Shaw and colleagues* have reported on cerebrospinal fluid tau concentration (and other biomarkers) for the detection of mild Alzheimer's disease (AD). Data describing the results of this test in a sample of 56 autopsy-confirmed people with AD and 52 cognitively normal (NC) people are reported in the figure on the next page. The authors constructed an ROC curve for Tau (area, 0.831) and identified a cutpoint that yielded the greatest diagnostic test accuracy (93 pg/ml).

Whether or not you agree with the authors' methods, use the information in the figure to:

Q1. Divide the Tau data into 3 strata (<70, ≥70 to <115, and ≥115), create the necessary Tau 2x2 tables, and plot the ROC curve that summarizes this multiple outcome test. Note: the strata are defined by the solid horizontal lines, NOT the dashed horizontal line. See bottom of figure for information about observations that appear to touch the lines or that overlap each other. Assume that the 52nd normal observation lies in the lowest Tau stratum).

Q2. If you are making a treatment decision for an older person for whom the pre-test probability of AD is 11% and – given we are not sure if there is much we can do if we are able to diagnose AD -- C_{FP}=.8C_{FN} (i.e., the ratio of the cost of false positive to false negative mistakes is .8) which 2x2 table cut-off would you use for a positive test? Using the optimal 2x2 table, what is the resulting post-test probability of disease given a test result between 70 and 115?

Q3. If the pre-test probability was 24% and the cost ratio remained unchanged, which cut-off would you use?

OPTIONAL: Given a cost ratio of 0.8, what is the lowest pre-test probability where you should first consider using a cut-off of ≥115?

Please show your work and report results to 3 decimals.

Plot of cerebrospinal fluid (CSF) tau concentration versus CSF amyloid-B 1 to 42 peptide (AB$_{1-42}$) concentration for 56 autopsy-confirmed (AD) cases (solid circles) and 52 elderly cognitively normal (NC) subjects (open circles). Horizontal lines added at Tau=70 and Tau=115. NOTE: All 3 solid circles that appear to touch the line at 70 fall above the line; one of the five solid circles that appear to touch the line at 115 is below the line. Of the 8 open circles that appear to touch the line at 70, only 1 falls above the line. In addition to the 5 visible partially overlapping open circles below a Tau of 70, consider one additional open circle to represent 2 cases.