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**Biostatistics, Epidemiology, and Research Design (BERD) Core**

**Clinical Epidemiology Unit**

**September 27th, 2019**

**Applied Example: Introduction to ROC Analysis in Clinical Research**

***A comparison of Injury Severity Score and New Injury Severity Score after penetrating trauma: A prospective analysis, Smith et al., 2015***

**Background (Smith et al., Journal of Trauma and Acute Care Surgery, Volume 79(2), 2015):**

The Injury Severity Score (ISS) has been validated in numerous studies and has become one of the most common trauma scoring systems since its inception. The ISS equation was later modified to create the New Injury Severity Score (NISS). By using the three most severe injuries regardless of body region, the NISS seems well suited to describe patients of penetrating trauma, where injuries often cluster within a single body region. We hypothesized that NISS would predict mortality better than ISS in patients with penetrating trauma.

1. Read into SAS the provided dataset (injsev1.sas7bdat), which is similar to the one used by Smith et al.
2. Note in the space below, the total sample size, number who died, number who survived, and the “prevalence” of mortality in this sample.

**Part I: ISS Test Performance**

1. Explore the distribution of ISS scores for patients who died and those who survived
2. The ISS (and the NISS) are both multilevel or continuous measures. Use SAS to create a new variable that dichotomizes the ISS at different “cutpoints” and explore how the ISS’ sensitivity and specificity differs at these cutpoints.
3. Examine the output from the two PROC LOGISTIC provided to verify that the AUC that PROC LOGISTIC calculated for the ISS is equal to the c statistic.

Report here, the estimated AUC (and its 95% CI) for ISS in terms of its accuracy in predicting mortality.

Comment on the predictive accuracy of ISS in predicting mortality following a penetrating injury

1. On the ROC curve produced via PROC SGPLOT, find the four cutpoints you explored in b, and compare your calculations of Sn and Sp with the plotted values.

Examine the ROC curve to identify the cutpoint that maximizes the sum of sensitivity and specificity (the one closest to the upper left corner) for predicting mortality following a penetrating injury.

**Part II: Comparison of ISS and NISS in Predicting Mortality and; Added Prognostic Value**

**Comparison of Correlated (Dependent) AUCs**

1. Using the SAS program provided, compare the performance of the ISS and the NISS in predicting mortality from penetrating injury. Does one predict mortality better than the other? *Also see STATA results provided re: parametric vs non-parametric results/graphs.*

**Added Prognostic Value**

1. Using the SAS program provided, assess the ‘added’ prognostic value of age i.e. once we know the patient’s injury severity score, does knowing their age improve our prediction of mortality?

**Comparison of Independent AUCs**

1. Using the SAS program provided, evaluate whether the NISS predicts mortality similarly in patients younger than 45 years and those 45 years and older

**Clinical Criteria Comparison: Assume ISS and NISS are two diagnostic tests. Compare ISS and NISS in minimizing false positives (favors high specificity) or in minimizing false negatives (favors high sensitivity).**

Use the **STATA output** provided (*Stata Output\_AUC and Partial AUC Analysis.pdf*).

1. Compare partial AUCs for the two tests at lower FPR ranges. Which test performs better at high specificities (Sp)?
2. Compare sensitivities at different FPRs at high FPR ranges.Which test performs better at high sensitivities (Sn)?

**Part III: Threshold Selection Using ISS**

**Mathematical Criteria**

1. Using the SAS program provided, identify the ISS cut-point that maximizes the sum of sensitivity and specificity for predicting mortality

**Cost Minimization /Decision-Making Criteria**

1. This method considers the financial cost, health impact, discomfort to patient and further investigative cost (downstream cost) for correct and false diagnosis taking into account the prior probability of disease.

To explore the idea of an optimal cutpoint for treatment/further testing decisions, we will make certain assumptions, recognizing they may be artificial or unrealistic:

1. We will use the ISS to decide whether to perform a potentially life-saving procedure for someone with a penetrating injury.

1. The procedure is expensive and carries a great deal of risk (C), but the unachieved benefit (B), which is survival for someone who will die if they do not undergo the procedure, is much greater (7\*C).

C=False-Positive Cost; B=False-Negative Cost

3. We cannot predict whose survival depends on the procedure by any means other than by using the ISS.

Use the formula proposed by Zweig et al that incorporates Sn, Sp, and expected cost ratio to identify the optimal ISS cut-off point that takes into account the misclassification costs (specified above) and prior probability of the outcome (mortality)

**Time-Permitting, we will also conduct a sensitive analysis**

1. Frequently it can be difficult to determine a value for the false‐positive/false‐negative cost ratio. So it is worth performing a sensitivity analysis (sensitivity here means how much one variable changes with changes in a second variable) to see whether the cutoff value changes significantly in the range of cost ratio values of interest. If the relative cost of a false‐negative is much greater than that of a false‐positive then the cost ratio is less than 1. But let’s assume that we don’t know exactly how much greater this false-negative cost is

Perform a sensitivity analysis by varying the cost ratio and identify a range where the cutoff value is insensitive to cost ratio. We used 1/7 above, explore cost ratios of 1/2, 1/3, 1/5, 1/10, 1/15, 1/20

**Time-Permitting, we will also explore the likelihood ratio (LR) threshold selection**