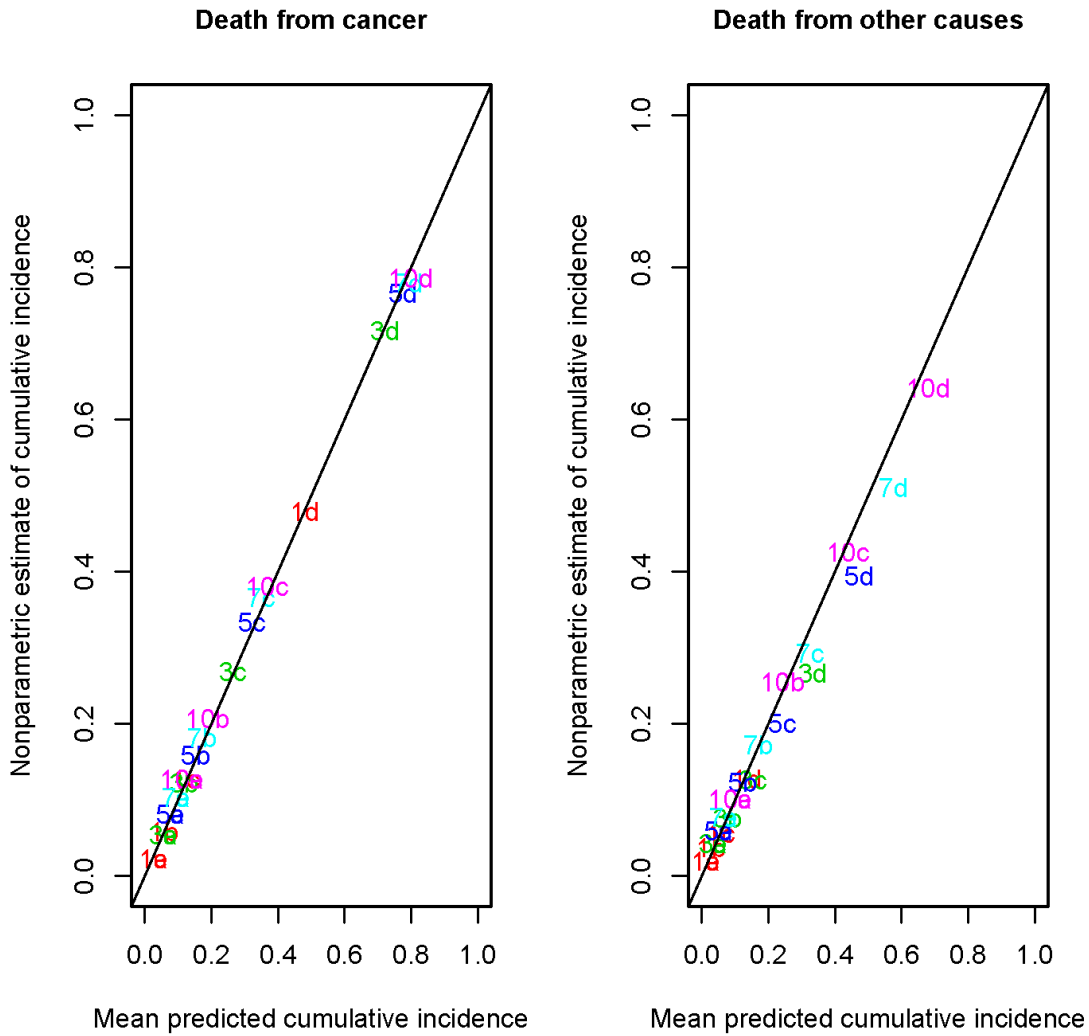
Rectal Ages 66+ With Comorbidity



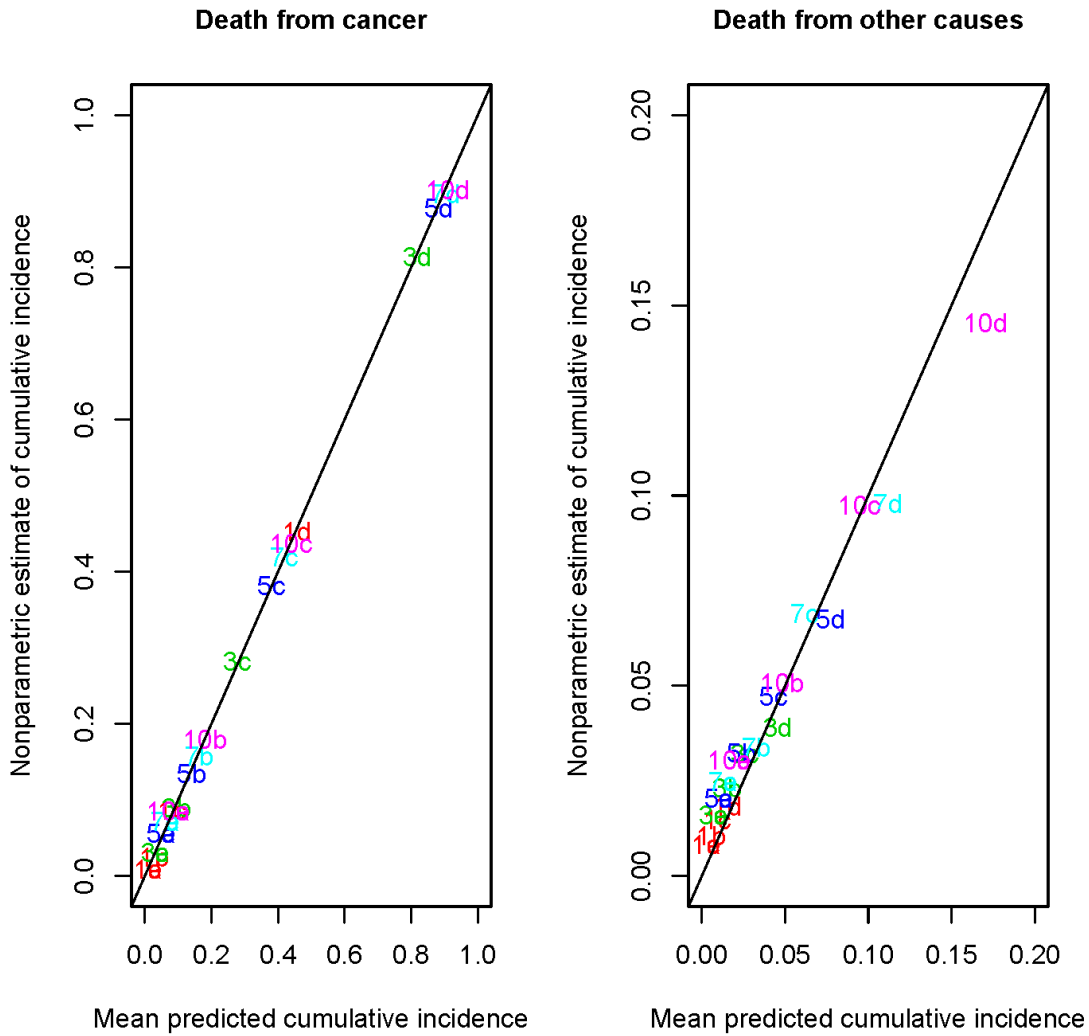
Rectal Ages <66 Without Comorbidity



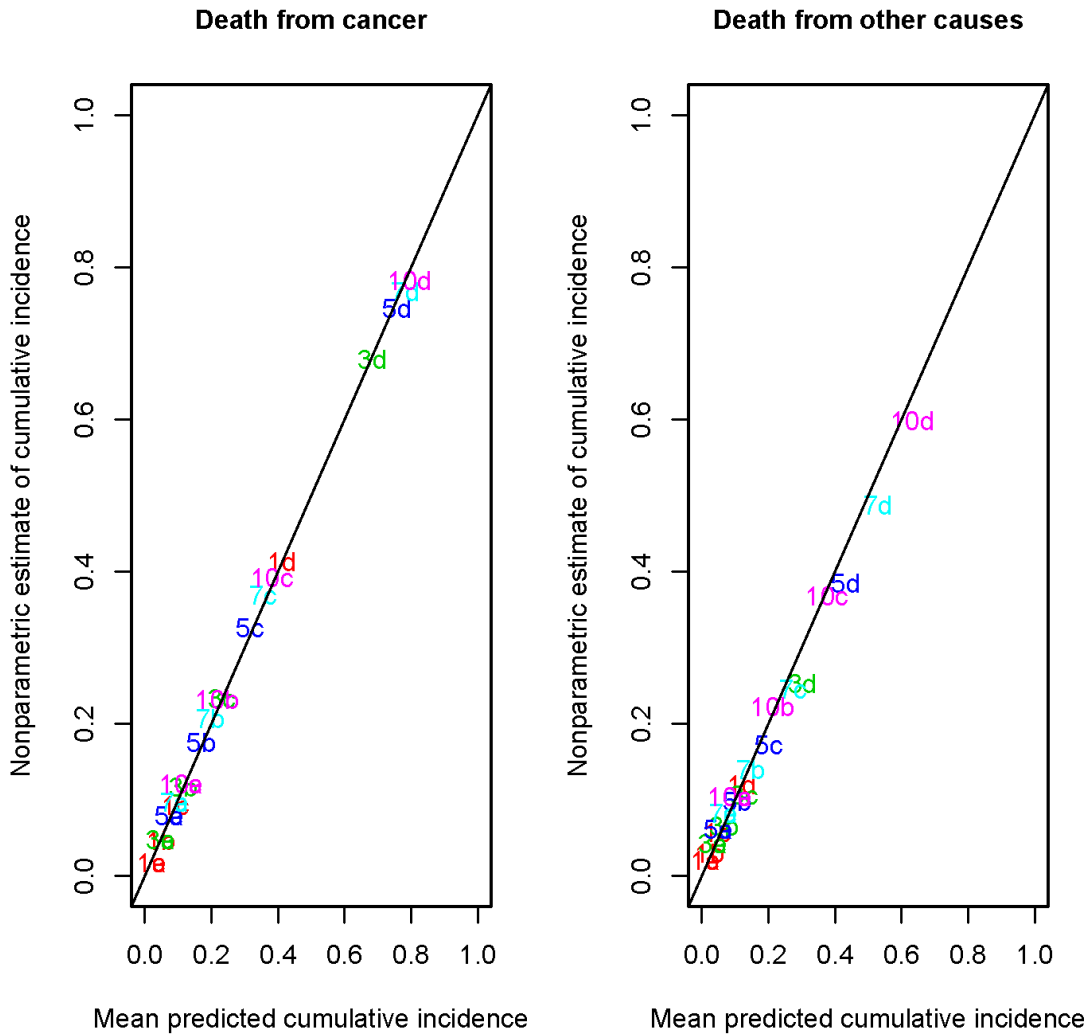
Proximal Ages 66+ With Comorbidity



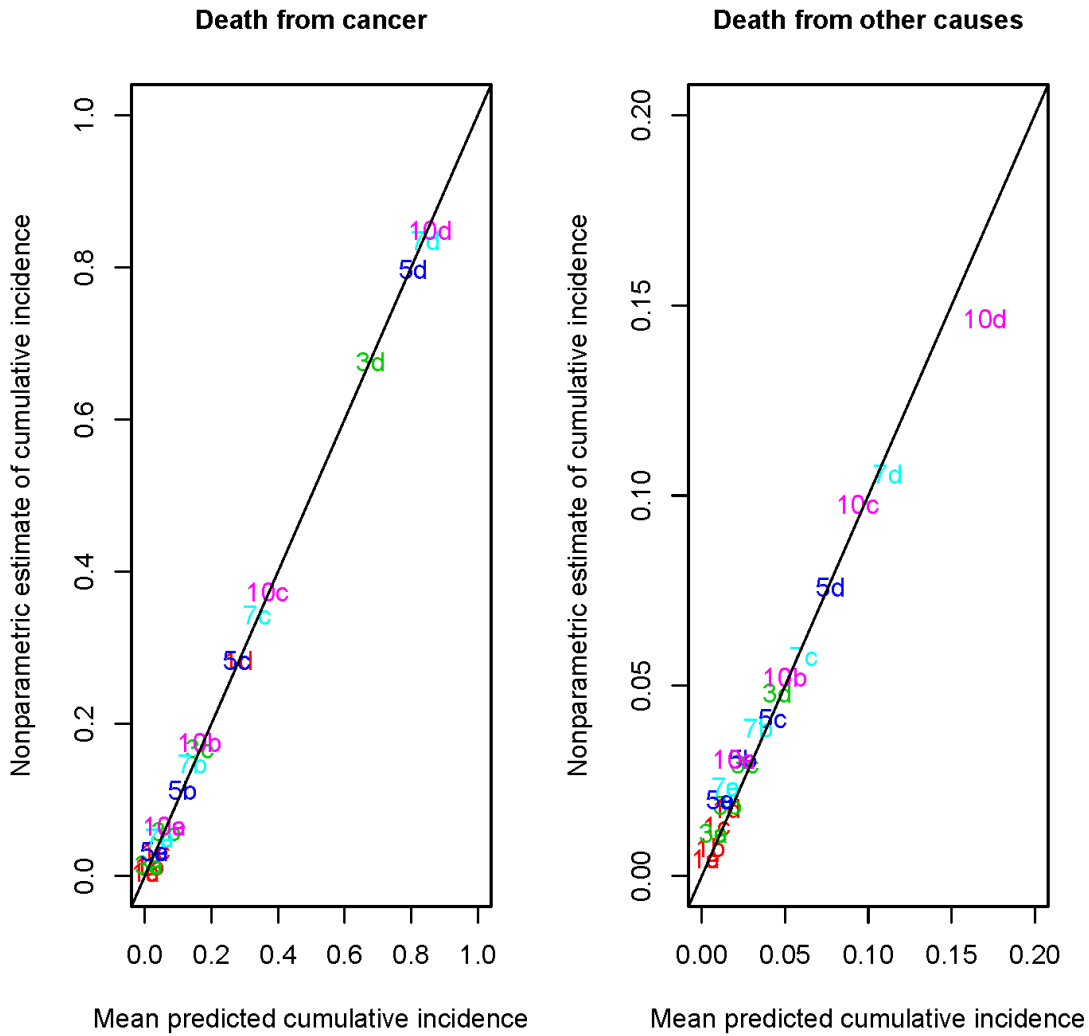
Proximal Ages <66 Without Comorbidity



Distal Ages 66+ With Comorbidity



Distal Ages <66 Without Comorbidity



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