**Appendix 2: Calculation of the hazard ratio for other-cause death**

Our goal was to determine how the risk of other-cause death among localized prostate cancer cases treated with RP differed from the mortality risk in the age-matched general population. We used the Surveillance, Epidemiology and End Results SEER\*Stat (seer.cancer.gov/seerstat) program to provide (other-cause) survival after diagnosis over a period of ten years and obtained estimates over a similar time period for a comparable population.

First we used SEER data to obtain observed all-cause survival and disease-specific survival rates for US men aged 40 years and over who were diagnosed with localized prostate cancer (T-stage less than T4, N-stage N0 or NX, and M-stage M0 or MX) between 1994 and 2007 inclusive and who received radical prostatectomy and no radiation therapy as primary treatment. For each year following diagnosis we obtained the interval survival estimates for any cause $(S\_{all cause})$ and prostate cancer ($S\_{ disease-specific})$. We then calculated the implied chance of other-cause death within the interval as $p\_{other cause}=S\_{all cause}-S\_{ disease-specific}$.

To obtain expected survival estimates, we used the SEER\*Stat survival run option to generate estimates of expected all-cause interval survival $(S\_{expected}$) for men in the US population matched to the case cohort by race, sex, and birth cohort, by year, over a similar time interval. Because prostate cancer death is relatively rare in the general population, we considered this to be a reasonable approximation of the expected other-cause survival in the general population. We denoted the expected chance of other-cause death in each interval as $S\_{all cause}$.

There are now two approaches to calculate a hazard ratio for other-cause death in prostate cancer cases who have had RP relative to the general population. The first considers the annual probabilities of death as discrete hazards and calculates a ratio each year as $p\_{expected}/p\_{other cause}$. The second considers the problem in continuous time and assumes that the distribution of survival in each interval is exponential. Then the hazard ratio comparing the other-cause death among cases with the expected other-cause death in the population is$ HR=log⁡(1-p\_{other cause})/log⁡(1-p\_{expected})$. The results of both approaches are very similar given the low risk of death in each interval. We used the second method. The Supplemental Figure 1 shows the hazard ratios by year for different age groups over the first 10 years following diagnosis. Although the hazard ratio differs across age groups, we use 0.4 as a summary value.

Details of calculating HR using SEER stat:

1. Restrict to the cases satisfying the inclusion.
2. Generate SEER relative survival table for each age group (Supplemental Table 1).

Supplemental Table 1: SEER relative survival table for localized prostate cancer cases diagnosed between 1994 and 2007.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Alive at |   | Lost to  | Observed | Expected |
| Year Interval | Start | Died | Follow-up | Interval | Cumulative | Interval | Cumulative |
| < 1 yr | 8,326 | 24 | 67 | **99.70%** | 99.70% | **99.50%** | 99.50% |
| 1-<2 yr | 8,235 | 27 | 67 | **99.70%** | 99.40% | **99.50%** | 99.00% |
| 2-<3 yr | 8,141 | 41 | 1,645 | **99.40%** | 98.80% | **99.40%** | 98.50% |
| 3-<4 yr | 6,455 | 28 | 1,456 | **99.50%** | 98.30% | **99.40%** | 97.90% |
| 4-<5 yr | 4,971 | 25 | 1,323 | **99.40%** | 97.80% | **99.40%** | 97.20% |
| 5-<6 yr | 3,623 | 23 | 1,309 | **99.20%** | 97.00% | **99.30%** | 96.60% |
| 6-<7 yr | 2,291 | 17 | 419 | **99.20%** | 96.20% | **99.30%** | 95.80% |
| 7-<8 yr | 1,855 | 14 | 386 | **99.20%** | 95.40% | **99.20%** | 95.10% |
| 8-<9 yr | 1,455 | 14 | 377 | **98.90%** | 94.40% | **99.10%** | 94.30% |
| 9-<10 yr | 1,064 | 7 | 329 | **99.20%** | 93.60% | **99.10%** | 93.40% |

1. Generate the SEER cause-specific survival table for each age group (Supplemental Table 2).

Supplemental Table 2: SEER cause-specific survival table for localized prostate cancer cases diagnosed between 1994 and 2007.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Alive at |   | Lost to  | Cause-Specific |
| Year Interval | Start | Died | Follow-up | **Interval** | Cumulative |
| < 1 yr | 8,326 | 9 | 82 | **99.90%** | 99.90% |
| 1-<2 yr | 8,235 | 5 | 89 | **99.90%** | 99.80% |
| 2-<3 yr | 8,141 | 16 | 1,670 | **99.80%** | 99.60% |
| 3-<4 yr | 6,455 | 7 | 1,477 | **99.90%** | 99.50% |
| 4-<5 yr | 4,971 | 13 | 1,335 | **99.70%** | 99.20% |
| 5-<6 yr | 3,623 | 14 | 1,318 | **99.50%** | 98.70% |
| 6-<7 yr | 2,291 | 9 | 427 | **99.60%** | 98.30% |
| 7-<8 yr | 1,855 | 6 | 394 | **99.60%** | 97.90% |
| 8-<9 yr | 1,455 | 7 | 384 | **99.40%** | 97.40% |
| 9-<10 yr | 1,064 | 5 | 331 | **99.40%** | 96.90% |

1. Merge Supplemental Table 1 and 2 as one table based on “Alive at Start” (Supplemental Table 3).

Supplemental Table 3: SEER observed interval survival and expected interval survival for localized prostate cancer cases diagnosed between 1994 and 2007.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Year Interval | Alive at start | Observed Interval(OBS) | Expected Interval(EXP) | Cause Specific Interval(CS) |
| < 1 yr | 8,326 | **99.70%** | **99.50%** | **99.90%** |
| 1-<2 yr | 8,235 | **99.70%** | **99.50%** | **99.90%** |
| 2-<3 yr | 8,141 | **99.40%** | **99.40%** | **99.80%** |
| 3-<4 yr | 6,455 | **99.50%** | **99.40%** | **99.90%** |
| 4-<5 yr | 4,971 | **99.40%** | **99.40%** | **99.70%** |
| 5-<6 yr | 3,623 | **99.20%** | **99.30%** | **99.50%** |
| 6-<7 yr | 2,291 | **99.20%** | **99.30%** | **99.60%** |
| 7-<8 yr | 1,855 | **99.20%** | **99.20%** | **99.60%** |
| 8-<9 yr | 1,455 | **98.90%** | **99.10%** | **99.40%** |
| 9-<10 yr | 1,064 | **99.20%** | **99.10%** | **99.40%** |

Based on Supplemental Table 3, we could calculate the probability of other-cause death in the case population as $p\_{other cause}=S\_{all cause}-S\_{ disease-specific}$, the expected probability of death in the age-matched population each year as $p\_{expected}=1-S\_{expected}$, and the hazard ratio as $HR=log⁡(1-p\_{other cause})/log⁡(1-p\_{expected})$.

**Supplemental Figure 1:** Hazard ratios of other-cause death among localized prostate cancer patients diagnosed between 1994 and 2007 in SEER relative to standard US life tables by year after diagnosis.

