**Epi 536 Homework #3**

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| **TABLE 1. Baseline characteristics of individuals with hormonally treated prostate cancer by remission status at 24 months** | | |
|  | **Relapse within 24 months (*n=*22)** | **No relapse within 24 months (*n=*28)** |
| Age (years), mean ± SD | 68 ± 5.68 | 67 ± 5.84 |
| Nadir PSA level (ng/mL), mean ± SD | 31.9 ± 52.5 | 4.12 ± 17.3 |
| PSA level prior to treatment (ng/mL), mean ± SD\* | 732 ±1360 | 617 ± 1250 |
| Bone scan score, n (%)\* |  |  |
| 1 | 0 (0) | 5 (18) |
| 2 | 4 (20) | 9 (32) |
| 3 | 16 (80) | 14 (50) |
| Tumor grade, n (%)\* |  |  |
| 1 | 3 (18) | 7 (29) |
| 2 | 7 (41) | 8 (33) |
| 3 | 7 (41) | 9 (38) |
| Performance status, n (%)\* |  |  |
| 50 | 1 (5) | 1 (4) |
| 60 | 2 (10) | 0 (0) |
| 70 | 5 (25) | 1 (4) |
| 80 | 8 (40) | 13 (46) |
| 90 | 3 (15) | 11 (39) |
| 100 | 1 (5) | 2 (7) |
| \*Presented values are of non-missing data | | |

2.a. On average, the odds ratio for relapse within 24 months of hormonally treated prostate cancer (from here on referred to as “relapse”) between subjects with levels of nadir PSA that vary by 1 ng/mL is estimated to be **1.03**, when adjusting for bone scan score and performance status. This odds ratio represents the ratio of the odds of relapse comparing subjects that differ by 1 ng/mL nadir PSA, with subjects with a higher nadir PSA having higher odds of relapse when holding bone scan score and performance status constant. This observation is within that which might be expected to occur by chance in the absence of a true difference (***p=*0.48**). The *95% CI* for the odds ratio is that the odds of relapse among men with hormonally treated prostate cancer with 1 ng/mL higher nadir PSA is **between 0.95 and 1.13** times that of the group of men with lower nadir PSA (robust SE 0.046).

b. On average, the odds ratio for relapse between subjects with varying levels of log nadir PSA is estimated to be **2.95**, when adjusting for bone scan score and performance status. This odds ratio represents the ratio of the odds of relapse comparing subjects that differ by 1 unit in log nadir PSA (i.e. 2.72 ng/mL), with subjects with a higher log nadir PSA having higher odds of relapse when holding bone scan score and performance status constant. This observation is beyond that which might be expected to occur by chance in the absence of a true difference (***p=*0.02**). The *95% CI* for the odds ratio is that the odds of relapse among men with hormonally treated prostate cancer with 1 unit higher log nadir PSA is **between 1.17 and 7.44 times** that of the group of men with lower log nadir PSA (robust SE 1.39).

c. This analysis is a bit difficult to interpret based on coefficient values as it would not be appropriate to interpret each spline component individually based on the modeled position of knots. None of the p-values for the splines were statistically significant, suggesting that when tested together any association between nadir PSA level when modeled as linear splines with knots at 1, 4 and 16 ng/mL would not be significant.

d. For each of the analyses above the intercept represents the odds of relapse among subjects with a bone scan score of 1 and performance status of 50 when nadir PSA is 0 ng/mL. This is not scientifically interesting as we are combining measures representative of low disease severity (low bone scan score and low nadir PSA) with a measure that represents poor performance status. Nonetheless, the intercept approximates 0 in all of the above models. (Of note, I used bone scan score and performance status as categorical rather than linear variables as we do know exactly how to interpret values that fall between reported ones for these measures).

3.a. I used linear regression with robust standard errors: outcome—nadir PSA as a continuous, untransformed variable; predictor of interest—relapse within 24 months as a binary variable; potential confounders—bone scan score and performance status as categorical variables (same categories presented in table 1).

On average, subjects who relapsed had an estimated mean nadir PSA that was **16.6 ng/mL higher** than that among subjects who did not relapse when holding bone scan score and performance status constant. This observation is within that which might be expected to occur by chance in the absence of a true difference (***p=*0.20**). The *95% CI* for the difference in nadir PSA among men who did and did not relapse suggests that the observed results were not unusual if the true difference in estimated mean nadir PSA were anywhere **between -9.05 and 42.3**.

b. As above, I used linear regression with robust standard errors, but this time I use the log-transformed outcome variable to perform inference on the geometric mean of nadir PSA: outcome—nadir PSA as a continuous, log-transformed variable; predictor of interest—relapse within 24 months as a binary variable; potential confounders—bone scan score and performance status as categorical variables (same categories presented in table 1).

On average, subjects who relapsed had an estimated geometric mean nadir PSA that was **12.3 ng/mL higher** than that among subjects who did not relapse when holding bone scan score and performance status constant. This observation is within that which might be expected to occur by chance in the absence of a true difference in geometric mean nadir PSA between these two groups (***p* <0.001**). The *95% CI* for the difference in geometric mean nadir PSA among men who did and did not relapse suggests that the observed results were not unusual if the true difference in estimated geometric mean nadir PSA were anywhere **between 3.70 and 41.0**.

4.a. The major merit of the analyses in question 2 is that the response variable is a future event with PSA measures being somewhat “real-time” which can be used to assess risk for future relapse and may impact treatment choices. This seems to be less directly interpretable from the analyses performed in question 3.

*A priori,* I would choose to perform the analysis in 2.a. using log-transformed PSA because of the way PSA is measured and the way values are usually distributed in a population.

b. This study is restricted to men who have already undergone and survived beyond hormonal therapy for prostate cancer. An inherent problem here stems from the survivorship bias imposed. The only way to address this would have been to change the study recruitment strategy.