Biost 518
Applied Biostatistics II

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Lecture 11:
Regression Based Prediction

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Lecture Outline

- General Setting
- Prediction of Summary Measures
  - Necessary Assumptions for Inference
  - Special cases
    - Means, Geometric Means, Odds, Probabilities, Rates, Hazard Ratios, Survival probabilities
- Prediction of Individual Observations
  - Necessary Assumptions for Inferences
  - Special cases
    - Continuous measurements, binary measurements

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Setting for Predictions

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General Classification

- Clustering of observations
- Clustering of variables
- Quantification of distributions
- Comparing distributions
- Prediction of individual observations

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1. Cluster Analysis

- Focus is on identifying similar groups of observations
  - Divide a population into subgroups based on patterns of similar measurements
    - Univariate, multivariate
    - Known or unknown number of clusters
  - (All variables treated symmetrically: No delineation between outcomes and groups)

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2. Clustering Variables

- Identifying hidden variables indicating groups that tend to have similar measurements of some outcome
  - Interest in some particular outcome measurement
  - Predictors that imprecisely measure some abstract quality
  - Desire to find patterns in predictors that more precisely reflect the abstract quality

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3. Quantifying Distributions

- Focus is on distributions of measurements within a population
  - Scientific questions about tendencies for specific measurements within a population
    - Point estimates of summary measures
    - Interval estimates of summary measures
      - Quantifying uncertainty
    - Decisions about hypothesized values
  - May desire estimates within subgroups
    - E.g., estimates by sex, age, race

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Example: Estimation of Median

- Statistical Tasks
  - Sample of patients newly diagnosed with stage II breast cancer
    - Follow for survival time (may be censored)
  - Statistical analysis
    - Best estimate of the median survival (K-M?)
    - Quantify uncertainty in that estimate
    - Compare to some clinically important time range (e.g., 10 years)

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4. Comparing Distributions

- Comparing distributions of measurements across populations
  - 4a. Identifying groups that have different distributions of some measurement
  - 4b. Quantifying differences in the distribution of some measurement across predefined groups (effects or associations)
  - 4c. Quantifying differences in effects across subgroups (interactions or effect modification)

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4a. Identifying Groups

- Identifying groups that have different distributions of some measurement
  - Focus is on some particular outcome measurement
  - Identify groups based on other measurements
    - E.g., quantifying distributions within subgroups
    - E.g, stepwise regression models
  - (cf: Cluster analysis where all measurements are treated symmetrically)

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Example: Identifying Groups

- Statistical Tasks
  - Sample subjects to measure risk factors and disease prevalence
    - Cohort study
    - Case-control study
  - Statistical analysis
    - Stepwise model building
      - (Rank most interesting variables by p value?)

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5. Prediction

- Focus is on individual measurements
  - Point prediction:
    - Best single estimate for the measurement that would be obtained on a future individual
      - Continuous measurements
      - Binary measurements (discrimination)
  - Interval prediction:
    - Range of measurements that might reasonably be observed for a future individual

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Example: Continuous Prediction

- Creatinine clearance
  - Creatinine
    - Breakdown product of creatine
    - Removed by the kidneys by filtration
      - Little secretion, reabsorption
  - Measure of renal function
    - Amount of creatinine cleared by the kidneys in 24 hours

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Example: Continuous Prediction

- Problem:
  - Need to collect urine output (and blood creatinine) for 24 hours
- Goal:
  - Find blood, urine measures that can be obtained instantly, yet still provide an accurate estimate of a patient's creatinine clearance

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Example: Continuous Prediction

- Statistical Tasks:
  - Training sample
    - Measure true creatinine clearance
    - Measure sex, age, weight, height, creatinine
  - Statistical analysis
    - Regression model that uses other variables to predict creatinine clearance
    - Quantify accuracy of predictive model
      - (Mean squared error?)

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Example: Discrimination

- Diagnosis of prostate cancer
  - Use other measurements to predict whether a particular patient might have prostate cancer
    - Demographic: Age, race, (sex)
    - Clinical: Symptoms
    - Biological: Prostate specific antigen (PSA)
  - Goal is a diagnosis for each patient

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Example: Discrimination

- Statistical Tasks:
  - Training sample
    - "Gold standard" diagnosis
    - Measure age, race, PSA
  - Statistical analysis
    - Regression model that uses other variables to predict prostate cancer diagnosis
    - Quantify accuracy of predictive model
      - ROC curve analysis
        - » Sensitivity vs 1 – Specificity
        - » True Positives vs False Positives

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Example: Interval Prediction

- Determining normal range for PSA
  - Identify the range of PSA values that would be expected in the 95% most typical healthy males
  - Age, race specific values

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Example: Interval Prediction

- Statistical Tasks:
  - Training sample
    - Measure age, race, PSA
  - Statistical analysis
    - Regression model that uses other variables to define prediction interval
      - (Mean plus/minus 2 SD?)
      - (Confidence interval for quantiles?)
    - Quantify accuracy of predictive model
      - (Coverage probabilities?)

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Regression Based Inference

- Estimation of summary measures
  - Point, interval estimates within groups
  - Tests hypotheses about absolute measurements
- Inference about associations
  - First order trends in summary measures across groups
    - Point, interval estimates of contrasts across groups
    - Tests hypotheses about relative measurements
- Inference about individual predictions
  - Point, interval estimates

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So far: Inference for Associations

- Necessary assumptions for classical regressions (no robust SE)
  - Independence of response measurements
  - Appropriate within group variance
    - Linear regression: Equal variance across groups
    - Other regressions: Appropriate mean-variance relationship
      - » Hence, some dependence on model fit
  - Sufficiently large sample size for asymptotic normal distribution of estimates to be a good approximation

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So far: Inference for Associations

- Necessary assumptions for first order trends using robust SE
  - Independence of response measurements across identified clusters
    - May have correlated response within identified clusters
  - (Robust SE accounts for heteroscedasticity in large samples)
    - Lack of "model fit" leads to conservative inference due to mixing systematic and random error
  - Sufficiently large sample size for asymptotic normal distribution of estimates to be a good approximation

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Now: Inference for Predictions

- Additional assumptions for predictions
  - Estimation of summary measures within groups
    - We need to know that our regression model accurately describes the relationship between summary measures across groups
  - Prediction of individual observations
    - We need to know the shape of the distribution within each group

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Estimation (Prediction) of Summary Measures

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Examples

- Estimate age, height, and sex specific mean (or geometric mean) FEV
  - Linear regression to obtain estimates and CI
- Estimate probability (or odds) of remaining in remission for 24 months by age, PSA
  - Logistic regression to obtain estimates and CI
- Estimate median time to liver failure in PBC patients by age, bilirubin, etc.
  - Proportional hazards regression for estimates (and CI?)

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Issues

- Which statistic provides the best estimate?
  - Definition of best?
    - Consistent (correct with infinite sample size)
    - Precise (minimal variability, minimal squared error)
  - Answer: Common regression models provide the best estimate in a wide variety of settings
- Is best good enough in particular setting?
  - Answer: CI for the value of true summary measure for each group

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General Methods

- Estimated summary measure involves a linear function of regression parameters
  - Linear, logistic, Poisson regression this is all that is needed
  - Proportional hazards regression also needs an estimate of the survival distribution in the reference group
    - We are not yet very good at putting confidence bounds on this part of the estimates

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Necessary Assumptions

- Independence
  - (between clusters for robust SE)
- Variance appropriate to the model
  - (relaxed for robust SE)
- **Regression model accurately describes relationship of summary measures across groups**
- Sufficient sample sizes for asymptotic distributions to be a good approximation

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Obtaining Point Estimates

- Substitution of predictor values provides the estimate of the modeled transformation of the summary measure
  - Linear regression: mean
  - Linear regression on logs: log geometric mean
  - Logistic regression: log odds
  - Poisson regression: log rate
  - Proportional hazards: log hazard ratio applied to baseline survival estimate

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Obtaining Interval Estimates

- Under the appropriate assumptions, we can obtain standard errors for each such estimate
  - Notable exception: Proportional hazards
    - More work to be done to get interval estimates
  - We generally find a confidence interval for the transformed summary measure, and then back transform to obtain the desired quantity

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Stata Commands: Predict

- After performing any regression command, the Stata command "`predict`" will compute estimates and standard errors
  - `predict` *`varname`*`, [`*`what`*`]`
    - *`varname`* is the name of the variable where you want the predictions stored
    - *`what`* is an option specifying what you want computed
      - xb = linear prediction (works for all types)
      - stdp = SE of linear prediction (works for all types)
      - p = probability (works for logistic)

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Computing CI for Predictions

- Just use the usual formula

  (est) +/- (crit val) * (std err)

  - In linear regression, we usually use the t distribution to obtain CI
    - Stata: (crit val) = `invttail(`*df*`,`$\alpha/2$`)`
    - degrees of freedom = n minus number of regression parameters
  - In all other regressions, we would use the standard normal distribution
    - (crit val) = `invnorm(1-`$\alpha/2$`)` (1.96 for 95% CI)

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Ex: Geom Mean FEV by ht, age

```
regress logfev height age
Number of obs =     654
logfev |  Coef.   Std. Err.   t    P>|t|     [95% CI]
height |   .044   .002    26.71   0.000     .041    .047
   age |   .020   .003     6.23   0.000     .014    .026
 _cons |  -1.97   .078   -25.16   0.000    -2.12   -1.82

predict flogfev
predict sefit, stdp
g gmfev= exp(flogfev)
g gmlofev = exp(flogfev - invttail(651, .025) * sefit)
g gmhifev = exp(flogfev + invttail(651, .025) * sefit)
list gmfev gmlofev gmhifev if age==10 & height==66
         gmfev    gmlofev    gmhifev
330.  3.097021   3.038578   3.156588
```

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Ex: Odds Relapse by NadirPSA

```
. logit relapse24 lognadir, robust
. predict lorel, xb
. predict selo, stdp
. g odds= exp(lorel)
. g oddslo= exp(lorel - 1.96 * selo)
. g oddshi= exp(lorel + 1.96 * selo)
. list odds oddslo oddshi if nadir==1
          odds     oddslo     oddshi
 10.  .4911836   .2388794   1.009971
```

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Ex: Prob Relapse by NadirPSA

```
. logit relapse24 lognadir, robust
. predict prel
. g prob = odds / (1+odds)
. g problo= oddslo / (1 + oddslo)
. g probhi= oddshi / (1 + oddshi)
. list prel prob problo probhi if nadir==1
          prel       prob     problo     probhi
 10.  .3293918   .3293918    .192819   .5024805
```

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Prediction in PH Regression

- Recall that there is no intercept in PH models
  - Instead there is a "baseline hazard function" which is related to the survival function in the reference group
- Stata will allow prediction of baseline survival function in their "stcox" command
  - Specify option `basesurv(`*`newvar`*`)` in `stcox`
  - Then use `stcurve, survival at( )`

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Stata Ex: Relapse in PSA Data

```
. g relapse=0
. replace relapse=1 if inrem=="no"
. stset obstime relapse
. g lnadir= log(nadir)
. stcox lnadir ps, robust basesurv(bslnS)
No. of subjects = 48          Number of obs =     48
No. of failures = 34          Time at risk  =   1408
                              Wald chi2(2)  =  33.18
Log pseudolklhd = -97.1       Prob > chi2   = 0.0000
        |      Robust
      _t |    HR   SE       z     P>|z|      [95% C I]
  lnadir | 1.56  .124    5.66   0.000    1.34     1.83
      ps | .960  .0162 -2.41   0.016    .929     .992
```

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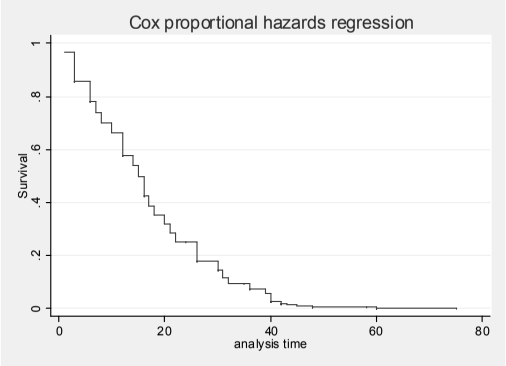
Stata Ex: Predicted Survival

- `stcurve, survival at(lnadir=2 ps=70)`



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Comments on PH Regression

- We can thus easily obtain estimated summary measures for any group based on semi-parametric PH assumption
  - Survival probabilities
  - Quantiles (median, etc.)
  - (Restricted mean (area under survival curve))
- We do not yet provide SE for those estimates

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Prediction (Forecast) of Individual Measurements

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Examples

- Estimate "normal range" for FEV by age, height, and sex groups
  - Linear regression
- Estimate probability (or odds) of remaining in remission for 24 months by age, PSA
  - Logistic regression
- Estimate range of times to liver failure in PBC patients by age, bilirubin, etc.
  - Proportional hazards regression

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Issues

- Which statistic provides the best estimate?
  - Definition of best?
    - Consistent (correct with infinite sample size)
    - Precise (minimal variability, minimal squared error)
  - Answer: Common regression models provide the best estimate in a wide variety of settings
- How variable is "best" in particular setting?
  - Answer: Prediction (Stata: Forecast) interval for the value of individual observation in each group

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Necessary Assumptions

- Independence
  - (between identified clusters for robust SE)
- Variance appropriate to the model
  - (NOT relaxed for robust SE)
- Regression model accurately describes relationship of summary measures across groups
- **Shape of distribution same in each group**
- Sufficient sample sizes for asymptotic distributions to be a good approximation

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Comments

- These are strong assumptions
  - Consequently, we do not have many methods that provide robust inference
    - Robust SE will only work here for correlated response, not for heteroscedasticity
  - For the most part, precise methods have only been well developed for
    - Binary or Poisson variables
      - All we need is an estimate of the probability or rate
    - Normally distributed data

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Obtaining Point Estimates

- Substitution of predictor values provides the estimate of the modeled transformation of the summary measure
  - Linear regression: mean
  - Linear regression on logs: log geometric mean
  - Logistic regression: log odds
  - Poisson regression: log rate
  - Proportional hazards: log hazard ratio applied to baseline survival estimate

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Obtaining Interval Estimates

- Under the appropriate assumptions, we can obtain standard errors for each such estimated summary measure
  - Notable exception: Proportional hazards
    - More work to be done to get interval estimates
  - We generally find a confidence interval for the transformed summary measure, and then back transform to obtain the desired quantity
- THEN: Add in variability within group

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Statistical Software

- No statistical package that I know of will provide prediction intervals except for normally distributed data
  - Even then, I do not think that they are behaving the way we want them to
    - Frequentist intervals describe behavior across repeated experiments, not within one experiment

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Prediction Intervals: Normal Data

- Obtaining point estimates
  - The point prediction is typically the mean (or log geometric mean) from the regression model

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Obtaining Interval Estimates

- Under the appropriate assumptions, we can obtain standard errors for each such prediction
  - The standard error accounts for
    - Uncertainty in estimating the regression parameters
    - The within group standard deviation
      - Spread of data about the group specific means

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Stata Commands: Predict

- After performing any regression command, the Stata command "`predict`" will compute estimates and standard errors
  - `predict` *`varname`*, [*`what`*]
    - *`varname`* is the name of the variable where you want the predictions stored
    - *`what`* is an option specifying what you want computed
      - stdf = standard error of forecast (works for linear regression)

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Computing Prediction Intervals

- Just use the usual formula

  (est) +/- (crit val) * (std err)

  - In linear regression, we usually use the t distribution to obtain CI
    - Stata: (crit val) = `invttail(`*df*`,`*α/2*`)`
    - degrees of freedom = n minus number of regression parameters

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Ex: Geom Mean FEV by ht, age

```
regress logfev height age
Number of obs =     654
logfev |  Coef.   Std. Err.   t    P>|t|     [95% CI]
height |   .044   .002    26.71   0.000     .041    .047
   age |   .020   .003     6.23   0.000     .014    .026
 _cons |  -1.97   .078   -25.16   0.000    -2.12   -1.82

predict flogfev
predict sefore, stdf
g predfev= exp(flogfev)
g predlofev = exp(flogfev - invttail(651, .025) * sefore)
g predhifev = exp(flogfev + invttail(651, .025) * sefore)
list predfev predlofev predhifev if age==10 & height==66
       predfev  predlofev  predhifev
330.  3.097021   2.320911   4.132662
```

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Compare: CI for Parameter

- Using the "standard error of the prediction"
  - 95% CI for geometric mean of 66" tall 10 yo
    - From slide 33: (3.039, 3.157)
  - Tells us how precisely we know the geometric mean, which is a single number
  - As n becomes infinite, the width of the CI goes to 0
    - We will know the geometric mean for that group exactly
      - (if our model is correct)

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Compare: Prediction Interval

- Using the "standard error of the forecast"
  - 95% PI for FEV measurements of 66" tall 10 year olds
    - From slide 52: (2.321, 4.133)
  - Tries to predict the range containing 95% of measurements in the population of 66" tall 10 year olds
  - As n becomes infinite, the width of the PI (on the log scale) would be +/- 1.96 SD

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Caveat

- This "forecast" or "prediction interval" assumes that the log FEV measurements are normally distributed
  - This is a pretty strong assumption

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Extensions

- I know how to get approximate intervals based on some slightly weaker semi-parametric assumptions
    - Uses nonparametric estimates of the error distribution
    - This would work for censored data as well
  - Most software packages will not do this

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Better Approaches

- It would be better to find nonparametric confidence intervals for
  - the 2.5th percentile
  - the 97.5th percentile

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But Still…

- All of these methods suffer from
  - Strong semiparametric assumptions
  - Multiple comparisons if more than one group
    - (But we do know how to get confidence bands)
  - Coverage probabilities defined across replicate experiments
    - On average (across experiments), 95% of observations will be within an interval
    - But in any given experiment, the intervals might truly cover less or more of the population

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Simulation Study

- Perform 1000 simulated regressions
  - X is normally distributed, mean 0, sd 1
  - N= 25 or 100
  - Generate 95% prediction intervals for
    - X = 0 (mean)
    - X = 1 (1 sd from the mean)
  - Calculate true coverage probability of each prediction interval
    - (I know the truth in this case)

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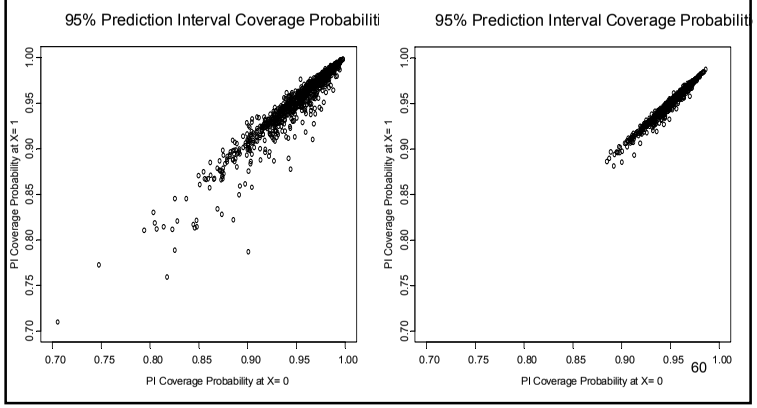
Plots of Coverage Probabilities



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Coverage Probabilities

- Sample size N= 25
  - Mean coverage probability: 0.950
  - Interquartile range: 0.935 – 0.978
  - Range: 0.706 – 0.998
- Sample size N= 100
  - Mean coverage probability: 0.950
  - Interquartile range: 0.941 – 0.962
  - Range: 0.885 – 0.986

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Joint Coverage of 2 Pred Intvl

- Sample size N= 25
  - Mean coverage probability: 0.906
  - Interquartile range: 0.874 – 0.956
  - Range: 0.501 – 0.996
- Sample size N= 100
  - Mean coverage probability: 0.903
  - Interquartile range: 0.884 – 0.926
  - Range: 0.784 – 0.974

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Correlated Response

- Prediction Intervals can be computed for correlated response
  - Stata, however, does not provide the obvious approximation
  - Thus for the SEP dataset we would have options of
    - Using mean p60 and adjusting the PI "by hand"
    - Identifying clusters and computing PI "by hand"
    - (More advanced models
      - mixed effects, repeated measures)

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Prediction Intervals

- Basic idea behind prediction intervals

Model:

$$Y_i \mid X_i \sim N\left(\beta_0 + \beta_1 \times X_i, \sigma^2\right)$$

$$Y_i \mid X_i = \beta_0 + \beta_1 \times X_i + \varepsilon_i$$

Estimated mean:

$$\hat{\beta}_0 + \hat{\beta}_1 \times X_i \sim N\left(\beta_0 + \beta_1 \times X_i, \sigma^2 V\right)$$

Predicted observation:

$$\hat{\beta}_0 + \hat{\beta}_1 \times X_i + \varepsilon_i \sim N\left(\beta_0 + \beta_1 \times X_i, \sigma^2 (1+V)\right)$$

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Computing Prediction Intervals

- We use an estimate for the within group variance
  - So we usually use the t distribution instead of the normal distribution
- With correlated response data, the degrees of freedom can be more complicated
  - But if n is large, it makes little difference

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With Correlated Response

- With a balanced design the "Root MSE" is still consistent for the within group standard deviation
- Hence, we can approximate the standard error of the forecast as

Estimated mean :

$$\hat{\beta}_0 + \hat{\beta}_1 \times X_i \sim N\left(\beta_0 + \beta_1 \times X_i, \sigma^2 V\right)$$

Predicted observation :

$$\hat{\beta}_0 + \hat{\beta}_1 \times X_i + \varepsilon_i \sim N\left(\beta_0 + \beta_1 \times X_i, \sigma^2 (1+V)\right)$$

$$\hat{se}(Forecast) = \sqrt{se^2\left(\hat{\beta}_0 + \hat{\beta}_1 \times X_i\right) + \hat{\sigma}^2}$$

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Prediction of Binary Measurements

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Classification (Discrimination)

- Sometimes the scientific question is one of deriving a rule to classify subjects
  - Diagnosis of prostate cancer
    - Based on age, race, and PSA, should we make a diagnosis of prostate cancer?
  - Prognosis of patients with primary biliary cirrhosis
    - Based on age, bilirubin, albumin, edema, protime, is the patient likely to die within the next year?

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Prediction of a Binary Variable

- Classification can be regarded as trying to predict the value of a binary variable
  - Before (slides 34-35) we were estimating the probability and odds of relapse within a particular group: A summary measure
  - Now we want to decide whether a particular individual will relapse: An individual measurement
- Obvious connection:
  - The probability or odds tells us everything about the distribution of values
  - The only possible values are 0 or 1

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Typical Approach

- Use regression model to estimate probability of the event in each group
- Form a decision rule based on estimated probability of the event
  - If estimate $\geq$ c, predict measurement is 1
  - If estimate < c, predict measurement is 0
- Quantify accuracy of decision rule
  - Sens, Spec, Pred Val Pos, Pred Val Neg

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Often: Stepwise Model Building

- Consider a large number of covariates that might possibly be predictive
  - Starting model
    - No covariates: "Forward stepwise regression"
    - All covariates: "Backward stepwise regression"
  - Add or remove covariates based on the corresponding partial t or partial Z test
    - "P to enter" and "P to remove"
    - Avoid infinite loops: "P to enter" < "P to remove"

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Caveats

- Stepwise model building "overfits" your data
  - "P values" are not true p values—instead they are anti-conservative
- You will quite often obtain different models depending upon whether you go "forward" or "backward"

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Use of Stepwise Model Building

- Exploratory data analyses
  - Statistical question 4a: Which covariates should we rigorously investigate first, because they seem to have the strongest association with response?
    - Provides an order that we might consider the covariates
    - Does not tell us whether any of the covariates are truly associated
      - Many false positives

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Use of Stepwise Model Building

- Predictive models
  - Statistical question 5: What is our best estimate for an individual's measurement?
    - We are not interested in the association between the covariates in the model and the response
    - We do not mind confounding or surrogate variables
    - We will judge accuracy of our predictive model by evaluating sens, spec, PV+, PV- in an independent sample

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Stata Commands

- Stata has prefix command "stepwise" that works with most regression commands

```
stepwise, pe(#) pr(#) [forward]:
```

  - "P to enter": a number between 0 and 1
  - "P to remove": a number between 0 and 1
  - forward or backward: backward is default

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Example

- Stepwise model building in inflammatory markers data set to predict who will die within 4 years
  - No subjects were censored before 4 years
  - Use logistic regression
  - Consider variables
    - age, male, smoker, prevdis, diab2, bmi ,systBP, cholest, cholsqr, crp, logcrp, fib
      - (Note that I am allowing cholesterol to have a U shaped trend, and I consider a transformation of CRP as well)

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Example: Forward Stepwise

```
. stepwise, pr(0.10) pe(0.05) forward: logistic
  deadIn4 age male smoker prevdis diab2 bmi systBP
  cholest cholsqr crp logcrp fib

begin with empty model
p = 0.0000 <  0.0500  adding   age
p = 0.0000 <  0.0500  adding   logcrp
p = 0.0000 <  0.0500  adding   male
p = 0.0000 <  0.0500  adding   prevdis
p = 0.0000 <  0.0500  adding   diab2
p = 0.0005 <  0.0500  adding   smoker
p = 0.0032 <  0.0500  adding   systBP
```

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Example: Forward Stepwise

```
Logistic regression      Number of obs   =     4861
                         LR chi2(7)      =   412.54
                         Prob > chi2     =   0.0000
Log likelihood = -1345   Pseudo R2       =   0.1330
```

deadIn4	OR	SE	z	P>|z|	[95% CI]	
age	1.115	.0095	12.81	0.000	1.097	1.134
logcrp	1.444	.0731	7.26	0.000	1.308	1.595
male	2.122	.2216	7.20	0.000	1.729	2.604
prevdis	2.056	.2181	6.80	0.000	1.670	2.531
diab2	1.824	.2193	5.00	0.000	1.441	2.309
smoker	1.698	.2555	3.52	0.000	1.264	2.281
systBP	1.007	.0023	2.94	0.003	1.002	1.011

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Example: Forward Stepwise

- Interpretation
  - Provides an ordering of the variables with respect to observed strength of association
    - In the case of forward stepwise, Stata lists variables according to “P value”
  - We cannot trust the P values due to the data driven analyses
  - It is possible that confounding relationships kept some variables out of the model

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Example: Backward Stepwise

```
. stepwise, pr(0.10) pe(0.05): logistic deadIn4 age
  male smoker prevdis diab2 bmi systBP cholest
  cholsqr crp logcrp fib
                        begin with full model
p = 0.2157 >= 0.1000  removing cholsqr
p = 0.3768 >= 0.1000  removing cholest

Logistic regression      Number of obs   =     4861
                         LR chi2(10)     =   421.22
                         Prob > chi2     =   0.0000
Log likelihood = -1341   Pseudo R2       =   0.1358
```

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Example: Backward Stepwise

deadIn4	OR	SE	z	P>|z|	[95% CI]	
age	1.111	.0097	12.06	0.000	1.092	1.130
male	2.123	.2232	7.16	0.000	1.728	2.609
smoker	1.577	.2414	2.97	0.003	1.168	2.129
prevdis	2.023	.2154	6.61	0.000	1.642	2.492
diab2	1.883	.2300	5.18	0.000	1.482	2.393
bmi	.979	.0120	-1.75	0.079	.956	1.003
systBP	1.007	.0023	2.88	0.004	1.002	1.011
logcrp	1.553	.1394	4.90	0.000	1.302	1.851
fib	1.002	.0009	1.98	0.048	1.000	1.003
crp	.980	.0111	-1.77	0.077	.959	1.002

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Example: Backward Stepwise

- Interpretation
  - Provides an ordering of the variables with respect to observed strength of association
    - In the case of backward stepwise, Stata lists variables according to original order
  - We cannot trust the P values due to the data driven analyses
  - Compare to forward
    - Some additional variables with P > 0.05
    - But also some additional with P < 0.05

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Stepwise for Classification

- We sometimes use stepwise model building to derive a classification rule
  - To ensure valid estimates of classification rates, we usually divide a sample into
    - Training sample used to build a regression model, and
    - Validation sample used to compute the classification rates
      - Sensitivity, specificity, predictive value of the positive, predictive value of the negative

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Example

- Prognostic model for death in 4 years
  - Training sample containing about 60% of data
  - Backward stepwise variable selection
  - Estimated probability of death used to classify
    - Some arbitrary threshold
  - Use all other cases (validation set) to compute
    - Sensitivity, specificity (condition on survival status)
    - PV+, PV- (condition on estimated p > threshold)

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Example: Model Building

```
. g training= uniform()
. stepwise, pr(0.10) pe(0.05): logistic deadIn4 age
  male smoker prevdis diab2 bmi systBP cholest
  cholsqr crp logcrp fib if training <= 0.60
begin with full model
p = 0.9919 >= 0.1000  removing cholsqr
p = 0.4914 >= 0.1000  removing cholest
p = 0.4475 >= 0.1000  removing fib
p = 0.1908 >= 0.1000  removing smoker
Logistic regression     Number of obs   =       2875
(output deleted - we do not care about it)
. predict pfit
```

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Example: Sens, Spec, PV+, PV-

- Consider a rule that predicts death if the estimated *pfit* is greater than 0.5
  - Create a variable indicating *pfit* > 0.5
  - Cross tabulate deadIn4 and pfit
    - Sensitivity and specificity from row percentages
    - PV+ and PV- from column percentages

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Example: Sens, Spec, PV+, PV-

```
. g pfitHigh= pfit
. recode pfitHigh 0/0.5=0 0.5/1=1
. tabula deadIn4 pfitHigh if training > 0.6, row col
           |        pfitHigh
   deadIn4 |          0            1 |     Total
---------------------------------------------------
         0 |      1,792            7 |     1,799
           |Spec: 99.61         0.39 |    100.00
           |PV-:  90.64        41.18 |     90.22
---------------------------------------------------
         1 |        185           10 |       195
           |      94.87  Sens:  5.13 |    100.00
           |       9.36  PV+:  58.82 |      9.78
---------------------------------------------------
     Total |      1,977           17 |     1,994
           |      99.15         0.85 |    100.00
           |     100.00       100.00 |    100.00
```

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Example: Other Thresholds

- Sensitivity, specificity will vary by threshold

Threshold	Specificity	Sensitivity
0.05	43%	87%
0.10	68%	73%
0.15	84%	48%
0.20	91%	37%
0.50	99.6%	5%

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ROC Curve Analysis

- Receiver Operating Curves (from Engr)
  - Compare sens and spec as threshold varies
  - Y axis: Sensitivity (True Positive rate)
  - X axis: 1 – Specificity (False Positive rate)
- Interpretation
  - Sometimes summarize area under curve (AUC)
  - A diagonal line: Like flipping a coin (AUC = 0.5)
  - ROC curve in upper left: Ideal (AUC = 1.0)
  - Comparing two rules:
    - If one ROC curve always above the other, that rule will always have better PV+ and PV- for all prevalences

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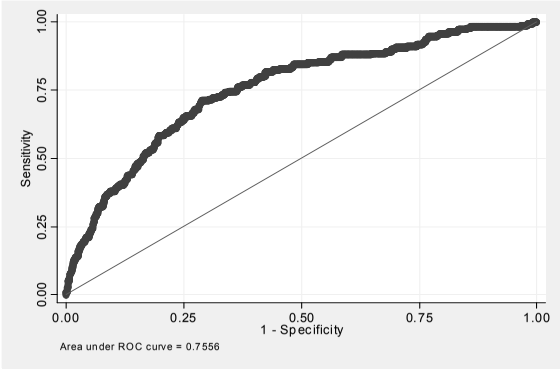
Stata Commands

```
. roctab deadIn4 pfit if training > 0.60, graph
```



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