Epidemiology VHM 8120 Course
Winter 2021, Atlantic Veterinary College, PEI
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Lecture 3a: Model building II (VER Ch. 15)

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- Learning objectives:
  - understand main steps to build a regression model
  - learn model selection strategies
  - learn the use of automated process to select predictors
  - evaluate reliability of a linear regression model
- Exercises: work on model building exercise
- Wednesday: Quiz #2

Model building strategies

- Parsimony vs fit
- Goals
  - estimates of effects
  - prediction
- Steps
  - specify maximum model
    - reduce number of predictors
    - address issues of missing values
    - functional form (linearity) of continuous predictors
  - criterion for selection
  - selection strategy
  - analysis
  - evaluate reliability
  - present results

Specifying the maximum model

- Outcome of interest
- Key predictors
- Important confounders/interactions
- Other variables of interest (lots / few)

Develop a causal model

- Identify exposure
- Identify confounders
- Identify intervening variables
- Identify exposure-independent variables
- Make a decision about what to use in model

Reducing the number of predictors

- Screening – descriptive statistics
  - keep predictors with few missing values
    - complete case analysis
      - any missing value – entire observation ignored
  - substantial variability
  - small number observations - re-categorize predictor
- Correlation / association
  - understand relationships among predictors
  - collinearity/confounding
- Unconditional associations
  - liberal P-value
- Multivariate analysis
  - factor analysis
  - principal component analysis

Functional form of continuous predictors (linearity)

- Detecting non-linearity – in final model
  - plot residuals vs fitted values
    - simultaneous evaluation of all predictors
  - plot of residuals vs predictor
- Detecting non-linearity – before / during model building
  - scatter plot of outcome vs predictor
    - smoothing functions
- Smoothed scatter-plots (L1a)
  - lowess – commonly used
  - cautions
    - potential to mask important local effects
    - behave poorly at ends

Detecting and correcting non-linearity

- Categorization of predictor (L2a)
  - indicator dummy variable
- Compare categorical and linear variables
  - linear model is a subset of a model with more categories (R)
  - test of linear regression against categorical model (F)
    - F-statistic to compare R vs F

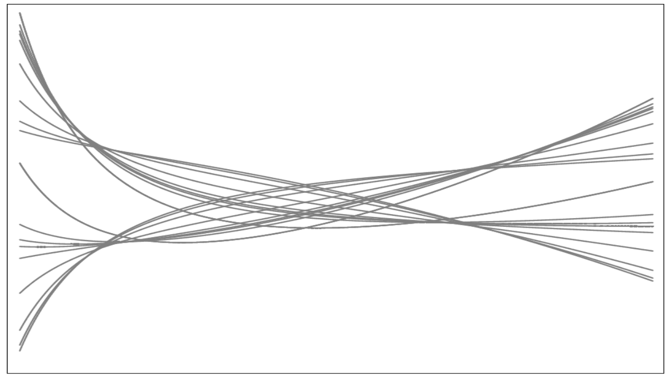
- Transformation of X
  - box-cox analysis
    - same idea as for the outcome (L1a)
      - eg. boxcox ln_cf milk120k , **model(rhs)**
  - polynomial functions of X
    - quadratic, cubic, etc
    - fractional polynomials

Polynomial functions of X

- Quadratic (details L1b and L2b)

- Fractional polynomials
  - extension polynomial regression (L1a)
    - allow log, non-integer powers, repeated powers
  - select terms (usually one or two) of the form x^p
  - where “p” is from the set -2, -1, -0.5, 0, 0.5, 1, 2, 3
    - p=0 is taken to be ln(X)
    - eg $\beta_1 X^{-1} + \beta_2 X^2 = \beta_1 (1/X) + \beta_2 (X^2)$
  - combination selected based on best fit (smallest log likelihood)
- Usually 2 power terms (2 degree) can fit most shapes
  - 2-degree FP: x(-2,2) … $x^{(-2)} + x^{(2)}$

- This graph shows some of the possibilities from a 2-degree FP



- Example – (ln) calving to first service and milk120

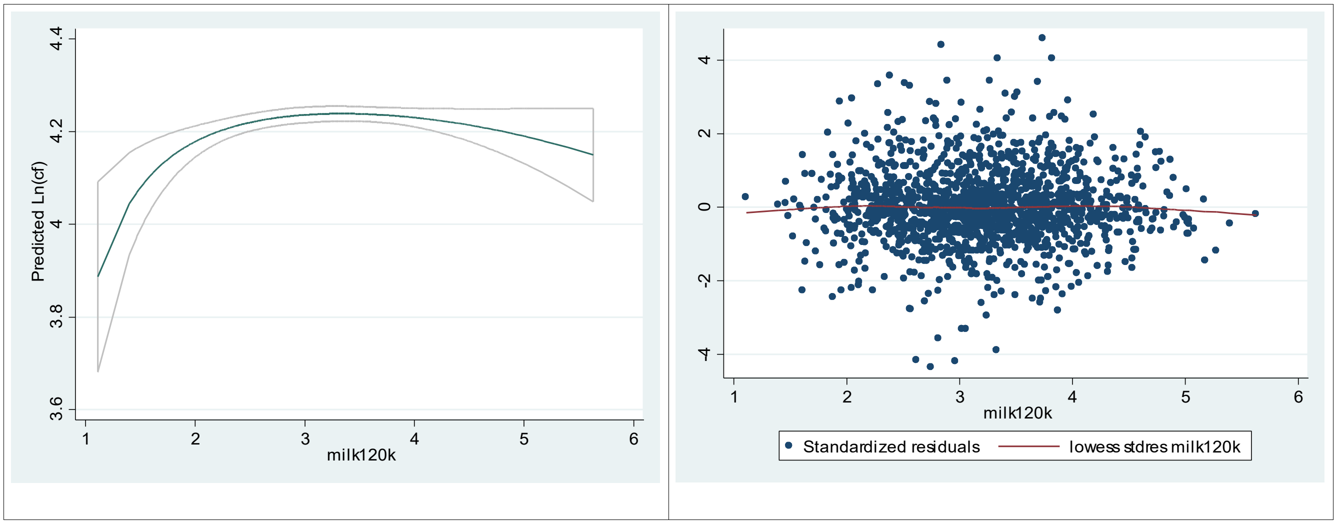
```
. fp <milk120k>,  scale center replace: reg ln_cf <milk120k>
(fitting 44 models)
(....10%....20%....30%....40%....50%....60%....70%....80%....90%....100%)

Fractional polynomial comparisons:
--------------------------------------------------------------------------------
    milk120k |   df    Deviance  Res. s.d.   Dev. dif.   P(*)   Powers
-------------+------------------------------------------------------------------
     omitted |    0    367.951      0.273     10.533    0.033
      linear |    1    366.159      0.273      8.741    0.033   1
       m = 1 |    2    361.396      0.273      3.978    0.138   -2
       m = 2 |    4    357.418      0.272      0.000       --   -2 3
--------------------------------------------------------------------------------
(*) P = sig. level of model with m = 2 based on F with 1520 denominator dof.

      Source |       SS       df       MS              Number of obs =    1525
-------------+------------------------------           F(  2,  1522) =    5.27
       Model |  .782289941     2  .391144971           Prob > F      =  0.0052
    Residual |  112.870944  1522  .074159622           R-squared     =  0.0069
-------------+------------------------------           Adj R-squared =  0.0056
       Total |  113.653234  1524  .074575613           Root MSE      =  .27232

------------------------------------------------------------------------------
       ln_cf |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
  milk120k_1 |  -.5301266   .1654544    -3.20   0.001    -.8546694   -.2055839
  milk120k_2 |  -.0008516   .0004271    -1.99   0.046    -.0016894   -.0000138
       _cons |   4.238434    .008295   510.96   0.000     4.222163    4.254704
------------------------------------------------------------------------------

.
```



- Interactions
  - 2 way
    - all possible
    - significant main effects
    - significant unconditional assoc.
    - biologically meaningful
    - with key predictor of interest
  - 3 way
    - rarely used in epidemiology

Selection criteria

- Non-statistical
  - predictor of interest
  - known confounder
  - evidence of being a confounder
  - component of an interaction term
- Statistical - nested models
  - F-test for the predictor (or t-test)
  - Wald test or Likelihood ratio test (LRT)
  - always use these tests if appropriate
- Statistical – non-nested models
  - adjusted $R^2 = 1 - \frac{MSE}{MST}$
    - R^2 adjusted for the # predictors, highest adjusted R^2 = best
    - linear regression models only
- Information criteria
  - AIC (Akaike's information criterion)
  - BIC (Bayesian information criterion)
  - not typically used in linear models (see logistic regression)

Selection strategies: Stepwise estimation

- Forward selection
  - start with a null model
  - adds terms based on statistical significance (one at a time, always choosing the most significant predictor not yet in the model)
  - stop when no more terms are significant when added

```
. stepwise, pe(0.1): reg y_test_scr x1_staff_sal x2_father_job x3_ses x4_test_teach
x5_edu_mother

                      begin with empty model
p = 0.0000 <  0.1000  adding  x3_ses
p = 0.0566 <  0.1000  adding  x4_test_teach

  ...output omitted

--------------------------------------------------------------------------------
   y_test_scr |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
--------------+-----------------------------------------------------------------
       x3_ses |   .5415607   .0500441    10.82   0.000     .4359768    .6471445
x4_test_teach |   .7498915   .3666402     2.05   0.057    -.0236517    1.523435
        _cons |    14.5827   9.175409     1.59   0.130    -4.775723    33.94112
```

- Backward elimination
  - starts with a full model
  - eliminates terms that are not significant (one at a time, starting with the “least significant”)
  - stop once all terms remaining in the model are significant

```
. stepwise, pr(0.1): reg y_test_scr x1_staff_sal x2_father_job x3_ses x4_test_teach
x5_edu_mother
                      begin with full model
p = 0.4267 >= 0.1000  removing x2_father_job
p = 0.6863 >= 0.1000  removing x5_edu_mother
p = 0.1616 >= 0.1000  removing x1_staff_sal
 ....output omitted
--------------------------------------------------------------------------------
   y_test_scr |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
--------------+-----------------------------------------------------------------
       x3_ses |   .5415607   .0500441    10.82   0.000     .4359768    .6471445
x4_test_teach |   .7498915   .3666402     2.05   0.057    -.0236517    1.523435
        _cons |    14.5827   9.175409     1.59   0.130    -4.775723    33.94112
--------------------------------------------------------------------------------
```

- Stepwise
  - combines forward and backward
  - generally preferred approach is stepwise backward
    - starts with a full model and works backward using a stepwise approach

```
. stepwise, pe(0.1) pr(0.11): reg y_test_scr x1_staff_sal x2_father_job x3_ses
x4_test_teach x5_edu_mother
                      begin with full model
p = 0.4267 >= 0.1100  removing x2_father_job
p = 0.6863 >= 0.1100  removing x5_edu_mother
p = 0.1616 >= 0.1100  removing x1_staff_sal

...outut omitted
--------------------------------------------------------------------------------
   y_test_scr |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
--------------+-----------------------------------------------------------------
       x3_ses |   .5415607   .0500441    10.82   0.000     .4359768    .6471445
x4_test_teach |   .7498915   .3666402     2.05   0.057    -.0236517    1.523435
        _cons |    14.5827   9.175409     1.59   0.130    -4.775723    33.94112
```

- daisy2red dataset
  - reg wpc_sqrt parity1 aut_clv c.hs_ct##c.hs_ct i.dyst##i.twin i.rp##i.vag_disch

```
stepwise, pe(0.05) pr(0.051) lockterm1: reg wpc_sqrt  parity1 aut_clv
(c.hs_ct##c.hs_ct) (i.dyst##i.twin) (i.rp##i.vag_disch)
estimates store sw_1
```

```
stepwise, pe(0.05) pr(0.051) lockterm1: reg wpc_sqrt  parity1 aut_clv
(hs_ct hs_sq)  i.dyst##i.twin i.rp##i.vag_disch
estimates store sw_2
```

```
stepwise, pe(0.05) pr(0.051) lockterm1: reg wpc_sqrt  parity1 (hs_ct
hs_sq) aut_clv  i.dys##i.twin (i.rp##i.vag_disch)
estimates store sw_3
```

```
estimates table sw_1 sw_2 sw_3, star(0.10 0.05 0.001)
--------------------------------------------------------------
    Variable |     sw_1            sw_2            sw_3
-------------+------------------------------------------------
     parity1 |  .05586593       .04388077       .04720258
     aut_clv | -.51283075***   -.52440137***   -.51422168***
       hs_ct |  .01232803***   -.02161068**    -.02240242**
     c.hs_ct#|
     c.hs_ct |   .0000713***
        dyst |
        yes  |  .62771805**
        twin |
        yes  |  1.6982381**     1.4787911**     1.4063402**
   dyst#twin |
    yes#yes  | -2.7727951
        1.rp |  .39042354                       .42079714
   vag_disch |
        yes  | -.04220258                       .07113917
rp#vag_disch |
      1#yes  |  1.4760578**     1.8317287***    1.3840389**
       hs_sq |                  .00006694***    .00006864***
       _cons |  7.5152743***    3.4048174**     3.2468497**
--------------------------------------------------------------
                          legend: * p<.1; ** p<.05; *** p<.001
```

Cautions with automated selection procedures

- R^2 and adjusted R^2 too high
- F-tests too large
- Ignores non-statistical considerations
    - exposures, confounders and intervening var.
- You need to take care of
    - dummy variables, interaction terms, polynomial terms
    - non significant confounders
- Useful when faced with large number of predictor variables
    - help to identify predictors that potentially are statistically significant associated with the outcome
- Perform residual and influential analysis of selected models

Evaluate reliability

- Validity - regression diagnostics
- Reliability
  - ability to predict future observations
  - leave-one-out analysis
    - fit the model using all data except one observation
    - generate prediction for the left-out obs.
    - compare the **P**redicted **R**esidual **S**um of **S**quares (PRESS) from predicted points to prediction error from full model
    - PRESS = sum{($residual_i$ / (1-$leverage_i$))^2}
    - R^2(prediction) = 1-(PRESS/Total Sum of Squares)
      - compare R^2 (prediction) vs R^2 (full model)
      - difference should not be "too large"
- Example: daisy2red dataset (PRESS analysis)

```
. reg  wpc_sqrt c.hs_ct##c.hs_ct parity1 i.aut_clv i.twin i.dyst##i.vag_disch

 ...output omitted...

predict res, res
predict lev ,lev
gen eq1=(res/(1-lev))^2

. summ eq1
    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+---------------------------------------------------------
         eq1 |      1574    7.851331     10.9765   1.85e-07   83.92817

. di "PRESS =" r(sum) //error sum square from predicted points
PRESS =12357.995

. di "R2(pred) = "1-(PRESS/  (e(mss) + e(rss)))
R2(pred) = .07126506

. di "R2 full model = " e(r2)
R2 full model = .08284007
```

Presenting the results

- Standardized coefficients
  - scales all coefficients so that they represent a change of 1 SD.

    $$\beta_{*}=\beta(\sigma_x/\sigma_y)$$

  - compare the relative magnitude of several predictors
    - use with caution to compare coeff. from different studies
- Interquartile range (IQR)
  - how big is the change in the outcome if the predictor changes through out the IQR
    - IQR = diff. between 75^{th} and 25^{th} percentile
      - parity IQR = 3, coef. = 0.06
      - effect = 0.06*3 = 0.18 units
    - avoid impact of outlying observations
- Predictors eliminated from the model
  - don't ignore predictors just because they have been eliminated from the model
    - not statistically sig. ≠ no effect
    - unconditional associations?
    - force back in to the final model?
- Scale of results
  - dealing with transformed data
  - compute some expected effects of key predictors on the original scale at various levels of the other factors

Strobe-Vet Reporting guidelines

- Strengthening the Reporting of Observational Studies in Epidemiology statement checklist for Veterinary medicine (the STROBE-Vet statement)
  - https://strobevet-statement.org/strobe-vet-statement/
- 22 items checklist for assessing reporting quality
- Items related to model building:
  - (7) Variables
  - (8) Data source measurements
  - (9) Bias
  - (11) Quantitative variables
  - (12) Statistical methods
- Explanation document
  - expanded document describing examples of reporting