Variable selection

Peter Geelan-Small, Stats Central, UNSW

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Statistical inference - main types of inference

- Parameter estimation - finding a plausible range of values for a parameter of interest - e.g. coefficient of a particular predictor
- Hypothesis testing - looking at the effect of a focal predictor - testing if the coefficient of the predictor is zero
- Predicting future values of the response from predictors
- Finding which predictors are associated with the response - *active* predictors versus *inactive* predictors

A good predictive model aids parameter estimation and hypothesis testing

Variable selection is a type of inference - one of many methods in general area of model selection

Example: Respiratory muscle strength in cystic fibrosis

Measurements of a number of clinical variables were taken on 25 patients with cystic fibrosis aged from 7 to 23 years. The response variable is maximum expiratory pressure (`pemax`).[1]

- What variables are associated with (active predictors of) `pemax`?
- What is a useful prediction model for `pemax`?

Response

- `pemax`: maximum expiratory pressure

[1]: Dalgaard 2008, Introductory Statistics with R, Springer; O'Neill et al. 1983, Am. Rev. Respir. Dis., 128:1051–1054.

Example: Cystic fibrosis

- `age`: age (yr)
- `sex`: coded 0: male, 1:female
- `height`: height (cm)
- `weight`: weight (kg)
- `bmp`: body mass pc. (% of normal) - indicator of malnutrition

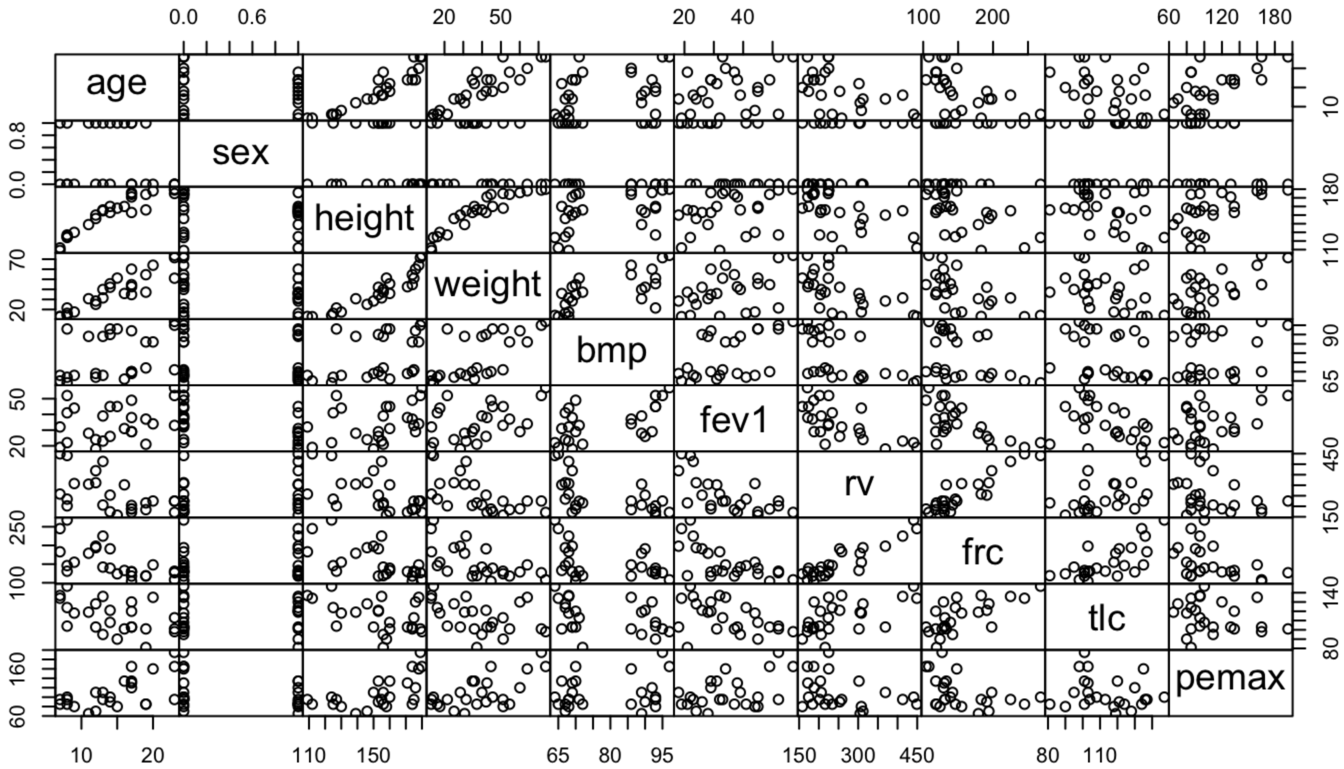
Lung function indicators

- `fev1`: forced expiratory volume
- `rv`: residual volume
- `frc`: functional residual capacity
- `tlc`: total lung capacity

Example: Cystic fibrosis - variables

```
## 'data.frame':    25 obs. of  10 variables:
##  $ age   : int  7 7 8 8 8 9 11 12 12 13 ...
##  $ sex   : int  0 1 0 1 0 0 1 1 0 1 ...
##  $ height: int  109 112 124 125 127 130 139 150 146 155 ...
##  $ weight: num  13.1 12.9 14.1 16.2 21.5 17.5 30.7 28.4 25.1 31.5 ...
##  $ bmp   : int  68 65 64 67 93 68 89 69 67 68 ...
##  $ fev1  : int  32 19 22 41 52 44 28 18 24 23 ...
##  $ rv    : int  258 449 441 234 202 308 305 369 312 413 ...
##  $ frc   : int  183 245 268 146 131 155 179 198 194 225 ...
##  $ tlc   : int  137 134 147 124 104 118 119 103 128 136 ...
##  $ pemax : int  95 85 100 85 95 80 65 110 70 95 ...
```

Example: Cystic fibrosis - all pairs plot



Example: Cystic fibrosis - summary statistics

```
##           mean         sd IQR   50%  n
## age     14.480  5.0589854   6  14.0 25
## sex      0.440  0.5066228   1   0.0 25
## height 152.800 21.5000000  35 156.0 25
## weight  38.404 17.8981256  26  37.2 25
## bmp     78.280 12.0052766  22  71.0 25
## fev1    34.720 11.1971723  18  33.0 25
## rv     255.200 86.0169557 117 225.0 25
## frc    155.400 43.7187984  56 139.0 25
## tlc    114.000 16.9681073  27 113.0 25
## pemax  109.120 33.4369058  45  95.0 25
```

Example: Cystic fibrosis - correlations

```
##          age   sex height weight   bmp  fev1    rv   frc   tlc pemax
## age     1.00 -0.17   0.93   0.91  0.38  0.29 -0.55 -0.64 -0.47  0.61
## sex    -0.17  1.00  -0.17  -0.19 -0.14 -0.53  0.27  0.18  0.02 -0.29
## height  0.93 -0.17   1.00   0.92  0.44  0.32 -0.57 -0.62 -0.46  0.60
## weight  0.91 -0.19   0.92   1.00  0.67  0.45 -0.62 -0.62 -0.42  0.64
## bmp     0.38 -0.14   0.44   0.67  1.00  0.55 -0.58 -0.43 -0.36  0.23
## fev1    0.29 -0.53   0.32   0.45  0.55  1.00 -0.67 -0.67 -0.44  0.45
## rv     -0.55  0.27  -0.57  -0.62 -0.58 -0.67  1.00  0.91  0.59 -0.32
## frc    -0.64  0.18  -0.62  -0.62 -0.43 -0.67  0.91  1.00  0.70 -0.42
## tlc    -0.47  0.02  -0.46  -0.42 -0.36 -0.44  0.59  0.70  1.00 -0.18
## pemax   0.61 -0.29   0.60   0.64  0.23  0.45 -0.32 -0.42 -0.18  1.00
```

Example: Cystic fibrosis - regression model

Model: multivariable linear regression

```
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept) 176.0582   225.8912  0.7794   0.4479
## age          -2.5420     4.8017 -0.5294   0.6043
## sex          -3.7368    15.4598 -0.2417   0.8123
## height       -0.4463     0.9034 -0.4940   0.6285
## weight        2.9928     2.0080  1.4905   0.1568
## bmp          -1.7449     1.1552 -1.5105   0.1517
## fev1          1.0807     1.0809  0.9998   0.3333
## rv            0.1970     0.1962  1.0039   0.3314
## frc          -0.3084     0.4924 -0.6264   0.5405
## tlc           0.1886     0.4997  0.3774   0.7112

## [1] Adjusted R-sq = 0.4197       p value = 0.032
```

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Example: Cystic fibrosis - collinearity

Global P value small, no P values for model coefficients small?

Correlations among variables are interfering with estimated standard errors - *collinearity*

Check via *variance inflation factor*

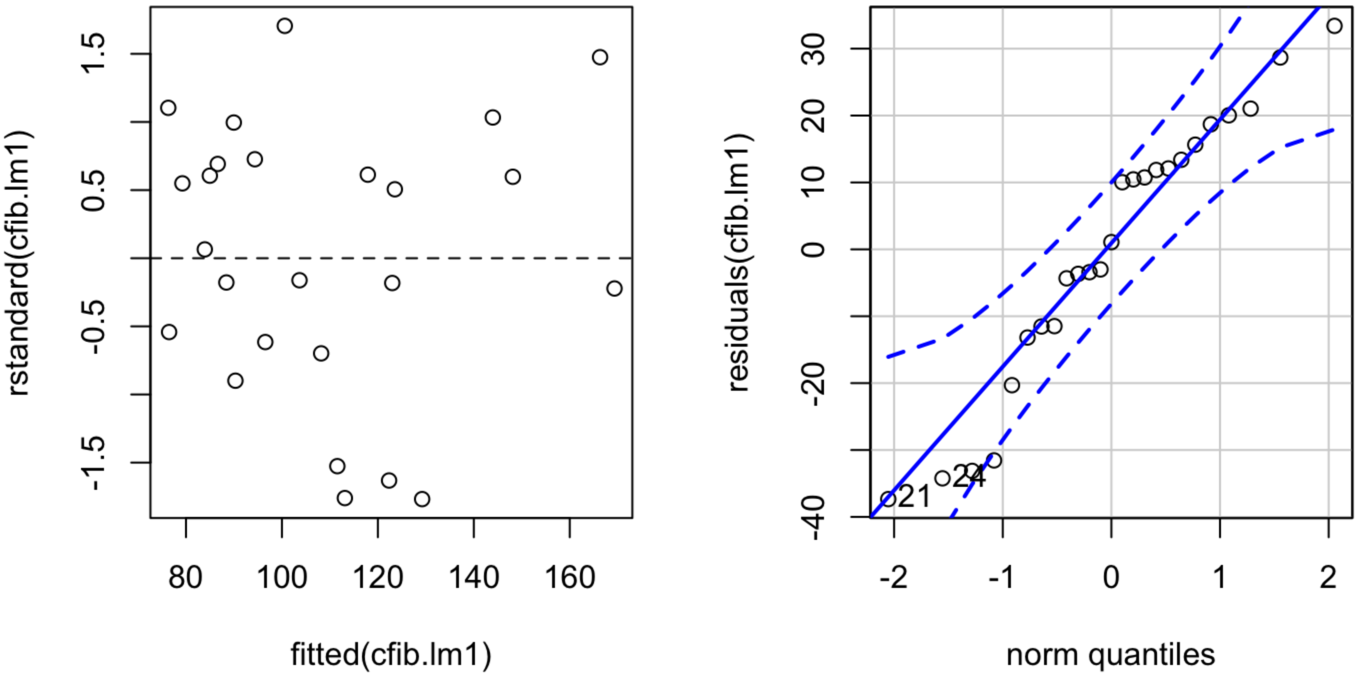
```
##    age    sex height weight    bmp   fev1     rv    frc    tlc
## 21.830  2.269 13.955 47.781  7.116  5.420 10.538 17.143  2.660
```

Values of VIF > 10 show concerning collinearity

VIF values show why individual P values are not smaller

Example: Cystic fibrosis - model assumptions

Check model assumptions



```
## [1] 21 24
```

Variable selection - criteria and methods

Criteria applied to a model (well or not!) for deciding the fate of a variable:

- P value derived from some statistic (t, F, χ^2)
- Measure of model fit - mean squared error (residual mean square), adjusted R^2
- Information criterion - AIC, BIC (combination of measure of model fit and penalty for larger model)

For these criteria, smaller is better, except for adjusted R^2, where larger is better

Variable selection - criteria and methods

Methods

- Stepwise methods - forwards, backwards, both (1960)
  - one variable added or removed at each step
- Validation methods
  - measure how well models predict using new data (1990s)
  - randomly split data set into training and test sets
  - all subsets combined with k-fold cross-validation
- Penalised estimation methods - model coefficient estimates forced towards zero
  - penalty term is based on magnitude of model coefficients
  - LASSO (1996)

Variable selection - criteria and methods

Consensus view is use expert knowledge first to *simplify* your model

- eliminate unnecessary predictors

Stepwise methods - can be useful but strongly criticised by some

- no statistical justification but if you must …
- do not use P values for decisions
    - hypothesis testing not appropriate for model selection as no a priori hypothesis is tested
    - multiple testing problems
- use information criterion (AIC, BIC)

Variable selection - criteria and methods

Validation methods

- common criterion is mean squared error
- good for comparing predictive capability of models and so variable selection
- choose appropriate “k” for k-fold cross-validation - one recommendation:
    - leave-one-out (i.e. N-fold c.v.) if n < 20
    - 10-fold c.v. for 20<n<100
    - 5-fold c.v. for n>100

Penalised estimation methods (e.g. LASSO)

- main goal is predictive capability of model
- good when many parameters or small sample

Variable selection - criteria and methods

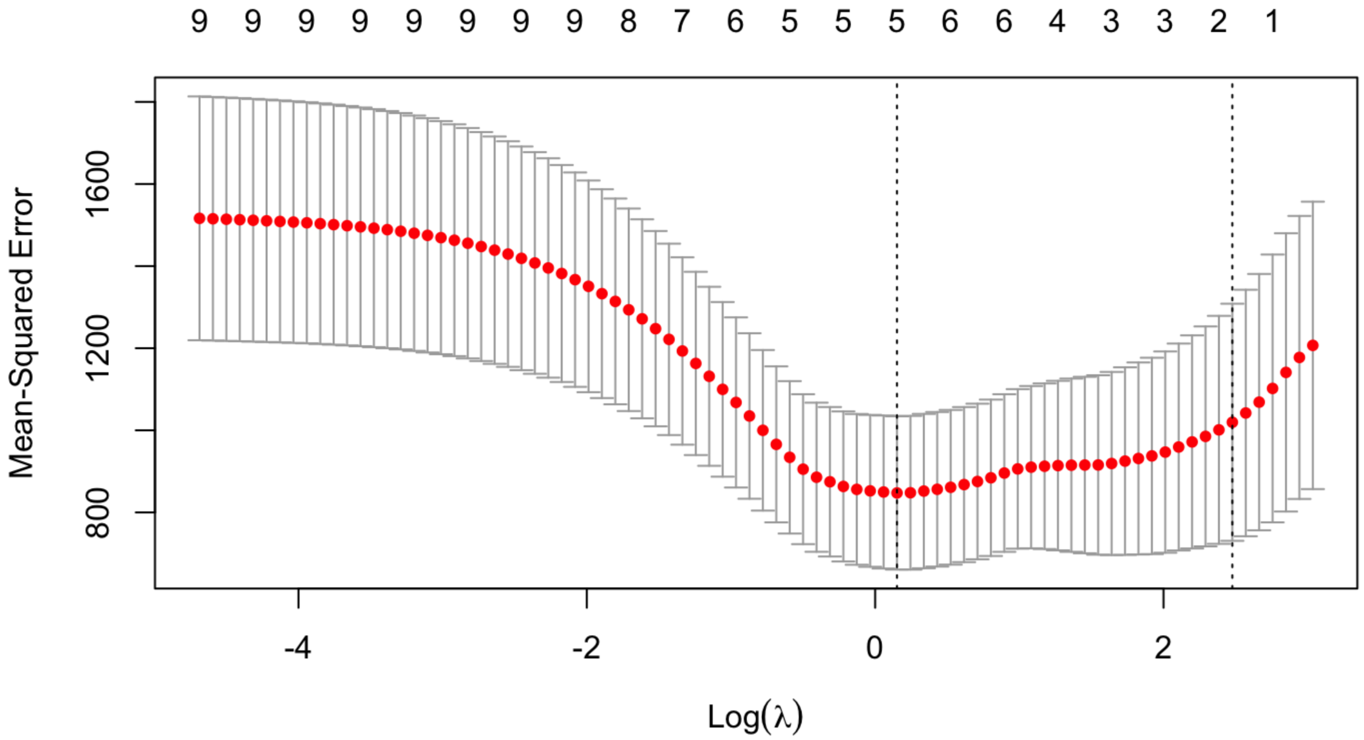
Each method also has its *limitations* and *disadvantages*

- Stepwise methods
  - can be undermined by collinearity
  - validity of multiple steps is questionable
- AIC and BIC rely on model being close to correct
- Cross-validation requires only independent splits for training and test data but different results for different “k”
- LASSO estimates are biased and no standard errors are available

Example: Cystic fibrosis - active predictors

- What variables are associated with (active predictors of) `pemax`?

LASSO



Example: Cystic fibrosis - active predictors

```
## 9 x 1 sparse Matrix of class "dgCMatrix"
##                 s0
## age      .
## sex      .
## height   .
## weight   1.48240558
## bmp     -1.03833881
## fev1     1.17164094
## rv       0.05732589
## frc      .
## tlc      0.12969407
```

Available output:

- active predictors and model coefficients
- no P values
- no standard errors

Example: Cystic fibrosis - prediction model

- What is a useful prediction model for `pemax`?

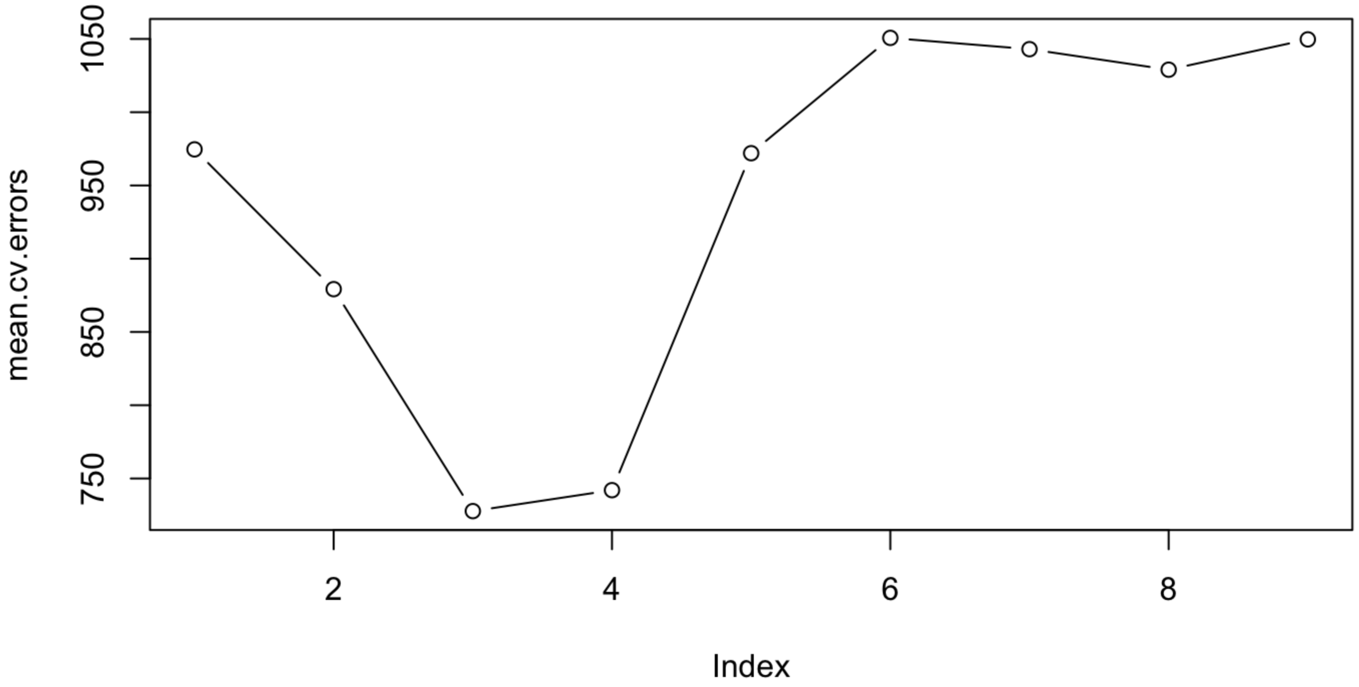
k-fold cross-validation (k = 1, leave-one-out) with all subsets in each fold

```
## folds
##  1  2  3  4  5  6  7  8  9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
##  1  1  1  1  1  1  1  1  1  1  1  1  1  1  1  1  1  1  1  1  1  1  1
## 24 25
##  1  1
```

```
##         1         2         3         4         5         6         7
##  974.6263  879.2297  727.7373  742.0240  972.0102 1050.7182 1043.0226
##         8         9
## 1029.0064 1049.6921
```

```
## [1] No. of predictors in final model = 3
```

Example: Cystic fibrosis - prediction model



Example: Cystic fibrosis - prediction model

```
## (Intercept)      weight         bmp        fev1
##  126.333557    1.536475   -1.465406    1.108629
```

Look at terms in 4-predictor model from c.v. runs

```
## (Intercept)      weight         bmp        fev1          rv
##  63.9466933   1.7489143  -1.3772433   1.5476984   0.1257152
```

Strange:

- both weight and bmp are in model when cor(weight, bmp) = 0.67
- coef of bmp is negative when cor(pemax, bmp) = 0.23

Possible overfitting?

Example: Cystic fibrosis - prediction model

Optimal model from cross-validation with all subsets fitted on full data set

```
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept) 126.3336    34.7199  3.6387   0.0015
## weight        1.5365     0.3644  4.2162   0.0004
## bmp          -1.4654     0.5793 -2.5297   0.0195
## fev1          1.1086     0.5144  2.1553   0.0429
```

```
## [1] Adjusted R-sq = 0.5086      p value = 4e-04
```

Example: Cystic fibrosis - prediction model

For prediction models:

- some overfitting is not a problem
- some collinearity is not a problem

Example: Cystic fibrosis - active predictors

Simplify the model

- use logic from expert knowledge - consider groups of predictors

Lung function: `fev1`, `rv`, `frc`, `tlc`

Remove these other lung function indicators as a group

Model comparison criteria:

- AIC - overfits, better for prediction model
- BIC - penalises larger models harder, good for active predictors
- As models are *nested*, can use an F test (see note at end of slides)

Example: Cystic fibrosis - active predictors

Simplify the model contd

```
## [1] AIC full model: 242.05
```

```
## [1] AIC reduced model: 239.56
```

```
## [1] AIC_full - AIC_red = 2.49
```

```
## [1] BIC full model: 255.46
```

```
## [1] BIC reduced model: 248.09
```

```
## [1] BIC_full - BIC_red = 7.37
```

Model without lung function variables appears better

Example: Cystic fibrosis - active predictors

Simplify the model contd

F test for nested models

```
## Analysis of Variance Table
##
## Model 1: pemax ~ age + sex + height + weight + bmp
## Model 2: pemax ~ age + sex + height + weight + bmp + fev1 + rv + frc +
##     tlc
##   Res.Df     RSS Df Sum of Sq      F Pr(>F)
## 1     19 12129.2
## 2     15  9731.2  4      2398 0.9241 0.4758
```

Smaller model is no worse than larger model

Example: Cystic fibrosis - active predictors

```
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept) 280.4482   124.9556  2.2444   0.0369
## age          -3.0750     3.6352 -0.8459   0.4081
## sex         -11.5281    10.3720 -1.1115   0.2802
## height       -0.6853     0.7962 -0.8607   0.4001
## weight        3.5546     1.5281  2.3261   0.0312
## bmp          -1.9613     0.9263 -2.1174   0.0476
```

```
## [1] Adjusted R-sq = 0.429       p value = 0.0064
```

Collinearity still present - possibly obscuring relationships

```
##       age       sex    height    weight       bmp
## 12.715251  1.038066 11.015970 28.123150  4.648941
```

Example: Cystic fibrosis - active predictors

Simplify the model contd

Remove `age`

```
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept) 251.3973   119.2859  2.1075   0.0479
## sex         -11.5458    10.2979 -1.1212   0.2755
## height       -0.8128     0.7762 -1.0472   0.3075
## weight        2.6947     1.1329  2.3787   0.0275
## bmp          -1.4881     0.7330 -2.0302   0.0558
```

```
## [1] Adjusted R-sq = 0.4371       p value = 0.0033
```

Collinearity still present

```
##       sex    height    weight       bmp
##  1.038062 10.620847 15.678850  2.953131
```

Example: Cystic fibrosis - active predictors

- Perhaps no neat ending here in specifying active predictors
    - cor(height, weight) = 0.92 so possibly one should have been removed at the start
- Different methods may lead to different results

Inference after model selection - Caveats

- Full fitted model is only model giving accurate standard errors and P values
- Data-driven model selection, esp. stepwise methods, produce estimated standard errors of coefficients and P values that are too small[2]
- Most parsimonious model may not give best parameter estimates or predictions[3]

[2]: Harrell 2015, Regression Modeling Strategies, Springer, 2nd ed., s. 4.3

[3]: Leeb & Pötscher 2005 https://doi.org/10.1017/S0266466605050036

Variable selection - Recommendations

- In study design, use expert knowledge to list predictors (do not use the data later to “help”!)
- Plan to collect adequate data on all variables
- Pre-specify a small number of candidate models
- Avoid including too many predictors for your sample size

Variable selection - Recommendations contd

- If variable selection is necessary:
    - use penalised or resampling methods or
    - if you must use stepwise methods
        - use a limited, structured approach (e.g. consider groups of predictor variables)
        - use *minimal* backwards elimination steps if you want parsimony (active predictors) rather than accuracy (good predictions)
        - validate the model using a resampling method or external test data[4]

[4] : Harrell 2015, Regression Modeling Strategies, Springer, 2nd ed., s. 4.12

Variable selection - Recommendations contd

- What is the role of modelling in your field?
  - systems biology - complex problems addressed by computational modelling and simulation[5]
  - business - big data - Netflix Prize (100 million records)[6]
  - clinical science and health - diagnostic and prognostic inferences … for care decisions … policy[7]
  - more generally - how statistical modelling decisions connect with answering scientific questions[8]

[5]: Macleod 2018 https://doi.org/10.1007/s40656-017-0183-9
[6]: Hastie 2015 Statistical learning with big data https://web.stanford.edu/~hastie/TALKS/SLBD_new.pdf
[7]: Henley 2020 https://doi.org/10.1080/24709360.2019.1618653
[8]: Navarro 2019 https://doi.org/10.1007/s42113-018-0019-z

Variable selection - future seminar topics?

Many issues not raised:

- how many variables is it feasible to start with in a model?
- after you’ve done model selection, how much can you trust P values for model parameter estimates?
- what methods can be used for models with multiple categorical predictor variables?
- what about mixed models with fixed and random effects - i.e. where the data records are not independent, such as observations made on subjects in different groups?
- what methods can be used with other types of model - e.g. non-linear models or where response variable is binary, small count, categorical, …?

Useful resources

Books

Dalgaard P 2008. *Introductory Statistics with R.* Springer, 2nd ed. (Contains description of example data set and analysis notes - UNSW Library e-book)

Harrell F 2015. *Regression Modeling Strategies,* Springer, 2nd ed.

James G et al. 2013. *An Introduction to Statistical Learning - with Applications in R.* Springer. https://doi.org/10.1007/978-1-4614-7138-7 **Extremely useful** (Free download available here: http://faculty.marshall.usc.edu/gareth-james/ISL/)

Useful resources

Journal articles

Heinze G & Dunkler D 2017. Five myths about variable selection. *Transplant International,* 30(1), 6–10. https://doi.org/10.1111/tri.12895

Heinze G et al. 2018. Variable selection – A review and recommendations for the practicing statistician. *Biometrical Journal,* 60(3), 431–449. https://doi.org/10.1002/bimj.201700067

Henley S et al. 2020. Statistical modeling methods: challenges and strategies. *Biostatistics and Epidemiology,* 4(1), 105–139. https://doi.org/10.1080/24709360.2019.1618653

Krzywinski M & Altman N 2015. Points of Significance: Multiple Linear Regression, *Nature Methods* 12(12): 1103-1104. https://doi.org/10.1038/nmeth.3665

Useful resources

Journal articles

Leeb H & Pötscher B M 2005. Model selection and inference: facts and fiction. *Econometric Theory* 21(1), 21-59. https://doi.org/10.1017/S0266466605050036

Sauerbrei W et al. 2020. State of the art in selection of variables and functional forms in multivariable analysis—outstanding issues. *Diagnostic and Prognostic Research,* 4(1). https://doi.org/10.1186/s41512-020-00074-3

Note on F test

To test whether *one* parameter in our regression model is zero, we can use a t test because a t test can handle one parameter at a time. The t test for whether the coefficient of `fev1` is zero, given all the other terms remain in the model, gives a P value of 0.33 (see slide 9).

If, however, we want to test whether the coefficients of a group of parameters are *all* zero, we cannot use a t test, which can handle only one parameter at a time, but we can use an F test, if the model without that group of parameters is nested within the larger model. It’s called an F test because the test statistic is an F statistic.

(continued over)

Note on F test contd

To test if the coefficients of `fev1`, `rv`, `frc` and `tlc` are *all* zero, we can use an F test to compare the model without those four predictors against the model with all the nine predictors because (1) the two models are nested and (2) we are testing more than one parameter at the same time (see slide 26).

See Quinn G & Keough M 2002. *Experimental Design and Data Analysis for Biologists,* Cambridge University Press, sect. 6.1.4 (UNSW Library e-book)

Note that if we were using a different type of model not fitted by least squares, we might need to use a different test, appropriate for that type of model, to answer this type of question.